Non-contrast-Enhanced Flow-Independent Peripheral MR Angiography with Balanced SSFP

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Flow-independent angiography is a non-contrast-enhanced technique that can generate vessel contrast even with reduced blood flow in the lower extremities. A method is presented for producing these angiograms with magnetization-prepared balanced steady-state free precession (bSSFP). Because bSSFP yields bright fat signal, robust fat suppression is essential for detailed depiction of the vasculature. Therefore, several strategies have been investigated to improve the reliability of fat suppression within short scan times. Phase-sensitive SSFP can efficiently suppress fat; however, partial volume effects due to fat and water occupying the same voxel can lead to the loss of blood signal. In contrast, alternating repetition time (ATR) SSFP minimizes this loss; however, the level of suppression is compromised by field inhomogeneity. Finally, a new double-acquisition ATR-SSFP technique reduces this sensitivity to off-resonance. In vivo results indicate that the two ATR-based techniques provide more reliable contrast when partial volume effects are significant. Magn Reson Med 61:1533–1539, 2009.

Key words: peripheral angiography; non-contrast-enhanced; magnetic resonance angiography; SSFP; fat suppression

INTRODUCTION

Magnetic resonance angiography (MRA) of the extremities can help in the diagnosis of conditions such as peripheral vascular occlusion, peripheral arterial disease, and Raynaud's disease. The main challenges for this application are the inherently slow blood flow and large volumetric coverage requirements in the lower extremities.

To date, there have been two main groups of MRA techniques for the extremities. Contrast-enhanced methods have been successfully used in the lower extremities (1–4); however, the bolus timing requirements limit the spatial resolution and signal-to-noise ratio (SNR). Furthermore, administration of gadolinium-based contrast agents introduces the risk of nephrogenic systemic fibrosis in patients with renal disease (5). Therefore, there has been renewed interest in non-contrast-enhanced MRA methods. Most of these techniques can effectively generate the desired blood-to-background contrast by relying on flow. However, the performance of flow-based techniques such as phase-contrast (6,7) or time-of-flight angiography (8,9) can be limited by reduced blood flow rate in the extremities, particularly with severe atherosclerotic disease. There are other flow-dependent techniques that can cope with slow flow more successfully such as fresh-blood imaging (FBI) (10,11). FBI subtracts diastolic- and systolic-triggered fast spin-echo acquisitions to produce high-resolution angiograms with reliable background suppression, but improper timing of the trigger delays can lead to blood signal loss in the subtraction images.

While most MRA techniques rely on contrast agents and/or flow to generate contrast, flow-independent angiography (FIA) (12,13) exploits differences in T1, T2, and chemical shift. This allows FIA to produce vessel contrast even in cases of slow flow. In early FIA work, magnetization-preparation schemes were combined with fast 3D imaging to generate contrast; however, the SNR efficiency was limited (13). Recently, FIA angiograms have been produced with magnetization-prepared balanced steady-state free precession (bSSFP) sequences (14, 15) and centric phase-encode ordering to overcome this limitation (16).

Although bSSFP yields high SNR within short scan times, bright fat signal often obscures the visualization of the underlying vasculature. In this study, we examined three different methods for reducing the fat signal in FIA angiograms: phase-sensitive (PS) SSFP (17), alternating repetition time (ATR) SSFP (18), and a new double-acquisition ATR-SSFP method (19). PS-SSFP is fast and efficient, but partial volume averaging can cause loss of blood signal in the vicinity of bone marrow and subcutaneous fat tissue. ATR-SSFP can instead be used to create a stopband around the fat resonance (18) and reduce partial volume artifacts with little increase in scan time. However, the level of suppression is more sensitive to field inhomogeneity than PS-SSFP. In these cases, a new double-acquisition ATR-SSFP method can be employed to improve the stopband at the expense of lengthened scan time (19).

