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Original Research

Artery and Vein Separation Using Susceptibility-Dependent Phase in Contrast-Enhanced MRA

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In magnetic resonance angiography, contrast agents are frequently used to help highlight arteries over background tissue. Unfortunately, enhancing veins hamper the visualization of arteries when data are collected over a long period of time after the arterial phase of the contrast agent. To overcome this problem, we have developed a novel imaging and postprocessing method that is capable of eliminating veins by utilizing the susceptibility difference between veins and surrounding tissue. This method was applied in the peripheral vasculature where the vessels are predominantly parallel to the main field and where the blood oxygen level-dependent effect is most pronounced. Results are presented for both long (15.8 msec) and short echo times (7.8 msec) and for sequential and centrally reordered acquisition schemes. The short echo scan approach appears to be the most promising, making it possible to obtain good suppression of the venous signal even when the timing is not perfect or when repeat scans are necessary. J. Magn. Reson. Imaging 2000;12: 661–670. © 2000 Wiley-Liss, Inc.

Index terms: MR angiography; contrast-enhanced MRA; susceptibility; phase imaging

HIGH-RESOLUTION MR angiography (MRA) of peripheral arteries has been technically difficult because flow is often so slow that the signal from the blood is suppressed in time-of-flight MRA. Hence, MRA of peripheral vessels requires a method that is independent of flow. One such approach has been the use of T2-weighted imaging techniques (1,2). The next major advance came through the use of contrast agents (3–6). A T_1-reducing contrast agent can dramatically enhance signal from all vessels independent of blood flow and, for this reason, is becoming more widely used (7). However, when three-dimensional (3D) gradient-echo techniques are used to acquire high-resolution data over several minutes, arteries and veins become equally enhanced when the contrast agent reaches an equilibrium distribution in the blood pool. Enhanced veins can obscure the visualization of arteries and reduce the diagnostic value of the images.

To avoid this problem, fast 3D gradient-echo techniques with limited resolution (usually about $1 \times 1 \times 2$ mm^3 voxel size) can be used to image the arteries selectively immediately after contrast agent injection prior to venous enhancement. At present, even experienced radiologists sometimes fail to catch the right timing for imaging arteries, since dose, length of the bolus injection, and the subject's blood circulation are not identical for each individual. Although there is recent progress in accurately determining the timing in dynamic studies (8), it has been reported that more than 20% of dynamic studies fail, mainly due to the venous blood enhancement (9). However, spatial resolution is a critical bottleneck, preventing MRI from challenging the conventional gold standard, X-ray angiography.

In this paper, we propose a flow-independent MRA method whereby the blood oxygenation level-dependent (BOLD) phase is used to separate arteries from veins. This is possible because deoxygenated hemoglobin is paramagnetic (as in venous blood), while oxygenated hemoglobin is diamagnetic (as in arterial blood) (10,11). Paramagnetic substances have a positive, larger absolute value of susceptibility compared with diamagnetic substances (12). Thus venous blood has a larger susceptibility-induced phase than the arterial blood. The actual phase behavior of the blood has been used by Haacke et al (13) to measure oxygen saturation in the brain in small vessels. Hence, susceptibility-induced phase provides, under certain conditions, direct, accurate, and easily acquired information that can be used to separate arteries from veins (14–16).

THEORY

The basic concept behind artery and vein separation using the BOLD effect is to use the susceptibility-induced phase difference between them to process the magnitude images in order to remove (mask) the veins. Generally, phase is difficult to deal with because of the multiple sources of phase in MRI and phase aliasing. Specifically, five internal effects can contribute to the

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phase in a contrast-enhanced MR image: susceptibility field changes from deoxyhemoglobin, susceptibility field changes from the presence of the contrast agent, static magnetic field variations, chemical shift, and flow. The first four all lead to phase changes of the form:

$$\Delta\phi(r) = -\gamma\Delta B(r)\mathrm{TE} \quad (1)$$

where $\Delta B(r)$ represents the local field change. The low spatial frequency nature of the spatial variations in $\Delta B(r)$ will be used to remove background field effects while a special choice of echo time can be used to remove chemical shift effects from fat. Flow effects will be removed by using velocity-compensated imaging sequences.

Blood Oxygen Saturation Effects on Phase

It has been previously demonstrated that the magnetic field susceptibility of blood is directly related to its oxygen saturation level (11). The change of susceptibility $\Delta\chi_0$ from fully oxygenated to deoxygenated blood per unit hematocrit has been measured to be $\Delta\chi_0 = 0.18$ ppm in cgs units (11). The resulting susceptibility change between arteries and veins for a given oxygen saturation can then be approximated as:

$$\Delta\chi = \Delta\chi_0\mathrm{Hct}(1 - Y) \quad (2)$$

where Hct is the average fractional hematocrit in the blood and Y is the fractional oxygenation of the blood's hemoglobin.

The susceptibility change in venous blood induces a phase variation that is dependent on the geometry of the vessel (10,13,16,17). Assuming the blood vessel is a very long cylinder (compared with its diameter), and that it makes an arbitrary angle θ to the static field, the susceptibility-induced phase can be expressed as:

$$\phi_b(\mathrm{TE}) = -2\pi\Delta\chi\gamma B_0(\cos^2\theta - 1/3)\mathrm{TE}. \quad (3)$$

The regions of interest can be defined as follows: region I, where the angle the vessel makes to the main field lies between $-55°$ and $55°$ or $-125°$ and $125°$; region II, where θ lies around $\pm 55°$; and region III, where θ lies between $55°$ and $125°$ or $-55°$ and $-125°$.

For a blood vessel parallel to the static field and assuming that Hct = 0.42 and $\mathbf{B}_0 = 1.5$ T, the phase shift of the vessel with respect to the background tissue will be (13):

$$\phi_b(\mathrm{TE}) \cong -40(1 - Y)\pi\mathrm{TE}. \quad (4)$$

Phase Dependence on Shape

The phase of a venous blood vessel will change as a function of the angle, θ, it makes to the magnetic field (Fig. 1). According to Eq. [3], the phase of the blood vessel will be zero if θ is near $55°$ (referred to as the magic angle), no matter what the oxygen saturation of the blood in the vessel. That is the case shown in region II of Fig. 1. Most of the vessels in our experiment belong to region I, since vessels in the leg tend to be parallel to the magnetic field. In theory, veins in region III (perpendicular to the magnetic field) can also be eliminated, since their susceptibility-induced phase will be positive compared with that of arteries. This angle-dependent effect was validated with a gelatin phantom using a series of cylinders doped with varying concentrations of gadopentatate dimeglumine (Gd-DTPA) to mimic the blood vessels (results not shown here).

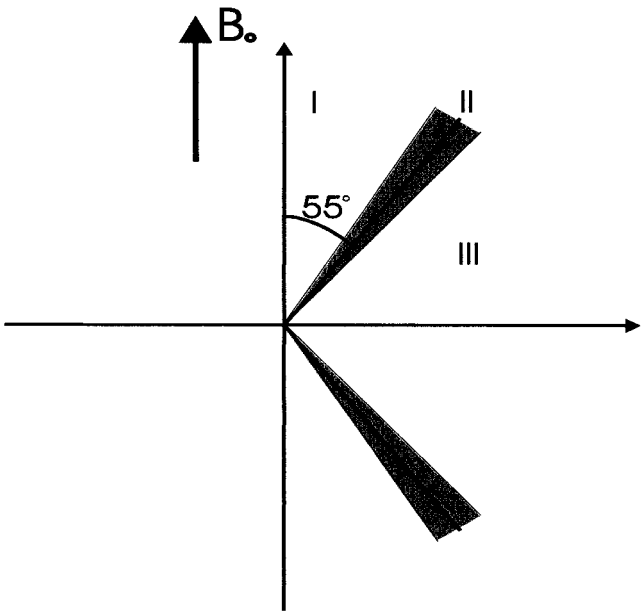

Figure 1. Demonstration of orientation dependence of the vessel phase. Region I; angles less than 55°; region II: angles in the neighborhood of 55°; and region III: angles larger than 55°.

T_1-Reducing Contrast Agents and Their Affect on Phase

The use of T_1-reducing, intravascular contrast agents offers the opportunity to enhance signal from blood selectively without altering signal from the surrounding tissue. Reducing the T_1 of blood will lead to an increase in the signal-to-noise ratio (SNR) of blood in the magnitude images while increasing phase shifts in the phase images. In most imaging applications, the contrast agent stays within the blood vessel for a certain period of time before it is washed out. However, for our application, one might fairly be concerned that the susceptibility of a contrast agent used to enhance the signal from the vessels could significantly alter the phase behavior of the blood. This will depend on the local concentration and susceptibility of the contrast agent in the blood at the time of imaging. We anticipate that there will be an equal shift in the phase of both arteries and veins when the contrast agent has reached equilibrium, ie, the phase effect of the contrast agent is additive. Therefore, any method based on the phase difference between arteries and veins should remain unaffected.

MATERIALS AND METHODS

In this section, we present a three-echo and a single-echo approach to extract arteries from veins. The se-

quences to be used are described first, followed by the proposed processing scheme that recognizes veins and suppresses them from the original images. The sequence design and image processing procedures were tested on both phantoms and human volunteers. A series of experiments was also performed to confirm that the contrast agent does not affect the expected phase relationship between arteries and veins. All experiments were performed on a Vision 1.5-T whole-body imaging system (Siemens Medical Systems, Iselin, NJ) with a circularly polarized extremity coil. All protocols for volunteer studies were preapproved by Washington University's Human Studies Committee.

Data Acquisition Methods

Multiple-Echo Scans

The goal was to collect high-resolution 3D data over the entire leg and to show that arteries could be distinguished from veins. A three-echo sequence with echo times of 6, 11, and 15.8 msec was used to allow for more phase development from the BOLD effect at the longer echo times. The bandwidth was 195 Hz/pixel. The sequence (including all other sequences used in the volunteer studies) was designed with a symmetric echo, using the following parameters: TR 21 msec, flip angle 12°, spatial resolution 0.5 mm in readout and 1 mm in both phase and slice-select directions, field of view (FOV) 256 × 256 mm^2, slab thickness 10–12 cm, and total imaging time 10–12 minutes depending on the number of slices needed to cover the calf. Phase images were also acquired. Care was taken in shimming to ensure that the static magnetic field was as uniform as possible. Either a single dose (four volunteers) or a double dose (one volunteer) of gadodiamide (Omniscan, Nycomed, New York, NY) was used to test the algorithm's ability to suppress the veins using the phase information. When a contrast agent was used, the flip angle was increased from 12° to 30° to enhance the signal from blood. A CP-extremity coil was used to cover the calf of one leg. A coronal cut was chosen to reduce the number of slices necessary to cover the lower extremity.

Single-Echo Scans

A single-echo sequence was also designed to see whether a shorter TE could be used to separate arteries and veins with future intravascular contrast agents (18) where an increase in SNR would allow a reduction of TE. A double dose of gadodiamide was administered to two volunteers to mimic the higher relaxativity associated with the intravascular contrast agents. A velocity-compensated gradient-echo sequence with TE of 7.8 msec was created to collect data from the same area as the multiecho sequence, but with the following imaging parameters: TR 12 msec, flip angle 30°, spatial resolution 0.5 × 0.5 × 0.7 mm^3, and total imaging time about 12 minutes, with 100 slices. The bandwidth was 195 Hz/pixel. This sequence was also created with central recordering of the phase-encoding lines and used to collect the data shortly after injection of a contrast agent.

