ON-LINE APPENDIX: ADDITIONAL APPLICATIONS OF TIME-VARIANT MULTIPHASE CT ANGIOGRAPHY COLOR MAPS

Detailed Multiphase CT Angiography Acquisition Technique

Multiphase CTA consists of 3 phases in all patients and was acquired as described previously.[1] After injection of 80 mL of contrast material (68% ioversol, Optiray 320; Mallinckrodt, St. Louis, Missouri) at a rate of 5 mL/s followed by a 50-mL saline bolus at 6 mL/s, images were acquired with a section thickness of 0.625 mm. The first phase, which covers the cervical and intracranial vasculature (aortic arch-to-vertex CTA), is triggered by bolus-tracking and timed to occur during the peak arterial phase. The second and third phases cover only the intracranial vasculature (skull base to vertex) and are acquired in the peak venous and late venous phases, ie, with 10- and 18-second delays. Scan duration is <7 seconds for the first phase and 3.4 seconds for the second and third phases.[1] For descriptive review, color-coded axial summation maps and coronal and sagittal reformations were reviewed on a workstation using the ColorViz module (GE Healthcare, Milwaukee, Wisconsin). The readers had access to information about the clinically affected side, baseline NIHSS score, and the time from symptom onset to imaging. The readers assessed the following imaging features: the presence, side, and location of any intracranial occlusion (single or multiple versus none); the thrombus itself (permeability); blood flow proximal and distal to the thrombus; and pial artery (collaterals) filling delay and extent. The average scan-interpretation time ranged within seconds (<10 seconds).

Detection of Multiple Intracranial Thrombi in the Same Vascular Territory

While detecting occlusions in different vascular territories is feasible with single-phase CTA and CTP, detection of occlusions distal to a large-vessel occlusion is often not possible; the proximal occlusion prevents sufficient contrast flow in the downstream territory to allow visualization on single-phase CTA and causes signal alterations in the entire ischemic territory on CTP maps so that downstream occlusions are not easily appreciated. mCTA can visualize multiple sequential thrombi in the same vascular territory through segmental contrast-sparing in a vessel with connected upstream flow alterations (Fig 7 and On-line Fig 1). Usually, the vasculature distal to an occlusion is displayed in 1 color. Rapid color changes within pial arteries distal to the primary occlusion (particularly a red-green-blue sequence from proximal to distal [On-line Fig 1] indicative of a blood flow gradient) usually precede distal occlusions. These distal occlusions can be appreciated by experienced readers on conventional mCTA images, too, but are more conspicuous on ColorViz.

Differentiating ICA Occlusions from Slow Flow and Pseudo-Occlusions

Differentiating a carotid occlusion from a pseudo-occlusion is useful in assessing recurrent stroke risk and in planning carotid endarterectomy or stent placement. It is, however, a challenge to differentiate these 2 entities without conventional angiography. Although multiphase imaging has been shown to be helpful in some studies,[2,3] its accuracy in differentiating true occlusions from pseudo-occlusions is low.[4] The faint intraluminal opacification caused by slow flow often does not sufficiently stand out against the nonopacified vessel lumen and soft tissues of the neck. Color-coded mCTA maps display slow flow in blue or green, which can be unambiguously appreciated. ICA pseudo-occlusions are therefore much more conspicuous when assessed using ColorViz (On-line Fig 2).

Assessing Intracranial Stenoses

Atherosclerotic intracranial stenoses are responsible for 5%–10% of acute ischemic strokes in whites and up to 33% of strokes in the Asian population.[5,6] Assessing the severity of intracranial stenoses is important because severe, flow-limiting stenoses might benefit from endovascular intervention and/or blood pressure management.[7] Single-phase CTA can help assess the morphology of the intracranial stenosis by assessing the degree of narrowing of the target artery. ColorViz summation maps can, in addition, show subtle blood flow patterns in the poststenotic arterial segment, thereby assessing the degree of stenosis better. On ColorViz, the vasculature proximal to a stenosis is red (indicating a zero-phase delay), whereas filling in the downstream vasculature is delayed. The color of pial artery filling in the poststenotic arterial segment and in the pial arteries distal to the stenosis provides an assessment of the degree of stenosis, which is more granular than a single-phase CTA or even a CTP (On-line Fig 3).

