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Emerging Functional MR Angiographic Techniques

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With recent advances in hardware and software, MR angiography can now demonstrate significant stenoses in most anatomic territories with sensitivities and specificities in the range of 90%. Most technology-assessment studies compare the accuracy of MR angiography with that of conventional arteriography, because both allow assessment of luminal dimensions, such as the percentage of diameter stenosis or cross-sectional area stenosis. Knowledge of the functional significance of a visualized stenosis often is more important than the percentage of the area affected, however.

With conventional angiography, the standard procedure entails measurement of the trans-stenotic pressure gradient before angioplasty or stent placement. If a pressure gradient exists across a stenosis, dilating the lumen to eliminate or decrease the stenosis will result in greater blood flow to the end organ. In the absence of a trans-stenotic pressure gradient, however, revascularization techniques will not augment blood flow but still pose the risk of procedure-related complications. Thus, a newer goal of MR angiography techniques is to determine noninvasively the trans-stenotic pressure gradient for discriminating between hemodynamically significant and non-significant lesions.

Collateral vessels

In the presence of a hemodynamically significant stenosis, end-organ ischemia stimulates vasodilatation of adjacent small-caliber arteries, which serve as collateral pathways. These collaterals may ameliorate the effect of occlusive disease at rest but may not provide sufficient blood flow for normal functioning, because insufficient flow reserve remains available for recruitment. Collaterals are relatively easy to distinguish from named arteries because they increase in length as well as in diameter, resulting in tortuosity (Fig. 1). Profoundly tortuous arteries are referred to as “corkscrew” collaterals because of their characteristic appearance.

Direct visualization of collateral vessels by MR angiography has been reported to be a reliable indicator of hemodynamic significance in patients with prior repair of coarctation of the aorta [1]. Failure to visualize collaterals on MR angiography does not imply the absence of a trans-stenotic pressure gradient, because, depending on the achievable spatial resolution, these vessels may be too small to resolve adequately on MR angiography. One challenge in the depiction of collaterals with MR angiography is to improve spatial resolution while minimizing detrimental effects on the signal-to-noise ratio (S/N).

Flow measurement with phase-contrast sequences

Two-dimensional (2-D) measurement of the cine phase-contrast (PC) flow volume can be a reliable technique for noninvasively measuring velocity and flow in the blood vessels at the voxel level. The PC technique is based on the principle that magnetic field gradients introduce phase shifts in the MR signal arising from the flowing spins that are proportional to their velocity, enabling the construction of velocity maps from which the

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Fig. 1. A 65-year-old man with claudication. 3-D bolus-chase MR angiography shows occlusion of bilateral superficial femoral arteries and formation of collateral arteries.

volume of flow can be calculated simply by integrating the velocity measurements over the vessel cross-section [2]. 2-D cine PC performed after gadolinium-enhanced MR angiography has a higher S/N than noncontrast imaging [3]. Using cardiac gating and breath-holding, cine PC can demonstrate flow variations between systole and diastole with high spatial and temporal resolution [4].

PC flow measurement results are most accurate if the imaging plane is perpendicular to the long axis of the vessel of interest and flow encoding is set to interrogate through-plane flow. Motion-related errors caused by cardiac motion and arterial pulsatility can occur in the torso, especially in the thorax (eg, falsely elevated ascending aortic peak flow during systole). Pulse sequences have been designed to correct for this error by prescribing an imaging plane that is synchronized with cardiac motion.

At rest, patients have high-resistance triphasic flow in their peripheral arteries, consisting of peak forward flow during systole with transient reversal and then a plateau substantially below the peak forward flow. During exercise, muscle ischemia stimulates vasodilatation and decreased capillary resistance, which increases blood flow to the peripheral muscles and create a flatter waveform indicating low-resistance flow. When there is a hemodynamically significant stenosis or occlusion in a peripheral artery, the waveform will tend to be high resistance (triphasic wave form) proximal to the lesion and low resistance distal to the lesion (biphasic or monophasic waveform) (Fig. 2). A transition from high-resistance to low-resistance flow across a stenosis is evidence of hemodynamic significance. Cine PC can be exploited to measure the pulsatile, high-resistance triphasic blood flow in normal lower extremity arteries as well as the low-resistance flow that occurs distal to hemodynamically significant occlusive disease.

Flow-volume data obtained by integrating velocity–time curves over a cross-sectional arterial region of interest on PC images show high accuracy and excellent correlation with direct flow measurements in animal models and with indirect techniques such as clearance of para-aminohippurate and ^{133}Xenon washout measurements [5–7]. On PC flow curves, significant renal arterial stenosis results in delayed or absent early systolic peak with reduction in renal capillary resistance [8]. Renal flow can be indexed to the total volume of renal parenchyma: a renal flow index less than 1.5 mL/min/cm^3 predicts successful outcome of revascularization [9].