We can produce FIA angiograms of the extremities with detailed depiction of the vasculature within several minutes, without the need for an intravenous contrast agent. The desired vessel contrast is generated by coupling magnetization-prepared three-dimensional Fourier transform (3DFT) bSSFP acquisitions with adequate fat suppression techniques. In cases where partial volume effects are not dominant (e.g., resolution <0.7 mm^3 in the

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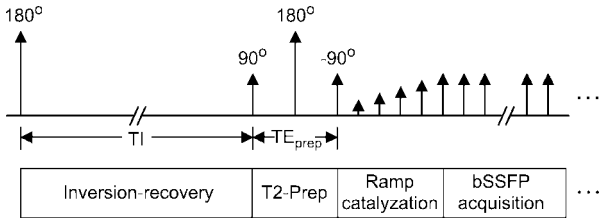

FIG. 1. Pulse sequence diagram. Optional inversion-recovery and T2-preparation sections form the magnetization-preparation module. The bSSFP acquisition starts immediately following a ramped series of RF excitations.

extremities), PS-SSFP might be preferred to decrease the sensitivity to field inhomogeneity. However, ATR-based techniques generate more reliable contrast in the presence of considerable partial voluming.

METHODS

Pulse Sequence Overview

A magnetization-prepared 3D bSSFP sequence with segmented *k*-space acquisition is used to produce FIA angiograms. The sequence starts with a magnetization-preparation module that has optional inversion-recovery and T2-preparation sections. When necessary, a nonselective inversion pulse is applied to reduce the signal from long-T1 fluids such as synovial fluid or edema. For improving the T2-dependent (blood/muscle, arterial/venous) contrast, a segmented adiabatic B1-insensitive rotation (BIR-4) pulse was used for T2-preparation (20). The BIR-4 pulse offers immunity to main field and radio-frequency (RF) excitation field inhomogeneities. A diagram of the sequence showing all the available modules is displayed in Fig. 1.

A limited number of phase encodes can be acquired with the desired contrast because of the transient nature of magnetization preparation. To capture this contrast effectively, centric phase-encode ordering [a square spiral for 3DFT (21)] is employed and *k*-space is segmented into several interleaves (16). After a certain number of phase encodes are acquired, the magnetization is allowed to recover to equilibrium and the preparation is repeated prior to the acquisition of the next interleaf. A linear ramp catalyzation is used, following magnetization preparation, to dampen transient signal oscillations (22).

Because frequent repetition of magnetization preparation reduces the scan efficiency, multiple phase encodes are acquired after a single preparation. This leads to a transient acquisition, where a mixture of prepared and steady-state contrast is captured. Figure 2 shows the transient bSSFP signal simulated for different preparation schemes: no preparation, only inversion recovery, only T2-preparation, and both inversion recovery and T2-preparation. The following approximate relaxation parameters were chosen from literature (13,23–25): T1/T2 = 1,000/220 msec for arterial blood, 1,000/120 msec for venous blood [assuming 70% oxygen saturation in peripheral venous blood (26)], 870/50 msec for muscle and 4,000/2,000 msec for synovial fluid. The sequence parameters were $\alpha = 60°$, TR/TE = 4.6/2.3 msec, TI (inversion time) = 2 sec, T2-preparation time = 80 msec, and a 10-excitation linear ramp catalyzation. The flip angle and T2-preparation time were chosen to optimize the initial blood/muscle contrast while maintaining as low a specific absorption rate (SAR) as possible. The inversion time was adjusted to produce

