Inclusion or Exclusion of Intratumoral Vessels in Relative Cerebral Blood Volume Characterization in Low-Grade Gliomas: Does It Make a Difference?

SUMMARY: We assessed the influence of inclusion (method 1) and exclusion (method 2) of intratumoral vessels when determining maximum relative cerebral blood volume (rCBVmax) in 3 types of low-grade gliomas (LGGs): astrocytomas, oligoastrocytomas, and oligodendrogliomas. Method 1 yielded significantly higher mean rCBVmax than method 2. However, only method 2 demonstrated a significant (P = .026) association between rCBVmax and membership of a differently ranked histologic category. Exclusion of intratumoral vessels appears, therefore, preferable when determining rCBVmax in LGGs.

Technique and Results
Thirty-four patients with LGGs, composed of 21 ACs, 8 ODs, and 5 OAs, had DSC GE-EPI (TR = 1200 ms; TE = 40 ms; flip angle = 20°; FOV = 26 cm; matrix = 96 x 128; section thickness = 5 mm) at 1.5T (GE Signa Horizon Echospeed LX9.1; GE Healthcare, Waukesha, Wis) with a bolus of 0.1 mmol/kg of body weight of gadoterate meglumine at 5 mL/s. Color maps of rCBV were generated with FuncTool 1.9 (GE Healthcare) and analyzed by 2 neuroradiologists (H.R.J. and G.B.C., with 15 and 7 years of experience, respectively), reaching a consensus for placement of ROIs. At least 6 intratumoral ROIs with a size of 9 pixels were placed over areas showing mostly elevated CBV on color perfusion maps. Blood vessels within the tumor were identified on unprocessed perfusion images acquired between the time points of maximum arterial and venous signal intensity drop. Sections above and below intratumoral vessels were viewed to identify potentially confounding large-vessel partial volume effects. We used 2 different methods for selecting the ROI with the maximum intratumoral CBV: method 1 included and method 2 excluded ROIs situated over intratumoral blood vessels and associated partial volume effects. The maximum rCBV (rCBVmax) was then obtained by dividing the highest intratumoral CBV by the mean CBV obtained from a contralateral normal-appearing white matter ROI (Fig 1).

Mean rCBVmax obtained for each group with each method are shown in the Table. Method 1 yielded higher mean values and wider ranges than method 2 in all 3 of the histologic tumor types, particularly in OA and OD. For the patient group as a whole, there was a significant difference between mean rCBVmax obtained using each method (P < .001, Wilcoxon test). Ordinal regression was used to assess the relationship of rCBVmax and tumor histology, categorized in 3 groups (0: OA; 1: AC; 2: OD). Only method 2 showed a significant association between rCBVmax and the risk of being in a histologic category with a higher ordinate. Using method 2, the odds ratio of being in a higher category was 4.25 (95% confidence interval: 1.19-15.14 for each additional unit rCBV increment; P = .026). Method 1 did not demonstrate a significant association between rCBVmax and the risk of being in a higher category (P = .638).

Discussion
Several studies have demonstrated increased rCBV in high-grade gliomas compared with low-grade tumors, suggesting that the presence of intratumoral vessels results in an overestimation of rCBVmax.

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They plateau at 3–4 mmHg/dL. We were able to demonstrate significant association between rCBVmax on MR perfusion imaging and histologic classification as OA versus OD has not been reported previously. The relationship between rCBVmax and histologic classification as AC, OD, and AO, but only when using method 2. As a preferred technique we, therefore, recommend exclusion of intratumoral vessels when determining maximum intratumoral rCBV from GE-EPI DSC-derived data. Although beyond the scope of this work, future research will address the influence of intratumoral vessels on rCBV measurements in high-grade gliomas, which are naturally subject to greater variability.

We demonstrated that inclusion of large intratumoral vessels significantly increases rCBVmax values in all types of LGG. Their identification may be difficult on rCBV color maps alone and necessitates reviewing of unprocessed perfusion data. The diameter of intratumoral vessels clearly identifiable on GE-EPI images lies in the millimeter range (approximating the size of peripheral leptomeningeal vessels), whereas glioma neangiogenetic vessels in animal models measure between 40 and 250 µm.6

In concordance with previous investigators, we found higher rCBVmax in tumors with oligodendral elements than in purely astrocytic tumors,5 explained by the “chicken wire” hypervascularity seen in the former. Cha et al8 chose intratumoral ROIs with an automated method targeting areas of maximum signal intensity decrease during the first pass of the gadolinium-based contrast bolus. This method probably incorporated intratumoral vessels and yielded mean rCBV for ODs of 3.68. Spampinato et al12 presented one of the few reports specifying exclusion of large intratumoral vessels for ROI analysis. Their mean rCBV measurement for a mixed group of low-grade OA and OD (1.61) lies between our group mean rCBV measurements of OA (1.53) and OD (2.21) using method 2. Our findings highlight the importance of using a consistent ROI placement technique, particularly if rCBV data are to be pooled in multicenter studies. The relationship between rCBVmax on MR perfusion imaging and histologic classification as OA versus OD has not been reported previously. We were able to demonstrate significant association between maximum intratumoral rCBV values and histopathologic classification as AC, OD, and AO, but only when using method 2.

### Table 1: rCBVmax obtained using methods 1 and 2

<table>
<thead>
<tr>
<th>Method</th>
<th>All Tumors, Mean (range)</th>
<th>AC (n = 21), Mean (range)</th>
<th>OA (n = 8), Mean (range)</th>
<th>OD (n = 5), Mean (range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Method 1</td>
<td>4.01 (1.54–6.99)*</td>
<td>3.30 (1.54–6.65)</td>
<td>5.33 (3.07–6.65)</td>
<td>5.04 (2.74–6.99)</td>
</tr>
<tr>
<td>Method 2</td>
<td>1.63 (0.70–3.51)*</td>
<td>1.44 (0.70–2.46)</td>
<td>1.53 (1.26–1.94)</td>
<td>2.21 (1.47–3.51)</td>
</tr>
</tbody>
</table>

Note: AC indicates astrocytoma; OA, oligoastrocytoma; OD, oligodendroglioma; rCBV max, maximum relative cerebral blood volume.

* P < .001 for method 1 versus method 2 by Wilcoxon test.

References: