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Repeatability of Non-Contrast-Enhanced Lower-Extremity Angiography Using the Flow-Spoiled Fresh Blood Imaging

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Purpose: The aim of this study was to prospectively evaluate the repeatability of non-contrast-enhanced lower-extremity magnetic resonance angiography using the flow-spoiled fresh blood imaging (FS-FBI).

Methods: Forty-three healthy volunteers and 15 patients with lower-extremity arterial stenosis were recruited in this study and were examined by FS-FBI. Digital subtraction angiography was performed within a week after the FS-FBI in the patient group. Repeatability was assessed by the following parameters: grading of image quality, diameter and area of major arteries, and grading of stenosis of lower-extremity arteries. Two experienced radiologists blinded for patient data independently evaluated the FS-FBI and digital subtraction angiography images. Intraclass correlation coefficients (ICCs), sensitivity, and specificity were used for statistical analysis.

Results: The grading of image quality of most data was satisfactory. The ICCs for the first and second measures were 0.792 and 0.884 in the femoral segment and 0.803 and 0.796 in the tibiofibular segment for healthy volunteer group, 0.873 and 1.000 in the femoral segment, and 0.737 and 0.737 in the tibiofibular segment for the patient group. Intraobserver and interobserver agreements on diameter and area of arteries were excellent, with ICCs mostly greater than 0.75 in the volunteer group. For stenosis grading analysis, intraobserver ICCs range from 0.784 to 0.862 and from 0.778 to 0.854, respectively. Flow-spoiled fresh blood imaging yielded a mean sensitivity and specificity to detect arterial stenosis or occlusion of 90% and 80% for femoral segment and 86.7% and 93.3% for tibiofibular segment at least.

Conclusions: Lower-extremity angiography with FS-FBI is a reliable and reproducible screening tool for lower-extremity atherosclerotic disease, especially for patients with impaired renal function.

Key Words: flow-spoiled fresh blood imaging, lower-extremity arteries, non-contrast-enhanced magnetic resonance angiography, repeatability

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Lower-extremity atherosclerotic disease is characterized by the atherosclerotic narrowing and/or occlusion of arteries, whose prevalence was estimated to be approximately 20% for persons older than 75 years with the main presentation of claudication and leg pain.¹ However, not all patients with peripheral arterial disease are symptomatic. Thus, precisely depicting the peripheral arteries disease is essential to make appropriate medical and/or surgical regimen. Furthermore, accurate depiction of lower-extremity artery is vital for revascularization planning and to determine if

amputation procedure is necessary.^{2,3} Therefore, accurately displaying the lower-extremity arteries system and reliable diagnosis of atherosclerosis are important.

Digital subtraction angiography (DSA) has been the reference standard for the diagnosis of atherosclerotic disease. Unfortunately, concerns about the arterial puncture, high ionizing radiation, and complications limit its use as a screening examination.⁴ During the last decade, duplex sonography, computed tomography angiography (CTA), and contrast-enhanced magnetic resonance angiography (CE-MRA) or non-contrast-enhanced MRA (NCE-MRA) have replaced DSA as screening tests for peripheral atherosclerosis. Although duplex sonography has been considered as the initial screening test because of its noninvasiveness and least expensiveness, the examination time is lengthy, and the procedure is operator dependent and has a lower sensitivity compared with CTA and CE-MRA.^{5,6} Current multi-detector-row computed tomography scanners and the development of 3-dimensional (3D) rendering techniques have made peripheral CTA promising and reliable tool for less-invasive imaging and treatment planning of lower-extremity arterial disease.⁷ However, CTA also has the obvious drawbacks of contrast material allergy, ionizing radiation, and nephrotoxicity.^{8,9} Contrast-enhanced MRA is a rapid and reliable technique that facilitates evaluation of the peripheral arteries without the exposure to ionizing radiation and has been established to have high diagnostic accuracy.^{10,11} The disadvantage of this technique is venous contamination, often occurring in the calves segments owing to the acquisition of central k-space, which may not coincide with the arterial summit of contrast bolus.¹² Moreover, with the use of gadolinium-based contrast material in CE-MRA, nephrogenic systemic fibrosis has been shown to occur almost exclusively in patients with glomerular filtration rate of less than 30 mL/min per 1.73 m² and should be used with deliberation in patients with a glomerular filtration rate of less than 60 mL/min per 1.73 m².^{13,14} Therefore, the development of NCE-MRA techniques becomes significant for lower-extremity atherosclerosis screening.

