Three noncontrast-enhanced MR venography techniques are presented for assessing deep vein thrombosis (DVT) at 0.5T in patients with metallic implants. Two cardiac-gated 3D half-Fourier FSE fresh blood imaging sequences with flow-refocusing pulses (FR-FBI) in the read-out (RO) direction and without FR pulses (non-FR-FBI) were developed for slower-flowing blood. For faster flowing blood, a swap phase-encode arterial double-subtraction elimination (SPADE) technique was developed. The three techniques were assessed both quantitatively using signal-to-noise (SNR) and contrast-noise-ratio (CNR) measurements and qualitatively by subjective image analysis in 15 volunteers. SPADE was compared to FR-FBI in the pelvic veins and FR-FBI was compared to non-FR-FBI in the thigh and calf veins. Both SPADE and FR-FBI techniques produced significantly higher SNRs, CNRs, and image quality in each comparative study (*P < 0.001). Five patients with metallic implants and confirmed DVT underwent SPADE (pelvic veins) and FR-FBI (thigh and calf veins) examinations and the results were compared to conventional venography. The SPADE and FR-FBI images showed all DVTs from all five patients without interference from implant susceptibility artifacts. The excellent image quality produced by both SPADE and FR-FBI throughout peripheral vasculature demonstrates their promise for detecting DVT in postsurgery patients. Magn Reson Med 61:907–917, 2009. © 2009 Wiley-Liss, Inc.

Key words: deep vein thrombosis; noncontrast-enhanced magnetic resonance venography; electrocardiography-triggered three-dimensional half-Fourier FSE; metallic implant

Deep venous thrombosis (DVT) and pulmonary embolism represent two clinical manifestations of the same venous thromboembolism (VTE). Over 90% of symptomatic pulmonary emboli originate from thrombi located in the pelvic and leg veins (1,2). DVT typically originates in the venous sinuses of the calf muscles but occasionally originates in the proximal veins, usually in response to trauma or surgery (2,3). The risk of pulmonary embolism with proximal DVT is ~50% and most fatal emboli probably arise from proximal thrombi (3). Calf thrombi rarely lead to symptomatic pulmonary embolism, but ~25% of untreated thrombi will extend into the proximal veins, usually within a week after presentation (3).

Risk factors for DVT include surgery, trauma, immobility, malignancy, cancer therapy, previous DVT, varicose veins, and increasing age. In particular, lower extremity orthopedic surgery carries a high risk for postoperative DVT (4). Therefore, an accurate diagnostic test that can detect both proximal and calf DVT in high-risk patients has enormous value as a screening procedure and is the motivation for this work.

Direct MR thrombus imaging using a black-blood $T_1$-weighted 3D gradient-echo type sequence is reported to be a highly sensitive and specific test for diagnosing DVT (5,6). The technique is based on the methemoglobin concentration induced $T_1$ shortening effect in thrombus, but has the potential for misdiagnosis because the $T_1$ shortening effect changes with time due to thrombus maturation (7).

Nonionizing, noninvasive, 2D time-of-flight (TOF) MR venography techniques are diagnostic for depicting DVT in the lower extremity (8–11) and have a reported sensitivity and specificity for above-the-knee DVT at 97% and 93%, respectively (11). However, 2D TOF-based methods suffer from flow and motion artifacts, poor depiction of blood vessels perpendicular to the slice orientation, and a relatively lengthy acquisition times (7,10,12–17). Recently reported noncontrast balanced steady-state free-precession (SSFP) MR venography work has demonstrated high blood signal intensity due to favorable $T_2/T_1$ contrast. Unfortunately, complex blood flow and pulsation artifacts, in addition to the strong $T_2/T_1$-based signal characteristics of thrombus itself, results in inaccurate DVT detection (18,19). Susceptibility artifacts on the veins adjacent to metallic implants are another possible limitation of balanced SSFP-based techniques (20).

Gadolinium (Gd)-enhanced MR venography, performed following recirculation of gadolinium contrast, was introduced to reduce the data acquisition time, which overcomes some of the TOF technical limitations (12,15,21).
Unfortunately, the rapidly enhancing soft tissue signal limits the data acquisition to a relatively short optimal venous enhancement time window (7,16,17,22). The time window limitation can be resolved by injecting a low dose of contrast agent directly into the pedal vein. However, such injections into foot veins are difficult in the presence of fresh thrombus and might not visualize the proximal veins (7,13).

Recently, MR venography using blood pool contrast agents has been reported to have longer intravascular half-life and resultant lower soft tissue enhancement than Gd-enhanced MR venography (7,14,16,17,22). These blood pool contrast MR techniques present superior accuracy for the diagnosis of DVT as compared to conventional venography or the other MR venography techniques (7,14,16,17). Nonetheless, the use of contrast agents is always accompanied by a potential risk of adverse effects (23,24) and cost issues, and the limit of one image acquisition per injection.

A noncontrast-enhanced MR angiographic technique, fresh-blood imaging (FBI), has been introduced using an electrocardiography (ECG)-gated 3D half-Fourier FSE (25) and can be applied with appropriate modifications to DVT imaging. The clinical usefulness of the basic technique has been reported in aortic diseases, arterial occlusive diseases, and assessment for the vascularity of musculoskeletal neoplasm (26–28). For fast flow thoracic and abdominal arteries, the technique intrinsically allows separation of arteries from veins, thereby providing MR venography with $T_2$-weighted images. The advantages of MR venography include no administration of contrast agent, the ability to immediately repeat the study, and visualization of slow and/or stationary veins in a $T_2$-weighted image. In addition, FBI venography is less susceptible to metallic implants because it is a spin-echo based sequence, allowing clear depiction of veins adjacent to metallic implants. However, an earlier study has demonstrated limited diagnostic utility in peripheral venous diseases due to poor delineation of the iliac veins as a result of signal dephasing due to their fast flow, thereby leading to false-positive results (29).

Flow-spoiled FBI (FS-FBI) in peripheral MRA is reported to improve the depiction of slow-flow peripheral arteries (30). The technique, as demonstrated at 1.5T, utilizes a short TR train spacing (ETS) of 4 or 5 ms and a flow-spoiler gradient pulse in the read-out (RO) direction to depict arteries in flow-void or black blood. The purpose of this study was to develop and demonstrate a noncontrast-enhanced MR venography technique for an entire clinical study of arteries from veins, thereby providing MR venography with $T_2$-weighted images. Alternatively, fast-flow veins will present as flow-void signals in both systolic and diastolic images due to the flow-dephasing effect as compared with $T_2$-weighted images (32). Conversely, increasing ETS enhances the dephasing effect, even in slow-flow arteries, and reduces blood signal intensities with increasing $T_2$ values (32). However, the thick section slice obscures the vascular system in the slice direction, which is a typical drawback of 2D imaging. In addition, the technique is limited in the calf region due to a long ETS.

Slice direction resolution is improved by acquiring thinner contiguous section slices with a 3D half-Fourier FSE sequence. For the particular application in this work at 0.5T, the optimal balance of factors was realized with an ETS of 6.5 ms and converting from flow spoiling (FS) to a 15% flow refocusing (FR) RO direction pulse. The percentage of FR is defined as a percentage relative to one-half the total acquisition window time, further reducing vessel flow-dephasing (25). Conversely, increasing ETS enhances the dephasing effect, even in slow-flow arteries, and reduces blood signal intensities with increasing $T_2$ blurring in the PE direction (31). It is reported that 2D FS calse MR venography (10.5 ms ETS, 7–10 mm slice) optimizes the venous contrast due to differences of artery and vein $T_2$ values (32). However, the thick section slice obscures the vascular system in the slice direction, which is a typical drawback of 2D imaging. In addition, the technique is limited in the calf region due to a long ETS.

Materials and Methods

Theoretical Background and Sequence Optimization

A 3D FS-FBI technique with systolic triggering produces black blood arteries and bright blood veins at 1.5T, when the RO direction is parallel to the vessel orientation and with the application of dephasing or spoiler gradient lobes (30). Shortening ETS in FSE and half-Fourier FSE minimizes motion-induced spin dephasing and decreases the total acquisition window time, further reducing vessel flow-dephasing (25). Conversely, increasing ETS enhances the dephasing effect, even in slow-flow arteries, and reduces blood signal intensities with increasing $T_2$ blurring in the PE direction (31). It is reported that 2D FS calse MR venography (10.5 ms ETS, 7–10 mm slice) optimizes the venous contrast due to differences of artery and vein $T_2$ values (32). However, the thick section slice obscures the vascular system in the slice direction, which is a typical drawback of 2D imaging. In addition, the technique is limited in the calf region due to a long ETS.

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(Fig. 2b), provides arterial images followed by MIP processing. Subtract1 (Fig. 2d). Further magnitude subtraction of arterial source images, Subtract1 (Fig. 2d), from the diastolic source images, Diastolic1 (Fig. 2a), provides Subtract2 or SPADE image (Fig. 2e) with bright-blood veins and black-blood arteries. Note that arterial signals are canceled out by magnitude subtraction of Subtract1 (Fig. 2d) from Diastolic1 (Fig. 2a), where Fig. 2a shows both arteries and veins and Fig. 2d shows arteries only.

Subjects
The Ethics Committee of our institution granted approval for this study and all participants gave written informed consent. Fifteen healthy volunteers (13 men and 2 women; mean age, 39.9 years; age range, 22–66 years) underwent a three-station (pelvic, thigh, and calf) noncontrast-enhanced MR venography examination for this comparative study. All healthy volunteers with no personal and family history of venous diseases, who had normal results, were recruited among personnel working at our institution.

Five patients (two women, three men; age range, 44–86 years; mean age, 64 years) with metallic implants were enrolled in this study. The inclusion criteria were the positive findings of lower extremity DVT with conventional venography and having a nonmagnetizing orthopedic implant confirmed as MR safe using a tissue-equivalent gel-phantom test on a 0.5T clinical imager (maximum temperature rises after 15 min of RF exposure ≤0.3°C). The measurement of RF heating of implants is based on American Society for Testing and Materials (ASTM) standards (34). The exclusion criteria were: contraindications to MRI, claustrophobia and inability to lie flat, and patients with unsafe orthopedic implants. The patients received the optimized three-station noncontrast-enhanced MR venography examination within 24 hr after their conventional x-ray venography. In all cases, symptoms were unilateral, and the duration of symptom was 1–9 days (mean, 4.6 days). Anticoagulation therapy was performed in four of five patients during the interval between conventional and MR venography. All patients have a history of fracture surgery and had a nonmagnetizing metal implant, ipsilateral to the symptomatic leg. Of these five cases, two had a trochanteric nail, one had a femoral intramedullary nail, one had a hip screw, and one had an L plate.

MRI
All noncontrast-enhanced MR experiments were performed on a 0.5T clinical imager (PLEXART/Hyper, Toshiba, Japan) (gradient strength of 17 mT/m and slew rate of 23 mT/m/msec). A whole-body QD coil was used for all studies without parallel imaging. All subjects were placed feet-first within the bore of magnet and examined in the supine position. Prior to 3D acquisition, a single-slice multiple phase ECG-Prep scan was used to determine appropriate systolic and diastolic phases (25). In each region the ECG delay that presented the entire arterial tree as black blood in systole-triggered image and as bright blood in diastole-triggered image were selected as the proper systolic and diastolic phases. The ECG-Prep scan was acquired as a series of multiple phase images with 50-ms incremental delays, starting with a zero R wave delay, using the following parameters: repetition time (TR) 3 RR interval, effective echo time (TEeff) 78 ms, inversion time (TI) 140 ms, matrix 128 × 256, section thickness 50 mm, field of view (FOV) 42 × 42 cm, and the total acquisition time of about 40 sec, depending on the cardiac rate.

A typical 3D acquisition was as follows; 3 RR intervals, TEeff 78 ms, TI 140 ms, ETS 6.5 ms, matrix 256 × 256, NAQ 1, section slice thickness of 2.7–3.5 mm, FOV 42 × 42 cm, two shots, 25–35 section slice encodings, and a total acquisition time of 2.0–3.5 min, depending on the cardiac rate. Each echo train shot was around 490 ms long. A typical systolic delay time was 50 ms and the diastolic delay time was around 400–450 ms for heart rates of around 75–80 bpm.
Table 1 shows a summary of acquisition techniques used in the healthy volunteers study. All three acquisitions (Diastole1, Diastole2, and Systole FR-FBI) were obtained in the iliac to generate the SPADE or Subtract2 image, and compared to the Systole FR-FBI image. In the thigh and calf, only Systole FR-FBI and non-FR-FBI were acquired similarly and the resulting images compared. In the iliac, the total acquisition time was about 9–11 min. The thigh and calf acquisition required about 6–7 min.