A dynamic scan was also performed by collecting data from 0 to 30 seconds after contrast agent injection. The artery-only image from the dynamic study was then used to compare with our phase-masked images from the steady-state approach. The imaging parameters for the dynamic scan were as follows: TR/TE 5/2 msec and total imaging time 40 seconds with a spatial resolution of 0.8 × 0.8 × 2 mm^3. The same FOV was used as in the steady-state scans.

Image Processing: Eliminating Background Field Inhomogeneity Effects on Phase

High Pass Filtering the Phase Image

Background field inhomogeneities tend to cause a low spatial frequency phase variation within the image. To remove this phase effect, we applied a 3D low-pass Hanning filter to the original *k*-space data. The field inhomogeneity information was removed from the original phase image by complex dividing the original image with the image created from the low-pass-filtered *k*-space data. Several different filter sizes were tested to ensure a minimum effect on the phase of the vessels. These filters contained 8 × 8, 16 × 16, 32 × 32, and 64 × 64 pixels.

Specifically, the original complex signal, $\rho_0(x)$, consists of components from both the background static field and the venous deoxyhemoglobin local field contribution:

$$\rho_0(x) = |\rho_0(x)|e^{i\varphi_f(x)+i\varphi_v(x)} = F^{-1}[S(k)] \qquad (5)$$

where $\phi_f(x)$ is the phase component from the local field inhomogeneity, $\phi_v(x)$ is the phase component of the blood, $S(k)$ is the original *k*-space data, and $\phi_0(x)$ is the complex data in the spatial domain, which is the inverse Fourier transform of $S(k)$.

We assume that the central part of *k*-space contains the main spatial behavior of the static magnetic field. If we use it as a filter and subtract its phase from the original phase, the resulting signal should be free of static field inhomogeneity effects. To accomplish this, we generate first a complex low-pass-filtered image:

$$\rho_h(x) = |\rho_h(x)|e^{i\varphi_f(x)} = F^{-1}[S(k)H(k)] \qquad (6)$$

where $H(k)$ is an n point *k*-space filter (this becomes an $n \times n$ filter in 2D) and $\rho_h(x)$ is the filtered complex data in the spatial domain.

Then we obtained the effectively high-pass-filtered image through a complex division of the original image with the filtered image:

$$\rho_f(x) = \frac{|\rho(x)|e^{i\varphi_f(x)+i\varphi_v(x)}}{|\rho_h(x)|e^{i\varphi_f(x)}} = |\rho_f(x)|e^{i\varphi_v(x)} \qquad (7)$$

The phase $\phi_v(x)$ is now used to create the phase mask. Practically, the value of the original image is examined to see whether it falls below some noise threshold. If it does, then that pixel is not evaluated in the new image $\rho_f(x)$.

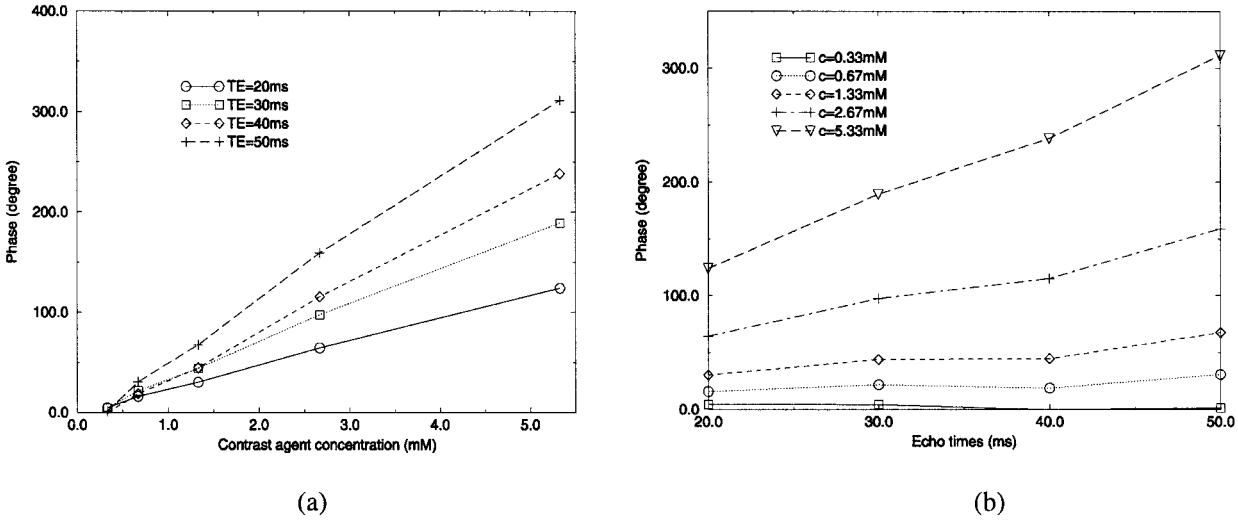

Figure 2. An example measurement from a single set of contrast agent dopings from a multiecho experiment. **a:** The phase versus concentration of the contrast agent for various echo times. **b:** The phase versus the echo time for different concentrations of the contrast agent.

Data Processing: Phase-Mask

In the filtered phase image, arteries and muscle have small positive phase values, while veins appear dark because of their susceptibility difference. To generate a phase mask from $\rho_f(x)$, phase values of 0 to π were set to unity, whereas phase values of less than zero were normalized to values that ranged linearly from 0 to 1, such that 0 corresponded to $-\pi$, and 1 corresponded to 0. Veins in the magnitude images were eliminated by multiplying the phase-mask on a pixel-by-pixel manner four times to suppress the venous signal. (This factor of four was found empirically to produce the best result (16)).

