Magnetic resonance angiography (MRA) can provide significant additional information to complement the routine spin-echo MR examination of the brain.1-13 The idea of a combined study has gained favor because it provides a noninvasive alternative for the complete study of patients with suspected cerebrovascular disease. Because of the relatively short time of acquisition, MRA sequences can be easily added to the traditional parenchymal study without significantly prolonging the overall examination time (Figure 1).

Magnetic resonance is able to create anatomic images through the use of radiofrequency (RF) excitation and refocusing pulses as well as spatial localizing magnetic field gradients. Motion (blood flow) in the presence of the RF pulse sequence creates time-of-flight (TOF) effects on the signal of moving protons, while proton motion during the application and in the direction of the magnetic field gradients produces spin phase phenomena. Each of these effects can be manipulated relatively independently to create vascular contrast within a given scan and thus angiographic images.

TOF techniques create vascular contrast via the inflow of blood protons into a region of interest previously prepared by an RF excitation, inversion, or saturation pulse. The most popular techniques consist of relatively simple gradient echo pulse sequences where the inflow of spins produces high signal within the vessels on the basis of the TOF effects known as “entry slice phenomenon” or “flow-related enhancement.” Angiographic images can then be derived from such data sets through the use of computer post-processing techniques which obviate the need for mask acquisitions to create a subtraction angiogram. Since TOF MRA requires only a single data set, the acquisition is less susceptible to problems, such as patient motion and eddy currents, which arise with longer examination times and multiple data sets.1-11 TOF data also require less computer memory and post-processing following the acquisition. Although the phase contrast techniques are more sensitive to very slow flow, the TOF techniques may be less vulnerable to the phase dispersion (and signal loss) that accompanies complex motion typically seen in regions of arterial flow (i.e., tortuous vessels, stenoses).12,13

All MRA techniques may be implemented in a 2D or 3D mode. Two-dimensional Fourier transform imaging (2DFT) acquires data in the conventional fashion in which individually acquired image slices are stacked sequentially. With 3D Fourier transform (3DFT) acquisitions an entire block or “slab” of anatomic digital data is acquired. This may then be displayed as individual slices reconstructed in any plane or perhaps subjected to a post-processing algorithm which displays only selected tissues (Figure 1). While 2D MRA examinations are superior for the demonstration of slow flow (e.g., venous) lesions, 3DFT sequences can provide thinner image slices with higher spatial resolution, as well as shorter echo times which minimize artifact responsible for the overestimation of (carotid) stenoses.

TOF techniques have been most extensively tested in the evaluation of carotid artery atherosclerotic disease and a variety of vascular abnormalities involving the larger vessels of the intracranial circulation. Both areas are particularly amenable to investigation by TOF studies because of the relatively rapid, constant flow in these vessels (particularly the carotids which results in high vascular contrast, the lack of significant physiologic motion (e.g., respiration), and the availability of coils which are especially well suited to these applications. With the exception of venous studies, intracranial investigations have been primarily performed with 3D sequences because of the complex flow and the demands for high spatial resolution.1-6,10 The carotid arteries have been studied with both 2D and 3D sequences.2,4

Extracranial Applications: Carotid Bifurcation

MRA techniques will likely have their greatest clinical impact in the evaluation of carotid bifurcation atherosclerotic disease.14,15 Traditional MR imaging is particularly sensitive to the parenchymal sequelae of cerebral vascular disease, and many patients are now evaluated by MR for the extent and distribution of ischemic damage. Hence the interest in developing a technique that can be combined with the traditional MR brain examination to evaluate the severity of carotid bifurcation occlusive disease in the same sitting.14

A number of studies have been conducted which demonstrate the efficacy of 2D and 3D-TOF MRA techniques in the evaluation of the carotid bifurcation.2,4,15,16,17 The sequential 2D-MRA technique has the advantage of high vessel/soft tissue contrast from strong flow-related enhancement which is maintained even in the setting of relatively slow flow (e.g., severe, long segment stenosis). On the other hand, minor motion by the patient during the scan can cause a severe star-step misregistration artifact. Also, higher gradient strengths are necessary to define thin slices in sequential 2DFT
Initial studies have shown a high degree of correlation in the degree of stenosis when comparing 3D-TOF MRA images (using a single thick volume) with the accepted gold standard, intra-arterial digital subtraction angiography (IADSA). Estimation of the vessel caliber was not significantly impaired by local field inhomogeneities or the complex motion within and immediately distal to the stenoses. The more severe stenoses (greater than or equal to 70%) tended to be slightly overestimated as a result of these higher order motion terms, but this degree of error was felt to be acceptable for the purpose of a screening examination. Other clinical studies have suggested that an accurate evaluation of carotid occlusive disease may be possible noninvasively through a combination of 2D or 3D-TOF MRA and ultrasound examinations of the carotid arteries.

