Acute MR Stroke Protocol in Six Minutes

Kambiz Nael; Rihan Khan; Kevin Johnson; Diego Martin

University of Arizona, Department of Medical Imaging, Tucson, AZ, USA

Background

Stroke is a common and serious disorder, with an annual incidence of approximately 795,000. Based on American Heart Association statistics update in 2010, approximately 610,000 of these are first attacks, and 185,000 are recurrent attacks. On average, every 40 seconds, someone in the United States has a stroke with an estimated mortality rate of 5.5%, claiming approximately 1 of every 18 deaths in the United States [1].

Neuroimaging plays a central role in the evaluation of patients with acute ischemic stroke (AIS). With improved technology over the last decade, imaging now provides information beyond the mere presence or absence of intra-

92-year-old man with sudden onset of right-sided weakness and aphasia presented to our emergency department after receiving IV-tPA at an outside institution. The acute stroke protocol was performed after 9 hours from the onset in our institution and selective images are shown.
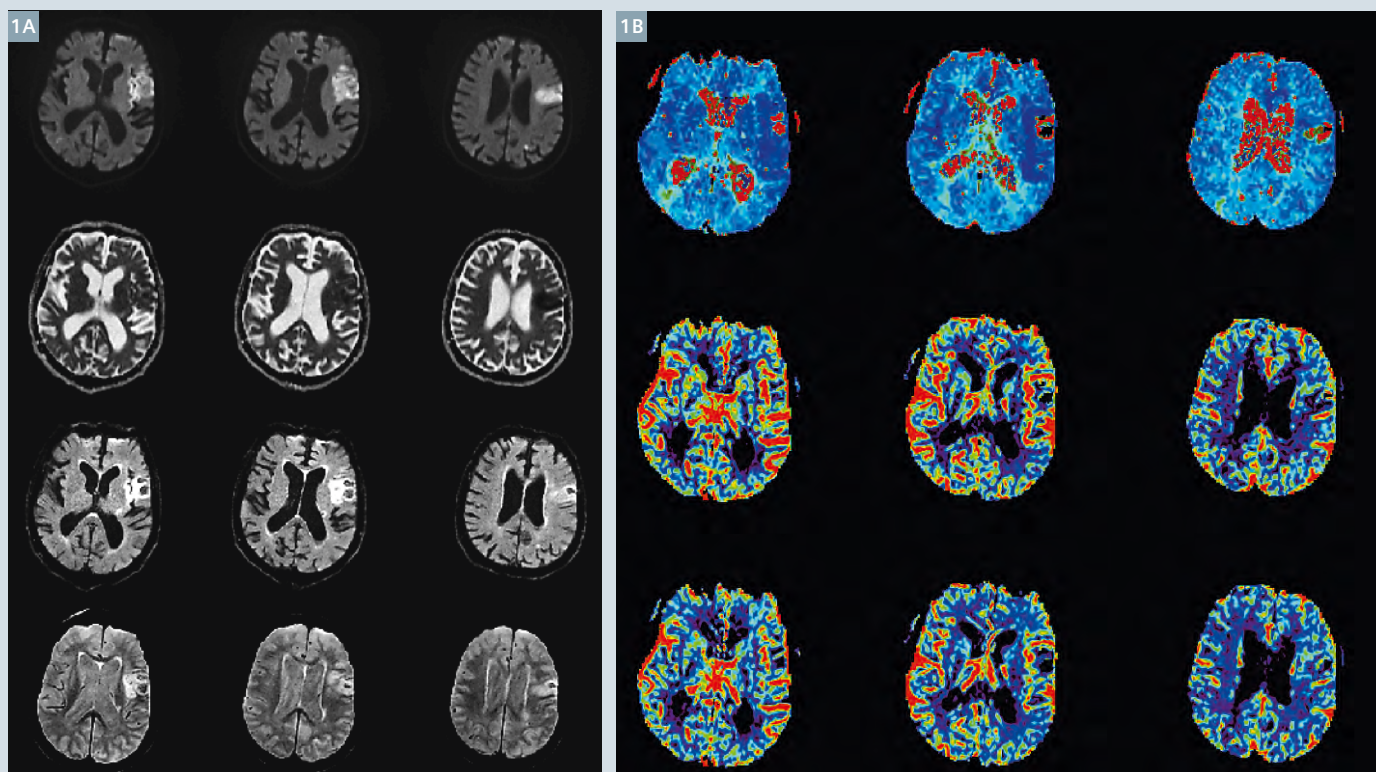
1A Serial aligned DWI, ADC, EPI-FLAIR and EPI-GRE images are shown. There is acute infarction of the left MCA distribution involving the left operculum and insula. Small focus of hemorrhagic conversion is present within the area of infarction seen on both EPI-FLAIR and EPI-GRE images.

1B Aligned DSC-Tmax, DSC-CBF and DSC-CBV images are shown. DSC maps show a heterogeneous pattern of perfusion deficit containing a small perfusion defect in the region of hemorrhage and predominant luxury perfusion along the left MCA territory seen on Tmax and CBF maps.

cranial hemorrhage including tissue viability, site of occlusion, and collateral status. While computed tomography (CT) is the most widely available and faster imaging modality, some comprehensive stroke centers favor streamlined MR protocols over CT in the acute stroke setting due to the higher specificity and superior tissue characterization afforded by MRI. The success of CT in initial evaluation of AIS is due, in part, to fast acquisition time, widespread availability and ease of interpretation in the emergency setting. The introduction of multi-slice technology has dramatically increased the speed and simplicity of CT techniques and has set a high standard for alternative

imaging techniques. A comprehensive CT stroke algorithm including parenchymal imaging (non-contrast head CT), CT angiography (CTA), and perfusion/penumbral imaging by CT perfusion can now be acquired and processed in less than 10 minutes [5, 6].

MRI has been demonstrated to be more sensitive for the detection of acute ischemia and more specific for delineation of infarction core volume when compared to CT [7, 8]. However, due to longer acquisition time and limited availability; it has been mainly used in large institutions and comprehensive stroke centers. A comprehensive MR protocol including parenchymal imaging, MRA and

MR perfusion can now be obtained in the order of 20 minutes as demonstrated in several clinical trials [9–13]. If MRI is to compete with CT for evaluation of acute stroke, there is need for further improvements in acquisition speed.

In this article we describe our modified acute stroke MRI protocol that can be obtained in approximately 6 minutes rivaling that of any comprehensive acute stroke CT protocol. We describe the technical aspects and review a few clinical examples based on our preliminary results.
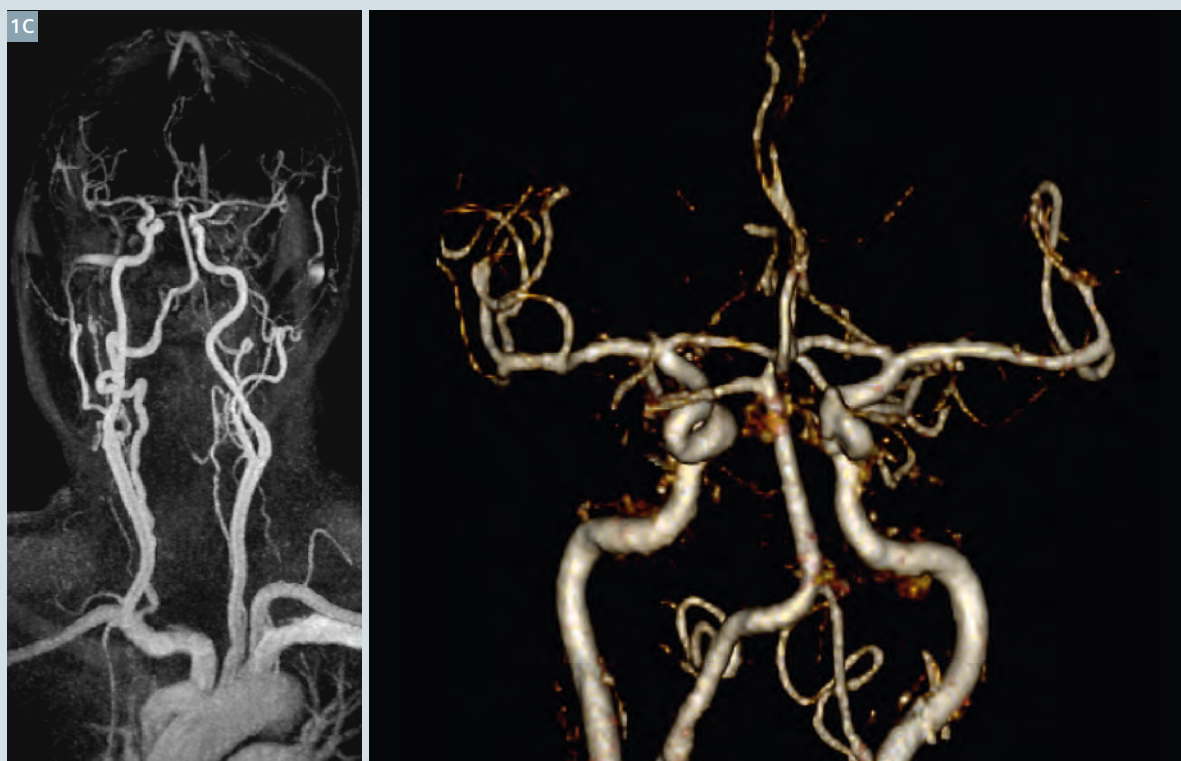
1C Coronal MIP from CE-MRA of the entire supra-aortic arteries and cropped volume-rendered reconstruction of the intracranial arteries show no evidence of hemodynamic significant arterial stenosis nor occlusion involving the proximal arteries. Note the high diagnostic image quality of the CE-MRA images which are obtained after administration of 8 ml of contrast.