Combining cine PC data with MR angiography reduces interobserver variability on stenosis grading [8]. In the setting of a metallic renal artery stent, intraluminal flow may be obscured by susceptibility artifact, but flow measurement distal to the stent can assess in-stent stenosis [10]. Cine PC renal blood flow measurements obtained before and after pharmacologic intervention provide more physiologic data. For example, an angiotensin-converting enzyme (ACE) inhibitor markedly reduces flow to a kidney being supplied by a renal artery with a hemodynamically significant stenosis [11]. Different studies have showed controversial results in evaluating the significances of ACE inhibitor, however [12]. Further experiments are needed to clarify its usefulness and accuracy.

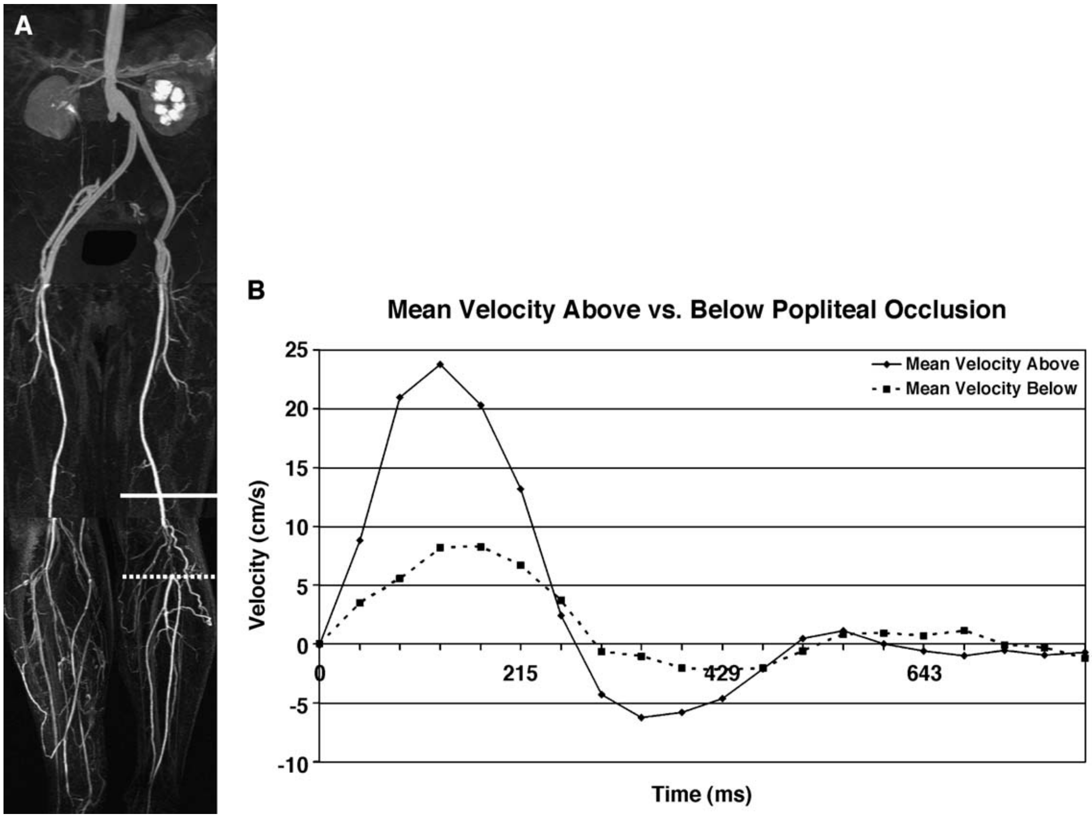

Fig. 2. A 56-year-old man with left calf pain at rest. (*A*) 3-D bolus-chase MR angiography shows left popliteal artery occlusion. (*B*) 2-D cine phase-contrast flow velocity measurements above and below popliteal occlusion show high-resistance, triphasic arterial flow proximal to the lesion and low-resistance flow distal to the lesion.

Ultrafast flow measurement

Ultrafast PC flow measurements are possible using echo planer imaging (EPI) and Fastcard PC (GE Medical Systems, Waukesha, Wisconsin). Multishot EPI PC imaging permits highly accurate flow measurement in pulsatile vessels during a breath-hold [13,14]. Particle-path visualization for time-resolved three-directional data sets in continuous slices covering the entire volume have been proposed to acquire time-resolved three-dimensional (3-D) velocity mapping of the flow in thoracic aorta [15].

