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Magnetic Resonance Imaging in the Management of Cerebrovascular Disease to Prevent Stroke

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Synopsis

Cerebrovascular disease is a heterogeneous disease that may require objective criteria for developing optimal recurrent stroke prevention strategies. Magnetic resonance (MR) imaging and angiography together with MR perfusion and functional MR imaging provide sufficient parameters to tailor medical and surgical interventions for each patient and to monitor disease compensation or progression. These MR imaging procedures are demonstrated by clinical cases of advanced cerebrovascular pathology in which treatment varied from medical management to surgical intervention.

Keywords

stroke prevention; brain; MR imaging; MR perfusion; BOLD fMRI; phase contrast MR angiography

Introduction

The capability of magnetic resonance (MR) imaging to make the diagnosis of acute stroke is not in dispute although its role in management of acute stroke is still limited. Ready access to computed tomography (CT) in emergency departments with 24/7 coverage by technologists has marginalized MR imaging. The primary management decision as to whether to use thrombolytic therapy for stroke is made based on randomized clinical trials that demonstrate improved outcome when used within 3 hours from time of symptom onset and the absence of hemorrhage on CT images. Thus, early clinical decisions do not require the use of MR imaging despite the limited use of thrombolysis, currently the only FDA approved pharmacological treatment. The historical precedent of CT in emergency departments hinders changes in practice and leaves MR imaging in a secondary role for stroke management in most medical facilities. Early adopters are moving towards customized patient treatment with decision-making directed by diffusion and perfusion MR imaging.

In patients with known cerebrovascular disease being evaluated for stroke etiology and prevention, MR imaging and MR angiography have a central role in medical decision-making. This application of MR imaging, away from the access and time constraints of acute treatment, will be discussed based on the author's experience. The use of quantitative perfusion and functional measurements will be emphasized through the use of representative case examples.

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Acute and Early Subacute Stroke

The occlusion of an arterial vessel supplying oxygenated blood to a region of brain tissue that lacks sufficient collateral circulation to maintain hemodynamic reserve, leads to a cascade of physiological, metabolic and functional changes that have been described elsewhere [1–5]. From the perspective of MR imaging, the immediate change in an acute non-hemorrhagic stroke can be visualized within a few minutes on diffusion-weighted images [6–15]. Although the mechanism of signal change remains controversial, the restricted diffusion of water in the stroke results in increased signal intensity on diffusion sensitized images [6,15]. One working hypothesis is that this signal increase is due to the rapid development of cytotoxic edema following compromise of aerobic metabolism due to cessation of blood flow with its supply of oxygen. This phenomenon can be characterized by the calculation of the apparent diffusion coefficient (ADC) map. Other MR images such as T2- and T1- weighted images and CT images may remain normal until hours later when vasogenic edema develops. If hemorrhage is present, signal loss will be readily apparent on magnetic susceptibility-sensitive gradient-echo images and less so on T1- and T2-weighted spin-echo images except through the mass effect from a hematoma and edema. Blood products from hemorrhage can persist in the brain parenchyma for decades and undergo an evolution of signal changes over days to months that reflect the changing biochemistry of iron metabolism [16–18]. CT readily detects most acute hemorrhages although MR is much more sensitive for small acute petechial hemorrhage and much more sensitive for detecting the iron storage products of hemosiderin and ferritin from old hemorrhages [19]. Once T2-weighted images show increased signal consistent with edema after a few hours, the diffusion weighted imaging becomes ambiguous. The increased signal on diffusion-weighted images can be due to the increased water content from vasogenic edema (so called “T2 shine through”) rather than just restricted diffusion from cytotoxic edema. The ADC map derived from the diffusion-weighted imaging readily resolves this dilemma. Cytotoxic edema shows reduced ADC whereas vasogenic edema shows increased ADC values. This ADC map is calculated in a few seconds on clinical MR scanners after acquiring the diffusion-weighted imaging at two different levels of diffusion weighting and is always readily available. The ADC map in acute and early subacute stroke shows low apparent diffusion coefficients, readily identified by comparing the abnormal side to the contralateral side. The differences can be 50% or more in most strokes but the region of stroke can also be heterogeneous. The ADC values remain low for a few days, begin to pseudo-normalize by 5–10 days and then become permanently supernormal as encephalomalacic changes take place [20]. During this early subacute time, the increasing edema initially produces mass effect that then resolves in the late subacute phase.

A patient with a non-hemorrhagic stroke by CT criteria and who is still within 3 hours of symptom onset, may be eligible for thrombolysis therapy [21]. Such lesions typically show increased T2 signal changes, low ADC values and no signal loss on gradient-echo images on MR imaging. The rationale for not routinely using MR imaging is to avoid delaying treatment when CT is usually more readily available.

