Time-Resolved MR Angiography in Wake-up Stroke:

An Innovative Application of a Proven Technique

Ravikanth Balaji, DMRD, DNB, EDIR

Stroke is a common disorder with high incidence of disability and death. Cerebral ischemia for even a minute leads to extensive neuronal death with catastrophic results for patients. Treatment strategies focus on minimizing neuronal loss and reviving neurons on the brink of ischemia. Imaging plays a critical role in assessing the cause of acute and transient ischemic strokes and extent of neuroparenchymal involvement (1). Accuracy and speed of diagnosis are important for initiating treatment within the golden hours or the window period to reduce morbidity and mortality. Computed tomography angiography (CTA), digital subtraction angiography (DSA), and magnetic resonance (MR) angiography (MRA) have all been widely used to study vascular conditions leading to strokes. DSA and CTA involve exposure to radiation and require administration of iodinated contrast media that are nephrotoxic (2,3).

MRA has replaced conventional DSA in screening for disease in intracranial and neck vessels because of its noninvasive and nonionizing character. Although the resolution of MRA is not as high as that of conventional angiography, it is sufficient to evaluate pathologic conditions in the carotid and vertebral arteries in the neck and arteries of Circle of Willis. MRA makes use of the MR effect in differentiation of blood flow motion and stationary vessel walls and tissues surrounding them. These techniques are not applicable in the case of patients with vascular disease having slow or disturbed flow (2). A wide array of MRA techniques such as time-of-flight MRA (TOF-MRA), phase-contrast MRA (PC-MRA), contrast-enhanced MRA (CE-MRA), and time-resolved (TR) three-dimensional (3D) MRA have been used for imaging of the neck and intracranial vasculature and to identify steno-occlusive vascular disease. CE-MRA is rapidly evolving as a clinically viable and diagnostically useful tool that is easy to implement in a routine stroke protocol, is minimally invasive, and provides high-contrast vascular images. Arterial catheterization and use of large volumes of iodinated contrast can thus be avoided. The technique uses T1 shortening gadolinium contrast, thereby diminishing the severity of flow-induced signal loss. High-resolution images of cerebral vascular vessels are obtained, wherein vascular pathology is demonstrated better than the images acquired using non–CE-MRA methods. CE-MRA to evaluate status of cervical and intracranial arteries and dynamic susceptibility contrast-perfusion imaging have been used in comprehensive stroke protocols to determine presence of hypoperfused "at-risk" tissue. In the evaluation of steno-occlusive disease, the 3D TOF-MRA technique is recommended for arterial evaluation and the two-dimensional (2D) TOF or 2D PC-MRA technique for venous evaluation. For the evaluation of aneurysms and arterio–venous malformations (AVMs), 3D CE-MRA technique was recommended, especially with dynamic sequences in AVMs (4). TR CE-MRA has evolved as a valuable technique for imaging dynamic vascular pathologies such as AVMs (5). The technical aspects, limitations, and optimization of these MRA techniques will be discussed together with their indications in intracranial disease. The 3D TOF techniques are currently used to evaluate stroke. The 3D TOF-MRA makes use of short echo time and flow compensation, and the flowing blood appears much brighter than the tissue. The 3D TOF tends to overestimate stenotic lesions and occluded arteries, giving rise to false diagnosis of strokes as slow flow leads to saturation of MR signal intensity.

Postcontrast 3D TOF demonstrates better diagnostic accuracy in delineating the extent of stenotic or occlusive arterial lesions than plain 3D TOF-MRA in patients with acute ischemic stroke. Postcontrast 3D TOF-MRA also provides additional information about the vessels distal to a lesion, which is useful for planning interventional therapy (6). Wake-up or unclear-onset strokes occur in up to one-fourth of patients with ischemic stroke. Although stroke severity and clinical outcomes appear to be poorer in wake-up strokes than non–wake-up strokes, many patients with wake-up strokes do not receive thrombolytic therapy because stroke onset time cannot be determined. Recent studies have suggested, however, that the actual onset time of wake-up stroke is close to the wake-up time (3,7). Furthermore, advanced imaging technologies may enable us to identify patients with favorable risk–benefit profiles for thrombolysis.