Spin dephasing on three-dimensional phase contrast

On 3-D PC MR angiography, flow is encoded in all three axes. Flowing blood appears bright, with signal intensity directly related to flow velocity, and stationery tissues appear dark. With mild stenoses, laminar flow accelerates, creating a blooming effect that makes stenoses appear less severe. Through hemodynamically significant stenosis (>70% luminal narrowing, with a trans-stenotic pressure gradient), however, flow also accelerates but becomes disorganized and turbulent [16]. Flow jets created by pressure gradients also destroy MR phase coherence, causing loss of MR signal. This dephasing is especially prominent on 3-D PC MR angiography because of the relatively long echo times and proton motion during application of flow-encoding gradients [17].

Thus, with 3-D PC imaging, the underestimation of mild stenoses and overestimation of severe stenoses accentuates differences between unimportant mild stenoses and hemodynamically significant stenoses (Fig. 3). One in vitro study shows that the degree of this spin dephasing is directly correlated with the trans-stenotic pressure gradient [16]. The severity of stenosis on digital subtraction angiography, considered the reference standard, shows better correlation with severity

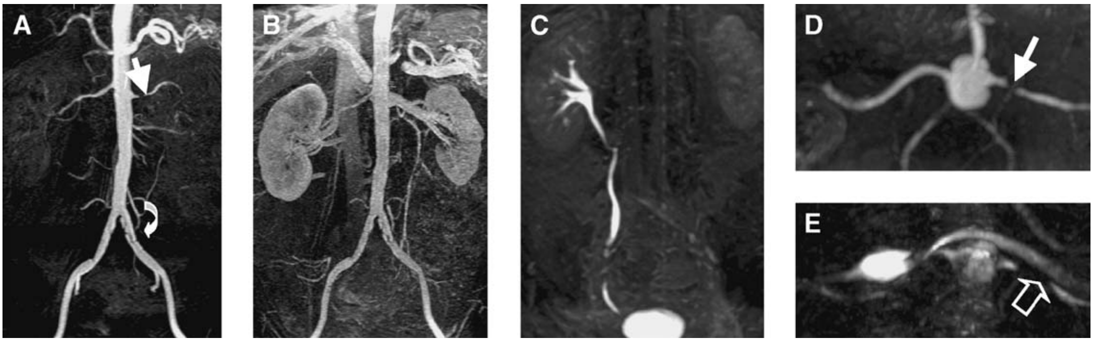

Fig. 3. Severe left renal artery stenosis (*arrow*) is better shown on arterial phase of 3-D gadolinium-enhanced MR angiography (*A*, *D*) with left kidney shrinkage, diminished cortical medullary differentiation in the venous phase (*B*), and asymmetrical gadolinium excretion on equilibrium phase (*C*). On 3-D PC (*E*), there is dephasing (*open arrow*) at the site of stenosis, indicating it is hemodynamically significant. Also noted is left common iliac artery dissection (*curved arrow*), which is useful for planning the approach to percutaneous angioplasty.

of spin dephasing on 3-D PC than with the length of dephasing [18].

3-D PC imaging is widely used in renal and carotid MR angiography [19–21]. Combining 3-D gadolinium MR angiography information with 3-D PC MR angiography offers more accurate grading of arterial stenosis by improving the specificity of MR angiography, because the number of false-positive interpretations of significant stenosis decreases with gadolinium-enhanced 3-D MR angiography.

Time-resolved MR angiography

Many techniques have been developed for obtaining functional information by temporally resolving the flow of contrast from arteries to veins. These methods include 2-D projection MR angiography, 3-D time-resolved imaging of contrast kinetics, fast 3-D spoiled gradient echo, vastly undersampled isotropic projection reconstruction (VIPR), periodically rotated overlapping parallel lines with enhanced reconstruction, four-dimensional spiral MR angiography with sliding window reconstruction, and parallel imaging [22–30]. These techniques can now reconstruct 3-D data with temporal resolution faster than one frame per second and 2-D data at several frames per second. Time-resolved MR angiography is especially useful in vascular territories where the path of blood flow is uncertain and cannot be determined from static images of the vasculature (eg, in cases of congenital heart disease or peripheral arterial occlusive disease) or in cases of overlapping vessels (eg, in the circle of Willis and portal venous system) (Fig. 4) [31]. For example, a time-resolved 3-D imaging technique for an extended field-of-view performed during continuous table motion to obtain both functional (hemodynamic) and morphologic information can be performed by capturing the leading edge of the bolus as it travels down peripheral arteries [32,33].

Time-resolved MR angiography is also possible without contrast by taking advantage of ECG gating to acquire multiple images over the cardiac cycle to show how flow varies in systole and

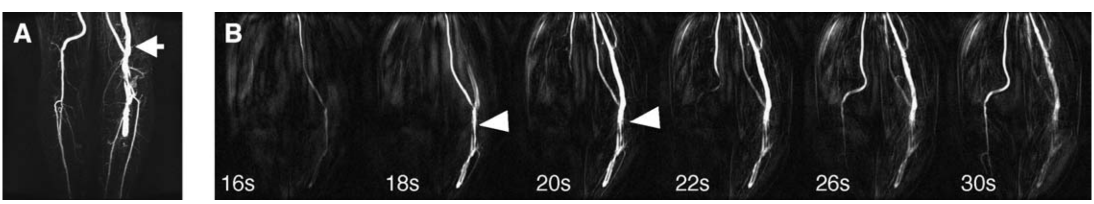

Fig. 4. A 59-year-old man with congestive heart failure after Fogarty balloon thrombectomy of a left femoral-popliteal bypass graft. (*A*) 3-D gadolinium-enhanced MR angiography is confusing because of venous contamination by left popliteal vein (*arrow*). (*B*) Time-resolved 2-D projection MR angiography, at 2 s/frame, shows an arterio-venous fistula (*arrowhead*) causing increased flow to the left leg. After the fistula was ligated, the congestive heart failure resolved.

diastole. A technique known as 'global coherent free precession' excites spins in the plane perpendicular to the artery and then acquires a projection image in the plane of the artery to illustrate flow pulsation over the cardiac cycle [34].

Functional evaluation of selected vascular pathology

Aortic coarctation and dissection

The morphologic severity of coarctation of the aorta may be difficult to evaluate, especially in the postrepair state. The physiologic severity of aorta coarctation can be assessed with cine PC MR imaging. Cine PC imaging is used to estimate flow volume at two locations in the aorta: one just distal to the coarctation site and the other at the level of the diaphragm. Normally, aortic flow decreases along its length. In cases of coarctation of the aorta, however, the more distal aortic flow at the level of the diaphragm is greater than the more proximal flow in the area just distal to the coarctation. This occurrence results from collateral filling of the descending aorta by the reversal of flow within the intercostal arteries, which represent a collateral pathway for arterial flow. The flow difference between the proximal and distal descending aorta can be quantified and represents the flow contributions of the collateral vessel. The presence of collateral filling accurately indicates the presence of a hemodynamically significant coarctation. This type of flow measurement can be helpful in cases where dilated collaterals may not be adequately demonstrated because of limited spatial resolution using spin echo imaging or 3-D contrast-enhanced MR angiography [35,36]. Determination of the peak velocity and flow volume also can be used to estimate the pressure gradient within the coarctation. A pressure gradient of more than 20 mm Hg as measured during cardiac catheterization is considered an indication for intervention [37].

In aortic dissection, as the overall aortic diameter increases, the ratio of the cross-sectional area of the false lumen to the true lumen increases, and the peak average velocity in the true lumen during systole decreases on cine PC imaging, a feature that can help determine prognosis and operability [38].

Renal artery stenosis

Loss of corticomedullary differentiation, poststenotic renal artery dilatation, asymmetry of kidney length, parenchymal thinning, and pattern of contrast excretion may help to diagnose renal artery stenosis [39]. Flow measurement with 2-D cine PC or 3-D PC imaging to detect spin dephasing is now a routine component of renal artery MR angiography in some institutions. Measurements of renal artery flow can be combined with additional pulse sequences (such as T1 measurements of flowing blood) to measure the gadolinium concentration in the renal artery (input) and renal vein (output), permitting exact calculation of the gadolinium clearance rate for each kidney and assessment of renal function [40]. Other functional techniques, including diffusion-weighted imaging, perfusion imaging, and the blood oxygen level–dependent (BOLD) effect, can be used to evaluate renal function and further determine the severity and hemodynamic significance of renal artery or mesenteric artery stenosis [41–44].

When evaluating renal arteries, the contrast arrival time in the renal cortex is similar for normal and ischemic kidneys, whereas the cortical transit time is much longer in kidneys with renal vascular disease and decreased function than in normal kidneys (40 seconds versus 15 seconds, respectively) [45]. Thus, in ischemic kidneys, the medullary enhancement rate is delayed and decreased. Low-dose gadolinium (2 mL) has been used to evaluate contrast enhancement of the renal cortex and medulla during MR renography [46].

