Angiographic Reconstructions From Whole-Brain Perfusion CT for the Detection of Large Vessel Occlusion in Acute Stroke

Andreas M.J. Frölich, MD; Marios N. Psychogios, MD; Ernst Klotz, Dipl-Phys; Ramona Schramm; Michael Knauth, MD; Peter Schramm, MD

Background and Purpose—Multimodal CT imaging consisting of nonenhanced CT, CT angiography (CTA), and whole-brain volume perfusion CT is increasingly used for acute stroke imaging. In these patients, presence of vessel occlusion is an important factor governing treatment decisions and possible endovascular therapy. The goal of this study was to assess the value and diagnostic accuracy of angiographic thin-slice volume perfusion CT reconstructions for the detection of intracranial large vessel occlusion in patients with stroke.

Methods—Fifty-eight patients with acute stroke received nonenhanced CT, CTA, and volume perfusion CT. All images were obtained on a 128-slice multidetector CT scanner. CT angiographic axial and coronal maximum-intensity projections of the head were reconstructed from conventional CTA and from the peak arterial scan of the volume perfusion CT data set (4-dimensional CTA). Images were assessed for the presence of intracranial vessel occlusion. The distribution of ischemic lesions was analyzed on perfusion parameter maps.

Results—On CTA, 30 patients (52%) had a total of 33 occluded intracranial artery segments. Twenty-eight occlusions were identified on 4-dimensional CTA, resulting in an 85% sensitivity with a positive predictive value of 97%. When combined with an analysis of the perfusion parameter maps, sensitivity of 4-dimensional CTA increased to 94% with a positive predictive value of 100%.

Conclusions—In acute stroke, angiographic volume perfusion CT reconstructions may be a feasible option to detect intracranial arterial occlusion and evaluate patients for endovascular therapy. Sensitivity for detection of intracranial arterial occlusion can be increased by simultaneous assessment of perfusion parameter maps. Future studies should assess whether time-resolved 4-dimensional CTA may offer additional diagnostically relevant information compared with single-phase CTA. (Stroke. 2012;43:97-102.)

Key Words: brain imaging ▪ CT perfusion ▪ stroke ▪ thrombosis ▪ vessel occlusion

In acute ischemic stroke, rapid detection of the location and extent of infarction is essential for making treatment decisions. One of the diagnostic key elements guiding the therapeutic approach in the acute phase of an ischemic stroke is the presence or absence of intracranial large vessel occlusion (LVO). For patients with intracranial LVO, the prognosis is expected to be worse and different endovascular recanalization techniques have shown the potential to improve outcome, even outside standard time windows for intravenous thrombolytic therapy. In addition, patients with LVO are less likely to benefit from intravenous therapy than patients with stroke without LVO, underlining the importance of detecting LVO as soon as possible. In a recent North American study, almost half of patients with acute ischemic stroke had an occlusion of a large intracranial artery. Although it cannot be inferred from this ratio that every second patient with stroke will need endovascular treatment and indeed the number is likely to be significantly lower, diagnostic information on the presence or absence of LVO will still be one of the most important factors in making a decision for or against an endovascular approach in the acute setting. Considering that clinical scores such as the National Institutes of Health Stroke Scale often do not adequately predict the presence of LVO, urgent imaging of the intracranial vascular system has become a standard at many stroke centers.

Options for visualizing the intracranial vasculature are included in standard stroke imaging protocols, which are based either on multimodal CT or MRI imaging. Multimodal CT consists of nonenhanced CT, perfusion CT, and CT angiography (CTA) and is increasingly selected for diagnostic imaging in patients presenting with acute stroke.
what simplified, the rationale of this diagnostic protocol is to rule out or demonstrate hemorrhagic stroke or clearly visible large infarcts (nonenhanced CT), define the location and extent of ischemic and salvageable brain tissue (perfusion CT), and assess for a possible underlying vessel occlusion or other vascular pathology (CTA).