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From the Department of Radiology, Apollo Specialty Hospital, #320, Padma Towers, Mount Road, CHENNAI, Tamil Nadu 600035, INDIA (R.B.). Received January 22, 2015; accepted January 22, 2015. **Address correspondence to:** R.B. e-mail: ravikanthbalaji@gmail.com

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Postcontrast signal enhancement was also evaluated and compared to dynamic susceptibility (DSC) imaging. The main application of DSC perfusion in patients with acute ischemic stroke is to identify perfusion–diffusion mismatch. Combined low-dose CE-MRA and DSC perfusion protocol in patients with stroke at 1.5 and 3 T is feasible with significant reduction in scan time and contrast dose. This protocol is faster and has better diagnostic accuracy compared to the usual stroke protocol using TOF-MRA and may be adopted into routine clinical practice to streamline imaging of patients with acute stroke (8). According to Thomalla et al. (9), mismatch between the acute ischemic lesion visible on diffusion-weighted imaging (DWI) but not visible on fluid-attenuated inversion recovery (FLAIR) imaging can identify patients within the time window for thrombolysis (≤4.5 hours from symptom onset). In the study by Huisa et al., comparison of DWI–FLAIR mismatch and the FLAIR/DWI ratio were carried out to estimate the time of onset in a group of patients with nocturnal strokes and unknown time of onset. It was found that the use of DWI–FLAIR mismatch in wake-up stroke is a promising approach to select patients for intravenous thrombolysis. The data obtained indicate that DWI–FLAIR mismatch is an optimal approach to estimate the time of stroke onset in patients with wake-up stroke (unknown time of onset) and suggest that a large group of these patients having DWI–FLAIR mismatch could be amenable to reperfusion therapies (10). Low-dose TR-MRA is rapid and gives better functional and anatomic information in patients with cardiac and vascular diseases but has limited spatial resolution in depicting finer vascular details compared to CE-MRA (4,11).

In this issue of *Academic Radiology*, the article by Seeger et al (12) investigates feasibility of TR-MRA to evaluate vessel morphology and pathology in patients with wake-up stroke. Image qualities of TR-MRA are correlated with those of TOF-MRA, CTA, conventional angiography, and sonography. TR-MRA is the fastest technique of all MR sequences available for vessel assessment, and the signal acquired at different phases can give information of cerebral perfusion too. TR-MRA resulted in the diagnosis of large vessel disease in 14 of 19 patients, involving the extracranial internal carotids (severe stenosis, $n = 1$; occlusion, $n = 3$), the extracranial vertebral arteries (stenoses, $n = 2$), and the Circle of Willis (severe stenoses of the middle cerebral artery, $n = 2$; occlusion, $n = 8$). TR-MRA gives additional information in four patients with stenosis or occlusion of the extra cranial internal carotid artery in comparison to TOF-MRA. However, TR-MRA helps in stroke classification and therapy decision by providing additional information of extracranial vessel morphology. It was concluded that TR-MRA is a valuable protocol in for imaging wake-up stroke because of its high sensitivity and negative predictive value. The authors used ultrafast TR-MRA and demonstrated the feasibility of this technique combined with DWI for detecting the core of ischemia, FLAIR for estimating the onset of ischemia as well as assessment of intracranial and extracranial arteries by TR-MRA and time-to-peak measurements. TR-MRA is fast and uses low-dose contrast, which may be helpful in the assessment of acute stroke setting. Furthermore, TR-MRA provides data with high in-plane resolution and can distinguish arterial from venous phases. This MR imaging protocol required scan duration of just 6 seconds and facilitated therapy decision in all cases. The feasibility of low-dose CE TR-MRA and correlation with DSC perfusion have been demonstrated by Seeger et al (12). Optimization of low-dose CE TR-MRA method can be adopted for prospective thrombolysis trials using imaging criteria and to test safety and efficacy of thrombolysis in patients with wake-up or unclear-onset strokes.

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