Flow-spoiled fresh blood imaging (FS-FBI) is a promising NCE-MRA technique by the use of electrocardiography (ECG)-gated 3D fast spin echo (FSE) sequence. The signal intensity within the vessel is varied according to different flow velocities in FSE T2-weighted images. In the T2-weighted images, the signal intensity within the fast-flowing artery is reduced because of flow void effects, and the venous flow always generates high signals in both diastole and systole gated images because of relatively slow and nonpulsation flow property. Thus, arterial and venous flow velocities can be differentiated in the systolic and diastolic phases of the cardiac cycle.^{15,16}

To date, many studies reported that FS-FBI was helpful in the clinical evaluation of lower-extremity arterial stenosis when compared with DSA and CTA^{17,18}; however, some literatures suggested that ECG-gated 3D FSE MRA lacks robustness relative to other examinations.^{19,20} In addition, if applying quantitative parameters to general clinical use, the technique must be demonstrated to be both precise and repeatable. There seems to be no

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study that investigated repeatability for FS-FBI of the lower-extremity arteries. Therefore, the aim of this study was to evaluate the repeatability and accuracy of this previously validated method.

MATERIALS AND METHODS

Subjects

From July 2014 to October 2016, 15 patients with lower-extremity arterial stenosis (9 men and 6 women; mean age, 66.3 [SD, 5.3] years; age range, 55–78 years; Fontaine classification: stage II, $n = 8$; stage III, $n = 6$; stage IV, $n = 1$) were enrolled in this study and underwent FS-FBI examination. None of the patients had undergone previous stenting procedures. Digital subtraction angiography was performed within a week after the FS-FBI. There were 2 patients who had a history of arrhythmia, and β -blocker, Betaloc, was taken 30 minutes before the FS-FBI examination. Forty-three healthy volunteers (20 men and 23 women; mean age, 24.3 [SD, 3.7] years; age range, 19–34 years; no history of smoking, hypertension, diabetes, and arrhythmia) recruited underwent FS-FBI. To assess the repeatability of the MRA measurements, we examined each subject twice after a median of 3 days. This prospective clinical study was approved by our institutional review board and with written informed consent from all participants.

MRI Protocol

All FS-FBI examinations were performed with a 1.5-T MRI scanner (Vantage-Altas; Toshiba Medical Systems, Otawara, Japan). Two Atlas SPEEDER body coils were used for 2-station examination with the automatic table moving technique. The examination covered the femoral and tibiofibular areas. The overlap of the 2 stations was 5 cm.

After the localization sequence, a coronal, single-slice, multiple-phase, half-Fourier FSE 2D “ECG-prep” scan was acquired to determine the appropriate diastolic and systolic ECG delay times with the following parameters: repetition time, 3 R-R intervals; echo time, 80 milliseconds; flip angle, 90 degrees; refocusing angle, 130 degrees; echo train spacing, 5 milliseconds; section thickness, 100 mm; matrix, 128×256 ; field of view, 37×37 cm to 40×40 cm; a single shot of 128 phase-encoding (PE) lines with parallel factor of 2.0; and a total scan time of 40 to 60 seconds depending on the heart rate. This ECG preparation scan was performed

on all participants each time because the triggering delayed time may vary on an individual basis. FBI-Navi, the automated analysis software, was used to determine the diastolic and systolic trigger delay times automatically. The readout curve diagrams signal intensity versus delay time, with low-intensity readings corresponding to systole phase and high-intensity readings to diastole phase (Fig. 1). The FBI-Navi algorithm is shown as follows: (1) determining a basic phase t_0 ; (2) producing subtracted images $Ps(x, y, t)$ of the basic phase t_0 from each phase images; (3) in $Ps(x, y, t)$ images, producing a maximum intensity projection (MIP) image, $Pm(x, y)$, in all phase images; (4) for a $Pm(x, y)$ image, performing the threshold processing to produce 2 sets of values and producing a mask image, $Pb(x, y)$; (5) for all phase images, producing an average value by multiplying with a mask image.²¹