Technical consideration

A comprehensive MR stroke protocol has three essential components:

1) Parenchymal imaging that identifies the presence and size of an irreversible infarcted core and determines the presence of hemorrhage;
2) MR angiogram to determine the presence of proximal arterial occlusion and/or intravascular thrombus that can be treated with thrombolysis or thrombectomy;
3) Pwerfusion imaging to determine the presence of hypoperfused tissue at risk for subsequent infarction if adequate perfusion is not restored.

Below we describe each of these components in detail and explain how recent technical advances can

be used to enhance the performance of the different aspects of acute stroke imaging.

1. Parenchymal imaging
This encompasses three parts:

1) DWI (diffusion-weighted imaging) that can detect ischemic tissue within minutes of its occurrence and has emerged as the most sensitive and specific imaging technique for acute ischemia, far beyond NECT or any other type of MRI sequences [14].
2) FLAIR that helps to age the infarction and permits the detection of subtle subarachnoid hemorrhage;
3) GRE to detect parenchymal hemorrhage with comparable accuracy for the acute intraparenchymal hemorrhage to CT [15].

Both FLAIR and GRE images have been used to detect intraarterial clot with variable sensitivity and specificity [16, 17].

Introduction of fast imaging techniques such as parallel acquisition [18] and EPI [19, 20] has significantly enhanced the performance of MR imaging in terms of acquisition speed. The main advantage of EPI, as in the case of DWI imaging, is rapid acquisition time, which is made possible by rapid gradient switching which permits the acquisition of all frequency and phase encoding steps during a single pulse cycle. The addition of parallel imaging can further enhance the acquisition speed and may also serve to mitigate the geometric distortion and susceptibility artifacts commonly