Only about 5% of eligible patients receive thrombolytic treatment in the United States because of the potential that a devastating hemorrhage, a known risk of thrombolytic therapy, may occur within the lesion and further compromise the patient. [21]. Attempts have been made to stratify risks by examining perfusion and diffusion MR imaging [22]. This concept is that large diffusion-perfusion mismatches identify patients who may benefit from treatment [23]. The mismatch has been conceptualized as being the ischemic penumbra - the region at risk for stroke progression. The mismatch paradigm has been used in ongoing research efforts to extend the treatment window for IV thrombolysis beyond 3 hours.

An alternative approach has been proposed in which sodium imaging is used to measure tissue sodium concentration (TSC) as a measure of tissue viability. Sodium ion homeostasis may directly reflect if tissue can be salvaged by appropriate treatment and indicate risk for hemorrhage. A quantitative TSC threshold of tissue viability would be an objective means of customizing treatment decisions in an individual patient [20,24,25].

Management of Stroke Risk in Patients with Known Cerebrovascular Disease

Every patient surviving a stroke or presenting with symptoms that may be explained by cerebral ischemia should undergo a thorough workup to determine the extent of both intra-cranial and extra-cranial etiologies that may underlie those signs and symptoms. This workup, away from the urgency of the acute stroke setting, should include quantitative evaluation of the integrity of the large vessels of the neck and head and estimation of the cerebral hemodynamic reserve. The lack of hemodynamic reserve puts the patient at high risk for subsequent stroke [26,27].

Different centers may elect to obtain such information in a variety of ways. As these patients may require on-going monitoring with subsequent follow-up imaging studies, quantitative parameters are valuable for temporal comparisons to measure disease progression. Methods using ionizing radiation should be minimized to avoid an accumulating radiation burden. For this reason, the roles of xenon CT, positron emission tomography (PET) and single photon emission tomography (SPECT) with vasodilatory challenges such as with acetazolamide will not be discussed in this report. The more invasive strategies such as conventional catheter angiography should be used sparingly and will also not be discussed further. MR imaging, MR angiography, MR perfusion and diffusion measurements are all readily available on clinical MR scanners, quantitative and can be repeated over time without concern for an increasing ionizing radiation burden, and noninvasive. These currently commercially available techniques will now be described. Newer research protocols will only be mentioned briefly although these may soon enter clinical practice.

MR Techniques for Evaluation of Cerebrovascular Physiology in the Setting of Stroke Prevention

1. MR Perfusion

Dynamic susceptibility contrast (DSC) perfusion imaging exploits the magnetic susceptibility effects produced by the blood-brain-barrier between the vascular space of the capillary bed and the surrounding brain parenchyma when a bolus of intravenously administered paramagnetic gadolinium-based contrast agent passes through the capillary bed [28–30]. This method requires a rapid imaging technique that is sensitive to these magnetic susceptibility effects. Gradient-echo, echo-planar imaging at high temporal resolution (Time to repeat, TR = 1 to 1.5s) is usually used. Using an intravenous bolus injection (5cc/s, antecubital vein, 20G Angiocath, standard full dose based on body weight, i.e., 0.1mmol/kg at 3.0 Tesla), the first passage of contrast through the brain is monitored as a washout curve in which the signal initially decreases and then increases as the contrast passes through the capillary bed (Figure 1). This washout curve can be analyzed in a number of ways. As the arterial input function (AIF) is not readily available and, in the setting of vascular disease, will vary across the different vascular territories of the brain, the simplest and fastest approach is the gamma variate fit to the experimental curve, introduced almost three decades ago [31], which allows the parameters of time to arrival (TTA), tissue transit time (TTT) and relative cerebral blood volume (rCBV) to be characterized. A relative cerebral blood flow (rCBF) can be estimated from the other parameters ($rCBF = rCBV/TTT$). These parameters are reproducible and can be used for studying disease progression over time. Details of this and similar methods are described elsewhere [28–31]. Although other methods of deconvolution of the AIF have theoretical value,

these methods often fail to recognize that it is unique for each voxel and can vary widely across a brain with regional cerebrovascular pathology. No generally acceptable method for finding an AIF on a voxel-by-voxel basis currently exists and best estimates are computationally intensive without benefit over the gamma variate approach [31].

