Six-Minute Magnetic Resonance Imaging Protocol for Evaluation of Acute Ischemic Stroke

Pushing the Boundaries

Kambiz Nael, MD; Rihan Khan, MD; Gagandeep Choudhary, MD; Arash Meshksar, MD; Pablo Villablanca, MD; Jennifer Tay, MD; Kendra Drake, MD; Bruce M. Coull, MD; Chelsea S. Kidwell, MD

Background and Purpose—If magnetic resonance imaging (MRI) is to compete with computed tomography for evaluation of patients with acute ischemic stroke, there is a need for further improvements in acquisition speed.

Methods—Inclusion criteria for this prospective, single institutional study were symptoms of acute ischemic stroke within 24 hours onset, National Institutes of Health Stroke Scale $\geq 3$, and absence of MRI contraindications. A combination of echo-planar imaging (EPI) and a parallel acquisition technique were used on a 3T magnetic resonance (MR) scanner to accelerate the acquisition time. Image analysis was performed independently by 2 neuroradiologists.

Results—A total of 62 patients met inclusion criteria. A repeat MRI scan was performed in 22 patients resulting in a total of 84 MRIs available for analysis. Diagnostic image quality was achieved in 100% of diffusion-weighted imaging, 100% EPI-fluid attenuation inversion recovery imaging, 98% EPI-gradient recalled echo, 90% neck MR angiography and 96% of brain MR angiography, and 94% of dynamic susceptibility contrast perfusion scans with interobserver agreements ($k$) ranging from 0.64 to 0.84. Fifty-nine patients (95%) had acute infarction. There was good interobserver agreement for EPI-fluid attenuation inversion recovery imaging findings ($k=0.78$; 95% confidence interval, 0.66–0.87) and for detection of mismatch classification using dynamic susceptibility contrast-Tmax ($k=0.92$; 95% confidence interval, 0.87–0.94). Thirteen acute intracranial hemorrhages were detected on EPI-gradient recalled echo by both observers. A total of 68 and 72 segmental arterial stenoses were detected on contrast-enhanced MR angiography of the neck and brain with $k=0.93$, 95% confidence interval, 0.84 to 0.96 and 0.87, 95% confidence interval, 0.80 to 0.90, respectively.

Conclusions—A 6-minute multimodal MR protocol with good diagnostic quality is feasible for the evaluation of patients with acute ischemic stroke and can result in significant reduction in scan time rivaling that of the multimodal computed tomographic protocol. (Stroke. 2014;45:1985-1991.)

Key Words: magnetic resonance angiography ■ magnetic resonance imaging ■ perfusion imaging ■ stroke

A cute ischemic stroke (AIS) is a common and often devastating disorder; however, acute treatments that reduce long-term disability are available if patients present within the window for treatment.1,2 Neuroimaging plays a critical role in the evaluation of these patients. Multimodal computed tomography (CT) or magnetic resonance imaging (MRI) has been used in comprehensive stroke centers, although the role of advanced imaging in improvement of stroke outcome remains controversial.3,4 These fast and more efficient imaging modalities provide information beyond the mere presence or absence of intracranial hemorrhage, including tissue viability, site of occlusion, and collateral status, although current guidelines emphasize that acute stroke multimodal imaging should not delay treatment with intravenous tissue-type plasminogen activator.5

Noncontrast CT is used in initial evaluation of AIS, in part, because of fast acquisition time, widespread availability, and ease of interpretation in the emergency setting. The introduction of multislice technology has expanded the CT armamentarium to make multimodal CT that includes CT angiography and whole-brain coverage perfusion CT feasible in the acute stroke setting. This technology has dramatically increased the speed and simplicity of CT techniques and has set a high standard for alternative imaging modalities. A comprehensive CT stroke algorithm, including parenchymal imaging (non-contrast head CT), CT angiography, and perfusion/penumbral
imaging by CT perfusion can now be acquired and processed in <10 minutes.5,7 Although CT is the most widely available and faster imaging modality, some comprehensive stroke centers favor streamlined magnetic resonance (MR) protocols instead of CT for 2 major reasons: (1) MRI has been demonstrated to be far more sensitive for the detection of acute ischemia and more specific for delineation of infarction core volume when compared with CT,8 and (2) lack of radiation. A comprehensive CT stroke protocol delivers a mean effective dose of 16.4 mSv,9 which is ≈6× the dose of an unenhanced CT head. This high dose usually prohibits repeating the study for follow-up of treatment in most clinical settings.