68-year-old man with left sided weakness and altered level of consciousness of unknown onset.
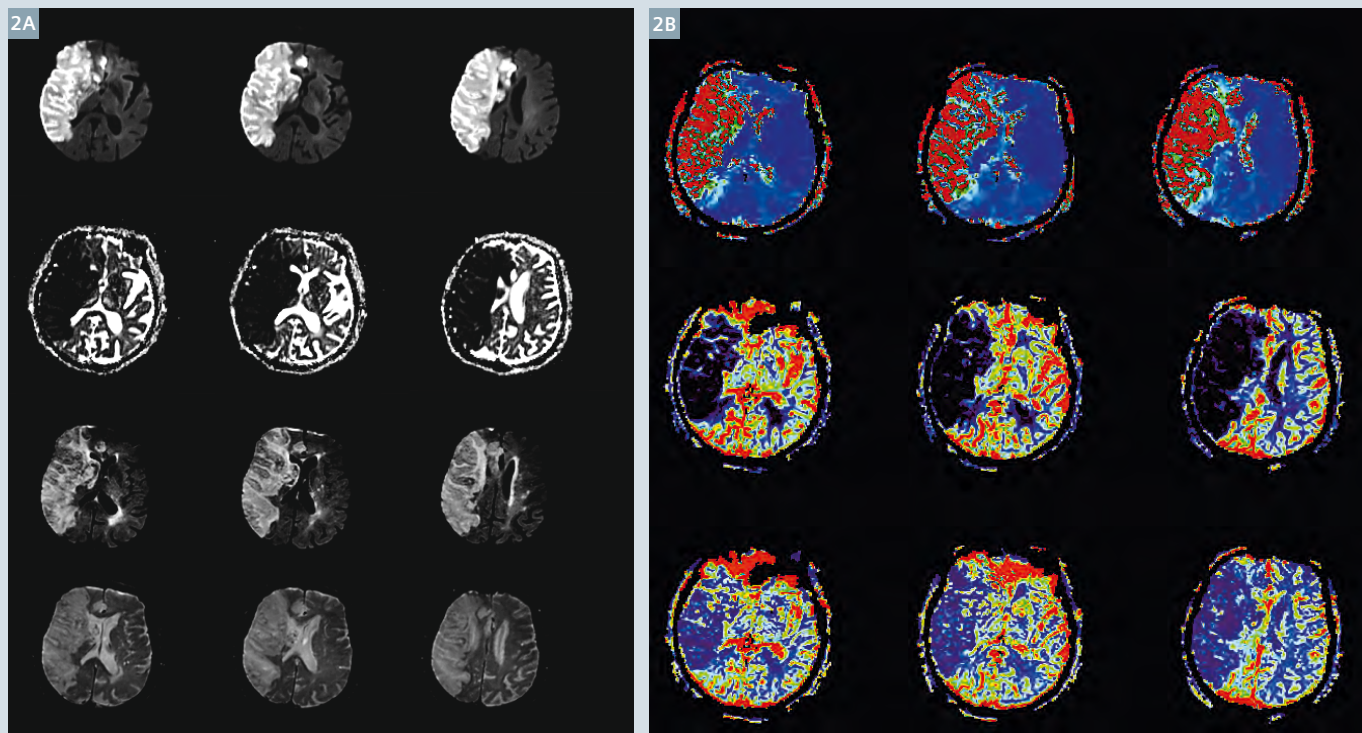
2A Serial aligned DWI, ADC, EPI-FLAIR and EPI-GRE images are shown. There is acute right hemispheric infarction involving both the ACA and MCA territories. The EPI-FLAIR images demonstrate corresponding hyperintensity suggestive of completed infarction. There is associated mass effect. No hemorrhage is identified on corresponding EPI-GRE images.

2B Aligned DSC-Tmax, DSC-CBF and DSC-CBV images are shown. There is a matched perfusion defect with the region of infarction.

associated with long echo-train sequences such as EPI [21, 22]. If their potential is realized, the application of EPI and parallel imaging techniques to the FLAIR and GRE sequences can result in reduction of image acquisition time of the entire brain to less than a minute, a three-fold reduction in scan time over conventional imaging [23, 24].

2. MR Angiogram

An important aspect of the workup of patients with AIS is the imaging of both the intracranial and extracranial vasculature. Precise imaging of the vascular tree is required during the initial assessment of patients with acute stroke to accurately detect the site of arterial disease, which in turn can be crucial in determining the

2C Coronal MIP from CE-MRA of the entire supra-aortic arteries shows complete occlusion of the right cervical ICA shortly after the origin. There is some reconstitution of flow signal at the supracliniod ICA likely via collaterals.

type of acute therapy they are given. Intravenous thrombolysis has been shown to be more effective in small distal vessels than in the large vessels [25]. Larger vessel occlusion may be more effectively treated with intra-arterial thrombolysis or clot retrieval devices while associated with fewer complications [26, 27]. In addition, MRA of the extracranial circulation (neck arteries) is essential to establish the mechanism of ischemia and to prevent subsequent episodes. Extracranial tandem stenoses with plaque involving the carotid or vertebral arteries can be the source of disease that triggers an acute stroke.

Time-of-flight MRA (TOF-MRA) has been traditionally used in routine stroke protocols to evaluate the status of neck and brain arteries. Despite its promising results [28], TOF-MRA has significant disadvantages including spin saturation and phase dispersion due to slow or turbulent flow [29, 30]. This can result in overestimation of arterial stenosis and increase false positive rates, usually due to slow flow distal to a subocclusive thrombus or clot. Most importantly the acquisition time usually is long, typically lasting 5–7 minutes.