For the detection of acute LVO, CTA offers excellent sensitivity and specificity. It has previously been shown that angiographic reconstructions from perfusion CT acquisitions may offer image quality comparable to traditional CTA, although it has been stated that images were grainier and showed less detail. Another previous study demonstrated good correlation for CTA and perfusion CT for vascular pathology with a reported sensitivity of 90% for all observed vascular changes (occlusion, stenosis, aneurysms, vascular malformations) in patients examined for suspected ischemic stroke or vasospasm. Another previous study was designed to demonstrate the sensitivity of 4-dimensional CTA examinations of the second half of the study population and CTA reconstructions for the other half of the population were provided. To reduce recall bias, the remaining CTA images of the first half and 4-dimensional CTA examinations of the second half of the study population were analyzed in randomized order after a break of 2 weeks. Vessel occlusion was defined as a focal loss of vascular opacity without distal vessel delineation. Specifically, the presence or absence of occlusion of the intracranial internal carotid artery, the proximal (A1) and distal (A2) segment of the anterior cerebral artery, the M1 and M2 segments of the middle cerebral artery, the P1 and P2 segments of the posterior cerebral artery, and the basilar artery were assessed. The intracranial vertebral arteries were frequently not covered by the 4-dimensional CTA scan range and were therefore excluded from analysis. In addition, image quality was rated on a 4-point scale (1, nondiagnostic; 2, diagnostic with limitations; 3, diagnostic with minor limitations; 4, excellent) assessing the visibility of the distal M2 segments. Relative distributions of vessel occlusions were obtained and diagnostic sensitivity, specificity as well as positive and negative predictive values of 4-dimensional CTA were calculated with CTA functioning as the standard of reference.

In patients with anterior circulation occlusion confirmed on angiography (n=6), biplanar angiographic images (Axiom Artis dBA; Siemens, Erlangen, Germany) were assessed for the presence of anterograde opacification distal to the occlusion. The corresponding 30 consecutive VPCT spiral scans were assessed by a different reader for opacification occurring in a retrograde fashion at the distal thrombus end.

Presence or absence of a perfusion deficit on the VPCT parameter maps was assessed in a separate reading session. Readers were presented with commonly used parameter maps (cerebral blood volume, cerebral blood flow, and time to peak) and were asked to assess the presence of an ischemic stroke (defined as a visual abnormality on cerebral blood volume and cerebral blood flow maps) and, if present, assign the perfusion deficit to 1 of the vascular territories defined previously. To assess whether the diagnostic yield of 4-dimensional CTA could be improved, raters were asked to re-evaluate the corresponding 4-dimensional CTA images for an underlying vascular occlusion in direct comparison with the perfusion parameter maps. The site of LVO was recorded and separate values for sensitivity, specificity, positive predictive value, and ...
negative predictive value were calculated for the combined approach.

The Wilcoxon signed ranked test was used to compare the image quality ratings; P<0.05 was used as the level of significance. All statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS 16.0; SPSS Inc, Chicago, IL). Effective dose values were calculated by multiplying dose–length–product values with published conversion factors.

**Results**

Of 62 patients identified, 4 were excluded because of lack of a complete imaging data set. Fifty-eight patients were included for analysis. Mean age was 70.5 years (range, 30.3–88.5 years) and female-to-male ratio was 25:33. Median National Institutes of Health Stroke Scale score was 12 (range, 4–30; mean, 13.6). Time from symptom onset was available in 30 of 58 patients with a mean 242 minutes (SD, 142 minutes) between symptom onset and multimodal CT; the remaining 28 patients presented with unknown time of symptom onset <24 hours. The effective dose was 5.3 mSv for the VPCT scan, 1.1 mSv for the craniocervical CTA portion (20 cm from vertex), and 2.1 mSv for the remaining more caudal CTA range (15 cm).

Table 1 shows the number and site of occlusions detected by 4-dimensional CTA and CTA in the 928 vessel segments analyzed in this study. Of the 58 patients included, 30 (51.7%) had an occlusion of an intracranial artery segment on CTA. Three patients (10%) had an occlusion of multiple intracranial vessels. When assessing the presence or absence of intracranial large vessel occlusion, 4-dimensional CTA offered an 84.9% sensitivity and a positive predictive value of 96.6% when compared with CTA (Table 2; Figure 1). In addition, 9 patients had an occlusion of an extracranial artery and 5 patients had a cervical carotid stenosis without occlusion as described in the final multimodal CT diagnostic report. Subgroup analysis of patients with anterior circulation occlusion and catheter angiography (n=6) revealed collateral filling to the distal thrombus end in a retrograde fashion on