The patients received the optimized protocol of SPADE in the iliac and only Systole FR-FBI in the thigh and calf. The total acquisition was about 17–25 min, including

<table>
<thead>
<tr>
<th>Region</th>
<th>SPADE</th>
<th>FR-FBI</th>
<th>Thigh</th>
<th>Non-FR-FBI</th>
<th>Calf</th>
<th>Non-FR-FBI</th>
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<tbody>
<tr>
<td>Image</td>
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<td>acquisitions</td>
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<tr>
<td>Diastole 1</td>
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<td>(RO = RL)</td>
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<td>Diastole 2</td>
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<td>(RO = HF)</td>
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<td>Systole FR-FBI</td>
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<td>(RO = HF)</td>
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<td>Systole FR-FBI</td>
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<td>without FR</td>
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<tr>
<td>pulse (RO = HF)</td>
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<td>Acquisition</td>
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<tr>
<td>Pelvic</td>
<td>9–11</td>
<td>N/A*</td>
<td>2.0–3.5</td>
<td>2.0–3.5</td>
<td>2.0–3.5</td>
<td>2.0–3.5</td>
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<tr>
<td>Thigh</td>
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<tr>
<td>Calf</td>
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</table>

Note.—Diastole 1 = diastolic-triggered FR-FBI with the readout (RO) direction in perpendicular (right-left, RL direction), Diastole 2 = diastolic-triggered FR-FBI with the RO direction in parallel (head-feet, HF direction), Systole FR-FBI = systolic-triggered FR-FBI with the RO direction (HF direction), Systole FR-FBI without FR pulse = systolic-triggered FR-FBI without flow-refocusing pulses acquired in the head-feet RO direction.

*Systole FR-FBI acquisition is included in SPADE.
to severe arterial contamination, reduction of assessable value). The mean venous visualization score (VVS) and arterial contamination score (ACS) were calculated in all segments of noncontrast-enhanced MR venography.

**Image Analysis for Clinical Studies**

To assess the feasibility of the proposed techniques in depicting DVT, findings in five patients were evaluated by one board-certified radiologist (T.T.), who did not know the results of conventional venography. In noncontrast-enhanced MR venography, patency was defined as homogeneous high-signal intensity within the venous segment and DVT was defined as hypointense signal defect seen within the venous lumen. These MR findings were then compared with conventional venography where DVT was defined as the presence of an intraluminal filling and non-filling of a venous segment with a sharp cutoff.

**Statistical Analysis**

The statistical evaluation was performed using the Statistical Package for Social Sciences software (SPSS, Chicago, IL, 14.0 J). Statistical analysis of the quantitative comparison for the noncontrast-enhanced venography datasets was based on a paired, two-sided Student’s t-test. Mean differences in VVS and ACS between the two imaging techniques were compared using the Wilcoxon signed rank test. Statistical significance was established at $P < 0.05$.

**RESULTS**

**Volunteer Studies**

SPADE produced the best quality images in the pelvic region and FR-FBI produced the best thigh and calf region images in all 15 volunteers. Figure 3 shows a three-station MIP and source images of the pelvic region obtained using SPADE and of the thigh and calf using FR-FBI on a healthy volunteer.

The mean SNR and CNR of the venous segments in all volunteers are summarized in Fig. 4. Quantitative analysis presented the SNR with a mean value of 152.6 ± 52.0 (range, 70.0 ± 16.0 and 188.7 ± 35.5) and the CNR with a mean value of 128.0 ± 49.7 (range, 45.4 ± 13.1 to 164.1 ± 30.9) in the pelvic segments using SPADE. In all pelvic segments, SPADE showed significantly higher SNR and CNR values than FR-FBI ($P < 0.001$). In the thigh and calf regions the SNR had a mean value of 137.5 ± 32.3 (range, 124.9 ± 23.3 and 156.5 ± 33.7) and the CNR had a mean value of 126.1 ± 31.3 (range, 113.9 ± 22.2 and 143.3 ± 33.6) using FR-FBI. These were significantly higher compared to non-FR-FBI ($P < 0.001$ in all venous segments).