Identifying Ante- and Retrograde Flow Patterns in Pial Arteries Distal to Stenosis/Occlusion

Antegrade flow distal to the site of an occlusion can predict success with intravenous alteplase treatment.[8] As opposed to mCTA, neither single-phase CTA nor CTP provide information about the direction of blood flow in pial arteries. In the color-coded summation map, a color sequence of red (no delay), green (1-phase delay), and blue (2-phase delay) just distal to the occlusion from proximal to distal indicates antegrade flow (On-line Fig 4), while a reverse (blue-green-red) blood flow pattern indicates retrograde blood flow through pial collaterals (On-line Fig 5). These pial artery flow patterns can reveal the degree of thrombus permeability, with antegrade flow immediately distal to a thrombus suggestive of a permeable thrombus.

Assessing Thrombus Permeability

Permeable intracranial thrombi are associated with improved functional outcome and higher intravenous alteplase success rates.[9-12] Thrombus permeability on CTP can be assessed using Tmax maps, which assess filling of contrast within pial arteries distal to the occlusion; the technique, however, requires complex postprocessing. Thrombus permeability on single-phase CTA is assessed by measuring thrombus attenuation on noncontrast CT and comparing it with that on single-phase CTA images.[9] A permeable thrombus on ColorViz will appear in color because of blood flow within the thrombus. Depending on the degree of thrombus permeability, the thrombus will appear either faint red, green, or blue (On-line Fig 6). Assessing antegrade flow distal to the thrombus (see the section above) also helps in assessing thrombus permeability. Nonpermeable thrombi, on the other hand, may not be displayed in color on ColorViz.

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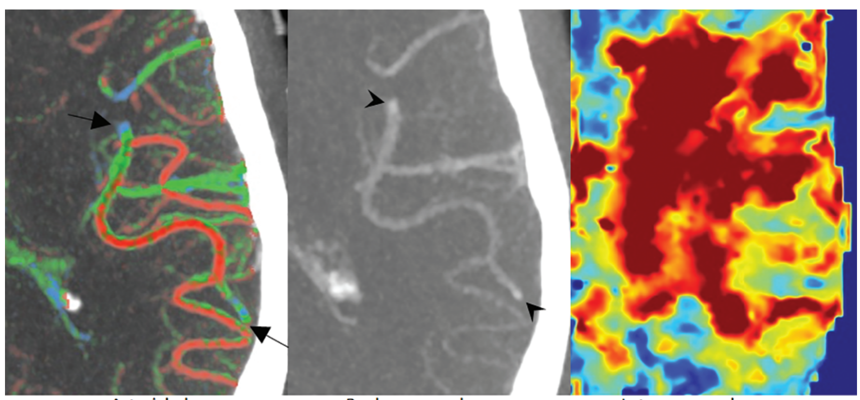
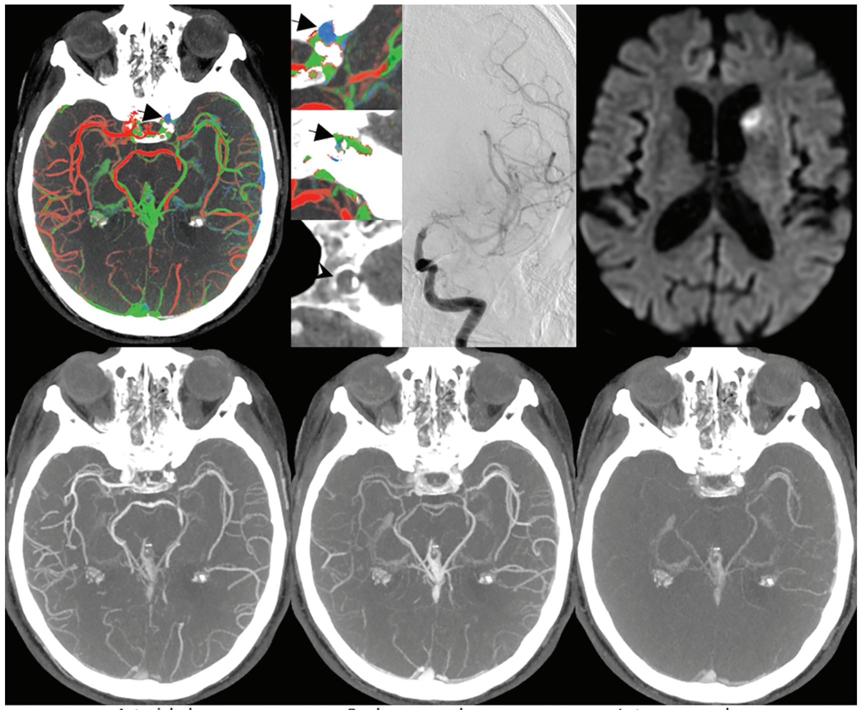
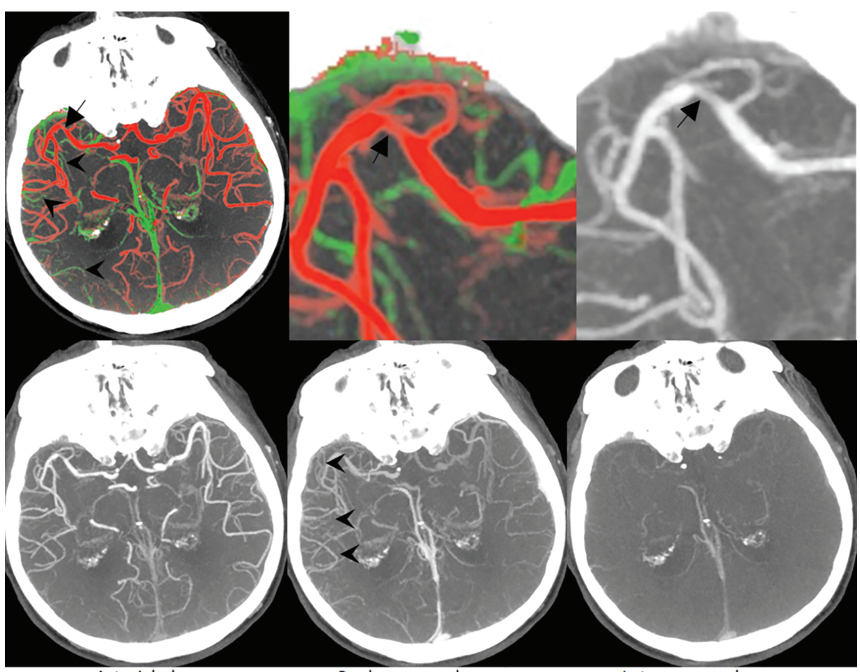


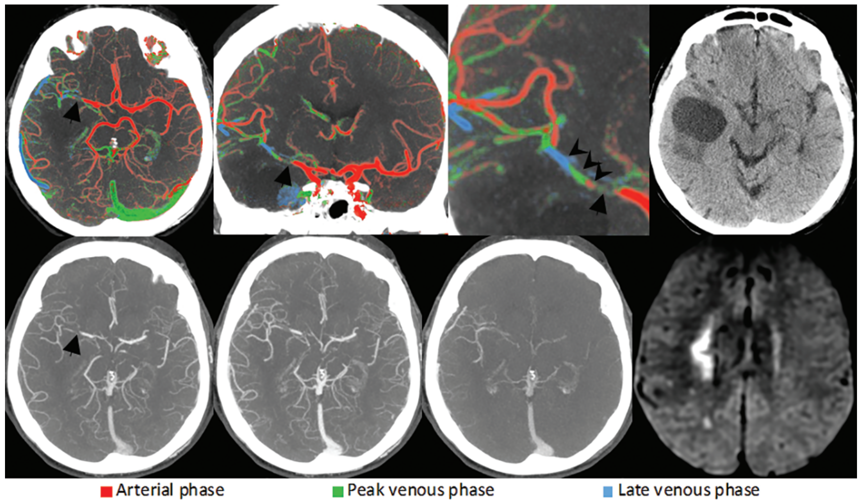
ON-LINE FIG 1. Magnified view of Fig 7 showing a part of the left temporal lobe. The abrupt ending of small peripheral arteries (*black arrows*) with preceding color changes indicates the presence of several thrombi within the left MCA territory. As is the case here, reduced blood flow within the pial artery proximal to the occlusion can often be seen through a typical color gradient of red, green, and blue proximal to the occlusion. The occlusions are also visualized in the late venous phase of the conventional mCTA images (*arrowheads*). CTP maps (time-to-maximum, *right image*) provide no information about the number and distribution of occlusions in the downstream ischemic vascular territory.