<table>
<thead>
<tr>
<th>Vessel Occlusion</th>
<th>CTA</th>
<th>4D-CTA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients with intracranial LVO</td>
<td>30 (51.7%)</td>
<td>27 (46.6%)</td>
</tr>
<tr>
<td>Total no. of LVOs</td>
<td>33</td>
<td>29</td>
</tr>
<tr>
<td>Site of occlusion</td>
<td>CTA</td>
<td>4D-CTA</td>
</tr>
<tr>
<td>Intracranial ICA</td>
<td>8</td>
<td>14%</td>
</tr>
<tr>
<td>A1</td>
<td>0</td>
<td>0%</td>
</tr>
<tr>
<td>A2</td>
<td>0</td>
<td>0%</td>
</tr>
<tr>
<td>M1</td>
<td>12</td>
<td>21%</td>
</tr>
<tr>
<td>M2</td>
<td>9</td>
<td>16%</td>
</tr>
<tr>
<td>P1</td>
<td>1</td>
<td>1.7%</td>
</tr>
<tr>
<td>P2</td>
<td>1</td>
<td>1.7%</td>
</tr>
<tr>
<td>Basilar artery</td>
<td>2</td>
<td>3.4%</td>
</tr>
</tbody>
</table>

CTA indicates CT angiography; 4D-CTA, 4-dimensional CT angiography; LVO, large vessel occlusion; ICA, internal carotid artery; A1, A2, M1, M2, P1, P2, segments of the anterior, middle, and posterior cerebral arteries.

4-dimensional CTA in 5 cases (80%; Figure 2). None of these demonstrated anterograde flow across thrombus on angiography.

VPCT parameter maps (cerebral blood volume, cerebral blood flow, time to peak) showed an ischemic lesion in 36 of 58 patients (62%; Table 3). The second rating of the 4-dimensional CTA data with simultaneous access to the perfusion parameter maps led to a different final decision regarding LVO in 5 of 58 cases (8.6%). In 1 patient with an M2 occlusion, an additional A2 occlusion that had been missed on both CTA and 4-dimensional CTA in the initial rating was identified with the combined approach (parameter maps and 4-dimensional CTA together) and could be retrospectively confirmed on CTA. The overall sensitivity of the combined approach for detection of LVO was 94.1% with a positive predictive value of 100% (Table 2).

In our study population, the median National Institutes of Health Stroke Scale score was higher in patients with intracranial LVO (17; range, 6–30) than in patients without intracranial LVO (8; range, 4–24). Finally, the median quality rating on an ordinal scale from 1 to 4 was 4 for both CTA (mean, 3.74) and 4-dimensional CTA (mean, 3.70). There was no statistically significant difference in the observed image quality (P=0.545).

Although image quality ratings were comparable for both examinations, vessel contours appeared slightly sharper on CTA when directly compared with 4-dimensional CTA (Figure 1). This is almost certainly due to the significantly lower spatial resolution and sampling in the z-direction of the 4-dimensional CTA data as compared with the standard CTA: 1.5 mm every 1.0 mm versus 0.75 mm every 0.4 mm. This is not a principal technical limitation, however, but rather due to the retrospective nature of our study. Images with the same z-resolution as in standard CTA can be reconstructed from the original VPCT raw data. Because the
primary goal of this study was to assess large vessel occlusion, we had decided at the beginning of data acquisition to keep the number of 4-dimensional CTA images at a more manageable level (2850 versus >7000 per study).

Discussion

In patients presenting with acute stroke, multimodal CT is a widely available, robust, and comparatively inexpensive imaging modality, which allows detection of acute ischemia and vascular pathology. Obtaining angiographic 4-dimensional CTA reconstructions from VPCT may be an option to assess acute intracranial large vessel occlusion. The present study shows that arterial phase 4-dimensional CTA reconstructions offer image quality comparable to CTA and can be used to assess intracranial LVO in patients with stroke with high sensitivity and positive predictive value. Because 4-dimensional CTA is just another reconstruction of the VPCT data, it is easy to include into the routine diagnostic workflow.