Flow-spoiled fresh blood imaging was performed in the coronal plane with the following parameters: repetition time, 3 R-R intervals; echo time, 80 milliseconds; flip angle, 90 degrees; refocusing angle, 180 degrees; inversion time, 190 milliseconds; echo train spacing, 5 milliseconds; matrix, 256×256 (interpolated to 512×512); section thickness, 3 mm (interpolated to 1.5 mm); approximately 30 to 50 slices partitions in tibiofibular area and 60 to 90 slices in femoral area; bandwidth, 651 Hz/pixel; field of view, 37×37 cm to 42×42 cm; 2 shots per 256 PE lines; parallel imaging factor of 2.0; and a total acquisition time of 5 to 8 minutes, depending on the heart rate. After image acquisition, the system automatically subtracted the systolic source images from the diastolic source images and reconstructed with an MIP algorithm with rotations on the coronal plane and through the craniocaudal axis.

Digital Subtraction Angiography

Standard intra-arterial DSA was performed according to routine protocol using a clinical DSA unit (Artis zee; Siemens, Erlangen, Germany), and anteroposterior and lateral views were obtained. Contrast medium (iopamidol [Isovue 300]; Bracco, Milan, Italy) was injected with a flow rate of 5 to 6 mL/s and a mean contrast injection volume of 30 mL per patient.

Image Analysis

All FS-FBI raw data were transferred to postprocessing workstation (Tethys 1.12, Myrian; Intrasure, Montpellier, France) for evaluation.

FIGURE 1. Flow-spoiled fresh blood imaging Navi result. Note that the highest signal intensities at 600 milliseconds represent diastolic delays, and lowest signals at 100 milliseconds represent systolic delays.

TABLE 1. Grading of Image Quality by FS-FBI in the Patient Group

Patient No.	Sex	Age, y	Image Quality							
			First Time				Second Time			
			Femoral Arterial Segment		Tibiofibular Arterial Segment		Femoral Arterial Segment		Tibiofibular Arterial Segment	
			Observer 1	Observer 2	Observer 1	Observer 2	Observer 1	Observer 2	Observer 1	Observer 2
1	M	64	1	1	1	1	1	1	1	1
2	M	65	1	1	1	1	1	1	1	1
3	M*	78	2	2	2	2	2	2	2	2
4	F	65	1	1	1	1	1	1	1	1
5	F	55	1	1	1	1	2	1	1	1
6	M	69	1	1	1	1	1	1	1	1
7	M	64	1	1	1	1	1	1	1	1
8	F*	71	2	2	2	2	2	2	2	2
9	M	68	1	1	1	1	1	1	1	1
10	F	67	1	1	1	1	1	1	1	1
11	F	59	1	1	2	2	1	1	1	1
12	M	72	1	1	1	1	1	1	2	2
13	F	66	1	1	1	1	1	1	1	1
14	M	67	1	1	1	1	1	1	1	1
15	M	65	1	1	1	1	1	1	1	1

*Patients with arrhythmia.
F indicates female; M, male.

The arterial tree was divided into 2 main regions, the femoral region and the tibiofibular region. The femoral region included 6 segments: bilateral common femoral artery, superficial femoral artery, and deep femoral artery. The tibiofibular region included 8 segments: bilateral popliteal artery, anterior tibial artery, posterior tibial artery, and peroneal artery.

Quality of arterial angiograms was classified using a 3-point scale: grade 1, good (no venous contamination and depiction of major arteries with good continuation); grade 2, fair (some venous contamination or less depiction of major arteries); and grade 3, poor (severe venous contamination, poor depiction of major arteries, or both). Grading of stenotic arteries was assessed using a 4-point scale: grade 1, no stenosis (0%); grade 2, mild stenosis (<50%); grade 3, moderate to severe stenosis (>50%); grade 4, complete occlusion. Two radiologists (Z.X. and D.S.) with 5 years' experience blinded to patient data independently evaluated the source images and the MIP reconstruction.