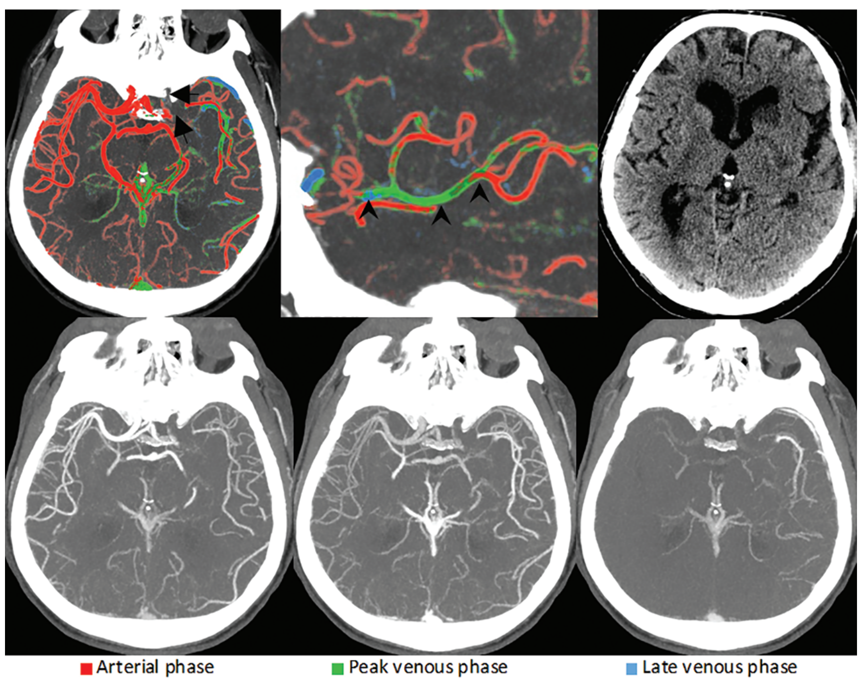
ON-LINE FIG 2. Left-sided intracranial ICA pseudo-occlusion with slow flow in the petrous and cavernous ICA proximal to the occlusion. The left cavernous and petrous ICA is blue and green (*arrows*), meaning that slow intraluminal flow is present. Single-phase CTA shows no opacification of the vessel (*arrowhead*) and is therefore not helpful for distinguishing pseudo-occlusion/slow flow from real occlusion. In the conventional mCTA images (*lower row*), opacification of the proximal intracranial ICA can be seen, but it is less conspicuous. The patient underwent mechanical thrombectomy (*third image*, *upper row*); follow-up MR imaging after 24 hours (*upper right image*) reveals a small left-sided caudate head infarct.