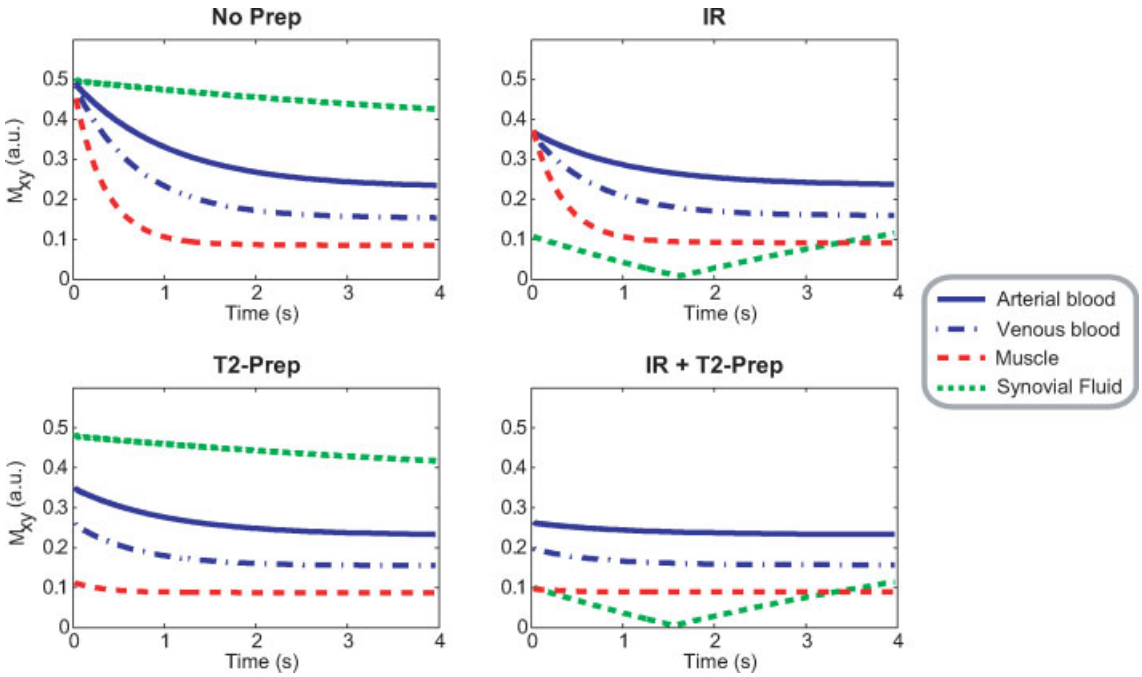

FIG. 2. The transient bSSFP signal is shown immediately after various types of magnetization preparation. The inversion-recovery sequence reduces the synovial-fluid signal for a finite time window at the expense of reduced blood signal. T2-preparation improves the initial blood/muscle and arterial/venous contrast.

low signal from synovial fluid during a 4–5 sec acquisition window.

Fat Suppression

PS-SSFP places the fat and water resonance peaks in the centers of adjacent passbands, which have a π-radian phase difference. To achieve this placement at 1.5 T, a TR of about 4.6 msec is needed. PS-SSFP provides uniform fat suppression, but it can underestimate the water signal within a voxel containing a mixture of fat and water. These partial volume effects can be mitigated with sufficient spatial resolution. However, the resultant artifacts can be significant when the achievable spatial resolution is limited by SNR and scan time considerations. Because of the large volumetric coverage requirements, the resolution needs to be lowered to maintain an adequate SNR for lower leg and foot angiograms. Hence, partial volume artifacts with PS-SSFP reduce the quality of these angiograms.

On the other hand, fat-suppressing ATR-SSFP uses two consecutive repetition times (TR1 and TR2) to create a stopband centered at the fat resonance (18). Because ATR-SSFP employs a different phase-cycling scheme than bSSFP, its response is equivalent to a frequency-shifted bSSFP response at on-resonance. This slightly reduces the tissue signal for higher T1/T2 ratios, and the magnitude of the signal change increases with T1/T2. Therefore, the ATR signal exhibits slightly more T2-dependent characteristics than the bSSFP signal, both in the steady state and throughout the progression from the initial prepared state to the steady state.

Arterial blood, venous blood, and muscle signals were simulated for the previously listed relaxation parameters assuming $\alpha = 60°$, TR1/TR2/TE = 3.45/1.15/1.725 msec, T2-preparation time = 80 msec, and a 10-excitation linear ramp catalyzation. The ATR-SSFP sequence, with 0-90-180-270 phase-cycling, yields higher signal and improved T2-contrast at the start of the acquisition following T2-preparation. The initial arterial blood/muscle contrast is approximately 3.9 for ATR-SSFP and 3.3 for bSSFP. This difference in signal behavior can lead to improved background suppression with ATR-SSFP. On the other hand, the arterial/venous contrast following T2-preparation is roughly 1.6 for both ATR-SSFP and bSSFP.