Measuring Phase Dependence on Contrast Agent Concentration

When a contrast agent, such as Gd-DTPA, is injected into blood vessels, because Gd-DTPA is paramagnetic, the phase in the vessels will be affected and the amount of phase change will depend on the contrast agent dosage (11,19,20). To ensure that the phase effects induced by the contrast agent are not deleterious to the process of separating the veins from the arteries, a phantom study was conducted to evaluate the phase change of the doped solution with different concentrations and echo times using a method similar to that described in ref. 21. Both Magnevist and AngioMARK (formerly MS-325, EPIX Medical, Boston, MA, and Mallinckrodt Medical, St. Louis, MO) were studied. To mimic the contrast agent concentration used in a volunteer, a series of 1, 2, 4, 8, and 16 ml of contrast agent was diluted into 1500 ml of tap water, sealed, and labeled in separate tubes of inner diameter 1 cm. The corresponding concentrations in these tubes were 0.33, 0.67, 1.33, 2.67, and 5.33 mmol/l (mM), respectively. The normal dose used in our volunteer studies was 0.1 mmol/kg. That is equivalent to a concentration in the blood of 1 mmol/l, if we assume the volunteer has 100 kg weight and 5,000 ml blood and a factor of two in extravasation of extracellular agents.

Each tube was then immersed in a water bath and imaged with a 2D four-echo, gradient-echo sequence with echo times of 8, 18, 28, and 38 msec, respectively. The imaging parameters were as follows: TR 62 msec, flip angle 30°, spatial resolution 1×1 mm^2 in-plane and 4 mm through-plane (slice thickness), and FOV 256×256 mm^2. To eliminate the effects of spatially varying field inhomogeneities, the test tubes were imaged individually in the same location by removing the original tube and replacing it with a new one for each experiment.

The image data (both magnitude and phase) were processed on a Sun Sparc-20 computer workstation (Sun Microsystems, Mountain View, CA). A region of interest (ROI) for each concentration at each echo time was drawn. The mean phase values for each concentration in the ROIs were used for the plot against echo time, and a slope was calculated for that concentration.

RESULTS

Measuring the Phase Dependence on Contrast Agent Concentration

The susceptibility as a function of concentration of the contrast agent was investigated with a series of five different tubes of water doped with contrast agent. The phase was clearly linearly proportional to the echo time, and the slope increased as the concentration of the contrast agent increased. Figure 2 shows the phase (in degrees) as a function of the concentration (mM) of the contrast agent (Fig. 2a) and the echo time (Fig. 2b) at each echo time. To avoid problems with phase offsets changing from one scan to the next, the slope was calculated for each concentration. All slopes were then normalized to concentration, and the mean of the normalized slopes used to find the phase per mM concentration per msec echo time. This experiment was run

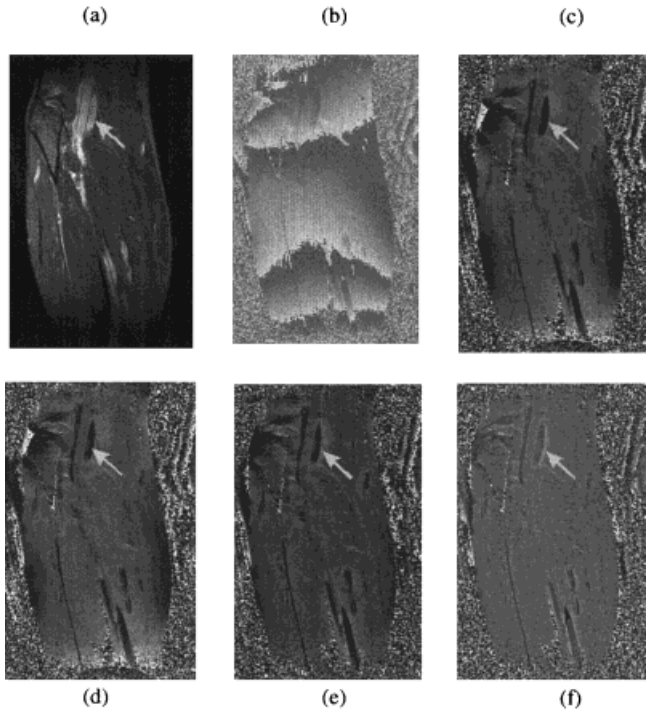

Figure 3. The effects of *k*-space filter size is shown here with a single slice in the calf of a volunteer. The magnitude (a) and phase (b) images were collected after the contrast agent reached steady state. The remaining phase images represent the results after *k*-space filtering with a filter size of 8 × 8 (c), 16 × 16 (d), 32 × 32 (e), and 64 × 64 (f), respectively.

three times to exhibit the repeatability of the measurements. The mean of the normalized slope for both studies combined for Magnevist was 0.960 ± 0.097 degrees/mM/msec. The results for AngioMark yielded a slope of 1.141 ± 0.23 degrees/mM/msec.

Assuming that the contrast agent concentration in a volunteer usually is 1 mM, the above results indicate that the contrast agent will induce a phase change of roughly the same in degrees as the echo time in msec. For example, at a TE of 8 msec, the expected phase from a single dose of contrast agent should be around 8°. This was much smaller than the expected phase shift of roughly 30° due to the veins at this echo time.

k-Space Filtering Results

Figure 3 shows the original magnitude (a) and phase (b) images from one slice of a 3D data set. The phase aliasing is automatically unwrapped by the complex-division process (Fig. 3c). As the 2D filter size increases, the resultant phase image becomes more uniform, but the phase difference between veins and the surrounding tissue decreases. The decrease of the contrast is dependent on the vessel size. For the extremity studies, with a 16 × 16 or 32 × 32 pixel size filter, the filtered phase images were sufficiently homogeneous, and the susceptibility-induced phase changes from the BOLD effect were mostly preserved.