The minor caliber was measured perpendicular to its long axis as a diameter of each artery using multiplanar reformatting. Oblique coronal, axial, and sagittal images of FS-FBI were generated

to provide accurate visualization of the entire length and course of the artery. In the healthy volunteer group, the measurements of the arterial diameter and area were performed in a distance of 1 to 1.5 cm from the bifurcation of each artery by the 2 aforementioned radiologists, respectively. In the patient group, the diameter of each arterial segment on FS-FBI was measured at the site of most significant stenosis or occlusion by a radiologist (Z.X.). Digital subtraction angiography images were analyzed by a radiologist (N.H., 7 years of experience in vascular radiology), who was unaware of patient information and other examination results. Digital subtraction angiography data were analyzed on a picture archiving and communication system (STARPACS 2.0; Start, Fuzhou, China).

Statistical Analysis

Interobserver and intraobserver agreements were assessed using intraclass correlation coefficients (ICCs) for each of the parameters for each observer and both observers. Intraclass correlation coefficient values were interpreted as follows: greater than 0.75 was excellent, 0.40 to 0.75 was fair to good, and less than

TABLE 2. Repeatability of the Intraobserver and Interobserver Evaluation of Image Quality by FS-FBI

Grading of Image Quality	ICC for Intraobserver Evaluation (95% CI)		ICC for Interobserver Evaluation (95% CI)	
	Observer 1	Observer 2	First Time	Second Time
Healthy volunteer group				
Femoral	0.792 (0.616–0.887)	0.884 (0.786–0.937)	0.918 (0.886–0.945)	1.000 (1.000–1.000)
Tibiofibular	0.803 (0.745–0.893)	0.796 (0.624–0.890)	1.000 (1.000–1.000)	1.000 (1.000–1.000)
Patient group				
Femoral	0.873 (0.621–0.957)	1.000 (1.000–1.000)	1.000 (1.000–1.000)	0.873 (0.621–0.957)
Tibiofibular	0.737 (0.216–0.912)	0.737 (0.216–0.912)	1.000 (1.000–1.000)	1.000 (1.000–1.000)

FIGURE 2. Non-contrast-enhanced MRA using FS-FBI of a 27-year-old healthy man with normal tibiofibular arteries acquired with FS-FBI on the first (A) and second (B) examinations. An excellent repeatability was achieved on the 2 examinations.

0.40 was poor. Sensitivities and specificities were calculated. The sensitivity, specificity, and area under the receiver operating characteristic curve (AUC) with 95% confidence intervals (CIs) were used to compare the diagnostic accuracy of FS-FBI with DSA for detecting diameter of stenotic lower extremities arteries. Statistical calculations were performed using PASW v18.0 (SPSS Inc, Chicago, Ill) and GraphPad Prism v6.0 (GraphPad Software, San Diego, Calif).

RESULTS

The grading of image quality of most data was satisfactory. Among the 43 volunteers, at least 93.0% and 90.7% were scored 1 for the femoral segment and tibiofibular segment, respectively. In the patient group, at least 80.0% were scored 1 for the femoral segment and tibiofibular segment (Table 1). Grade 3 was not evaluated in either healthy or patient group.

Repeatability of Image Quality Grading

Table 2 summarizes the repeatability of FS-FBI image quality grading. In the healthy volunteer group, the ICCs for the first and second measures were 0.792 and 0.884 in the femoral segment

and 0.803 and 0.796 in the tibiofibular segment, indicating excellent agreement. Interobserver agreements were almost perfect, with ICCs ranging from 0.918 to 1.000. Figures 2 and 3 show the representative FS-FBI lower-extremity angiography images from 2 different healthy volunteers. There were 5 cases of vessel ghosts occurring in the PE direction in the healthy volunteer group (Fig. 4).

In the patient group, the ICCs for the first and second measures were 0.873 and 1.000 in the femoral segment and 0.737 and 0.737 in the tibiofibular segment, which also indicate good agreement. Interobserver agreements ranged from 0.873 to 1.000. Figure 5 displays the arterial stenosis of femoral and tibiofibular segment examined by FS-FBI and DSA of the same patient.