Table 2 shows a mean VVS of various segments using SPADE, FR-FBI, and non-FR-FBI in all volunteers. Qualitative analysis of the pelvic segments revealed a significantly higher score in venous visualization using SPADE as compared to FR-FBI ($P < 0.001$ in all venous segments)—ranging between 4.4 ± 0.9 and 5.0 ± 0.0 for SPADE versus 2.4 ± 1.0 and 3.5 ± 1.1 for FR-FBI. In the pelvic region, none of the venous segments were classified as hardly assessable or unassessable in SPADE (VVS ≥3).
whereas a total of 32 venous segments were scored as hardly assessable or unassessable (VVS = 2) in FR-FBI. In the thigh and calf regions, mean VVSs of the superficial femoral and popliteal veins were significantly higher in FR-FBI as compared to non-FR-FBI (P < 0.001 for both comparisons)—4.5 ± 0.8 and 4.8 ± 0.5 for FR-FBI versus 3.5 ± 0.9 and 3.6 ± 0.7 for non-FR-FBI. The anterior tibial, posterior tibial vein, and peroneal veins were rated similarly in VVSs without significant differences. There were no venous segments categorized as hardly assessable or unassessable in FR-FBI MR venography (VVS ≥ 3). In contrast, non-FR-FBI gave a total of eight venous segments SFV (n = 6) and PV (n = 2) judged as hardly assessable or unassessable (VVS ≤ 2). Figure 5 shows typical thigh venography images of a volunteer obtained using non-FR-FBI and FR-FBI. On the non-FR-FBI image, N/2 artifacts (30) caused by the fast flow of superficial femoral and popliteal veins, which reduced the venous signals and deteriorated overall image quality. Regarding the ACS, overall good correlation between SPADE and FR-FBI was demonstrated in the pelvic region. FR-FBI provided all segments with no arterial signal, meaning an ACS of 3. SPADE gave all segments an ACS of 3, except IVC (n = 2) and CIV (n = 1) with an ACS of 2, meaning slight arterial contamination but without any impairment of venous assessment. In the thigh and calf regions good ACS concurrence was obtained in both FR-FBI and non-FR-FBI, with an ACS of 3.

Clinical Studies

In all five patients, SPADE for pelvic and FR-FBI for thigh and calf present venous vasculature without contamination of overlapped arteries. The presence and location of DVT as determined by conventional venography were detected as hypointense signal defects by both the SPADE and FR-FBI images for all patients, as shown in Table 3. The veins adjacent to implants were clearly visualized without metal artifacts. In three patients who underwent MR examination within 14 days after surgery, increased signal intensities was observed in association with postoperative edema or hematoma, resulting in a contrast reduction between veins and surrounding tissue. However, the source images permit one to differentiate veins from those tissues, confirming the presence of DVT, as shown in Fig. 6.

In two patients diagnosed with a large DVT extending up to the left CFV by conventional venography, the proximal extent of the left common iliac thrombosis was depicted using SPADE and FR-FBI. In one of these two cases, hyperintense signal areas due to edema in the surrounding tissue obscured the calf veins on MIP images using FR-FBI; however, the source images revealed the hypointense sig-

FIG. 3. Noncontrast-enhanced MR venography using SPADE for pelvis and FR-FBI for thigh and calf in a 33-year-old volunteer. a: MIP images, all venous segments of all three stations from the pelvis to calf are conspicuously visualized in high signal intensity without overlapping of arteries. b: the source images of the same three stations present homogeneously high venous signals.

FIG. 4. Mean signal-to-noise ratio (SNR) and contrast-to-noise ratio (CNR) values of the venous segments in all 15 volunteers. a: Bar graph shows mean SNR ± SD of the venous segments of SPADE as compared to FR-FBI. b: Bar graph shows mean CNR ± SD of the venous segments of FR-FBI as compared to non-FR-FBI. IVC, inferior vena cava; CIV, common iliac vein; EIV, external iliac vein; CFV, common femoral vein; SFV, superficial femoral vein; Pop.V, popliteal vein; ATV, anterior tibial vein; PTV, posterior tibial vein; PV, peroneal vein.
nal thrombus in the peroneal vein, as shown in Fig. 7. Both MIP and source images of SPADE and FR-FBI offer interpretation of all veins, whereas conventional venography provides thrombi in the peroneal, popliteal, superficial and common femoral veins, excluding the iliac vein. Table 3 presents that SPADE and FR-FBI provided information of six thrombosed veins in four patients which were non-diagnostic in the conventional venograms due to incomplete filling. However, these differences in results were not verified, because no additional examinations were performed.