Our data show that the diagnostic accuracy of 4-dimensional CTA can be improved by simultaneous assessment of the perfusion parameter maps. This combined approach further improved sensitivity (94%) and positive predictive value (100%) for the detection of LVO in comparison to CTA. In 1 patient with an occluded M2 segment, coexisting occlusion of the ipsilateral A2 segment had been missed on both CTA and 4-dimensional CTA ratings alone and was only detected after an abnormality was seen on the perfusion parameter maps, underlining the use of VPCT to aid in stroke diagnosis.

Our results do not suggest, however, that standard CTA can be omitted. In the present study, 9 patients had an occlusion of a cervical artery not depicted in the used intracranial reconstructions, which may affect treatment decision regarding intravenous or endovascular thrombolysis. Figure 1 shows an example of basilar artery occlusion in which the extent of proximal involvement cannot be identified on VPCT because the scan volume was placed largely supratentorially, probably because an anterior circulation lesion was suspected clinically. Previous investigators have observed that in some patients, the dynamic attenuation of intracranial vessels over time may indirectly point to a more proximal site of vessel occlusion outside the VPCT scan range.\textsuperscript{13} We have made similar observations; however, we deem it unlikely that these indirect findings will provide enough diagnostic certainty to guide clinical decisions. Thus, cervical CTA including the carotid bifurcation will remain mandatory to detect relevant extracranial pathology and allow access planning for intra-arterial procedures. Increasing the VPCT z-coverage by approximately 5 cm over the roughly 10 cm used in our study would probably always cover the complete intracranial vasculature but would also increase the

Figure 1. Examples of CTA and 4-D-CTA scans demonstrating intracranial large vessel occlusion. A–B, Coronal MIP reconstructions of CTA (A) and 4D-CTA (B) from a patient with a proximal occlusion of a left M2 segment (asterisk). In addition, there is faint proximal contrastation of a temporal M2 branch (arrow) consistent with subtotal occlusion. C–D, Coronal MIP reconstructions of CTA (C) and 4D-CTA (D) from a patient with distal basilar and proximal left posterior cerebral artery occlusion (arrow). CTA indicates CT angiography; 4D-CTA, 4-dimensional CT angiography; MIP, maximum intensity projection; M2, middle cerebral artery branch.

Figure 2. Early-arterial and late-arterial phases of 4D-CTA. Four-dimensional CTA images from a patient with right-sided carotid T-occlusion. A, Peak arterial phase demonstrating lack of opacification of the right ICA, M1, and M2. B, Late-arterial phase image shows delayed opacification of the distal ICA up to the proximal thrombus end as well as opacification of the distal M2 segments consistent with collateral flow. 4D-CTA indicates 4-dimensional CT angiography; ICA, internal carotid artery; M1, M2, middle cerebral artery branches.
Finally, correlation of 4-dimensional CTA data with imaging and clinical outcome may show whether 4-dimensional CTA could be of value in selecting patients for intravenous or intra-arterial therapy and its possible role as an imaging biomarker should be further assessed.

In conclusion, 4-dimensional CTA is a promising additional option for the assessment of intracranial large vessel occlusion in patients presenting with acute ischemic stroke. Joint analysis of 4-dimensional CTA and perfusion parameter maps increases the sensitivity for detecting vessel occlusion. Complete visualization of the cervical vasculature by CTA or other modalities will usually still be required in most patients with stroke to detect coexisting extracranial pathology and 4-dimensional CTA is likely to complement rather than replace intracranial CTA in the foreseeable future. Additional research is required to maximize the diagnostic potential of 4-dimensional CTA in patients with stroke; especially promising applications include assessment of collateral flow, distinction of partial from complete occlusions, and delineation of intravascular thrombus.

Sources of Funding
The department has a research agreement with Siemens AG, Forchheim, Germany.

Disclosures
E.K. is a full-time employee of Siemens AG, Forchheim, Germany. P.S. received speaker’s honoraria from Siemens AG, Forchheim, Germany.

References


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Stroke. 2012;43:97-102; originally published online October 27, 2011;
doi: 10.1161/STROKEAHA.111.630954
Stroke is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0039-2499. Online ISSN: 1524-4628

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