However, because of longer acquisition time and limited availability; MRI has been mainly used in large institutions and comprehensive stroke centers. A comprehensive MR protocol, including parenchymal imaging, MR angiography (MRA), and MR perfusion, can be obtained in the order of 20 minutes.6,7 Introduction of fast imaging techniques, such as parallel acquisition13 and echo-planar imaging (EPI),14,15 has significantly enhanced the performance of MRI in terms of acquisition speed. If their potential is realized, the application of EPI and parallel imaging techniques can significantly enhance the performance and speed of MR to compete with multimodal CT for evaluation of AIS and can be used to facilitate imaging-based stroke research. The purpose of this study was to establish the feasibility of a fast MR protocol that can be obtained in ≈6 minutes rivaling that of any comprehensive acute stroke CT protocol. We describe the technical aspects and present our initial clinical experience using this protocol.

Table 1. MR Imaging Protocol and Sequence Parameters

<table>
<thead>
<tr>
<th>DWI</th>
<th>EPI-FLAIR</th>
<th>EPI-GRE</th>
<th>CE-MRA</th>
<th>DSC</th>
</tr>
</thead>
<tbody>
<tr>
<td>TR/TE, ms</td>
<td>4600/65</td>
<td>1000/82</td>
<td>1860/48</td>
<td>3.3/1.2</td>
</tr>
<tr>
<td>FA, °</td>
<td>90</td>
<td>90</td>
<td>90</td>
<td>25</td>
</tr>
<tr>
<td>Matrix, mm</td>
<td>160</td>
<td>128</td>
<td>192</td>
<td>448</td>
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<tr>
<td>FOV, mm</td>
<td>220</td>
<td>220</td>
<td>220</td>
<td>340</td>
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<tr>
<td>Slices (n×thickness), mm</td>
<td>30×4</td>
<td>30×4</td>
<td>40×3</td>
<td>120×0.8</td>
</tr>
<tr>
<td>GRAPPA</td>
<td>3</td>
<td>3</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Acquisition time, s</td>
<td>58</td>
<td>52</td>
<td>56</td>
<td>22</td>
</tr>
</tbody>
</table>

CE-MRA indicates contrast-enhanced magnetic resonance angiography; DSC, dynamic susceptibility contrast perfusion; DWI, diffusion-weighted imaging; EPI, echo-planar imaging; FA, flip angle; FLAIR, fluid attenuation inversion recovery imaging; FOV, field-of-view; GRAPPA, generalized autocalibrating partially parallel acquisition; GRE, gradient recalled echo; MR, magnetic resonance; TE, echo-time; Tmax, time-to-maximum; and TR, repetition time.

Methods

Patients

This prospective single institutional study was performed with institutional review board approval. Patients with suspected AIS from January to December 2013 were enrolled using the following inclusion criteria: (1) high clinical suspicion of AIS determined by the neurology stroke team and baseline National Institutes of Health Stroke Scale scores ≥3; (2) interval between the onset of neurological deficits to MRI of <24 hours; (3) absence of contraindication to MRI. Patient demographic data, median time from last known well to MRI, and median National Institutes of Health Stroke Scale were documented for each patient.

Image Acquisition

All patients underwent MRI on a 3.0T (Siemens Skyra, Erlangen, Germany) MR system. Figure 1 shows a schematic of the imaging protocol, which included diffusion-weighted imaging (DWI), EPI-fluid attenuation inversion recovery imaging (FLAIR), EPI-gradient recalled echo (GRE), contrast-enhanced MRA (CE-MRA), and dynamic susceptibility contrast (DSC) perfusion imaging. The combination of EPI sequence design and a generalized autocalibrating partially parallel acquisition algorithm13 resulted in a fast MRI protocol with total acquisition time of ≈6 minutes. Detailed sequence parameters are summarized in Table 1. The 6-minute time is an estimate calculated on all steps required to complete the image acquisition. It should be noted that acquisition time may vary on a case by case basis depending on factors, such as patient cooperation and technical difficulties. In a subset of patients (n=40), conventional FLAIR and GRE were obtained for comparison purposes. A detailed description of image acquisition and the technical components are provided in the online-only Data Supplement. The sequence parameters for conventional imaging are detailed in the online-only Data Supplement.

Image Analysis

Image analysis was performed by 2 board certified neuroradiologists independently and in separate reading sessions. The readers were blinded to the result of conventional MRI. The source data and reconstructed MRA images using maximum intensity projection were used for image analysis. DSC images were processed using commercially available Food and Drug Administration–approved software (Olea Sphere; Olea Medical SAS, La Ciotat, France). DSC analysis consisted of the following steps: (1) truncation of the first 5 time points in the DSC time series because the MR signal does not reach steady state before this time, (2) calculation of prebolus signal intensity on a voxel-wise basis, and then (3) conversion of truncated DSC time series to a concentration–time curve based on the T2* relaxivity of the contrast agent. The arterial input function was selected automatically using a block-circulant singular value decomposition technique.16 The Tmax maps with threshold of ≥6 s were then automatically generated and exported from the software for subsequent analysis.

Image Quality

The readers were asked to grade DWI, EPI-FLAIR, EPI-GRE, and DSC-Tmax maps using a 3-scale scoring system with regards to susceptibility mediated distortion at tissue interfaces, noise, motion, and...
Clinical Imaging Findings

The readers filled a questionnaire for each patient consisting of the following questions:

1. DWI:
   1. AIS (+/−)
   2. If (+), determine the location and mechanism (territorial, embolic, lacunar, and watershed).
2. EPI-FLAIR
   1. Determine the presence of hyperintensity corresponding to the area of restricted diffusion (+/−).
   2. Calculate the signal:intensity ratio (SIR) of the DWI-positive lesion to contralateral normal white matter. This was performed using a region of interest–based analysis method, as recently published.17
   3. The same analysis was performed in a subset of patients (n=40), who had conventional FLAIR images in a separate reading session. The patients with acute infarction were categorized into 2 groups based on time from onset to MRI of lesser or greater than 4.5 hours as the cutoff for thrombolysis. The mean±SD of the SIR values on EPI-FLAIR and conventional FLAIR were correlated in these 2 groups.
3. EPI-GRE
   1. Determine the presence of acute intracranial hemorrhage. This was compared with the finding of conventional GRE in a subset of patients (n=40).
   2. Determine the presence of clot in proximal intracranial arteries. The observers were asked to determine the presence of susceptibility-related blooming on EPI-GRE or hyperintense signal on EPI-FLAIR within the proximal intracranial arteries.
4. DSC perfusion
   1. Determine the presence of perfusion deficit using DSC Tmax≥6 s.
   2. The volumes of DWI abnormality, hypoperfused region using Tmax≥6 s, and DWI–diffusion mismatch ratios were generated by each observer. Using the modified Diffusion and Perfusion Imaging Evaluation for Understanding Stroke Evolution criteria,18 the patients were categorized into 3 groups (1) mismatch: perfusion abnormality volume >180% of infarction core volume, (2) matched: perfusion abnormality volume >70% but <180% of the infarction core volume, (3) reperfused: perfusion abnormality volume <70% of the infarction core volume. These scores were then used to perform comparative analysis between observers.
5. CE-MRA

Arterial segments were examined for stenoses independently by 2 neuroradiologists. Arterial stenosis were quantified using established methods, including The North American Symptomatic Carotid Endarterectomy Trial (NASCET)19 criteria for neck and The Stroke Outcomes and Neuroimaging of Intracranial Atherosclerosis (SONIA) trial20 criteria for brain arteries. When ≥2 stenoses were detected in the same vessel segment, the most severe stenosis was used for grading and analysis. The extracranial arteries evaluated included origin of supra-aortic arteries, common carotid arteries, cervical internal carotid arteries, and cervical vertebral arteries. The intracranial arteries were divided in to the following segments: petrocavernous internal carotid arteries, supraclinoid internal carotid arteries, anterior cerebral arteries (A1 and A2 segments), middle cerebral arteries (M1 and M2 segments), intradural segments of vertebral arteries, basilar artery, and posterior cerebral arteries (P1 and P2 segments).