**Intracranial Applications**

TOF MRA has been applied in the head to the evaluation of patients with intracranial aneurysms, large vessel atherosclerotic disease, arteriovenous malformations, and dural sinus occlusions. Each of these entities has its own unique parenchymal sequelae which are investigated by the accompanying spin-echo examination. The MRA images enhance the specificity of the traditional brain study and provide additional information to the clinician and neuroradiologist to aid in making a decision regarding a subsequent invasive study or management.

**Aneurysms**

With an acute subarachnoid hemorrhage and a presumed intracranial aneurysm, patients are more appropriately studied by nonenhanced CT and conventional arteriography. The combination of an MRA and a conventional spin-echo study is better implemented in patients with a subacute onset of symptoms in whom an aneurysm might explain the clinical presentation. TOF MRA images with IADSA have yielded promising results. Ross et al detected aneurysms as small as 3-4 mm with sensitivities of 67% when evaluating the MRA images alone and 86% when evaluating the MRA images along with the original 3D slices and spin-echo images.

Nevertheless, TOF images are still somewhat limited by the nature of the pathology, the technique itself, and hardware limitations. Hypointense thrombus in the aneurysm lumen (e.g., acute or chronic thrombosis) may artificially reduce or obliterate the aneurysm’s lumen, but the same problem exists with catheter arteriography. Correlation with the spin-echo exam, the original 3D slices, or multiplanar reconstructions of these slices provides a more accurate assessment of the aneurysm lumen in this situation. Parenchymal and subarachnoid hemorrhage can also be misleading because the high intensity of subacute hemorrhage will also be picked up by the reconstruction program and may obscure the aneurysm. A large aneurysm or one that is compressing the lumen of the parent vessel may be poorly or
incompletely visualized because of impaired inflow of the fresh, unsaturated spins which provides the flow-related enhancement necessary to see the aneurysm lumen.\textsuperscript{9} Vasospasm may have the same effect. (Phase contrast techniques may not be subject to such problems.\textsuperscript{12,13}) Although less a problem with the 3D-TOF method, the parent vessel may be difficult to see if the spins moving within this segment demonstrate a large amount of higher order motion. Regardless, the 3D relation between the aneurysm and the parent vessel is
Arterial Occlusive Disease

Preliminary clinical studies have also demonstrated the ability of 3D-TOF MRA to identify occlusive disease of the larger intracranial vessels. Confirmation of a tandem lesion in the distal internal carotid artery or an isolated stenosis in the proximal middle cerebral artery can have a significant impact on the clinical decision-making process in a patient with atherosclerotic narrowing at the carotid bifurcation. This may lead to a more definitive catheter study, for example, in a patient who has had a prior ultrasound examination documenting mild to moderate carotid bifurcation disease. On the other hand, a negative study may avoid a conventional angiogram. This option would be particularly valuable in older patients with suspected occlusive disease of the posterior circulation where the risk of the procedure itself is quite high. MRA may also permit noninvasive imaging of acute middle cerebral artery embolic occlusion, which is potentially treatable with thrombolytic agents.

The studies conducted to date have demonstrated occlusion or stenosis of the distal internal carotid artery or the M1 segment of the middle cerebral artery. A group of infants with a ligated internal carotid artery and internal jugular vein (for extracorporeal membrane oxygenation) were studied to confirm adequate cross-filling and venous drainage for both cerebral hemispheres. These results provided significant long-term prognostic information about the children. Children with sickle cell disease were also studied to identify large vessel occlusive disease.

The combination of MRA and a spin-echo parenchymal study can directly visualize the vascular stenosis and the parenchymal consequences in the corresponding vascular territory at the same sitting. Without additional acquisition time the corresponding phase images can be examined to document the direction of flow in other large vessels that may be supplying collateral flow. Selective MRA studies have also been designed to confirm the contributions from other vascular territories. An appropriately positioned saturation pulse, for example, can eliminate the inflow from one internal carotid artery to determine the extent of collateral flow (from the circle of Willis) to the territory of a severely stenotic carotid siphon.

Little has been done to evaluate occlusive disease of the posterior circulation specifically. Since the vascular disorders of the posterior fossa, such as dissection and partial basilar artery thrombosis, tend to have relatively slow flow, an appropriately designed sequential 2D study would be the most successful TOF study. Although the vascular abnormality is frequently apparent on the spin-echo images, MRA can be helpful to confirm the pathology in those cases with confusing intraluminal signal. The TOF images themselves can be confusing with incomplete, subacute thrombosis of the basilar artery. Evaluation of the corresponding phase images can settle the issue.
Difficulties similar to those which arise in the evaluation of stenosis of the carotid bifurcation are also demonstrated in the examination of intracranial occlusive disease. Because of higher order motion terms in the blood flowing within and immediately distal to the stenoses, the resulting phase dispersion causes an overestimation of the degree of stenosis. An additional complicating factor in the head is the size of even the larger intracranial vessels. Hardware limitations (i.e., system gradient capability) in the commercially available whole-body imaging systems impose restrictions on the echo time and spatial resolution which affect the degree to which these problems can be addressed.

