Each of the recent positive endovascular trials in acute ischemic stroke used a slightly different imaging paradigm for patient selection with a common goal to identify patients with proximal vessel occlusion and a small ischemic core. A non-contrast head computed tomography (CT) ASPECTS (Alberta Stroke Program Early CT) score was used to evaluate the ischemic core; this was supplemented by CT angiogram (CTA) collateral assessment in Endovascular Treatment for Small Core and Anterior Circulation Proximal Occlusion with Emphasis on Minimizing CT to Recanalization Times (ESCAPE)\(^1\) or CT perfusion (CTP) core measurement in Extending the Time for Thrombolysis in Emergency Neurological Deficits–Intra-Arterial (EXTEND IA)\(^2\) and Solitaire With the Intention for Thrombectomy as Primary Endovascular Treatment (SWIFT PRIME) trials.\(^3\) Collaterals can influence the rate of infarct growth, and perfusion may give indirect information about this downstream collateral sustenance of ischemic tissue, although the relationship between collaterals and perfusion is uncertain.

Our objective was to explore the relationship between CTA collaterals and perfusion imaging in a cohort of patients with baseline CTA and CTP in the Interventional Management of Stroke (IMS) III trial. We hypothesized that better collaterals are associated with smaller ischemic core and larger mismatch, reflecting compensation from the collateral network preserving blood flow in the setting of acute ischemia.

**Methods**

**Study Population**

IMS III was a phase 3, randomized, open-label trial of endovascular treatment after intravenous tissue-type plasminogen activator versus...
testing for ischemic core did not show a significant difference between good and intermediate \( (P=0.3950) \) or between intermediate and poor collateral grade \( (P=0.0728) \).

### Discussion

We found that, among patients with M1/M2±internal carotid artery occlusions, better collaterals are associated with smaller ischemic cores and greater mismatch. The CTA collaterals correlated moderately well with CTP measured core with an inverse relation. The strength of our study is that we have demonstrated association between CTA collateral status and CTP parameters in a randomized trial setting.

It is well established that patients with better collaterals have smaller infarcts and better functional outcomes.\(^6\)\(^,\)\(^8\)\(^,\)\(^9\) Using this premise, the recent ESCAPE trial used collateral assessment using multiphasic CTA for patient selection without additional CTP acquisition.\(^1\) Although the EXTEND IA\(^3\) and SWIFT PRIME\(^3\) trials used CTP for patient selection utilizing automated software for CTP processing, it is important to note that there are numerous challenges for CTP imaging when performed outside of a well-controlled trial environment. These include variability in CTP acquisition and postprocessing methodology, as well as controversy, regarding readiness of CTP for prime time usage.\(^10\)

Because of the positive endovascular trials, baseline CTA has become standard of care for acute stroke workup. Although, concurrent assessment of collateral status is relatively straightforward and can provide a good estimate of ischemic core, CTA collateral evaluation is a relatively new imaging tool with heterogeneity in CTA acquisition

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**Table 1. Subject Characteristics**

<table>
<thead>
<tr>
<th>Variables</th>
<th>Total, n=53</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y, median (minimum–maximum)</td>
<td>69 (33–83)</td>
</tr>
<tr>
<td>Men, n (%)</td>
<td>27 (50.9)</td>
</tr>
<tr>
<td>NIHSS, median (minimum–maximum)(^*)</td>
<td>18 (7–40)</td>
</tr>
<tr>
<td>ASPECTS, n (%)</td>
<td></td>
</tr>
<tr>
<td>0–5</td>
<td>16 (30.2)</td>
</tr>
<tr>
<td>6–10</td>
<td>37 (69.8)</td>
</tr>
<tr>
<td>Core volume, mL, median (minimum–maximum)</td>
<td>8.3 (0.0–81.6)</td>
</tr>
<tr>
<td>Hypoperfused volume, mL, median (minimum–maximum)</td>
<td>70.6 (2.1–383.4)</td>
</tr>
<tr>
<td>Mismatch ratio</td>
<td>4.9 (1.0–371.5)</td>
</tr>
<tr>
<td>Vessel occlusion, n (%)</td>
<td></td>
</tr>
<tr>
<td>ICAT</td>
<td>13 (24.5)</td>
</tr>
<tr>
<td>M1</td>
<td>37 (69.8)</td>
</tr>
<tr>
<td>M2</td>
<td>3 (5.7)</td>
</tr>
<tr>
<td>Randomized to endovascular therapy, n (%)</td>
<td>35 (66.0)</td>
</tr>
</tbody>
</table>

ASPECTS indicates Alberta Stroke Program Early Computed Tomography score; CTA, computed tomography angiogram; ICAT, internal carotid artery terminus; and NIHSS, National Institutes of Health Stroke Scale.

\(^*\)Subject missing (n=1).
and collateral grading. Our study suggests that collaterals and perfusion are measuring similar aspects of the ischemic pathophysiology. This finding is clinically relevant as CTA collateral assessment may be an alternative for CTP, potentially obviating the need for an additional CTP study.

Our study adds to the accumulating body of evidence related to association of collaterals and perfusion in acute ischemic stroke. A malignant CTA collateral profile, specific for large core volume on baseline magnetic resonance diffusion study correlated with poor outcomes. Better collateral flow measured by magnetic resonance perfusion was associated with larger diffusion–perfusion mismatch and smaller baseline diffusion-weighted imaging lesion volume. However, Bang et al found no difference in the magnetic resonance mismatch depending on the angiographic collateral grade, but did show that patients with good collaterals had larger areas of milder perfusion delay than those with poor collaterals. Similarly, Marks et al showed a relationship between angiographic collaterals and severity of magnetic resonance perfusion deficit but did not show an association between collaterals and DWI core and mismatch. A key explanation for the conflicting findings is the fact that angiographic collaterals were used in these studies, which may not necessarily quantify posterior cerebral artery middle cerebral artery collaterals.

Our study limitations include those inherent in a post hoc analysis along with a small sample size. Another important limitation is that the IMS III trial was a multi-institutional trial with significant heterogeneity in the CTP acquisition technique, although this resembles real-world circumstances. Although CTP techniques have evolved during and beyond the trial period (2006–2012), a large proportion of subjects (86%) had CTP brain coverage of <4 cm, and 95% subjects had <90-s duration of CTP acquisition. The CTA studies obtained were all single-phase acquisitions, which are dependent on bolus characteristics and can underestimate collateral status when compared with the newer multiphasic CTA techniques.

**Conclusions**

Better collaterals were associated with smaller ischemic core and higher mismatch in the IMS III trial. CTA collateral assessment and perfusion imaging identify the same biological construct about ischemic tissue sustenance.

**Disclosures**

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speaker’s bureau for Covidien (Significant). Dr Hill has received research grant from Covidien AG (Medtronic) to the University of Calgary for partial funding of the Endovascular Treatment for Small Core and Anterior Circulation Proximal Occlusion with Emphasis on Minimizing CT to Recanalization Times (ESCAPE) trial (Significant) and has ownership interest in Calgary Scientific Inc, Imaging company (Significant). The other authors report no conflicts.

References
Association Between CT Angiogram Collaterals and CT Perfusion in the Interventional Management of Stroke III Trial
Achala Vagal, Bijoy K. Menon, Lydia D. Foster, Anthony Livorine, Sharon D. Yeatts, Emmad Qazi, Chris d'Esterre, Junzi Shi, Andrew M. Demchuk, Michael D. Hill, David S. Liebeskind, Thomas Tomsick, and Mayank Goyal

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