Statistical Analysis

Statistical analyses were performed using MedCalc (version 12.2.1; MedCalc Software, Ostend, Belgium). The qualitative scores were plotted as median and range and tested for statistical significance using a Wilcoxon signed-rank test. The quantitative SIR values between FLAIR and EPI-FLAIR were tested with a t test. A weighted k test with calculation of 95% confidence interval was used to evaluate the interobserver agreement in comparative analysis of DWI, EPI-FLAIR, EPI-GRE, CE-MRA, and DSC perfusion. The significance level was defined as P<0.05 (2-sided).

Results

A total of 62 patients (37 M, 25 F) with a mean age of 69.8 (range, 36–94) years met our inclusion criteria. National Institutes of Health Stroke Scale scores at baseline ranged from 3 to 30 with a median of 6. The median time from last well known to MRI was 14 (range, 1–23) hours.

Twenty-two patients underwent a second MRI examination during their hospital course resulting in a total of 84 sets of acute MR stroke protocols for analysis. The median time between the 2 MRIs in this group was 7 (range, 3–28) hours. The indication for repeat MRI included follow-up endovascular recanalization (n=6), follow-up intravenous tissue-type plasminogen activator (n=11), and decline in mental status (n=5).

Image Quality

Images were rated as having adequate diagnostic image quality in 100% of DWI, 100% of EPI-FLAIR, 97.6% (82/84) of EPI-GRE, 97.6% (82/84) of brain MRA, 94% (80/84) of neck MRA, and 94% (80/84) of DSC-Tmax (Figure 2). There was no statistically significant difference between the observers for image quality scores (P>0.2) with good to excellent interobserver agreement with k values ranging from 0.64 to 0.84. The image quality scores by each observer and the interobserver agreement for each imaging parameter are detailed in Table 2.

Two CE-MRA studies were rated nondiagnostic because of poor contrast timing. Two of the neck CE-MRA studies were nondiagnostic because of significant motion artifact. Four DSC perfusion studies were nondiagnostic because of poor contrast bolus profile, likely because of small bore intravenous lines (n=2) and significant motion artifact (n=2).

Clinical Imaging Findings

Infarction

A total of 59/62 (95%) had positive DWI lesions (acute infarction), identified by both observers. In 3 patients without infarction, 2 were ultimately considered to have had a seizure
(Figure 3) and I had a hemorrhagic mass. The distribution of the infarctions was territorial n=31, embolic n=16, lacunar n=10, and watershed n=2.

**EPI-FLAIR**

In 43/59 (73%) patients with acute infarction, EPI-FLAIR had concordant lesion/hyperintensity to the DWI lesion. The time from onset to MRI ranged from 2.5 to 23 hours in this group. In 16/59 (27%) of patients with acute infarction, EPI-FLAIR did not show corresponding signal abnormality. Time from presentation to MRI ranged from 1 to 6 hours in this group. In 8 (13%) patients, vascular FLAIR hyperintensity was detected (carotid n=3, middle cerebral artery stem n=2, and middle cerebral artery distal sylvian branches n=3) suggestive of sluggish flow or clot formation. There was an overall good agreement (κ=0.78; 95% confidence interval [CI], 0.66–0.87) between the readers for EPI-FLAIR findings. The mean of the SIR values on EPI-FLAIR was 1.17 for patients with time of onset to MRI of <4.5 hours (n=26) and 1.36 for patients with time of onset to MRI of >4.5 hours (n=36), respectively, concordant with the result of recently published report.21

In a subset of patients (n=40), conventional FLAIR image findings concurred with EPI-FLAIR findings in 39/40 (97%). In only 1 case, EPI-FLAIR was discordant with FLAIR and unable to show subtle FLAIR hyperintensity, corresponding to a small cerebellar lacunar infarction. The overall mean±SD of the SIR values on EPI-FLAIR and FLAIR for DWI-positive lesions were 1.25±0.15 and 1.22±0.13, respectively (P=0.3).

**EPI-GRE**

Acute intracranial hemorrhage was identified in 6/62 (9%) patients (parenchymal hemorrhage, n=3; petechial hemorrhage associated with infarction, n=2; hemorrhagic mass, n=1). In 22 patients with follow-up MR studies, 7 additional intracranial hemorrhages were identified (1 parenchymal hemorrhage after revascularization and 6 petechial hemorrhages associated with areas of infarction). In 5 patients (8%), blooming artifact was identified in main proximal arteries (carotid, n=2; middle cerebral artery stem, n=3) suggestive of clot formation. In a subset of patients (n=40) who had conventional GRE, EPI-GRE findings were concordant in 100% for detection of acute intracranial hemorrhage. There was an overall excellent agreement (κ=0.95; 95% CI, 0.88–0.96) between the readers for EPI-GRE findings.

**DSC Perfusion**

On evaluation on DSC-Tmax, all patients had a perfusion deficit: mismatch n=21; matched n=49; and reversed mismatch n=14. The interobserver agreement for mismatch classification using Diffusion and Perfusion Imaging Evaluation for Understanding Stroke Evolution criteria was κ=0.92, 95%
CI, 0.87 to 0.94 (Table I in the online-only Data Supplement). Among 22 patients who had follow-up MRI, 14 patients had reversed mismatch (endovascular recanalization, n=6; intravenous tissue-type plasminogen activator, n=5; and spontaneous recanalization, n=3).

**CE-MRA**

In evaluation of neck CE-MRA, from a total of 252 available arterial segments, 23 high-grade segmental stenoses (9%) and 9 segmental occlusions (3.5%) were identified. In evaluation of brain CE-MRA, from a total of 839 arterial segments available, 26 high-grade segmental stenoses (3%) and 29 segmental occlusion (3.4%) were identified. The interobserver agreements were $\kappa=0.93$, 95% CI 0.84 to 0.96 for neck CE-MRA and $\kappa=0.87$, 95% CI 0.80 to 0.90 for brain CE-MRA. The distribution of brain and neck arterial stenoses detected by CE-MRA is detailed in Table II in the online-only Data Supplement.

**Discussion**

As such, a comprehensive MR stroke protocol currently has 4 major components: (1) sequences that allow detection of acute hemorrhage (T2* and FLAIR), (2) parenchymal imaging that identifies the presence and size of an irreversible infarcted core and determines the presence of hemorrhage, (3) MRA to determine the presence of proximal arterial occlusions, stenosis, and intravascular thrombus, and (4) perfusion imaging to determine the presence of potential hypoperfused tissue at risk. The use of multimodal imaging has been advocated for the evaluation of AIS because it has the potential to provide additional information beyond that of noncontrast CT. However, although some studies suggest that this information has some clinical use, no study or trial to date has demonstrated improved outcomes or overall benefit from this approach.

In this study, we demonstrated that a 6-minute MR stroke protocol is feasible while maintaining a high degree of image diagnostic quality. Across our cases, we obtained diagnostic image quality in $\geq 90\%$ of studies with a high interobserver agreement to demonstrate the reproducibility of our technique. In this regard, we were able to demonstrate that EPI-FLAIR provides comparable qualitative and quantitative values to those obtained from conventional FLAIR and resultant reduction in acquisition time as recently shown.

In this study, we obtained high diagnostic image quality with EPI-FLAIR and comparable image quality and imaging findings with conventional FLAIR in a subset of patients (n=30). The application of FLAIR imaging as part of acute MR stroke protocol provides diagnostic value for detection of subtle cerebral subarachnoid hemorrhage, added diagnostic value to GRE images for detecting intra-arterial clot, and can be used to estimate the age of infarction in patients with both known and unknown time of onset of neurological deficit (wake-up stroke). In this study, using EPI-FLAIR, the mean of the SIR value of $>1.3$ consistently identified patients with time of onset to MRI of $>4.5$ hours concordant with the result of recently published reports with use of FLAIR and EPI-FLAIR.

In this cohort of patients, we found that EPI-GRE is comparable with conventional GRE in terms of image quality and detection of intracranial hemorrhage in a subset of patients (n=30) but with a 3-fold reduction in scan time. GRE has been successfully used in acute stroke protocol to detect acute parenchymal hemorrhage with comparable accuracy with CT. In our study, both EPI-FLAIR and EPI-GRE were able to detect intra-arterial clot concordant with the use of FLAIR and GRE.

Finally, our results suggest that combined CE-MRA and DSC perfusion is feasible, resulting in significant reduction in scan time as previously suggested. We used a modified 2-phase contrast injection scheme to perform both CE-MRA and DSC perfusion imaging, without the need for additional contrast.