Since ATR-SSFP reduces the fat signal at the time of data acquisition, the corresponding partial volume effects are reduced. It is important to note that the level of suppression in the ATR stopband is a function of off-resonance. At the edges of the stopband where large field inhomogeneity is experienced, the signal reaches up to ~50% of the passband signal, yielding ineffective fat suppression. Methods with improved stopbands are needed when the fat signal cannot be sufficiently reduced through the whole imaging volume. Although ATR-SSFP achieves adequate fat suppression in the lower leg, high field inhomogeneity is observed in regions such as the foot because of their irregular shape. In this case, an improved fat suppression method that relies on two ATR-SSFP acquisitions can be used instead (19).

In regular ATR-SSFP, the phase of the RF excitation prior to the TR2-interval is selected to place the central null of the stopband at the fat-resonance (−220 Hz at 1.5 T). This selection divides the stopband into two equal-width segments, where one segment is in-phase and the other is out-of-phase with the on-resonant water signal. By decreasing the RF phase, we can shift the central null toward higher frequencies and extend the width of the in-phase segment. Alternatively, the out-of-phase segment can be extended by increasing the RF phase.

Fat suppression can be achieved by summing two separate acquisitions where the whole stopband is respectively in-phase and out-of-phase with the water signal (19). In one variation of this method, RF phases of 45° (0-45-180-225) and 135° (0-135-180-315) are used to create a stopband as wide as the regular ATR-SSFP stopband, assuming TR1/TR2 = 3. Because the magnitude profiles of the two acquisitions are very similar around the fat resonance, the resulting stopband suppression is significantly improved. In another variation, RF phases of 45° and −45° are used to generate in-phase and out-of-phase acquisitions for all frequencies in the spectrum except for the ones within the passband. This choice of RF phases increases the width of the stopband three times (for TR1/TR2 = 3).

Figure 3 compares the simulated magnetization profiles for the aforementioned fat suppression methods. The following parameters were assumed: $\alpha = 60°$, TR/TE = 4.6/2.3 msec (bSSFP) and TR1/TR2/TE = 3.45/1.15/1.725 msec (ATR-SSFP and the double-acquisition fat suppression method), and T1/T2 = 260/80 msec for fat (25). PS-SSFP uses the bSSFP profile, which has high passband signal at the fat resonance (−220 Hz at 1.5 T). ATR-SSFP reduces this signal by creating a stopband; however, the amount of suppression is limited with field inhomogeneity. The ATR-based double-acquisition method can yield substantially reduced remnant signal in the stopband. Alternatively, the stopband can be widened to further improve the immunity to field inhomogeneity at the expense of a lower level of suppression and ~11% reduction in the passband signal.

Imaging Parameters

Lower leg and foot angiograms were produced with the 3DFT bSSFP FIA sequence using a single-channel transmit-receive linear extremity coil (26 cm in length, 18 cm in diameter). The experiments were performed on a 1.5 T GE Signa Excite scanner with CV/i gradients. The fat signal was suppressed with PS-SSFP, ATR-SSFP, and the double-acquisition ATR method. The acquisition parameters were $\alpha = 60°$, TR/TE = 4.6/2.3 msec for PS-SSFP, and TR1/TR2/TE = 3.45/1.15/1.7 msec for ATR-SSFP, 1 mm isotropic resolution, 25.6 cm × 12.8 cm × 12.8 cm FOV, ±125 kHz bandwidth, 256 × 128 × 128 encoding matrix, T2-preparation time = 80 msec, a 10-excitation catalyzation, 4 interleaves, at 19 sec data acquisition window for each interleaf, and a 4 sec recovery time. The acquisition time for a single dataset was 1 min 28 sec. The irregular shape of the foot led to high field inhomogeneity. Therefore, the double-acquisition method was modified to widen the stopband as previously mentioned. All datasets were zero-padded to twice the initial matrix size prior to a maximum-intensity projection (MIP) to improve the visualization of the vasculature.