Multi-Echo Results

Figure 4 shows one slice from a 3D image set with and without contrast agent. The imaging parameters were

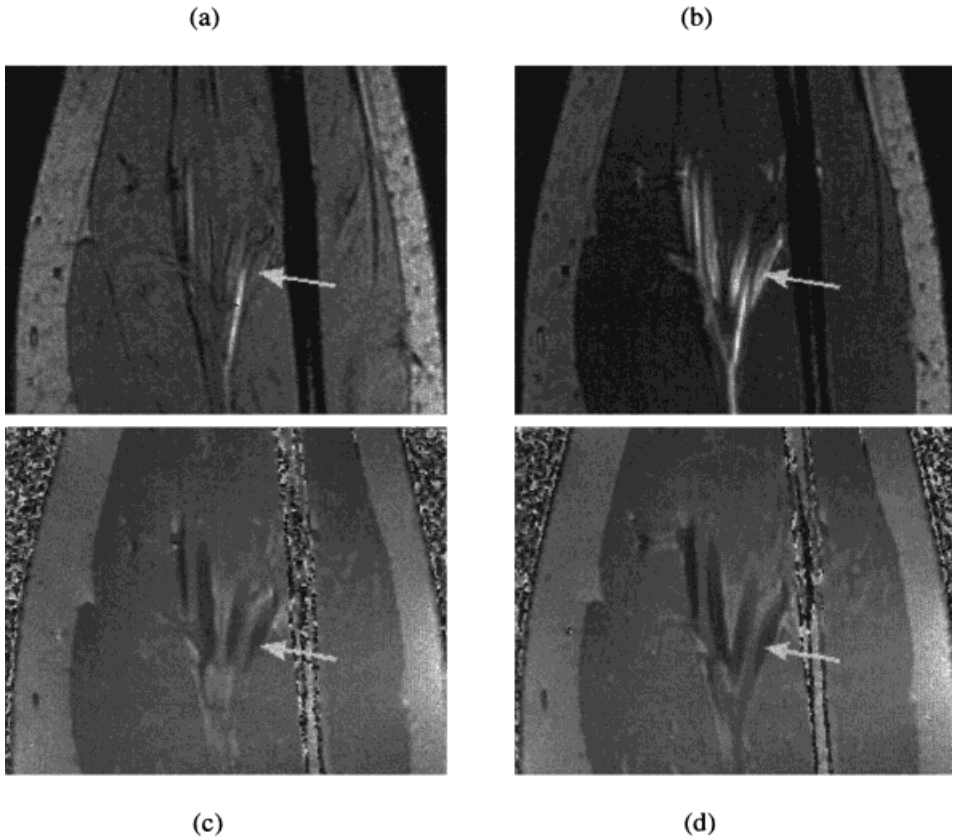

Figure 4. Single slice from a contrast-enhanced 3D data set collected from the calf of a human volunteer. In the non-contrast-enhanced image (a), the artery was enhanced by inflow effects while the veins were saturated (arrow). Both arteries and veins were clearly enhanced in the postcontrast image (b). As expected, the phase images before (c) and after (d) contrast agent administration demonstrated a similar phase difference between arteries and veins.

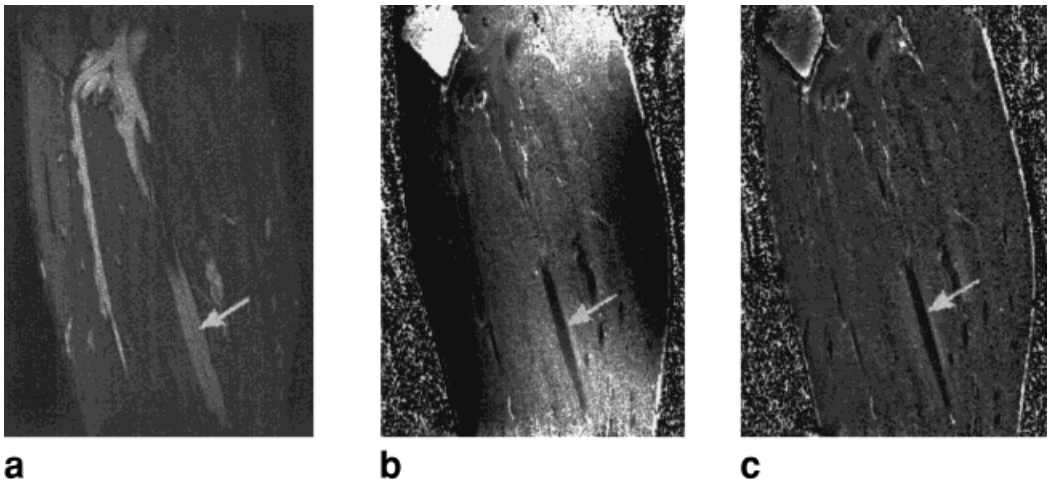

Figure 5. Original magnitude image (a) and phase image (b) of a single slice extracted from a 3D data set with a TE of 15.8 msec. c: The resulting phase-filtered image. Note that the large phase variations in the upper and lower parts of the middle image are gone after phase filtering. The major vein in the lower part of the leg is demarcated by the arrow. The phase image in c is now much more uniform.

as follows: TR/TE 30/15.8 msec, slice thickness 1 mm, and flip angle 15° before contrast agent injection and 30° after injection. In magnitude images, vessels were poorly delineated in precontrast images but both arteries and veins were markedly enhanced in postcontrast images. In contrast, the associated phase images showed little phase difference change between arterial and venous blood vessels from pre- to postcontrast images. The mean of the phase difference between a vein and an adjacent artery was 39.4 ± 2.2° before contrast agent enhancement, and 42.3 ± 1.8° after a single dose of contrast agent. The phase difference was 18° at the same ROI as used in the above measurements inside a vessel before and after contrast agent enhancement. This phase difference was from the susceptibility effect of the contrast agent.