Time-of flight MRA has been traditionally used in routine stroke protocols to evaluate the status of neck and brain arteries. Some of the potential disadvantages of time-of flight MRA include long acquisition time in the order of 5 to 7 minutes and potential for spin saturation and phase dispersion secondary to slow or turbulent flow, which in turn can result in overestimation of arterial stenosis.
By introduction of MR scanners with higher gradient performance and fast imaging tools, such as generalized auto-calibrating partially parallel acquisition, CE-MRA images of the entire head and neck can be obtained with millimeter voxel sizes and acquisition times on the order of 20 sec as shown in this study and others. Despite its relatively lower spatial resolution in comparison with time-of-flight, the described CE-MRA technique seems to be sufficient for accurate evaluation of proximal intracranial arteries.

We were able to reduce image acquisition time because of numerous recent technological advances in MRI, including introduction of fast imaging tools such as EPI and parallel acquisition techniques such as generalized auto-calibrating parallelly parallel acquisition. Rapid acquisition time in EPI is made possible by rapid gradient switching that permits the acquisition of all frequency and phase encoding steps during a single pulse cycle. The addition of parallel imaging has a 2-fold synergistic effect to EPI: (1) further enhancement of the acquisition speed because of undersampling in phase or slice-encoding direction and (2) mitigation of the geometric distortion and susceptibility artifacts commonly associated with long echo-train sequences, such as EPI.

In addition, during the past decade improvements in MRI hardware technology, including introduction of multicoil technology for better signal reception and higher magnetic fields (23T) with higher afforded signal-to-noise ratio, have increased the efficiency to apply fast imaging tools. Because the described technology is commercially available, fast and effective MRI protocols are on the horizons for the next decade with comparable acquisition time and proficiency with other cross-sectional techniques, such as CT.

In this study, we obtained a comprehensive MR stroke protocol in 6 min, a 4-fold reduction in scan time instead of conventional MR stroke imaging. For comprehensive stroke centers that choose MRI as their imaging modality, the described protocol allows for a comparable acquisition time and efficiency with that of multimodal CT protocol, while taking advantage of superior tissue resolution and higher sensitivity and specificity for delineation of infarction afforded by MRI. Another major advantage of MR instead of CT is lack of radiation. This is particularly important for patients who need repeat examination after the treatment or have change in their neurological examination (35% in this study), in whom the repeat CT can be prohibitive because of accumulated radiation dose. MR interpretation is more challenging than noncontrast CT, and this should be considered as a potential limitation in the settings where different levels of trainees or readers are expected to provide initial interpretation. Another potential disadvantage of MRI is the potential time-delay required to complete the MR safety questionnaire to exclude an MRI contraindication in acute stroke setting. This study has several limitations, including (1) a relatively small sample size drawn from a single institution possibly introducing a sample bias, (2) limited availability and technical demands because of the need of 3.0T MR scanners and multicoil technology that is required for parallel imaging. This technology may not be available in a broad clinical setting, (3) requirement for Gadolinium contrast excludes some patients with contraindications to contrast, (4) specific design of the described imaging paradigm for detection of acute stroke may result in underdetection of other pathologies and stroke mimics (we tried to minimize this limitation by inclusion of only patients with a high suspicion for AIS and National Institutes of Health Stroke Scale >3 that were screened by the stroke neurology team), (5) the subjective/arbitrary nature of our image quality scoring system, and (6) dilution of contrast to perform DSC perfusion, which may affect the perfusion analysis. Although we did not perform a comparative analysis between the diluted and nondiluted contrast DSC in this study, high image quality scores and interobserver agreement in defining the perfusion abnormality indicate that lower contrast-dose was not a major limiting factor for the diagnostic interpretation. Broader clinical studies are required to investigate the application of diluted DSC perfusion further, in particular if quantitative analysis is needed.

In summary, a 6-minute multimodal MRI protocol is feasible for the evaluation of patients with AIS and can result in significant reduction in scan time rivaling that of the multimodal CT protocol. This paradigm can be used in comprehensive stroke centers to enhance imaging-based research in acute stroke; however, additional clinical studies are required to determine the clinical role and effect of this protocol in diagnosis and evaluation of patients with AIS.

Disclosures

None.

References

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The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://stroke.ahajournals.org/content/45/7/1985

Data Supplement (unedited) at:
http://stroke.ahajournals.org/content/suppl/2014/06/10/STROKEAHA.114.005305.DC1

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SUPPLEMENTAL MATERIAL

Supplement to Image acquisition:

A combination of a 16 element array coil [(head n=12), (neck n=4)] were used for signal reception. The coil design allowed for application of parallel acquisition in both the phase and slice encoding directions.