This perfusion method can also be enhanced using a vasodilatory challenge such as acetazolamide (1g, IV injected slowly and a delay of 10 minutes to allow vasodilation) to measure hemodynamic reserve. Acetazolamide is a carbonic anhydrase inhibitor that limits clearance of carbon dioxide (CO₂) from the brain by slowing its conversion to bicarbonate ions. This accumulated CO₂ causes cerebral vasodilation. This technique, requiring two perfusion studies, is demonstrated in the case examples described below. Other approaches to measuring hemodynamic reserve using a CO₂ rebreathing technique may soon become available for clinical use [32].

Other perfusion methods are also available. Arterial spin labeling methods avoid the need for intravenous contrast but are currently more time consuming and not yet commercially available on all MR scanners [33].

2. Functional MR Imaging

Functional MR imaging uses blood oxygenation level dependent (BOLD) contrast to localize brain function [34]. When a region of the brain increases its activity in response to a stimulus, there is a focal increase in blood flow and blood volume. The magnetic susceptibility of the blood in the capillary bed becomes more like the surrounding diamagnetic brain parenchyma as the increased blood flow displaces paramagnetic deoxyhemoglobin for diamagnetic oxyhemoglobin. This loss of the magnetic susceptibility difference between the capillaries and tissue eliminates one of the transverse relaxation mechanisms that cause loss of MR signal intensity. Thus, a small increase in MR signal intensity occurs that can be detected on magnetic susceptibility-weighted (T2*) images. This signal increase is small (1–5% at 3 Tesla) but can be detected statistically by comparing the average signal intensity of the control condition (without stimulus) with that of the active condition (with stimulus) after signal averaging of many images. Although this approach is normally used to map cortex for presurgical planning, the method can also be used to detect hemodynamic reserve. As the hemodynamic reserve decreases, the brain becomes more vasodilated. BOLD contrast is reduced and eventually undetectable when no further vasodilation can occur. The stimulus paradigm is designed to efficiently interrogate all vascular territories. Motor, visual and auditory stimuli are combined to allow assessment in the anterior (primary motor, somatosensory, auditory) and posterior (visual, cerebellar motor) circulation in a single short paradigm.

The paradigm consists of a two-condition, block design with 4.5 cycles with each block of 30 seconds duration. The control condition is a silent, static visual fixation on a central white cross (2° visual angle) on a black background, presented to the patient on a rear projection screen inside the magnet. The stimulus condition consists of audiovisual commands to open and close both hands at a fixed frequency (1Hz). The words OPEN and CLOSE are presented visually and centrally with peripheral bilateral alternating black and white checkerboards on the same rear projection screen. The verbal commands are also simultaneously presented stereophonically through earphones. The activation map for this paradigm for a healthy adult without cerebrovascular disease is shown in Figure 2.

3. Quantitative MRA

MR angiography can be performed with both time of flight (TOF) and phase-contrast (PC) techniques. Whereas the TOF method defines vascular anatomy at high resolution in 3D or 2D modes in acceptable acquisition times, quantitative flow rates are not determined. The PC

method is quantitative and able to determine blood flow (from flow velocity and vessel diameter) through specified large vessels but is time consuming. As these approaches were evolving in the preceding decades, the TOF technique became more popular for anatomical disease screening. However, the quantitative PC technique with improved analysis software is again becoming recognized as being potentially very useful for following disease progression. The complete description of this method goes beyond the scope of this text and can be found elsewhere [35]. This technique provides large vessel conductance flow measurements for specified vessels as shown in Figure 3. Such flow measurements can be obtained before and after pharmacological challenge with acetazolamide to assess hemodynamic reserve. Additionally, large vessel flow values can be used to determine the presence, quantity, and pattern of collateral flow and tissue level flows can be obtained directly by MR perfusion. The use of such measurements is illustrated by the clinical cases described below.

Clinical Cases

Case 1

A young right-handed woman presented with variable complaints of right face numbness, left arm weakness, short term memory loss and migraine headaches. Her workup included a conventional catheter angiogram that showed an occluded supraclinoid portion of her left internal carotid artery and significant stenosis of the distal right internal carotid artery. Numerous small collateral vessels at the Circle of Willis were typical of moya moya disease. Figure 4 illustrates the anatomy, MRA and perfusion studies for this case. The anatomic images show diffuse cortical atrophy for age with multiple small foci of T2 hyperintense, non-enhancing, non-hemorrhagic, signal abnormalities in the white matter of both cerebral hemispheres consistent with chronic small vessel distribution ischemia. The MR angiogram shows diminished flow enhancement in the left internal carotid artery and left middle cerebral artery compared to the right side. The perfusion studies show essentially normal TTT, TTA and rCBV values without left-right or anterior-posterior asymmetries. The TTA values in the white matter appear to be slightly longer than normal, especially on the left side. The clinical question for the management of this symptomatic patient is whether the complaints and the anatomic changes resulted from emboli or reduced flow with concomitant loss of hemodynamic reserve. The perfusion study was performed before and after pharmacological vasodilation with intravenous acetazolamide and is shown in Figure 5. Vasodilation produces no left-right asymmetries with minimal change in TTA values and slightly reduced TTT values. Similarly, no gradient is present between the anterior and posterior circulation. With bilateral disease such as moya moya, anterior-posterior circulation comparisons become important although no gradients are apparent in this case. As there is no redistribution and the perfusion values are in the normal range, collateral circulation through the multiple vessels at the Circle of Willis and through the leptomeningeal collateral circulation is sufficient to maintain hemodynamic reserve. This is further supported by the fMRI activation map in Figure 6. Activation is present in all vascular territories, indicating that there is sufficient hemodynamic reserve to support BOLD contrast. However, close follow-up is required as moya moya disease is often progressive. This patient was treated with antithrombotic medication and instructed to maintain hydration.

Case 2

A middle aged right-handed former smoker had a previous stroke with left hand weakness and slurred speech that recovered to near baseline after 2 months. Initial workup at an outside hospital suggested high-grade stenosis of the right internal carotid artery. Subsequent workup was done several months later after referral to determine if there was adequate collateral circulation or reduced hemodynamic reserve. MR imaging identified chronic non-hemorrhagic small subcortical strokes in the right frontal lobe (Figure 7) and right basal ganglia (not shown).

The MR angiogram showed the absence of flow enhancement in the right internal carotid artery and the bilateral anterior and right middle cerebral arteries (Figures 7, 8). The diffusion weighted imaging showed no evidence of restricted diffusion to suggest acute or early subacute ischemia (Figure 7). This pattern of white matter involvement suggested limited hemodynamic reserve that affects white matter prior to gray matter [36]. The perfusion study was performed before and after vasodilation with intravenous acetazolamide and the perfusion maps are shown in Figure 9. Prior to vasodilation, the rCBV is relatively symmetric, the TTT map is slightly asymmetric (1–2s difference from right to left) and prolonged in the posterior aspect of the right middle cerebral artery territory while the TTA is very asymmetric (2–3s) being delayed on the right, more so in the white matter than the gray matter. These asymmetries all increase after vasodilation, as expected in the setting of limited hemodynamic reserve. The explanation for this effect is that once a territory is fully vasodilated, any further decrease in vascular resistance in other regions of the brain causes a selective redistribution of increased blood flow towards the regions of lower resistance. This finding is further supported by functional MR imaging using BOLD contrast in which increased neuronal activity causes a localized increase in blood flow and blood volume [34]. The simple 4.5-minute audiovisual block-design paradigm from Figure 2 has been used to give the activation map in Figure 10. Activation has been lost from the right anterior circulation.

Such patients are at high risk for subsequent stroke. This patient requires aggressive medical management to limit emboli from the slow flow (“string sign”) in the right internal carotid artery. Vascular augmentation with angioplasty and stenting or a superficial temporal artery-middle cerebral artery bypass could be considered if the patient’s symptoms progress despite aggressive medical management.

Case 3

A young right-handed woman presented with bifrontal non-hemorrhagic early subacute infarctions involving the anterior cerebral arteries (Figure 11). The MR angiogram (Figure 12) confirmed the presence of moya moya disease with the internal carotid arteries ending at the posterior communicating arteries that contribute to her expanded posterior circulation. Although present, the leptomeningeal collateral circulation from the posterior cerebral arteries had not been sufficient to reach the anterior cerebral artery territories leading to stroke. A perfusion study was performed before and after vasodilation with intravenously administered acetazolamide (Figure 13). Antero-posterior gradients in TTA and TTT are demonstrated. TTA becomes longer from the posterior to the anterior circulation indicative of the leptomeningeal collateral circulation. Vasodilation increases these gradients, indicating compromised hemodynamic reserve. This was confirmed with the functional activation map (Figure 14) that fails to show detectable BOLD contrast in the anterior and middle cerebral artery territories (motor, somatosensory, auditory areas) but activation is present in the posterior circulation for the cerebrum (visual cortex) and cerebellum (motor). Quantitative flow measurements also confirm low flow and compromised hemodynamic reserve in the anterior circulation (e.g., right and left MCA flow: pre- acetazolamide flows = 42 and 63 ml/minute, post- acetazolamide flows = 59 and 62 ml/minute; compared to basilar artery flows: pre- acetazolamide flows = 189 ml/minute, post- acetazolamide flows = 244 ml/minute).

The recent stroke and the imaging demonstrating compromised hemodynamic reserve place this patient at high risk for further stroke. Cerebrovascular augmentation via bilateral superficial temporal artery-middle cerebral artery bypasses and synangiostomies were performed. The follow-up studies were performed at 6 weeks and 6 months after the surgery.

The MR imaging and MR angiogram at the 6-week follow-up (Figure 15) demonstrate bilateral craniectomies and increased flow enhancement through the right superficial temporal artery. Flow through the left side does not appear to be augmented as much as the right side but this

may be from the more severe surgical artifacts. All of the images show the magnetic susceptibility effects around the bilateral craniectomies that compromise delineation of the anastomoses of the bypasses. The perfusion studies (Figure 16) also are affected immediately adjacent to the surgical bed but the previous perfusion gradients have normalized even following vasodilation. The activation studies (Figure 17) show restored BOLD contrast in the previously compromised areas but with a left-right asymmetry that suggest that the left cerebral hemisphere has less reserve than the right side.

The MR imaging and MR angiogram at the 6-month follow-up showed no significant changes (not shown). The perfusion study (Figure 18) showed minor variability in the perfusion parameters in the gray matter but the white matter showed perfusion asymmetries that worsened with vasodilation. This is consistent with the reduced hemodynamic reserve of the white matter compared to the gray matter and may be an early sign of re-compromise. The activation study (Figure 19) shows further improved BOLD contrast in the superior areas of the anterior circulation but reduction in activation in the distal more inferior middle cerebral artery territories covering the auditory cortex. These patterns of change may reflect the ongoing readjustment of blood flow between white and gray matter as well as through the bypasses and the previously well-established leptomeningeal collateral circulation. It is clear that these tissue level changes are not reflected in the qualitative flow patterns of the large vessels in the MR angiogram.

Case 4

A young right-handed woman was evaluated for bilateral stenoses of the supraclinoid portions of the internal carotid arteries consistent with moya moya disease. The anatomic images (Figure 20, left column) show bilateral ischemic changes in the white matter, worse in the left cerebral hemisphere. The MR angiogram (Figure 20, middle column) shows the bilateral internal carotid artery stenoses with expansion of the posterior circulation indicating leptomeningeal collateral flow. The MR perfusion study (Figure 20, right column) demonstrates worsening gradients in TTT values between the anterior and posterior circulation, especially in the white matter, after vasodilation indicating compromise of the hemodynamic reserve in the anterior circulation, as expected from the anatomic changes. These findings are confirmed with the activation study (Figure 21). No motor and somatosensory activation is detected in the superior portions of the cerebral hemispheres, markedly reduced auditory activation remains in the distal middle cerebral artery territories of the superior temporal gyri and normal visual activation and cerebellar motor activation persists in the occipital and cerebellar regions supplied by the posterior circulation.

This patient underwent angioplasty and stenting of the right-sided stenosis where the remaining flow was higher and which was more anatomically amenable to increase flow into the anterior circulation although the long-term outcome of this procedure remains to be determined. The post stent perfusion and activation results are shown in Figures 22 and 23, respectively. The hemodynamic reserve was improved on the right side as indicated by the improved perfusion TTT and TTA parameters to match the posterior circulation (Figure 22) and restoration of the BOLD responses (Figure 23). The left side remains compromised in the distal middle cerebral artery territory by both asymmetric perfusion TTT and TTA values and loss of auditory activation compared to the right side. The quantitative flow measurements after stenting confirm that hemodynamic reserve was improved to the right cerebral hemisphere (e.g., right MCA flow: pre- acetazolamide = 116ml/minute, post acetazolamide = 171ml/minute) but still compromised on the left side (e.g., left MCA flow: pre- acetazolamide = 93ml/minute, post acetazolamide = 70ml/minute). Consideration was subsequently given to a left-sided flow augmentation procedure.

Summary

These 4 cases are representative of many hundreds of cases of cerebrovascular disease examined over the last 7 years in our center in which management decisions have been guided by these MR imaging procedures. Symptoms in the presence of hemodynamic reserve suggest a need for aggressive medical treatment such as risk factor control and antithrombotic medication. The symptomatic patient with loss of hemodynamic reserve who has recurrent symptoms despite medical management may be the optimal candidate for flow augmentation procedures such as angioplasty with or without stenting and bypass surgery. The role of MR imaging for initial evaluation and for following disease progression in these patients allows tailored care for each patient based on the unique cerebrovascular pathophysiology of their disease. The long-term outcome of these medical and surgical interventions guided by MR imaging remains to be established. The cost of such imaging procedures for guiding clinical decisions towards appropriate management strategies is justified only if strokes are successfully prevented. These outcome measures are difficult to obtain without controlled clinical trials but warrant further investigation.

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Figure 1.

Representative voxel-based time course of brain MR signal intensity for a bolus of gadolinium-based MR contrast administered intravenously at the antecubital vein (5cc/s, 20 gauge Angiocath, 0.1mmol/kg). The initial decrease in the signal in the first 3 points is due to progressive T1 relaxation spin saturation effects followed by the baseline (3 – 12s) and then the arrival of the bolus at the capillary bed (TTA) when the signal intensity undergoes a rapid decrease and then recovers as the bolus washes out (TTT) of the capillary bed. Recirculation of contrast from the rest of the body prevents the signal intensity from returning completely to baseline and produces a second dip in the washout curve.

Figure 2.

Representative slices from an activation map superimposed over high-resolution T1-weighted (upper row, dark CSF) and T2-weighted (lower row, bright CSF) anatomical images for a subject performing the audiovisual motor paradigm showing bilateral primary motor and somatosensory activation in superior middle cerebral artery territory (lateral, left column) and supplementary motor activation in anterior cerebral artery territory (medial, left column), bilateral auditory activation in distal inferior middle cerebral artery territory (middle column) and bilateral visual activation in posterior cerebral artery territory (posteriomedial, right column). These activations interrogate each of the cerebral artery vascular territories.

Figure 3.

Schematic summary (NOVA analysis, Vasol, Inc., Chicago, IL) of the quantitative phase contrast MR angiographic measurements of blood flow for the large intracranial vessels for a patient with right middle cerebral artery stenosis. Flow through the right middle cerebral artery is only 76 ml/minute compared to that of the left middle cerebral artery flow of 202 ml/minute. Collateral pial-pial circulation from the right posterior cerebral artery explains its increased flow of 243 ml/minute compared to that of 99 ml/minute in the left posterior cerebral artery.

Case 1

Figure 4.

Anatomic, angiographic and perfusion MR imaging of Case 1. (upper left) T2-weighted FLAIR image showing multiple foci of high T2 signal abnormalities; (upper middle) MR angiogram of the anterior circulation showing attenuation of flow enhancement in the left internal carotid artery and left middle cerebral artery; (upper right) intravenous contrast enhanced T1-weighted image showing no enhancement. The perfusion maps are shown on the lower row with (lower left) tissue transit time (TTT); (lower middle) time to arrival (TTA); and (lower right) relative cerebral blood volume (rCBV). No large asymmetries between left and right cerebral hemispheres and between anterior and posterior circulation are identified.

Figure 5.

The perfusion maps for Case 1 before (upper) and after (lower) vasodilation with Diamox showing no significant asymmetries and normal perfusion parameters for TTT and TTA. Hemodynamic reserve remains intact in all vascular territories.

Figure 6.

The activation maps using the bilateral motor, auditory and visual stimulus paradigm for Case 1 superimposed over (upper) dark CSF T1 weighted images and over (lower) bright CSF T2-weighted images. Somatosensory, primary motor and supplementary motor cortex (upper and lower left), auditory and visual cortex (upper and lower middle) and cerebellar motor activation demonstrate sufficient hemodynamic reserve to maintain BOLD contrast responses in all vascular territories.

Case 2 **Figure 7.**

MR anatomy and intracranial MR angiogram obtained at 3.0 Tesla of a patient with history of stroke and known right internal carotid artery occlusion who is currently asymptomatic. (upper left) T2-weighted FLAIR image showing ischemic lesions (white arrow) in the white matter of the right frontal lobe; (upper middle) unenhanced T1-weighted 3D gradient echo image showing ischemic lesions (white arrow); (upper right) intravenous contrast enhanced T1-weighted 3D gradient echo image showing no enhancement in lesions (white arrow); (lower left) T2-weighted gradient echo image showing no hemorrhage in lesions (white arrow); (lower middle) TOF MR angiogram of the anterior circulation showing absence of flow enhancement in the right internal carotid artery (white arrow) and in the bilateral anterior and right middle cerebral arteries and ADC map showing ischemic, CSF-filled cavitory lesions (white arrow).

Figure 8.

MR angiogram of Case 2 from Figure 7 showing: (upper left and middle) maximum intensity projection reconstructed TOF angiogram of the (upper left and middle) anterior circulation in which the right internal carotid artery (arrows) is missing; (upper right) base images showing reduced flow (string sign, arrow) in the precavernous portion of the right internal carotid artery; (lower left and middle) normal posterior circulation and (lower right) combined anterior and posterior circulation showing the absence of flow enhancement in the right internal carotid artery (arrow), bilateral anterior cerebral arteries and the right middle cerebral artery.

Figure 9.

MR perfusion maps before (upper row) and after vasodilation (lower row) with 1 g intravenously administered acetazolamide derived from DSC perfusion MR imaging of the same patient as in Figure 7. (upper left) tissue transit time (TTT) map with values for cortex showing slight asymmetry with longer values on right, especially in the posterior right middle cerebral artery territory; (upper middle) time to arrival (TTA) map showing prolonged arrival times in the right middle cerebral artery territory; (upper right) relative cerebral blood volume (rCBV) map showing slightly increased right-sided values; (lower left) TTT map after vasodilation shows markedly increased asymmetry with little change in the values in the left cerebral hemisphere; (lower middle) TTA map shows increased asymmetry and (lower right) rCBV map also shows asymmetry. The black voxels in the right frontal lobe are areas of such abnormal perfusion that the data cannot be accurately fitted. The worsening perfusion following vasodilation is indicative of lack of hemodynamic reserve in the right middle cerebral artery territory and places the patient at high risk for a subsequent second stroke if aggressive management is not instituted.

The color scales are based on standard deviations from the mean values of the whole brain for each parameter. Black voxels have insufficient contrast change during the first pass of the bolus to perform a gamma variate fit to obtain perfusion parameters.

Figure 10.

Activation maps (color) superimposed over (upper row) T1-weighted (dark CSF) images and (lower row) T2-weighted (bright CSF) images for the bilateral audiovisual hand movement task. The maps show marked asymmetry with loss of activation in the right anterior and middle cerebral artery territories, indicating loss of hemodynamic reserve, insufficient to maintain the BOLD hemodynamic response. Right auditory cortex (upper and lower left) fails to activate as does the right motor and somatosensory cortex (upper and lower middle) indicating compromised hemodynamic reserve in the anterior circulation on the right side compared to the left but no compromise in the posterior circulation as the visual cortex (upper and lower right) activates bilaterally.

Case 3 **Figure 11.**

Anatomical images of a young woman with Moya Moya disease who presented with bilateral subacute infarctions. (upper left) un-enhanced T1-weighted image with minimally visible bifrontal infarction (arrow); (upper middle) enhanced T1-weighted image showing enhancement (arrow) in the bilateral anterior cerebral artery territories; (upper right) T2-weighted FLAIR image showing edema/gliosis in the infarction; (lower left) diffusion weighted image showing restricted diffusion (arrow) that is confirmed on (lower middle) ADC map (arrow); and (lower right) T2-weighted gradient-echo weighted image showing no hemorrhage (arrow).

Figure 12.

MR angiogram of the patient in Case 3 with Moya Moya disease showing the truncation of flow enhancement in the proximal middle and anterior cerebral arteries (arrows) but intact posterior communicating arteries (upper row, arrows) providing some collateral flow into the expanded posterior cerebral arteries (lower right) which provide pial-pial collateral circulation into the anterior circulation. The basilar artery is supplied by one dominant vertebral artery that is normal in caliber so that the expanded posterior circulation is due to the posterior communicating arteries from the anterior circulation.

Figure 13.

Perfusion imaging of the patient in Case 3 with Moya Moya disease showing perfusion maps (upper row) prior to vasodilation and (lower row) after vasodilation with intravenously administered acetazolamide. The tissue transit times (TTT, first column) show low values in the anterior cerebral artery territories (9.2 – 9.4s) because of the infarction. Away from the infarctions, there are longer TTT values (right MCA: 10.8 – 11.9s; left MCA: 11.2 – 11.4s) in the middle cerebral artery (MCA) territories compared to values (10.3 – 10.4s) in the posterior cerebral artery (PCA) territories. These differences increase (right MCA: 10.9 – 13.7s; left MCA: 9.8 – 11.2; PCA: 9.2 – 9.9s) in right MCA after vasodilation, indicating compromised hemodynamic reserve. The time to arrival (TTA, middle column) values also show asymmetry between the anterior and posterior circulation that further widens after vasodilation. The relative cerebral blood volume (rCBV, right column) is insensitive to the perfusion asymmetries. The color scales are based on standard deviations from the mean values of the whole brain for each parameter. Black voxels have insufficient contrast change during the first pass of the bolus to perform a gamma variate fit to obtain perfusion parameters.

Figure 14.

Activation pattern for the audiovisual motor task showing no activation in the primary motor and somatosensory areas (left column, vertical upward arrows); but activation in the motor cerebellar regions (right column, angled downward arrows) indicating that the motor task was performed as also observed directly. The visual cortex activation (horizontal arrows) is readily apparent. The colored activation is superimposed over the T2-weighted, fast gradient-echo, echo-planar images.

Figure 15.

Anatomic images and MR angiogram following bilateral superficial temporal artery-middle cerebral artery bypasses (arrows). (upper left) T1-weighted image showing bilateral craniectomy post surgical changes; (upper middle) contrast enhanced T1-weighted image; (upper right) T2-weighted FLAIR images shows progressive encephalomalacic changes in the frontal lobes from previous infarction; (lower left) MR angiogram and a (lower middle) base image from that angiogram showing enhanced flow through the right superficial temporal artery compared to the left due to the susceptibility artifacts from the surgery; and (lower right) ADC map showing no restricted diffusion to suggest acute or early subacute stroke.

Figure 16.

The 6-week follow-up perfusion studies (upper row) before and (lower row) after vasodilation with acetazolamide show that the previous pre-bypass perfusion gradients in TTT (left column); TTA (middle column) and rCBV (right column) have been eliminated. Vasodilation results in no asymmetries indicating that hemodynamic reserve has been restored.

Figure 17.

The activation study at 6-week follow-up from the bilateral bypasses demonstrates restoration of activation in the motor and somatosensory cortex (left column, vertical arrows), and in auditory cortex (upper middle, arrows) and maintained in the posterior circulation (lower middle and right column, visual cortex shown by horizontal arrows, cerebellar motor activation shown by angled arrows)). The asymmetry in activation with greater activation in the right cerebral hemisphere suggests that better flow augmentation was achieved on the right side. This is reflected in the better flow enhancement on the right side on the MR angiogram in Figure 15.

Figure 18.

The 6-month follow-up perfusion studies (upper row) before and (lower row) after vasodilation with acetazolamide show that some variability in distribution of perfusion has occurred since the 6-week follow-up study in TTT (left column); TTA values (middle column) are worsened by vasodilation especially in white matter and the rCBV maps (right column) remain insensitive to changes. This changes are more evident in the white matter but not in the gray matter following vasodilation.

Figure 19.

The activation study at 6-month follow-up from the bilateral bypasses demonstrates further improvement with less asymmetry in the bilateral activation in the motor and somatosensory cortex (left column, vertical arrows), but with loss of activation in the auditory cortex (upper middle, arrows) since the 6-week follow-up study. Activation is maintained in the posterior circulation (lower middle and right column). The improved motor and somatosensory activation with loss of the auditory activation suggests that the distal middle cerebral artery territories may be affected by the reduced hemodynamic reserve in the white matter evident on the perfusion study (Figure 18).

Figure 20.

Representative MR images (left column), MR angiogram (middle column) and MR perfusion TTT maps (right column) of Case 4. There are bilateral ischemic changes in the white matter of both cerebral hemispheres as shown on the T2-weighted FLAIR (upper left) and T1-weighted (lower left) images. There are very high-grade stenoses of the supraclinoid portions of the internal carotid arteries bilaterally but with greater flow remaining through the right internal carotid artery (upper middle, arrow). The posterior circulation (lower middle) shows expansion of the posterior cerebral arteries supplying pial-pial collateral flow, greater on the left side. The MR perfusion study shows longer TTT values in the white matter, especially on the left (upper right) and a worsening anterior-posterior gradient after vasodilation (lower right), also more severe in the white matter on the left.

Figure 21.

Representative slices from the activation map of Case 4 showing no activation in the expected motor and somatosensory areas (left column, upward arrows), reduced activation in auditory cortex (middle column, sloping arrows) and normal activation in the visual (right column, horizontal arrow) and cerebellar motor (right column, downward arrows) areas. These observations indicate reduced hemodynamic reserve in the superior anterior circulation, insufficient to support BOLD contrast.

Figure 22.

Representative perfusion studies before (upper row) and after (lower row) vasodilation for Case 4 following angioplasty and stenting of the right internal carotid artery showing improved anterior-posterior symmetry in both TTT (left column) and TTA (middle column) values but residual asymmetries on the left, particularly in the white matter. The rCBV maps remain symmetric and insensitive to these changes.

Figure 23.

Activation study after angioplasty and stenting of the right internal carotid artery showing restoration of activation in the motor and somatosensory areas (left column, upward arrows) but greater asymmetry in auditory activation (middle column, horizontal arrow) compared to prestenting in Figure 21. The activations in the visual (upper right, arrow) and cerebellar motor (lower right, arrow) cortex are unchanged.