Peripheral arterial occlusive disease

Often a borderline stenosis is not flow limiting at higher flow rates (eg, during exercise). During conventional angiography, a vasodilator such as priscoline can be used to increase flow to unmask a flow-limiting lesion. With MR angiography, flow to an extremity can be increased by inflating a blood pressure cuff to suprasystolic pressure (~200 mm Hg) for 3 minutes to induce transient ischemia. Upon cuff deflation, the time needed for the BOLD effect in calf muscles to return to normal can be measured. The BOLD effect is delayed in the presence of significant occlusive disease [47].

Phantom studies demonstrate that highly pulsatile flow, as in the limbs, needs ECG synchronization for flow measurement, increasing the duration of the PC scan. Fortunately, with cine PC, the blood flow volume can be examined in several vessels simultaneously in the same plane with a large field of view. A recent study in 50 healthy volunteers showed the mean blood flow was 353 mL/min in the femoral artery and 61.9 mL/min in the popliteal artery [48]. Femoral blood flow was related to age and gender, whereas popliteal blood flow was more related to calf muscle volume, after adjusting for age and gender. Another study showed that blood flow volume at rest was similar in volunteers and in patients. After exercise, however, patients with abnormal ankle–brachial indexes had diminished lower extremity arterial flow augmentation (a 2.6-fold increase in flow) compared with normal volunteers (a 4.8-fold increase in flow), indicating MR measurement of blood flow volume may aid in evaluating peripheral vascular disease [49].

In patients with occlusive peripheral arterial disease, the blood flow in the leg with occlusion or severe stenosis can be slower or faster than in the contralateral normal leg, because of the smaller cross-sectional diameter of collateral vessels or distal ischemia, which stimulates vasodilatation distal to occlusions [50]. Thus, time-resolved MR angiography must be interpreted with caution.

Pulmonary embolism

Pulmonary arteriography is not the preferred modality to diagnose pulmonary embolism because of its risk profile. In about 4% of patients with pulmonary embolism, acute pulmonary hypertension develops, causing diminished pulmonary flow and right ventricular dysfunction. MR angiography can demonstrate pulmonary arterial filling defects consistent with emboli with high accuracy [51,52]. Cross-sectional cine cardiac MR allows precise calculation of stroke volume, cardiac output, and ejection fraction to evaluate right heart function. Cine PC measurements of flow through the aorta and central pulmonary arteries enable calculation of the magnitude of right-to-left shunting in the setting of pulmonary hypertension [53,54]. In addition to demonstrating pulmonary emboli and their potential cardiac effects, MR imaging also can demonstrate deep vein thrombosis [55,56].

Portal venous system abnormality

Portal vein thrombosis is an important indication for MR angiography of the portal venous system. Cavernous transformation indicating chronic portal vein occlusion can be demonstrated easily by MR portography (Fig. 5). MR portography with PC flow measurement can provide a functional evaluation of portal hypertension and surgical portosystemic shunts. Contrast-enhanced MR angiography is promising as a noninvasive means to determine the resectability of pancreaticobiliary tumors involving the portal venous system. MR PC flow measurement is a simple and rapid technique for the assessment of portal venous patency, flow direction, and flow velocity. Pharmacologic stimulation of portal flow with nicardipine hydrochloride is useful for the evaluation of liver function [57]. Using MR techniques to measure flow in the azygous and hemiazygous veins may estimate the amount of portal flow being shunted from the liver in patients with cirrhosis [58–60].

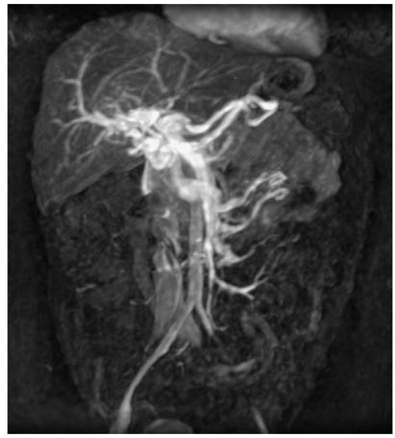

Fig. 5. A 21-year-old woman with lupus and abdominal pain. 3-D MR portography shows cavernous transformation of the portal vein.

Summary

As the accuracy of MR angiography approaches that of conventional digital subtraction angiography, further refinements of vascular analysis will focus on providing functional information about the normal and pathologic vasculature. In particular, PC flow measurement, time-resolved contrast-enhanced MR angiography, and detection of turbulent flow jets help to establish the functional significance of stenoses.

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