Repeatability of Diameter and Area Measurements of Lower-Extremity Arteries in the Volunteer Group

As shown in Table 3, intraobserver reliability of both diameter and area measurements was good with ICC of at least 0.747 and 0.752, respectively. Most interobserver agreements on measurements of diameter and area between the 2 examinations were greater than 0.750.

FIGURE 3. Non-contrast-enhanced MRA using FS-FBI of a 23-year-old healthy woman with normal femoral arteries acquired with FS-FBI on the first (A) and second (B) examinations. A very good repeatability was achieved on the 2 examinations.

FIGURE 4. The arrow indicates a ghost in the PE direction.

Repeatability of Stenosis Grading of Lower-Extremity Arteries in the Patient Group

Bilateral lower-extremity arteries were respectively calculated among 15 patients. There were 10 cases of stenosis in common femoral artery, 21 in superficial femoral artery, 15 in popliteal artery, 24 in anterior tibial artery, 25 in posterior tibial artery, and 19 in peroneal artery. The repeatability of stenosis grading is summarized in Table 4. Flow-spoiled fresh blood imaging also showed excellent intraobserver agreement (ICCs from 0.784 to 0.862, and from 0.778 to 0.854, respectively) and interobserver agreement (ICCs from 0.773 to 0.844, and from 0.765 to 0.843, respectively) on reproducibility.

Comparison of FS-FBI Versus DSA for Lower-Extremity Arteries in the Patient Group

Diagnostic ability was evaluated for independent readers for femoral, calf, and tibiofibular arterial diameters (Table 5, Fig. 5). Compared with DSA, the sensitivity, specificity, and AUC of FS-FBI to detect significant stenosis or occlusions were 90.0%, 80.0%, and 0.98 for common femoral artery; 95.2%, 90.5%, and 0.97 for superficial femoral artery; 86.7%, 93.3%, and 0.95 for popliteal artery; 90.9%, 91.1%, and 0.81 for anterior tibial artery; 92.7%, 86.7%, and 0.85

FIGURE 5. Lower-extremity arteries of a 65-year-old patient with Fontaine classification stage III. A and D were the DSA images obtained after the FS-FBI. B and E, and C and F, were femoral and tibiofibular arteries acquired with FS-FBI on the 2 examinations, respectively. In the femoral segment, occlusion was displayed in both DSA and FS-FBI images (black and white arrows). High consistency was achieved between DSA and FS-FBI, as well as the 2 examinations. In the femoral and tibiofibular segments, multiple collateral developments (black and white arrowheads) were clearly shown in DSA and FS-FBI images with excellent agreement.

TABLE 3. Repeatability of the Intraobserver and Interobserver Measures of Diameter and Area by FS-FBI in the Healthy Volunteer Group

	ICC for Intraobserver Measures (95% CI)		ICC for Interobserver Measures (95% CI)	
	Observer 1	Observer 2	First Time	Second Time
Diameter of right CFA	0.929 (0.872–0.961)	0.840 (0.724–0.910)	0.831 (0.709–0.905)	0.813 (0.654–0.903)
Area of right CFA	0.957 (0.922–0.976)	0.914 (0.847–0.953)	0.811 (0.676–0.893)	0.849 (0.737–0.894)
Diameter of left CFA	0.934 (0.882–0.964)	0.897 (0.817–0.943)	0.832 (0.710–0.905)	0.758 (0.653–0.869)
Area of left CFA	0.948 (0.906–0.972)	0.922 (0.861–0.957)	0.827 (0.702–0.902)	0.864 (0.749–0.926)
Diameter of right SFA	0.852 (0.743–0.917)	0.889 (0.804–0.938)	0.761 (0.599–0.863)	0.752 (0.540–0.795)
Area of right SFA	0.887 (0.800–0.937)	0.909 (0.838–0.950)	0.758 (0.595–0.861)	0.824 (0.674–0.904)
Diameter of left SFA	0.924 (0.865–0.958)	0.883 (0.794–0.935)	0.736 (0.562–0.848)	0.727 (0.619–0.886)
Area of left SFA	0.925 (0.866–0.959)	0.911 (0.842–0.951)	0.762 (0.600–0.863)	0.755 (0.644–0.897)
Diameter of right DFA	0.766 (0.607–0.866)	0.926 (0.867–0.929)	0.783 (0.685–0.895)	0.755 (0.633–0.893)
Area of right DFA	0.854 (0.730–0.921)	0.915 (0.860–0.953)	0.737 (0.548–0.842)	0.776 (0.608–0.877)
Diameter of left DFA	0.869 (0.712–0.928)	0.885 (0.798–0.936)	0.786 (0.589–0.887)	0.755 (0.582–0.863)
Area of left DFA	0.821 (0.693–0.899)	0.926 (0.867–0.959)	0.753 (0.650–0.843)	0.813 (0.755–0.903)
Diameter of right PoA	0.747 (0.588–0.846)	0.773 (0.578–0.879)	0.765 (0.610–0.865)	0.789 (0.593–0.889)
Area of right PoA	0.796 (0.653–0.884)	0.883 (0.794–0.935)	0.783 (0.632–0.876)	0.771 (0.615–0.869)
Diameter of left PoA	0.776 (0.586–0.861)	0.863 (0.761–0.923)	0.755 (0.590–0.859)	0.763 (0.609–0.881)
Area of left PoA	0.793 (0.649–0.882)	0.870 (0.772–0.927)	0.774 (0.619–0.871)	0.749 (0.602–0.872)
Diameter of right ATA	0.783 (0.633–0.876)	0.822 (0.761–0.897)	0.769 (0.562–0.861)	0.788 (0.609–0.903)
Area of right ATA	0.827 (0.703–0.902)	0.840 (0.797–0.916)	0.753 (0.568–0.874)	0.752 (0.569–0.855)
Diameter of left ATA	0.850 (0.722–0.919)	0.878 (0.802–0.938)	0.842 (0.708–0.914)	0.824 (0.674–0.904)
Area of left ATA	0.831 (0.709–0.905)	0.844 (0.765–0.928)	0.803 (0.664–0.887)	0.776 (0.622–0.872)
Diameter of right PTA	0.816 (0.684–0.896)	0.919 (0.873–0.961)	0.876 (0.783–0.931)	0.870 (0.773–0.927)
Area of right PTA	0.857 (0.752–0.920)	0.911 (0.852–0.943)	0.848 (0.737–0.915)	0.866 (0.766–0.925)
Diameter of left PTA	0.824 (0.697–0.901)	0.878 (0.803–0.928)	0.830 (0.708–0.904)	0.783 (0.633–0.876)
Area of left PTA	0.815 (0.684–0.896)	0.904 (0.830–0.947)	0.828 (0.703–0.904)	0.796 (0.654–0.884)
Diameter of right PA	0.783 (0.638–0.864)	0.885 (0.798–0.936)	0.773 (0.617–0.870)	0.766 (0.632–0.856)
Area of right PA	0.794 (0.608–0.869)	0.829 (0.753–0.921)	0.766 (0.701–0.858)	0.789 (0.714–0.876)
Diameter of left PA	0.823 (0.696–0.900)	0.909 (0.874–0.963)	0.850 (0.739–0.916)	0.862 (0.756–0.930)
Area of left PA	0.811 (0.778–0.893)	0.918 (0.852–0.942)	0.805 (0.669–0.886)	0.865 (0.775–0.913)

ATA indicates anterior tibial artery; CFA, common femoral artery; DFA, deep femoral artery; PA, peroneal artery; PoA, popliteal artery; PTA, posterior tibial artery; SFA, superficial femoral artery.

for posterior tibial artery; and 94.7%, 89.4%, and 0.95 for peroneal artery.

DISCUSSION

Recent studies have shown a lot of concerns about the use of gadolinium-based contrast material in patients with severe renal

failure for possible induction of nephrogenic systemic fibrosis. Accordingly, contrast-free imaging techniques, NCE-MRA, are favored to use repeatedly and prevent any contraindications to gadolinium-based contrast medium. According to a different mechanism, NCE-MRA can be categorized into 4 groups: inflow-based (2D/3D time of flight [TOF]), cardiac phase dependent

TABLE 4. Repeatability of the Intraobserver and Interobserver Evaluation of Stenosis Grading by FS-FBI in the Patient Group

Stenosis Grading	ICC for Intraobserver Evaluation (95% CI)		ICC for Interobserver Evaluation (95% CI)	
	Observer 1	Observer 2	First Time	Second Time
CFA	0.858 (0.775–0.953)	0.849 (0.736–0.934)	0.821 (0.714–0.917)	0.833 (0.715–0.932)
SFA	0.862 (0.793–0.937)	0.854 (0.773–0.926)	0.844 (0.727–0.933)	0.841 (0.756–0.923)
PoA	0.856 (0.737–0.934)	0.841 (0.725–0.924)	0.838 (0.753–0.885)	0.843 (0.767–0.912)
ATA	0.823 (0.722–0.895)	0.836 (0.753–0.881)	0.827 (0.756–0.891)	0.815 (0.743–0.878)
PTA	0.796 (0.748–0.853)	0.778 (0.726–0.841)	0.773 (0.719–0.834)	0.782 (0.735–0.855)
PA	0.784 (0.735–0.846)	0.814 (0.765–0.883)	0.803 (0.742–0.876)	0.765 (0.711–0.829)

ATA indicates anterior tibial artery; CFA, common femoral artery; DFA, deep femoral artery; PA, peroneal artery; PoA, popliteal artery; PTA, posterior tibial artery; SFA, superficial femoral artery.

TABLE 5. Diagnostic Accuracy of FS-FBI Relative to DSA for Detection of Lower-Extremity Arteries Diameter in the Patient Group

	Sensitivity (95% CI)	Specificity (95% CI)	AUC (95% CI)
CFA	90.0 (85.5–98.9)	80.0 (74.4–97.5)	0.98 (0.93–0.99)
SFA	95.2 (76.2–99.8)	90.5 (69.9–98.8)	0.97 (0.94–0.99)
PoA	86.7 (59.5–98.3)	93.3 (68.0–99.8)	0.95 (0.88–0.97)
ATA	90.9 (80.0–97.1)	91.1 (78.8–97.5)	0.81 (0.68–0.93)
PTA	92.7 (82.4–98.0)	86.7 (73.2–95.0)	0.85 (0.75–0.95)
PA	94.7 (74.1–99.8)	89.4 (66.9–98.7)	0.95 (0.89–0.98)

ATA indicates anterior tibial artery; CFA, common femoral artery; DFA, deep femoral artery; PA, peroneal artery; PoA, popliteal artery; PTA, posterior tibial artery; SFA, superficial femoral artery.

(FS-FBI), flow encoding (2D/3D PC-MRA), spin labeling (time-spatial labeling inversion pulse), and relaxation based (balanced steady-state free precession).²² TOF is the most widely used and has high accuracy in the evaluation of the lower extremity, but it is time consuming because of extensive scan coverage.²³ Besides, TOF is sensitive to patient motion, easy to cause systematic overestimation of the grade of the stenosis, and prone to artifacts from in-plane flow.^{24,25} Flow-spoiled fresh blood imaging is an ECG-gated 3D FSE sequence using readout flow-spoiled pulses. Diastolic triggering images provide bright blood arteries and veins, whereas systolic triggering images result in black blood arteries and bright blood veins. After subtraction of these 2 independently acquired images can obtain the artery-only image. To reduce indistinction in the PE direction, each division of the sequence was acquired in 2 shots.

Many studies anticipated that FS-FBI would become invaluable in atherosclerotic patients who have chronic kidney disease, owing to being free from intravenous gadolinium administration. In this study, high sensitivity and specificity were acquired in the patient group in contrast to DSA, similar to what has previously been found. Because repeatability or margin of error is one of the fundamental characteristics of any measurement, the assessment of reliability is essential. Thus, compared with previous publications, this study mainly aimed at exploring repeatability of normal volunteers and patients with lower-extremity atherosclerotic disease using FS-FBI. The main observation from this study was that diagnostic image quality and quantitative data using FS-FBI could be reliably obtained in both healthy subjects and those with atherosclerosis. Intraobserver and interobserver agreements were sufficient.