This study was approved by our institutional review board. Four volunteers were scanned to produce FIA

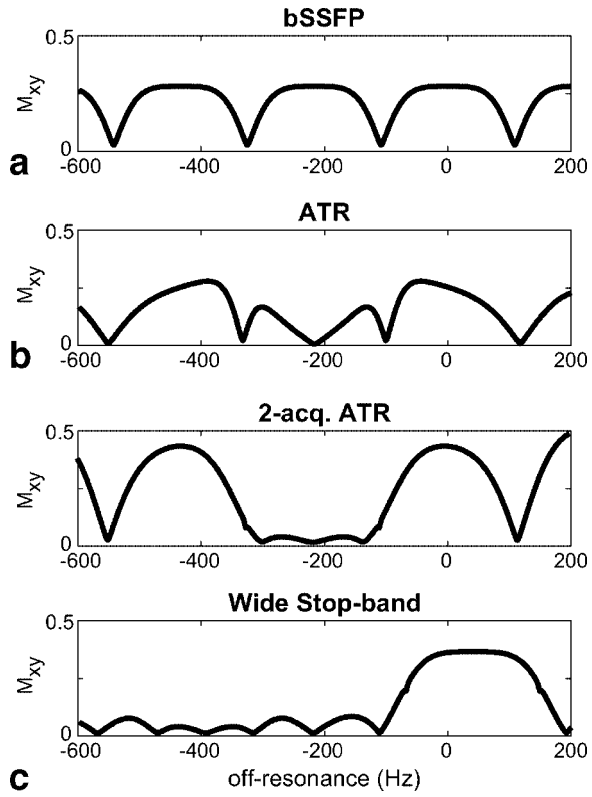

FIG. 3. The transverse magnetization profiles were simulated for the **a:** bSSFP, **b:** ATR-SSFP sequences, and **c:** the ATR-based double-acquisition fat suppression method. ATR-SSFP creates a stopband around the fat resonance; however, the residual stopband signal with increasing field inhomogeneity limits the level of achievable suppression. On the other hand, the double-acquisition method robustly suppresses the fat signal. Furthermore, this method can be modified to widen the stopband and provide increased immunity to field inhomogeneity.

angiograms of the lower leg and foot. Written, informed consent was obtained from all subjects. To quantitatively compare the level of background suppression and the reliability of vessel contrast, the arterial/venous and arterial blood/muscle contrast as well as scan-time-normalized contrast-to-noise-ratio (CNR) were measured. In the lower leg, the measurements were performed in the popliteal, peroneal, and posterior tibial arteries. The arterial blood/muscle CNR was computed with the mean arterial signal. In the foot, the lateral plantar artery and dorsal metatarsal arteries were used to measure the arterial blood/muscle CNR. Homogeneous regions of arterial as well as neighboring venous and muscle signal were selected on the source images for the measurements. The noise was then estimated by computing the standard deviation in the muscle region. The same tissue regions were used when comparing different techniques. The measurements from all subjects were averaged.

RESULTS

Representative PS-SSFP, ATR-SSFP, and double-acquisition ATR angiograms of the lower leg are displayed in Fig. 4. The techniques mainly differ in their sensitivity to field inhomogeneity and partial volume effects. PS-SSFP uniformly removes the fat signal (Fig. 4a), whereas the level of suppression degrades in regions of high field inhomogeneity with ATR-SSFP (Fig. 4b). The double-acquisition ATR method improves the fat suppression in these regions (Fig. 4c).

Partial volume cancellation creates stripe-like artifacts on vessels in the vicinity of fat tissue in the PS-SSFP image. On the other hand, the ATR-based methods are more robust against these artifacts and dramatically improve the visualization of small vessels. Furthermore, the blood/muscle contrast is higher as a result of the increased blood/muscle signal difference following magnetization preparation for ATR-SSFP compared with bSSFP.