DISCUSSION

A combination of SPADE and FR-FBI presents the venous vasculature from the pelvis to calf without arterial contamination in all volunteers and patients. In the calf region of the volunteer studies, non-FR-FBI provides a similar visualization of veins as FR-FBI, because there is less signal loss due to slower flow in the calf. However, quantitative assessment reveals that FR-FBI provides significant improvements in both SNR and CNR values, as compared to non-FR-FBI. In the SFV and popliteal veins, FR-FBI provides high venous signal intensities and visualization without the arterial overlap, whereas the SPADE technique in the pelvic veins provides good visualization of faster venous flow, especially in the IVC and CIV. In the SPADE technique, a double subtraction method was utilized to eliminate arterial signals. A few cases with slight arterial contamination in the IVC and CIV were observed in volunteers. These arterial contaminations are thought to be caused by an arterial signal difference between the diastolic-systolic subtraction of the systolic HF RO direction and the diastolic RL RO direction. A weighted subtraction technique may help to reduce the arterial contamination. Nevertheless, qualitative analysis results indicate no significant difference in venous assessment. The combination of SPADE for pelvis and FR-FBI for the thigh and calf is an excellent way to visualize the overall venous vasculature in the lower extremity.

Table 2
Mean Venous Visualization Scores (VVSmean) for Vessel Segments in SPADE, FR-FBI and Non-FR-FBI MR Venography

<table>
<thead>
<tr>
<th>Vessel Segments</th>
<th>No. of Segments</th>
<th>SPADE</th>
<th>FR-FBI</th>
<th>Non-FR-FBI</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inferior vena cava</td>
<td>15</td>
<td>4.7 ± 0.5*</td>
<td>2.4 ± 1.0</td>
<td>N/A</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Common iliac vein</td>
<td>30</td>
<td>4.4 ± 0.9*</td>
<td>3.1 ± 1.0</td>
<td>N/A</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>External iliac vein</td>
<td>30</td>
<td>5.0 ± 0.8*</td>
<td>3.5 ± 1.1</td>
<td>N/A</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Common femoral vein</td>
<td>30</td>
<td>4.5 ± 0.7*</td>
<td>3.0 ± 1.4</td>
<td>N/A</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Superficial femoral vein</td>
<td>30</td>
<td>N/A</td>
<td>4.5 ± 0.8**</td>
<td>3.5 ± 0.9</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Popliteal vein</td>
<td>30</td>
<td>N/A</td>
<td>4.8 ± 0.5**</td>
<td>3.6 ± 0.7</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Anterior tibial vein</td>
<td>30</td>
<td>N/A</td>
<td>4.4 ± 0.7</td>
<td>4.4 ± 0.7</td>
<td>1.000</td>
</tr>
<tr>
<td>Posterior tibial vein</td>
<td>30</td>
<td>N/A</td>
<td>4.8 ± 0.4</td>
<td>4.8 ± 0.4</td>
<td>.317</td>
</tr>
<tr>
<td>Peroneal vein</td>
<td>30</td>
<td>N/A</td>
<td>4.8 ± 0.4</td>
<td>4.8 ± 0.4</td>
<td>.317</td>
</tr>
</tbody>
</table>

Note.—Data are mean ± standard deviation.
*VVS mean is significantly higher in SPADE venography than in FR-FBI MR venography.
**VVS mean is significantly higher in FR-FBI venography than in non-FR-FBI MR venography.

FIG. 5. Noncontrast-enhanced MR images of the veins in the thigh region obtained with non-FR-FBI and FR-FBI. a: MIP image of non-FR-FBI. b: MIP image of FR-FBI. The bilateral superficial femoral veins (arrows) were judged hardly assessable in non-FR-FBI due to insufficient signal intensities and flow void in the center of the lumen, whereas delineation of both superficial femoral veins can be improved in FR-FBI, which were judged fully assessable on FR-FBI. N/2 artifacts originated from superficial femoral and popliteal veins are well suppressed in b as compared with a (arrowheads).
These initial clinical data demonstrate the ability to detect DVTs as hypointense signal defects within the venous lumen. This depiction is based on the intrinsic $T_2$ properties of arterial and venous blood and thrombi. Several authors have reported that acute and subacute venous thrombi depict as hypointense signals on $T_2$-weighted images (29,32). In general, the composition of the thrombus is affected by local blood flow characteristics. Red thrombi form in low-pressure, reduced blood flow venous systems, from activation of the coagulation cascade (35). Therefore, it is generally accepted that the venous thrombi are mainly composed of red thrombi. Red thrombi are rich in fibrin and trapped erythrocytes (35). Blood clots pass through a sequential stage of degradation from oxyhemoglobin to deoxyhemoglobin and methemoglobin, and then hemosiderin. The presence of unpaired electrons in deoxyhemoglobin gives the thrombus a hypointense appearance on MRI.

Table 3
Results of Conventional Venography and MR Venography using SPADE and FR-FBI in Five Patients with Orthopedic Implants

<table>
<thead>
<tr>
<th>Patient no.</th>
<th>Implant</th>
<th>Time from operation</th>
<th>Symptom duration*</th>
<th>Location of DVT detected at conventional venography</th>
<th>Location of DVT detected at SPADE and FR-FBI MR venography</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Hip Screw$^a$</td>
<td>9.5years</td>
<td>3days</td>
<td>Left; CFV, SFV, Pop. V, PTV, PV</td>
<td>Left; CIV†, EIV†, CFV, SFV, Pop. V, PTV, PV</td>
</tr>
<tr>
<td>2</td>
<td>Trochanteric Nai$^b$</td>
<td>11 days</td>
<td>9days</td>
<td>Left; SIV, Pop. V, PV</td>
<td>Left; SFV, Pov V, PTV†, PV</td>
</tr>
<tr>
<td>3</td>
<td>Femoral IM Nail$^a$</td>
<td>14 days</td>
<td>6days</td>
<td>Right; Pop. V, PV</td>
<td>Right; Pop. V, PTV†, PV</td>
</tr>
<tr>
<td>4</td>
<td>Trochanteric Nai$^b$</td>
<td>8days</td>
<td>1day</td>
<td>Right; PV</td>
<td>Right; PV</td>
</tr>
<tr>
<td>5</td>
<td>L Plate$^b$</td>
<td>20days</td>
<td>4days</td>
<td>Left; CFV, SFV, Pop. V, PV</td>
<td>Left; CI†, EIV†, CFV, SFV, Pop. V, PTV</td>
</tr>
</tbody>
</table>

Note.—Femoral IM nail = femoral intramedullary nail, CIIV = common iliac vein, EIV = external iliac vein, SFV = superficial femoral vein, Pop. V = popliteal vein, CFV = common femoral vein, SFV = superficial femoral vein, Pop. V = popliteal vein, PTV = posterior tivial vein, PV = peroneal vein.

$^a$These implants were made from titanium-based alloy. $^b$This implant was made from titanium.

Symptom duration* is the time between the onset of symptoms and conventional venography.

$^†$This venous segment was nondiagnostic at conventional venography due to poor filling.

These initial clinical data demonstrate the ability to detect DVTs as hypointense signal defects within the venous lumen. This depiction is based on the intrinsic $T_2$ properties of arterial and venous blood and thrombi. Several authors have reported that acute and subacute venous thrombi depict as hypointense signals on $T_2$-weighted images (29,32). In general, the composition of the thrombus is affected by local blood flow characteristics. Red thrombi form in low-pressure, reduced blood flow venous systems, from activation of the coagulation cascade (35). Therefore, it is generally accepted that the venous thrombi are mainly composed of red thrombi. Red thrombi are rich in fibrin and trapped erythrocytes (35). Blood clots pass through a sequential stage of degradation from oxyhemoglobin to deoxyhemoglobin and methemoglobin, and then hemosiderin. The presence of unpaired electrons in deoxyhemoglobin gives the thrombus a hypointense appearance on MRI.
globin, methemoglobin, and hemosiderin gives them paramagnetic properties, which induce shortening of $T_2$ relaxation times (36). Therefore, the sources of the hypointense signals during the acute and subacute phase of venous thrombi can be explained by increasing concentration of deoxyhemoglobin and methemoglobin in trapped blood cells. Likewise, increasing of hemosiderin concentration in old thrombus may also depict as hypointense signals.

MR Direct Thrombus Imaging (MRDTI) visualizes thrombi on a $T_1$-weighted image with high signal intensity using the shortening of $T_1$ relaxation time caused by increased methemoglobin concentration in a thrombus (5,6). However, the time course of thrombus maturation means that the increase of methemoglobin concentration in a thrombus is later than those of deoxyhemoglobin concentration. In addition, deoxyhemoglobin in blood cells and hemosiderin are indicated to have marked shortening of $T_2$ relaxation time but no change to the $T_1$ relaxation time (36). The SPADE and FR-FBI techniques allow reduction of the blood flow effects and artifacts within the veins. Moreover, the effective TE of 78 ms provides $T_2$-weighted images, which reflect the $T_2$ shortening effect of venous thrombi. For this reason, noncontrast MR venography using SPADE and FR-FBI has the potential of detecting thrombi earlier and in various stages of formation than MRDTI.