Figure 5 shows one slice of a 3D image at a TE of 15.8 msec after contrast agent administration. The field inhomogeneity effect caused significant phase variations at this TE even after careful shimming. The low spatial frequency components in the phase image were eliminated by using the previously described *k*-space filter with a 32×32 matrix size. The resulting phase image was then used as a mask and applied to each individual slice to eliminate the veins. Figure 6a and b shows an example of a single slice before and after masking the image. This image demonstrates a good suppression of veins, even those very close to the arteries. A maximum intensity projection (MIP) was then performed to demonstrate the effectiveness of the method. Figure 6c and d shows the MIPs of the calf before and after the phase-masking process. On the processed MIP images, the veins were largely suppressed when parallel to the main field. As expected, veins at the magic angle to the field were not eliminated.

Short TE Results

Figure 7 demonstrates the application of this method to a TE 7.8-msec sequence. The resolution in these images was $0.5 \times 0.5 \times 0.7$ mm^3. The higher spatial resolution significantly enhanced the visibility of the vessel wall and sharpened the edges of the vessels. Figure 7 shows the MIPs from the dynamic scan (a), the original steady-state (b), and our phase processing (c) for the same volunteer. Although it is not perfect, the phase filtered high-resolution MIP image (Fig. 7c) shows better defined edges of the blood vessels and many more small vessels. This edge definition is important in the diagnosis of stenoses. The MIP from the conventional 40-second dynamic scan (Fig. 7a) serves as a reference to demonstrate which vessels were arteries. Some of the veins suppressed in Fig. 7c are still causing a visual blurring effect in Fig. 7a. As occurs on occasion, it is difficult a priori to say which veins will enhance with dynamic scanning.

Centric Reordering Acquisition Results

Figure 8 shows two examples of centrally reordered data. The first (Fig. 8a) shows the effect of collecting the data a little late after injection of the contrast agent (15–30 seconds); hence the venous blood is bright but not as intense as the arterial blood. The second example (Fig. 8b) shows the successful suppression of most venous blood when the timing is perfect (0–15 seconds after injection) and the central part of the data set is collected during the arterial phase. On closer examination, one can see the high spatial frequency edge effects in the veins. These images were not processed with phase multiplication because the phase of both arteries and veins was significantly modified by the high concentration of the contrast agent. However, it is clear that when this occurs, the high-resolution acquisition combined with the low spatial frequency suppression of the venous signal does a reasonable job.

DISCUSSION

Several conditions have been assumed in our research that are generally satisfied in most MR imaging exper-

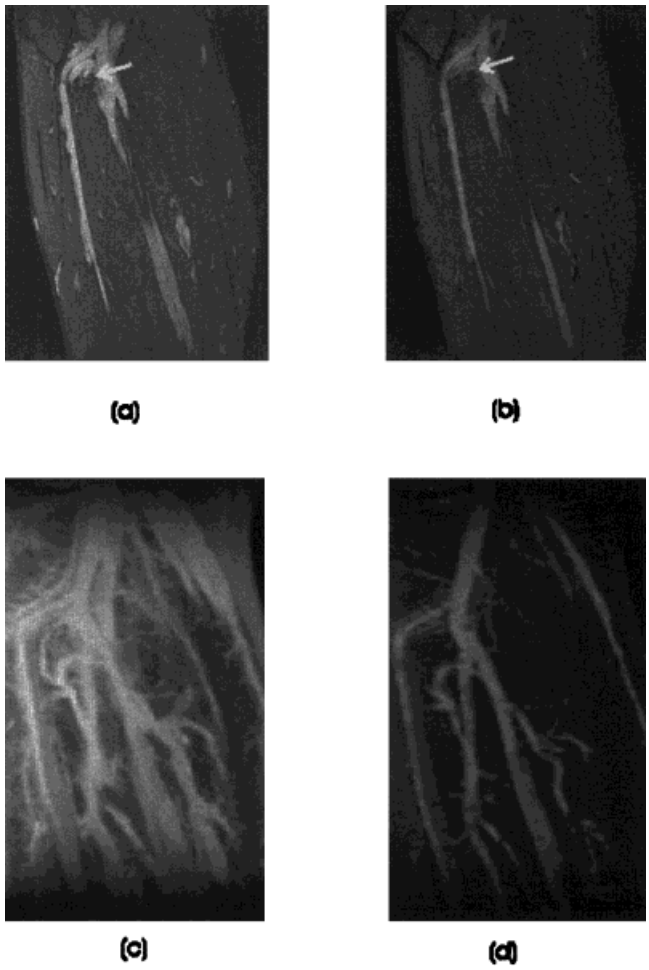

Figure 6. A single slice of a 3D data set with a TE of 15.8 msec is shown in the upper panel, before (**a**) and after application of the phase-mask (**b**). The veins parallel to the main field have been successfully suppressed in b. However, veins in the area indicated by the arrow are still not completely eliminated. The arrow indicates one vein that was not suppressed. The maximum intensity projection of blood vessel after contrast agent administration (c) was calculated from all slices before processing (**c**) and after phase-mask processing (**d**). The resulting MIP in d shows an artery-dominated image for most areas.

iments. First, there are two terms that contribute in an additive fashion to the phase in a gradient-echo experiment: ϕ_0 (a time-invariant phase term) and ϕ_1 (a linear time-dependent phase term). Second, blood vessels in the lower extremity behave as infinitely long cylinders, for the most part. Third, the contrast agent will also induce certain phase shifts in the vessels, but the phase difference between arteries and veins will remain invariant before and after contrast agent administration. Fourth, blood flow in peripheral vessels is slow so that a well flow-compensated sequence should keep flow-induced phase to a minimum. Finally, intravascular contrast agents will lead to a better SNR for both magnitude and phase images and make it possible to keep echo times and imaging times short despite the small effect on phase of the BOLD phenomena. The goal of this paper is to show that the background field effects on phase can be removed and the remnant phase used as a means to reduce signal from the veins, leaving arteries as the main source of signal in the images.