ATR-SSFP is a very effective direct fat suppression method; however, the width of its stopband may be insufficient in the presence of high field inhomogeneity. ATR-SSFP usually yields significant remnant fat signal in the foot angiograms. For this case, the double-acquisition ATR method—tailored to increase the stopband width—offers improved performance. MIPs of typical PS-SSFP, ATR-SSFP, and double-acquisition foot angiograms are shown in Fig. 5.

PS-SSFP again suffers from partial volume artifacts deteriorating the depiction of the vasculature (Fig. 5a). ATR-SSFP improves the depiction in regions of robust fat suppression; however, the residual fat signal reduces the visibility of the vessels in the remaining regions (Fig. 5b). Finally, the double-acquisition method sufficiently reduces the fat signal in these regions, and suffers less from partial volume artifacts compared with PS-SSFP (Fig. 5c). The improved fat suppression of the double-acquisition method yields superior depiction of the vasculature.

Table 1 lists the arterial/venous and arterial blood/muscle CNR (scan-time-normalized) and contrast measurements in the lower leg and foot angiograms. PS-SSFP and the double-acquisition ATR method have similar SNR efficiencies, while that of ATR-SSFP is ~22% higher because of its initially higher transient blood signal. Furthermore, the ATR-based techniques demonstrate 14% higher arterial blood/muscle contrast than bSSFP on average, which closely matches with the theoretical estimate of 17%. In turn, higher CNR values are achieved with the ATR-based methods. Meanwhile, similar arterial/venous contrast values are observed for all three techniques, as predicted by theory.

DISCUSSION

FIA with magnetization-prepared bSSFP exploits the intrinsic MR properties to suppress the background signal. Therefore, it can yield high, isotropic spatial resolution even in cases of slow and nonpulsatile flow. Because reliable fat suppression is crucial for this application, we have investigated three methods with relatively short acquisition times: PS-SSFP, ATR-SSFP, and a double-acquisition ATR method.

There are several criteria for comparing the performance of these techniques: partial volume effects, sensitivity to field inhomogeneity, minimum scan time, and reconstruction complexity. In terms of partial volume effects, the ATR-based techniques perform better and reduce small