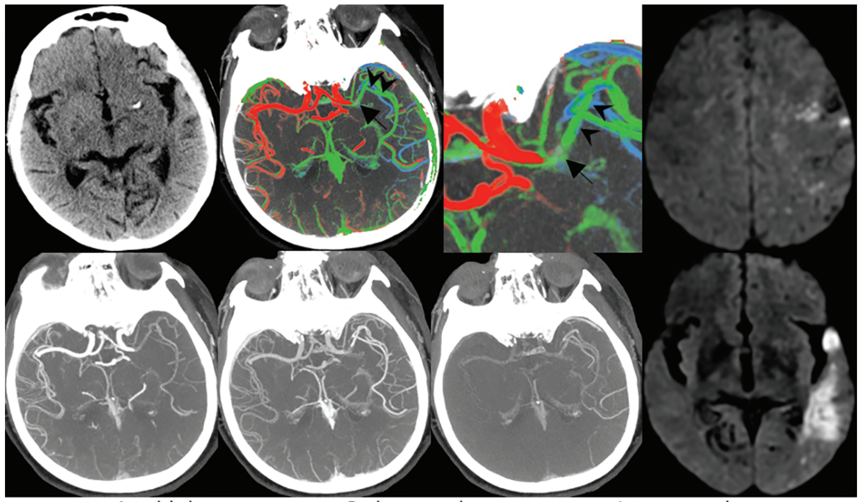
ON-LINE FIG 3. Right-sided proximal M2 stenosis (*arrows*) with green vessels in the downstream territory, indicating a 1-phase delay (*arrowheads upper row*). The delay can be appreciated in the conventional mCTA images as well (*arrowheads, lower row*), but it is less apparent compared with the color-coded summation maps.



ON-LINE FIG 4. Right-sided M1 segment MCA occlusion (*arrows*) with antegrade flow distal to the thrombus. The red, green, and blue color sequence immediately distal to the occlusion (*arrowheads*) indicates forward flow distal to the thrombus, suggestive of thrombus permeability. On conventional mCTA images (*lower row*), the flow direction cannot be determined. Baseline noncontrast CT (*upper right image*) shows a right-sided cystic temporal lesion but no early ischemic changes. The patient received intravenous alteplase. Follow-up MR imaging after 24 hours (*lower right*) reveals a small infarct in the right corona radiata.



ON-LINE FIG 5. Left-sided ICA occlusion (*arrows*) with a retrograde flow pattern distal to the occlusion. Sagittal color-coded reformations (*middle image*, *upper row*) show a blue-green-red color sequence (*arrowheads*) distal to the thrombus, indicating retrograde filling of the vessel from nearby collaterals and a nonpermeable thrombus. Conventional mCTA images (*lower row*) do not provide this information. The patient underwent mechanical thrombectomy. Follow-up CT after 24 hours (*upper right*) shows a small infarct in the left caudate head and lentiform nucleus.



ON-LINE FIG 6. Left-sided M1 segment MCA occlusion with permeable thrombus and good pial artery filling in the affected territory. The faint green color depicting the thrombus (*arrows*) indicates thrombus permeability, which explains the mild (1-phase) filling delay in the downstream vasculature displayed in green (*arrowheads*). Thrombus opacification can also be seen in the conventional mCTA images (*lower row*), but it is less obvious. The patient was treated with mechanical thrombectomy. Follow-up MR imaging after 24 hours (*upper and lower right*) shows infarction of the left M2 and M3 area and only a few small, scattered infarcts in the remaining MCA territory.

On-line Table: Baseline characteristics of the PRoveIT patient cohort

Patient Baseline Characteristics ($n = 596$)	
Sex (%) (No.)	52.3% (312) male; 47.5% (283) female; 0.2% (1) not known
Patient age (median) (IQR) (yr)	72 (62.5–80)
NIHSS score	13 (6–19)
Time from symptom onset to imaging (median) (IQR) (min)	114 (82–163)
ASPECTS (median) (IQR)	10 (8–10)
Treatment decision (patients with vessel occlusions only) ($n = 495$) (%) (No.)	
No treatment	0.8 (4)
IV alteplase	27.7 (137)
IV tenecteplase	2.2 (5)
EVT	19.6 (97)
EVT + IV alteplase	33.3 (165)
Antithrombotics	15.0 (74)
Not known	1.4 (7)

Note:—IQR indicates interquartile range; EVT, endovascular therapy.