Other Sources of Phase Variation

The problem remains to separate background static field effects and other unwanted sources of local field inhomogeneities from these local BOLD effects. Fortuitously, the background field is usually of low spatial frequency in nature, except for some circumstances near air/tissue interfaces (these do not occur in the leg, but do in the brain). As described earlier, a phase filter is used to eliminate this low spatial frequency component of the magnetic field inhomogeneity. Since the central part of *k*-space contains the background static field inhomogeneity information, it is used to produce a phase image with the low spatial frequency components of the field inhomogeneities suppressed. Although this processing may change the relative phase between arteries and veins if too much of *k*-space is used to filter the data, with the filters we have used (central *k*-space filter sizes less than or equal to 32 in any direction) this has not been a problem (22).

Once all other sources of phase are removed, in theory, only the phase effects from the BOLD phenomena remain. This final, processed phase image, in turn, can be used to tell which vessels are arteries and which are veins. This is made particularly easy because the phase of other background tissue such as muscle is also zero, similar to that for arteries. (The signal from muscle appears to be negligibly affected in the steady state.) Hence, the negative phase of the vein is a signature from which the veins can be suppressed. The phase itself can also be used to measure the oxygen saturation. For example, from one subject we found a phase shift of 40° at a TE of 15.8 msec. This corresponds to a fractional oxygen saturation of $Y = 0.68$, quite consistent with the expected value of oxygen saturation in the venous blood.

The success of this artery/vein separation method relies on two critical features: first, that the oxygenation difference between arteries and veins is large enough to allow for a phase discrimination between them for reasonably short echo times and, second, that the vessels remain nearly parallel to the field. The first point is, fortuitously, not a problem. However, we have noticed that this is not always the case for all veins in the leg, some perhaps having a much higher oxygenation level than expected. A similar observation has been made by Brittain et al (2). We know of no cure for this problem, unless a second feature can be absorbed into the data acquisition scheme to help avoid this. That second part may come from the combined concept of acquiring the low *k*-space part of the data during the arterial phase of the contrast agent uptake, as discussed later in this section.

Sequence Considerations

The results shown in Fig. 7 indicate that a short echo time of 7.8 msec is still long enough to develop a significant phase difference between arteries and veins, at least for vessels parallel to the field. As the angle to the

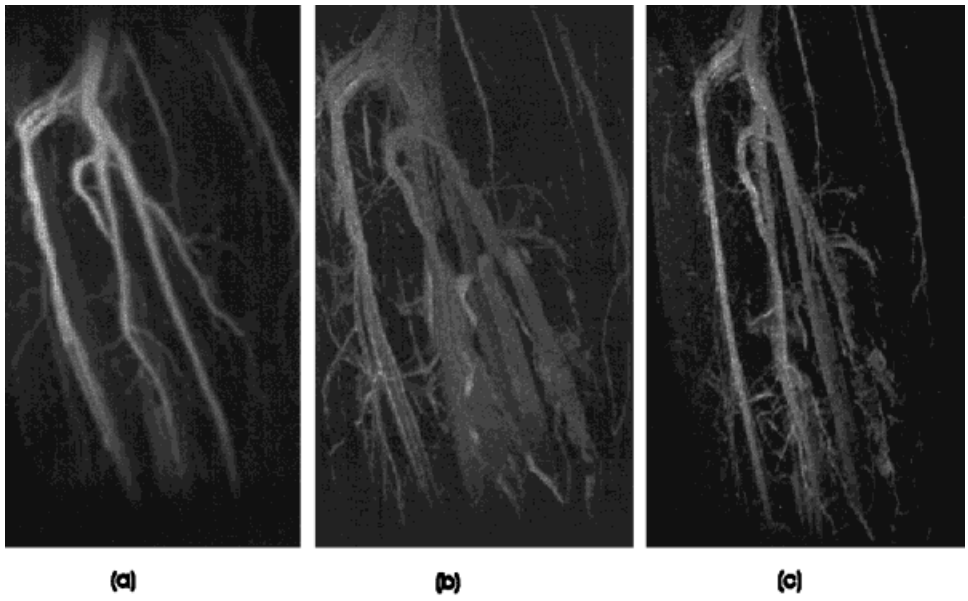

Figure 7. Maximum intensity projection images of the blood vessels in the calf of another volunteer shortly after contrast agent administration using a dynamic scan (**a**), a steady-state scan (**b**), and the steady-state scan after phase processing (**c**). Here the TE was 7.8 msec. Many of the major veins have been removed.

main field increases, so the phase difference decreases. A short TE makes the background field easier to remove, and so the processing should become even more stable. Generally, flow-induced phase errors have not been a problem, and with new gradients and shorter field echo times of roughly 2–4 msec, rapid flow near stenoses should have little effect on phase in leg vessels.

The multiecho sequence was used for the following reasons: the two phase terms, ϕ_0 (a time-invariant phase term) and ϕ_1 (a linear time-dependent phase term), can be separated; T2* can be concurrently estimated from the multiple echo data; a phase slope could be used instead of the absolute phase value to estimate effects as a function of concentration; and a complex division could be used to find the phase difference between the adjacent echo times to avoid potential phase aliasing problems in the presence of a large ϕ_0. One practical issue is the total imaging time accompanying longer echo times. Total imaging time is dependent on the size of the leg. A short TE sequence would help to reduce the imaging time. We hypothesize that newer intravascular contrast agents will result in a higher SNR, which should enable us to use shorter echo times to separate arteries and veins. Furthermore, high spatial resolution may be achieved, and the whole data set could be collected in 10–12 minutes for a $0.5 \times 0.5 \times 0.7$ mm^3 voxel resolution, if the number of slices is 100. However, if only the area containing blood vessels is covered, and if the number of slices could be reduced to 40, then the imaging time could be cut down to about 4–6 minutes, albeit at the expense of reduced SNR and a more limited FOV. Further developments in fast imaging, including partial Fourier methods applied in two dimensions and the use of multiple coils would also help make this approach more feasible. The use of variable TE and variable TR may also prove viable in reducing acquisition times even further with this approach.

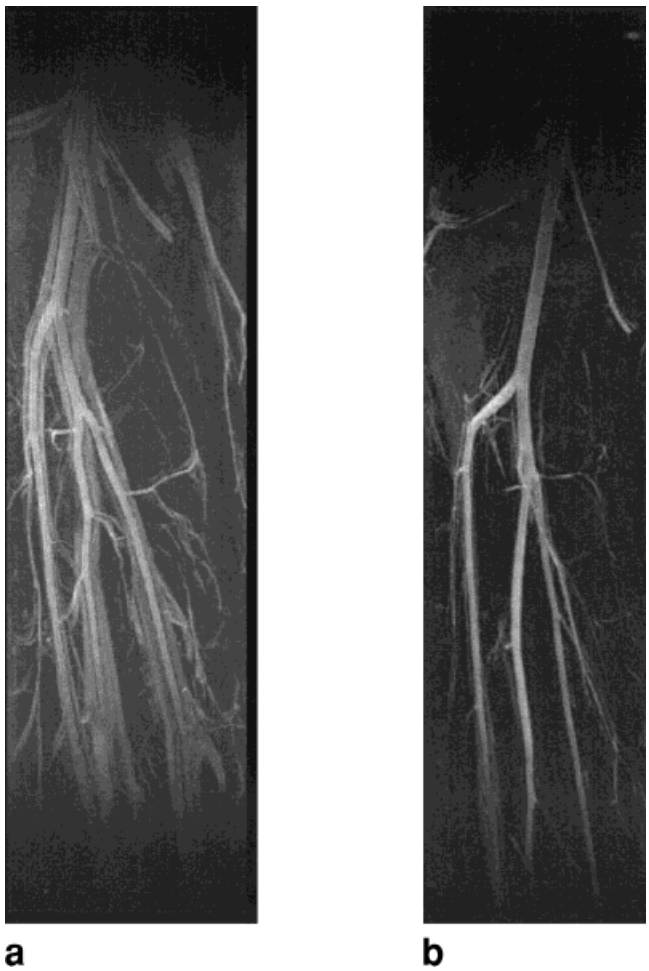

Figure 8. Two examples of centrally reordered data. **a:** Effect of collecting the data a little late after injection of the contrast agent (15–30 seconds). The boundaries of both the arteries and the veins are well delineated because of the high resolution of the scan. **b:** Successful suppression of most venous blood when the timing is perfect (0–15 seconds after injection) and the central part of the data are collected during the arterial phase.

Processing Issues

From a processing perspective, shorter echo times reduce the background field effect and may allow for the use of a smaller filter window. The smaller filter size then offers a better contrast between venous phase and the surrounding tissue. It may also be possible to reduce the static field effects by using water pads surrounding the legs.

Multiecho imaging may have another advantage. As we know, fat signal also appears bright in contrast-enhanced MRA because of its short T_1. A modified two-point Dixon method (23) can also be used to suppress fat, which will further enhance the arterial vasculature. This requires collecting two echoes, one with water and fat in-phase and the other with water and fat out-of-phase. The in-phase nature of one echo also helps reduce artifacts associated with edges when the phase filter is used. Processing of the positive phase to eliminate veins is also possible but requires a highly uniform background field. It has recently been shown that this processing can improve venous suppression (24) and may be a better way to suppress veins near 90° to the main field.

Central Reordering

Central reordering in a square spiral sense (or in an elliptical fashion) (25,26) immediately after injection makes it possible to obtain high-quality images even if the timing is not perfect. The practical approach is to attempt to use this method so that no phase processing is required. However, if the timing is bad, then the images will have veins in them. At that point, all the information will be present to phase process the data to eliminate the veins.

Using a double dose of conventional contrast agent and imaging the center of *k*-space immediately after injection has the disadvantage that the concentration and, hence, the susceptibility of the contrast agent are very high and will confound the use of the phase masking. However, with the use of a half dose of the new intravascular agents such as AngioMark, this problem should be significantly alleviated.

Practically, we suggest that the combination of centric reordering with this BOLD-related venous suppression technique could lead to a very robust procedure. For example, when the arterial phase is successfully captured, there is little need for suppressing the veins further. (This is not exactly true, as the edges of the veins still show even then, but they are much reduced in amplitude.) When the arterial phase is mistimed, then the venous suppression should complement the still somewhat enhanced arterial phase. Finally, if the arterial phase is entirely missed or if a second injection is given and remnant venous signal remains, then this approach should significantly help suppress the veins.

CONCLUSIONS

Intravascular agents are an important step in improving MR angiographic methods in humans (27). However, steady-state methods still suffer from the simultaneous enhancement of arteries and veins. We have shown that the phase information available in velocity-compensated MR angiography sequences is a potential means to separate arteries and veins. By appropriately phase filtering images with an echo time as short as 7.8 msec, background magnetic field effects can be removed and veins suppressed. Preliminary results demonstrated that the method successfully separates arteries from veins when the vessel makes an angle less than 55° to the main magnetic field. This method will not be able to suppress veins near 55° but should still offer a complementary means to process data with no danger of misregistration artifact. It will make the timing issue for the arterial phase less important and make multiple imaging post injection more viable.

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