The general consensus is that contrast-enhanced MR angiography (CE-MRA) provides more accurate imaging of extracranial vessel morphology and of the degree of stenosis than TOF-MRA techniques [31–33]. However, CE-MRA has not been widely incorporated into acute stroke protocols for several reasons. First, CE-MRA has lower spatial resolution relative to TOF-MRA, since the competing requirements of coverage and acquisition speed generally force a compromise in spatial resolution for CE-MRA [34]. A second potential limitation to incorporation of CE-MRA into clinical stroke protocols is related to the requirement of an extra contrast dose, which would be in addition to the intravenous contrast bolus normally utilized for perfusion imaging. With introduction of high performance MR scanners and recent advances in fast imaging tools such as parallel acquisition (GRAPPA) [18], high matrices can now be spread out

over a large field-of-view encompassing the entire head and neck, resulting in acquisitions with submillimeter voxel sizes and acquisition times on the order of 20 seconds [35, 36].

3. MR Perfusion

MR perfusion imaging has been used broadly in the identification of potentially salvageable tissue to determine the best treatment strategy in patients with acute ischemic stroke. Although the concept of perfusion-diffusion mismatch remains controversial [37, 38], it has been used with some success to identify patients who may respond favorably to revascularization therapies in several clinical trials [12, 13, 39].

Faster image acquisition combined with higher signal-to-noise ratio (SNR) resulting from the use of gadolinium contrast agents has helped dynamic susceptibility contrast (DSC) perfusion become a more robust and widely accepted technique in comparison to arterial spin labeling (ASL) to identify the presence of perfusion abnormalities in patients with AIS.

A refined MR stroke protocol that can combine both CE-MRA and DSC-perfusion with improved acquisition time and diagnostic image quality as previously suggested [47, 48] may have important therapeutic and prognostic implications in the management of patients with acute stroke. Higher inherent SNR of higher magnetic fields such as 3T with improved multi-coil technology has resulted in acquisition of low dose CE-MRA of the supra-aortic arteries with contrast dose as low as 8 ml [40, 41]. A modified 2-phase contrast injection scheme [46] can be used to perform both CE-MRA and DSC perfusion imaging, without the need for additional contrast. The influence of contrast dose reduction on DSC perfusion has been evaluated by several investigators [42, 43] and contrast dose as low as 0.05 mmol/kg has been used to perform DSC perfusion with promising results [44, 45].

Advances in MR technology including hardware and software, faster gradient performance of MR scanners, improved sequence design and fast imaging tools such as EPI and parallel
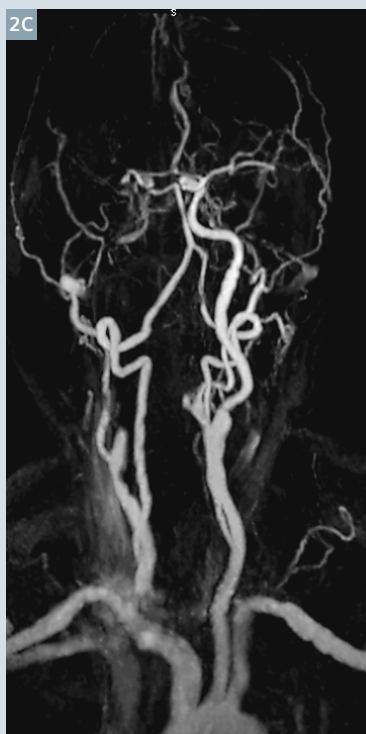
acquisition have promised the potential for a fast but comprehensive MR stroke protocol that can be performed in approximately 6 minutes rivaling those of CT protocols. Next we review our stroke protocol in terms of image acquisition and sequence parameters and show some of the clinical examples that were performed at our institution.

How we do it

At our institution, absent contraindication, MR is the default imaging modality for AIS. An MR safety questionnaire is administered, and MR compatible ECG leads are placed in the emergency department as patients are being evaluated by the neurology team. Patients are then placed onto an MR compatible table and wheeled to the MR magnet for rapid imaging.

We use both 3T and 1.5T MR scanners (MAGNETOM Skyra and MAGNETOM Aera, Siemens Healthcare, Erlangen, Germany), with 3T the default scanner for acute stroke imaging when available. For signal reception, a combination of a 16-element array coil [head (n = 12), neck (n = 4)] will be used. The coil design allows for application of parallel acquisition in both the phase and slice encoding directions. Our 6-minute MR imaging protocol consist of DWI, EPI-FLAIR, EPI-GRE,

CE-MRA and DSC perfusion. The clinical indications for using this acute MR stroke protocol are patients with acute (< 9 hours) presentation from the onset of symptoms, unknown onset of symptoms, NIHSS > 4, or aphasia. Table 1 shows the sequence parameters of our acquisition protocol.