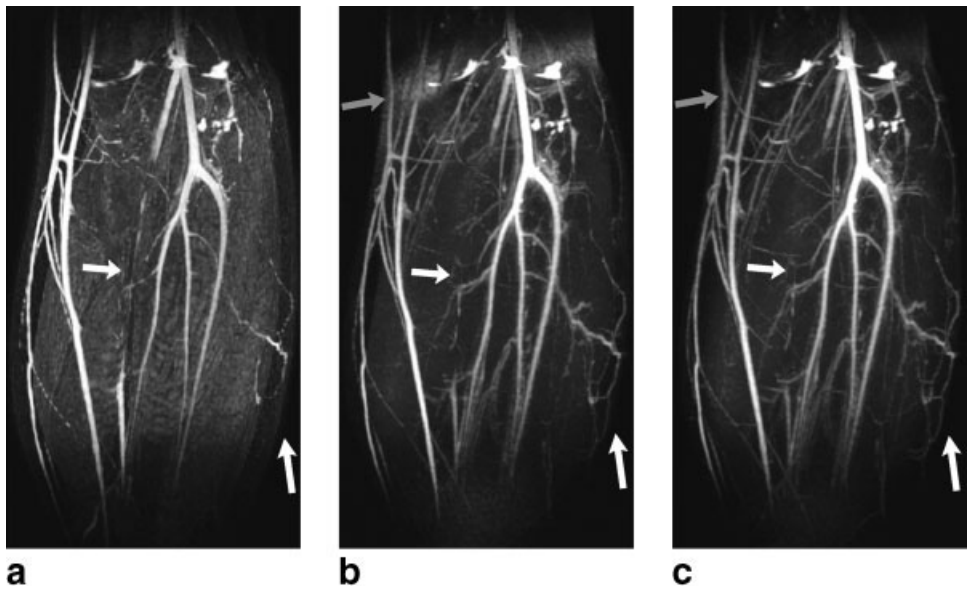

FIG. 4. Lower leg angiograms were produced with **a:** PS-SSFP, **b:** ATR-SSFP, and **c:** the double-acquisition ATR fat suppression method. The white arrows point to regions of vessel signal loss due to partial volume effects with PS-SSFP. In contrast, the ATR-based methods reduce these artifacts and significantly improve small vessel visualization. It is important to note that higher blood/muscle contrast is observed in the ATR angiograms. The gray arrows point to the regions where field inhomogeneity limits the level of fat suppression in the ATR-SSFP angiogram, whereas the double-acquisition method reliably reduces the fat signal.

vessel loss compared to PS-SSFP. In terms of immunity to off-resonance, PS-SSFP and the double-acquisition method outperform ATR-SSFP. With regard to scan time, the double acquisition method requires twice the image acquisition time compared to PS- and ATR-SSFP. Image registration might be needed with considerable patient motion between the two acquisitions. Finally, PS-SSFP requires the most complicated reconstruction including a region-growing phase-correction algorithm (17).

The investigated techniques can be extended to acquire larger FOVs and image at higher field strengths (3 T). The FOV was limited to 26 cm because of the size of the extremity coil used in this work. In fact, a FOV of 38 cm can be acquired in the readout (superior–inferior) direction without introducing severe artifacts, assuming the current parameter values of 4.6 msec TR and 1 mm resolution. In our experience, banding artifacts become more severe if the FOV is extended in the other two dimensions. To mitigate these artifacts without reducing the TR, dual-acquisition phase-cycling (27) can be used for PS-SSFP, whereas partial-dephasing in the slice direction is compatible with ATR-based techniques (28).

Similar to large-FOV imaging, banding artifacts experienced at higher field strengths can be reduced with the aforementioned strategies. For fat suppression at 3 T, PS-SSFP requires an optimal TR of 2.3 msec (17), while the TR can be kept the same with ATR-based techniques (18,19). Although ATR deposits higher RF power at 1.5 T, the reduced TR of PS-SSFP at 3 T yields equivalent SAR values for both methods. The flip angles must be reduced to an approximate maximum of 50° at 3 T to comply with the SAR limits. Although this yields reduced blood/muscle contrast, the improved venous suppression at higher field strengths will be more beneficial (29).

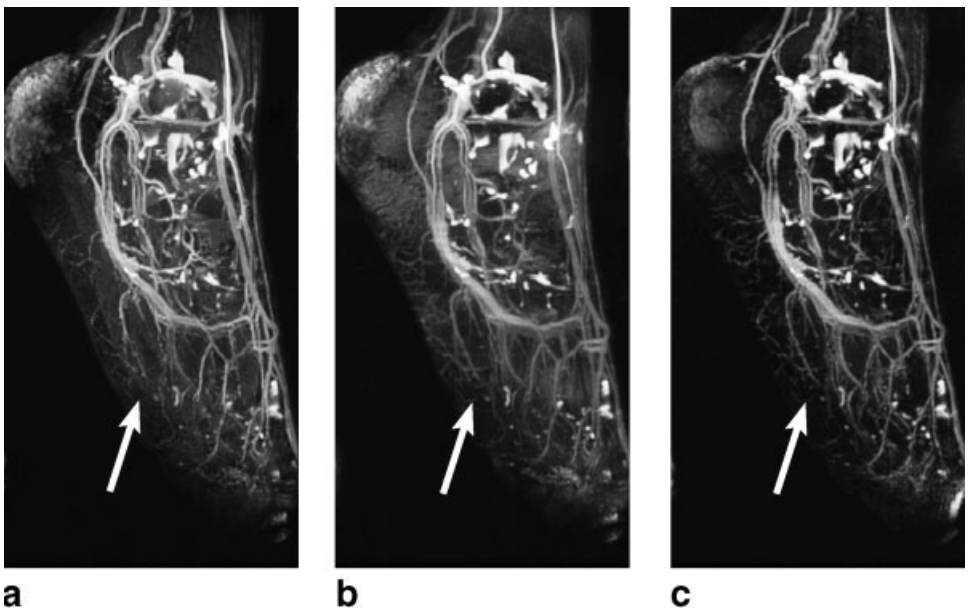

FIG. 5. Foot angiograms acquired with **a:** PS-SSFP, **b:** ATR-SSFP, and **c:** the double-acquisition ATR fat suppression. PS-SSFP achieves uniform suppression, but suffers from partial volume artifacts. On the other hand, ATR-SSFP reduces the fat signal to varying levels, deteriorating the visualization of the underlying vessels toward the ankle. Finally, the double-acquisition method achieves a level of suppression adequate for clearly depicting the vasculature. The arrows point to the regions where partial volume artifacts lead to the loss of blood signal with PS-SSFP. In these regions, the blood/background contrast is higher with ATR-SSFP compared to PS-SSFP.

Table 1
The Arterial/Venous (A/V) and Arterial Blood/Muscle (A/M) CNR (Scan-Time-Normalized) and Contrast Measured in the PS-SSFP, ATR-SSFP, and Double-Acquisition ATR Angiograms.

Method	PS-SSFP	ATR-SSFP	Double acq.
A/V 1: CNR	14.48	20.80	16.22
(Calf) Contrast	2.01	2.07	2.04
A/V 2: CNR	8.98	11.12	8.92
(Calf) Contrast	1.68	1.64	1.62
A/M : CNR	16.13	22.91	18.81
(Calf) Contrast	2.73	3.01	3.16
A/M 1: CNR	11.31	15.65	16.00
(Foot) Contrast	2.63	2.76	3.29
A/M 2: CNR	7.16	9.42	9.47
(Foot) Contrast	2.03	2.06	2.36

In the lower leg, the first set of arterial/venous measurements were performed in the popliteal artery itself, whereas the second set was collected in the peroneal and posterior tibial branches. In the foot, the first and second sets of measurements were performed in the lateral plantar artery and dorsal metatarsal arteries respectively.

Several other fat suppression methods for bSSFP reduce the fat signal without introducing significant partial volume artifacts. An efficient method is to apply spectrally selective RF saturation pulses during the steady-state acquisitions (30); however, RF inhomogeneities and transient signal oscillations lead to artifacts. These problems can be avoided with linear-combination SSFP (31). This method effectively suppresses the fat signal, but places more demanding limitations on the TR selection than PS-SSFP or ATR-SSFP. A very simple double-acquisition method comprising a summation of in-phase and out-of-phase images has been proposed by Huang et al. (32,33). Although this method gives flexibility in the choice of TR, its stopband width is limited.

Intriguing alternatives for fat suppression that are also robust to main-field inhomogeneity are multiecho Dixon techniques (34,35). In order to be able to acquire three echoes within a single TR for the peripheral angiography applications, the TR has to be increased. Two phase-cycled datasets may need to be acquired to remove the resultant banding artifacts. Hence, the total scan time can be longer compared with the double-acquisition ATR fat suppression method used in this work, increasing the susceptibility to motion artifacts. Furthermore, multiecho techniques require a complicated reconstruction as opposed to the simple pixelwise summation of the datasets in the double-acquisition ATR method.

CONCLUSION

Magnetization-prepared 3D bSSFP sequences can be coupled with fast fat suppression techniques to acquire FIAs over 26 cm of the extremities in less than 3 minutes and without the need for contrast agents. If partial volume effects are mitigated by sufficiently high resolution, PS-SSFP may be preferred. However, the ATR-based techniques generate improved vessel contrast in the lower extremities, where the limitations on the achievable resolution can lead to significant partial volume averaging. When necessary, the modified double-acquisition method can provide increased immunity against field inhomogeneity for ATR-SSFP.

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