In hyperacute thrombus, the main component may still be oxyhemoglobin, which does not have a paramagnetic property. Therefore, these thrombi may not be detected by using noncontrast MR venography techniques, since high signal intensity will be obtained (17). However, hemoglobin desaturation from oxyhemoglobin to deoxyhemoglobin in thrombus may be complete within a short time after the event. Because the venous oxygen pressure is essentially low, this seems inadequate to delay the development of deoxygenation in venous thrombi.

Patients undergoing surgery for fractures of the hip or leg are at high risk of DVT (4). Many of these patients have
various types of metallic orthopedic implants, which may cause susceptibility artifacts and disturb the assessment of veins close to the implants in MR venography. Our data show that SPADE and FR-FBI provide clear depictions of veins adjacent to those metallic implants. The SPADE and FR-FBI techniques utilize a fast spin-echo type sequence, which minimizes the susceptibility artifacts of implants, and permits diagnosis of DVT even in patients with metallic orthopedic implants.

The elevated signals in background tissues associated with edema may limit the thrombus assessment based on MIP images. The elevated signals in $T_2$-weighted images are caused by a prolonged $T_2$ of tissues with increased water proton component. A potential limitation of thrombus assessment was reported, which was solely evaluated from the MIP image only (7,15). The interpretation of a single MIP venogram may lead to failure to detect nonocclusive thrombus, resulting in underestimation of the full extent of thrombosis, which can be eliminated by evaluating the source images. The interpretation of source images is extremely useful in the differentiation of veins from edema and other tissues accompanied with high signal intensities. Consequently, the thrombus assessment based on both MIP and source images of SPADE and FR-FBI provide a DVT diagnostic tool in patients after orthopedic surgery for fractures of the hip or leg.

Other considerations such as the specific absorption rate (SAR) and heating problems can be encountered in patients with metallic implants. When FSE and other pulse sequences using high amounts of RF energy are performed in a high-field-strength MR system, the patients with metallic orthopedic implants have a risk for RF radiation-induced heating of the implants. Because RF heating during MR examinations is attributed mainly to electric currents induced by RF radiation (37), an increase of SAR leads to the temperature rise near the metallic implant (38). Theoretically, the SAR increases in proportion to the second power of magnetic field strength; therefore, the use of low-field-strength MR systems provides a remarkable decrease of whole-body averaged SAR. In higher fields, special methods would be required to lower the RF power requirements, such as employing low refocusing flip angles in FSE and half-Fourier FSE (39,40). All of our examinations were performed on patients using a 0.5T imager and the whole-body averaged SARs were below 0.001W/kg. Thus, RF-induced heating of implants can be neglected in this SAR range. This study was limited to patients who underwent surgery for fractures of the hip or leg. Further studies involving a larger number of patients with various types and materials of implants are required.

Possible disadvantages of our technique may be limitations in recruiting patients with arrhythmia because of the requirement of cardiac gating, and less spatial resolution, which may be difficult to depict small veins and clots, as compared to conventional venography. However, small calf veins were visualized in all volunteers. Furthermore, in our preliminary clinical cases, all calf DVTs diagnosed on patients by conventional venography were clearly depicted by the SPADE and FR-FBI techniques. In our study we acquired the systolic and diastolic 3D data separately, increasing the possibility of misregistrations between scans. However, misregistrations can be reduced by a sequential acquisition of both systolic and diastolic scans (20). In consideration of other noncontrast venography techniques, such as 2D TOF and balanced SSFP, we did not include them in this study, mainly due to lengthy scan times. As mentioned previously, TOF suffers from a long acquisition time and dependency of flow velocity and orientation of veins (17) and balanced SSFP limits the depiction of venous thrombi, due to intrinsic $T_2/T_1$ contrast (18). A further drawback of our techniques may be heavy $T_2$ components such as joint fluid and urine signals remaining in both the FR-FBI and SPADE images.

In conclusion, the noncontrast MR venography with SPADE and FR-FBI allows depiction of veins in the lower extremity without delineation of overlapped arteries. Quantitative and qualitative analyses demonstrate that the FR-FBI technique is suitable in venous imaging of superficial, popliteal, and calf veins and the SPADE technique for the pelvic veins. Clinical advantages of these techniques are the ability to use them for screening and follow-up of DVT, without the adverse effects of MR contrast agents. Our preliminary clinical studies indicate the potential clinical benefit for diagnosing DVT in patients with orthopedic metallic implants; however, further clinical assessment is required.

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REFERENCES
Deep Vein Thrombosis MR Venography