A modified 2-phase contrast injection scheme [46] is used to perform both CE-MRA and DSC perfusion imaging, without the need for additional contrast. To accomplish this, the total volume of 20 ml of gadolinium (Multihance, Bracco Diagnostics Inc., Princeton, NJ, USA) that is used routinely for MR perfusion is diluted with normal saline to a total 50 ml volume. Using a timing bolus, a total of 3 ml of contrast solution (1.2 ml of gadolinium) is injected at 1.5 ml/s to determine the transit time from the arm vein to the cervical carotid arteries. Then, a total of 22 ml contrast solution (8.8 ml of gadolinium) is injected at the same flow rate as the timing injection for the CE-MRA acquisition. A centric ordering *k*-space is used for CE-MRA to minimize intracranial venous contamination. Subsequently, the remaining 25 ml of contrast solution (10 ml of gadolinium) is injected at 5 ml/s for the MR perfusion scan which is performed at the end.

Image analysis

Following data acquisition, CE-MRA image processing is performed on the scanner console with standard commercial software using a maximum intensity projection (MIP) algorithm. All of the reconstructed data, as well as the source images are available on the workstation for image analysis. Perfusion analysis will be performed off-line on a dedicated FDA-approved workstation (Olea-sphere, Olea Medical SA, France). The arterial input function is selected automatically and multi-parametric perfusion maps including time-to-peak (TTP), time-to-maximum (Tmax) cerebral blood flow (CBF) and cerebral blood volume (CBV) are then calculated using a block-circulant singular value decomposition technique [49].

Our initial results using the described stroke MR protocol have been promising. We have scanned more than 600 patients with ASI since January 2013. More than 97% of our studies have been rated with diagnostic image quality. The EPI-FLAIR sequence has been used in parallel to conventional FLAIR in a subset of patients with comparable qualitative and quantitative results [24]. In a study of 52 patients with AIS, the mean ± SD of the signal intensity ratios on EPI-FLAIR and FLAIR for DWI positive lesions were 1.28 ± 0.16 and 1.25 ± 0.17 respectively with sig-

Table 1: Imaging protocol

	DWI	EPI-FLAIR	EPI-GRE	CE-MRA	DSC
TR (ms)	4600	10000 (TI:2500)	1860	3.36	1450
TE	65	88	48	1.24	22
FA (degrees)	–	90	90	25	90
Matrix	160	192	192	448	128
FOV	220	220	220	340	220
Slices (n × thickness)	30 × 4	30 × 4	40 × 3	120 × 0.8	30 × 4
Bandwidth (Hz/pixel)	1250	1488	964	590	1502
Parallel acquisition (GRAPPA)	3	3	–	3	3
Acquisition time	58 sec	52 sec	56 sec	20 sec	1 min and 30 sec

nificant correlation (r = 0.899, z value = 8.677, p < 0.0001). The EPI-GRE sequence has been also used in parallel to conventional GRE in a subset of patients with comparable results in terms of detection of hemorrhage (Fig. 1) and blood clot in proximal arteries.

The combination of CE-MRA and DSC has been successfully tested in our institution [48] with diagnostic image quality. In a cohort of 30 patients with acute stroke, the specificity of CE-MRA for detection of arterial stenosis > 50% was 97% compared to 89% for TOF-MRA when compared to DSA as the standard of reference [48]. DSC perfusion imaging with reduced contrast dose is feasible with comparable quantitative and qualitative results to a full-dose control group [48]. Importantly, the presence of contrast in the circulating blood of the CE-MRA half-dose group does not negatively impact the image quality nor the quantitative analysis of perfusion data when compared to the control full-dose group.

Conclusion

Described multimodal MR protocol is feasible for evaluation of patients with acute ischemic stroke with total acquisition time of 6 minutes rivaling that of the multimodal CT protocol.

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Contact

Kambiz Nael, M.D.
Assistant Professor of Radiology
Director of Neuroradiology MRI
University of Arizona
Medical Center
Department of Medical Imaging,
Neuroradiology Section
1501 N. Campbell,
PO Box 245067
Tucson, AZ 85724-5067
USA
Phone: +1 520-626-2138
Fax: +1 520-626-7093
kambiz@radiology.arizona.edu