To avoid subjective and objective factors that may influence the repeatable result, before the FS-FBI scan, we made some efforts to exclude the deviation caused by the technical factors. First, the localization of the first examination was recorded as a reference for the second time, which could make the scanning field at the same level. Besides, as an ECG-triggered sequence, suitable heart rates and stable rhythm are crucial for FS-FBI imaging. All the volunteers and patients were required to keep a quiescent state for at least 30 minutes. Two patients with history of arrhythmia took β -blockade drug 30 minutes before the scan. While relative consistent rhythms were achieved, the image quality of these 2 patients was all grade 2 in 2 examinations; some venous contamination or less depiction of major arteries may arise, but it is still useful for clinical diagnosis especially for those with renal failure. Therefore, the deviation control of heart rates is important for a confident diagnosis. In addition, to determine the optimal diastolic and systolic trigger delay times for effortlessly navigating to a

3D FBI scan, a specialized software algorithm, FBI-Navi, was used. Subjective bias can be eliminated using such algorithm. According to our experience, individually diastolic and systolic trigger delay times were reproducible between examinations carried out twice, which also lays the foundation for achieving repeatable 3D FS-FBI images. According to our preliminary experience, most of systolic and diastolic trigger delay times in healthy volunteer were composed by 100 and 500 milliseconds, or 100 and 600 milliseconds. But in the patient group, the combination with trigger delay time fluctuates without obvious regularity, especially in patients with arrhythmia. Even if β -blocker was used before FS-FBI examination, systolic and diastolic trigger delay time could be 200 and 700 milliseconds, or 500 and 1000 milliseconds. Be it in the volunteer group or patient group, however, trigger delay time was almost reproducible between scans carried out twice in individuals. Some literatures demonstrated limitation of subtraction 3D ECG-gated FSE MRA, including susceptibility to motion artifacts and dependence on blood flow characteristics.^{19,20} Thus, to avoid long examination time for subjects to tolerate, bilateral iliac arteries and foot arteries were not evaluated in our study. Besides, effective communication with the subjects and suitable foam pads fixed before FS-FBI examination might help to control the motion artifact. We did not observe severe motion artifacts of FS-FBI that hampered vessel evaluation in this study. In some cases, absence of signal from proximal right femoral artery was noted, whereas the left is well depicted. This may be due to B1 inhomogeneity. This is an inherent feature of the interaction between the circularly polarized radiofrequency field and the human form. The superficial location of proximal femoral artery accords with B1 minimum, which explains the lack of signal on sequences sensitive to B1 variations.²⁶ Some degree of signal loss has also been observed in arteries with small caliber, such as collateral vessels; this was probably caused by incomplete systolic dephasing. By applying the readout flow-spoiled pulses in parallel with the vessel orientation, an intrinsic dephasing effect can be obtained from near the center or low frequencies of the k-space in half-Fourier FSE imaging.²⁷

In our study, we found an excellent consistency in the grading of image quality in both volunteer and patient groups. We detected that there were 5 cases of vessel ghosts occurring in the PE direction, which shows weak repeatability. The appearance of vessel ghosts can be explained in view of even-echo rephasing of spin-echo pathways that could cause a modulation of k-space in the PE direction, especially at the highest flip angle.^{27,28} However, this did not affect the evaluation and interpretation of lower-extremity MRA features using FS-FBI.

Our study had a few limitations. First, bilateral iliac arteries and foot arteries were not evaluated in our study. One reason was the relatively long examination time for subjects to tolerate, and a more important reason was that the iliac region sometimes showed artifacts likely caused by the bowel movement and venous contamination; the latter one may due to the poor delineation of the iliac vessels because of signal dephasing of their fast flow.^{29,30} Technical modification and improvement would be needed in further studies. Second, the correlation between heart rates and image quality was not explored in the present study, because the FBI angiography was ECG gated. Thus, the deviation and stability of heart rates are important for a confident diagnosis. Therefore, further study should involve a larger sample size of patients with statistical analysis of heart rate and image quality.

CONCLUSIONS

This study demonstrates that lower-extremity angiography with FS-FBI is a reliable and reproducible screening technique

for lower-extremity atherosclerotic disease, especially for patients with impaired renal function.

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