**Vascular Malformations**

TOF MRA images can provide useful information in the evaluation of parenchymal and dural arteriovenous (AV) fistulas. A venous angioma typically appears on conventional MR as a single large vessel extending from the ventricular margin to the cortical surface. The very slow flow and small size of the feeding vessels in cavernous angiomas and capillary telangiectasias prevent their visualization by any form of MRA. In any event the clinically significant cavernous angiomas are generally recognizable on the spin-echo examination by the blood products from prior hemorrhage.

Parenchymal AV fistulas are visible because of the cluster of flow voids representing the nidus, the associated ischemic steal, or the results of prior intervention (e.g., surgery, embolization). Preliminary clinical results have shown that MRA is useful in demonstrating the 3D relations between the vascular nidus and the primary afferent and efferent vessels. Dural fistulas are unique in that they are frequently undetectable with routine spin-echo images of the head. This is best evaluated on the late echo T2-weighted images, which are oriented perpendicular to the primary direction of flow for the sinus in question. With this arrangement the spins in the sinus are least apt to experience both the 90 and 180 pulses such that a flow void will be seen in the images if flow is present. For example, axial images would be most likely to demonstrate a flow void in the sigmoid sinus in a patient who was studied because of severe mastoiditis or a cholesteatoma which had caused bony destruction of the petrous ridge. Alternatively, coronal images would be the most appropriate orientation for patients with a parasagittal mass lesion compressing the adjacent superior sagittal sinus.

On occasion the spin-echo images demonstrate confusing intraluminal signal in the sinuses, particularly if the T2-weighted study is not optimally oriented for the sinus in question (e.g., atypical anatomy), the slices are relatively thick, the second echo is relatively short, the venous flow is quite slow, or the sinus contains acute thrombus (isointense on T1- and hypointense on T2-weighted images). In such cases TOF MRA studies of the dural sinuses can provide more definitive information with little additional examination time. The slow flow in the dural sinuses demands the use of a 2D-TOF study. Visualization of the dural sinuses would be impaired by saturation effects in a 3D-TOF study unless the slices are optimally oriented for the sinus in question (e.g., atypical anatomy), the slices are relatively thick, the second echo is relatively short, the venous flow is quite slow, or the sinus contains acute thrombus (isointense on T1- and hypointense on T2-weighted images). In such cases TOF MRA studies of the dural sinuses can provide more definitive information with little additional examination time. The slow flow in the dural sinuses demands the use of a 2D-TOF study. Visualization of the dural sinuses would be impaired by saturation effects in a 3D-TOF study unless the 3D study was performed after intravenous gadolinium administration.

Potentially, 2D-TOF studies can provide misleading information if the sinus contains subacute thrombus and this is not apparent on the spin-echo study. The high signal intensity of the extracellular methemoglobin can mimic flow-related enhancement and suggest patency. Reconstructing the phase images from the spin-echo study can eliminate this ambiguity without prolonging scan time. Sequences can be designed such that the images are sensitive to flow in the slice-select direction as slow as 0.5 cm/sec or as slow as 2.5 cm/sec in the frequency direction. It is also possible to quantitate the flow velocities in the sinuses through the use of paired gradient-recalled sequences or narrow in-plane saturation pulses (i.e., bolus tagging).

**Future Prospects**

Large, carefully controlled, prospective clinical trials must still be conducted to define more clearly the role
MRA will play in the evaluation of patients with clinically suspected cerebral vascular disease. At the moment TOF-MRA images cannot replace traditional arteriography of the carotid arteries and intracranial vasculature. The discrepancy between the modalities is particularly evident in the intracranial circulation where the spatial resolution demands are high. Irregularity of the vessel caliber is related, in part, to errors introduced by the maximum intensity projection post-processing algorithm used with present TOF angiography sequences. The most commonly used maximum intensity projection technique may be unable to identify accurately the vessels in the original data because of variations in the background signal intensity, inadequate flow-related enhancement, and/or volume averaging effects. These problems have stimulated the development of alternative more sophisticated post-processing algorithms and the use of various background suppression techniques for the MRA acquisitions.

Another important factor contributing to the irregularity of a vessel lumen and focal discontinuities in a vessel is the intravascular phase dispersion secondary to complex motion and local field inhomogeneities. Reducing the minimum field echo time limits the motion-induced dephasing and was shown to be possible on routine imaging systems through the use of truncated RF pulses and asymmetric data sampling. Other innovations in data post-processing and image reconstruction should complement these strategies and improve the clinical usefulness of the MR arteriograms. Further reductions in the field echo time and voxel dimensions have been achieved through the use of specialized head coils with self-contained gradients. These coils have higher peak gradient strengths and permit more rapid switching times than the standard imaging coils. Preliminary tests with prototype gradient RF head coils have shown the expected but nevertheless exciting results in phantoms and normal volunteers. Although these sequences have not yet been extensively tested in patients, it is expected that the MR arteriograms will display a significantly higher correlation with the traditional angiographic images than was demonstrated previously and the technique will therefore be of greater diagnostic value.

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