Localizer images were obtained using a fast multiplanar gradient echo (FLASH: Fast Low Angle Shot) sequence (TR/TE: 8.6/4ms, flip-angle: 20º; field of view: 35 cm, matrix size: 256 mm; 3 slice groups (sagittal, coronal, transverse) each containing 3 x 3mm slices, acquisition time 15 sec). Using a large field-of-view allowed for positioning of both head MRI and neck MRA without the need for additional localizers.

For CE-MRA, a fast 3D spoiled-GRE sequence was performed just before the perfusion imaging to obtain a near isotropic submillimeter voxel size covering from the aortic arch to the cranial vertex during a 22 second acquisition. A centric ordering K-space was used for CE-MRA to minimize intracranial venous contamination. A modified 2-phase contrast injection scheme was 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)] that is normally used routinely for MR perfusion was diluted with normal saline to a total 40 ml volume. Using a timing bolus, a total of 3 ml of contrast solution was injected at 1.5 ml/s to determine the transit time from the arm vein to the cervical carotid arteries. Then, the contrast solution divided in to halves, the first half was injected at 1.5 ml/s for the CE-MRA acquisition and the 2nd half was injected at 5 ml/s for the MR perfusion scan which was performed at the end (Figure 1). An acquisition time of 30 seconds for timing bolus in addition to 30 seconds for calculation of transit time were added to overall image acquisition time.

Conventional FLAIR was obtained using a spin-echo sequence during a 3 minute acquisition time with the following sequence parameters (TR/TE: 9000/88 ms; inversion time 2500ms; flip-angle: 150º; field of view: 22 cm, matrix size: 256 mm; 35 x 4mm slices, GRAPPA x2).

Conventional GRE was obtained using a gradient-echo sequence during a 2:30 minute acquisition time with the following sequence parameters: TR/TE: 900/20 ms; flip-angle: 90º; field of view: 22 cm, matrix size: 256 mm; 35 x 4mm slices, GRAPPA x2.
## Supplemental Tables:

### Table-I: Perfusion-diffusion mismatch classification using modified DEFUSE criteria

| Mismatch classification | Observer-1 | | | |
|------------------------|------------|------------|------------|
|                        | Observer-2 | Mismatched | Matched    | Reperfused |
| Mismatched             |            | 21         | 1          | 1          |
| Matched                |            | 0          | 48         | 1          |
| Reperfused             |            | 0          | 0          | 12         |
| Total                  | 21 (25%)   | 49 (58%)   | 14 (17%)   |

Perfusion-diffusion ratio was < 0.7, 0.7 ≤ 1.8, and ≥ 1.8 for reperfused, matched and mismatched patients respectively. The interobserver agreement + 95%CI for the mismatch classification was $k = 0.92$, 0.87 - 0.94.

### Table-II: Distribution of arterial stenoses detected by CE-MRA

<table>
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<tr>
<th>Arterial segment</th>
<th>High grade stenosis</th>
<th>Occlusion</th>
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</thead>
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<td>Common carotid artery</td>
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<td>1</td>
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<tr>
<td>Cervical ICA</td>
<td>12</td>
<td>4</td>
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<tr>
<td>Cervical Vertebral artery</td>
<td>9</td>
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</tr>
<tr>
<td>Pterocavernous ICA</td>
<td>3</td>
<td>5</td>
</tr>
<tr>
<td>Supraclinoid ICA</td>
<td>5</td>
<td>2</td>
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<tr>
<td>Middle cerebral artery</td>
<td>M1 (5), M2 (3)</td>
<td>M1 (6), M2 (7)</td>
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<td>Anterior cerebral artery</td>
<td>A1 (0), A2 (1)</td>
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<td>9</td>
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<tr>
<td>Brain</td>
<td>26</td>
<td>29</td>
</tr>
</tbody>
</table>

ICA: cervical internal carotid artery
M1 and M2 are 1st and 2nd order branch of middle cerebral arteries
A1 and A2 are 1st and 2nd order branch of anterior cerebral arteries
P1 and P2 are 1st and 2nd order branch of posterior cerebral arteries

Reference: