Arterial spin labeling as an ancillary assessment to postoperative conventional angiogram in pediatric moyamoya disease

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OBJECTIVE Digital subtraction angiography (DSA) is commonly performed after pial synangiosis surgery for pediatric moyamoya disease to assess the degree of neovascularization. However, angiography is invasive, and the risk of ionizing radiation is a concern in children. In this study, the authors aimed to identify whether arterial spin labeling (ASL) can predict postoperative angiogram grading. In addition, they sought to determine whether patients who underwent ASL imaging without DSA had similar postoperative outcomes when compared with patients who received ASL imaging and postoperative DSA.

METHODS The medical records of pediatric patients who underwent pial synangiosis for moyamoya disease at a quaternary children’s hospital were reviewed during a 10-year period. ASL-only and ASL+DSA cohorts were analyzed. The frequency of preoperative and postoperative symptoms was analyzed within each cohort. Three neuroradiologists assigned a visual ASL grade for each patient indicating the change from the preoperative to postoperative ASL perfusion sequences. A postoperative neovascularization grade was also assigned for patients who underwent DSA.

RESULTS Overall, 21 hemispheres of 14 patients with ASL only and 14 hemispheres of 8 patients with ASL+DSA were analyzed. The groups had similar rates of MRI evidence of acute or chronic stroke preoperatively (61.9% in the ASL-only group and 64.3% in the ASL+DSA group). In the entire cohort, transient ischemic attack (TIA) (p = 0.027), TIA composite (TIA or unexplained neurological symptoms; p = 0.0006), chronic headaches (p = 0.035), aphasia (p = 0.019), and weakness (p = 0.001) all had decreased frequency after intervention. The authors found a positive association between revascularization observed on DSA and the visual ASL grading (p = 0.048). The visual ASL grades in patients with an angiogram indicating robust neovascularization demonstrated improved perfusion when compared with the ASL grades of patients with a poor neovascularization.

CONCLUSIONS Noninvasive ASL perfusion imaging had an association with postoperative DSA neoangiogenesis following pial synangiosis surgery in children. There were no significant postoperative stroke differences between the ASL-only and ASL+DSA cohorts. Both cohorts demonstrated significant improvement in preoperative symptoms after surgery. Further study in larger cohorts is necessary to determine whether the results of this study are validated in order to circumvent the invasive catheter angiogram.

https://thejns.org/doi/abs/10.3171/2021.7.PEDS21302

KEYWORDS moyamoya disease; arterial spin labeling; angiogram; pediatric; perfusion; outcomes; vascular disorders
MOYAMOYA disease is a cerebrovascular disease characterized by the progressive stenosis of the terminal portion of the internal carotid arteries and the subsequent formation of brittle, branch-like collateral vessels in the basal cisterns and brain.\textsuperscript{1-3} These collaterals give the angiographic appearance of a “hazy puff of smoke” (moyamoya in Japanese\textsuperscript{2,4}). Although moyamoya affects both children and adults, the presenting symptoms and treatment strategies may be different between these populations.\textsuperscript{2,5}

The diagnosis of moyamoya disease typically involves preoperative MRI/MRA with or without perfusion sequences. Additionally, most patients undergo catheter-based digital subtraction angiography (DSA), with a classification system as originally described by Suzuki et al.\textsuperscript{1,4,5,6,7} Medical and surgical treatments are complementary and are not stand-alone; the definitive treatment is surgical.\textsuperscript{2} The main medical management strategies involve avoiding dehydration or hypotension given patients’ decreased cerebrovascular reserve, and administration of single antiplatelet therapy (usually aspirin).\textsuperscript{2,8} Surgery for moyamoya is focused on revascularization of the ischemic brain. Because of the small caliber of blood vessels, an indirect bypass procedure is usually chosen over a direct bypass in the pediatric population.\textsuperscript{3,11-14} Although many techniques have been described, indirect bypass techniques such as encaphaloduroarteriosynangiosis or pial synangiosis are the most widely practiced forms of indirect bypass in children.\textsuperscript{15} In the pial synangiosis procedure, the superficial temporal artery is used as a donor vessel and affixed into the pia with a suture or laid on top of the pia after a wide arachnoid dissection.\textsuperscript{11,13,15,16}

When treating pediatric patients with moyamoya disease surgically, it is important to assess the hemodynamics of the pathological hemisphere before and after a revascularization procedure.\textsuperscript{3} The Matsushima grading system, based on postoperative DSA, was created to evaluate the extent of collateralization after bypass surgery.\textsuperscript{12} Many pediatric neurosurgeons consider DSA and postprocessing variations useful for assessing postoperative flow dynamics\textsuperscript{17} and calculating the Matsushima grade.

There has been interest in developing arterial spin labeling (ASL)\textsuperscript{18} for use in preoperative and postoperative moyamoya assessments. ASL is an MRI sequence that allows imaging of cerebral blood flow without a contrast agent\textsuperscript{18,19} and has emerged as a promising technique for noninvasive postoperative monitoring of patients with moyamoya.\textsuperscript{20} ASL quantitatively assesses cerebral perfusion by first tagging a voxel of water within the blood.\textsuperscript{18} After a predetermined delay to allow the voxel to perfuse the targeted territory, a repeat image is taken to subtract from the baseline, and then perfusion is calculated. While ASL has been used for many years, in the last decade its use has increased due, in part, to improvements in MRI scanner technology and wider distribution of 3T units at hospitals.\textsuperscript{19}

In this study, we reviewed a cohort of pediatric patients with moyamoya who underwent a pial synangiosis revascularization procedure at a quaternary children’s hospital. The aims of this study were threefold. First, we considered the potential of noninvasive ASL to serve as an alternative to invasive DSA by determining whether ASL imaging was able to predict postoperative angiogram results. Second, we assessed the correlation between ASL imaging and postoperative clinical outcomes. Lastly, we assessed the agreement among 3 neuroradiologists on a visual grading system for the postoperative ASL imaging sequences.

**Methods**

This retrospective study was conducted at the Children’s Hospital of Philadelphia, a quaternary children’s hospital. The protocol was approved by the Committee for the Protection of Human Subjects (IRB).

**Data Collection**

Surgical billing records from the Division of Neurosurgery were reviewed to identify pediatric patients (< 18 years of age) who underwent a pial synangiosis procedure between May 2009 and January 2019. Patient data, including demographic characteristics, clinical presentation, imaging results, treatment course, and follow-up data were extracted from the electronic medical record and entered into a standardized database. Medical records were reviewed through the last neurological examination performed in outpatient follow-up over a 2-year period. If a patient had bilateral pial synangiosis surgery, their age at the time of the first surgery was used as the age at surgery.

**Inclusion Criteria**

Patients were included if they had a confirmed diagnosis of unilateral or bilateral moyamoya disease based on preoperative DSA and Suzuki stage, underwent pial synangiosis surgery, had interpretable preoperative and postoperative imaging with ASL sequences with or without postoperative DSA, and had clinical follow-up through at least 12 months postoperatively.

**ASL Protocol**

Pulsed ASL perfusion MRI was performed on 3T scanners (Siemens MAGNETOM Trio and Prisma). Two-dimensional pulsed ASL acquisition was performed with proximal inversion with a control for off-resonance effects, quantitative imaging of perfusion with a single subtraction with thin-section TI1 periodic saturation, echoplanar readout, TE 12–14 msec, TR 2500 msec, bolus time 700 msec, inversion time 1900 msec, slice thickness 8 mm, 64 × 64 matrix, 41–44 averages, and a generalized autocalibrating partially parallel acquisition acceleration factor of 2. The total scan time was 4 minutes 30 seconds. Cerebral blood flow was calculated based on a general kinetic model for ASL quantitation.\textsuperscript{21}

**Radiographic Interpretation**

All patients were assigned a Suzuki stage based on preoperative DSA.\textsuperscript{3} Patients who had postoperative DSA were assigned a scoring of their revascularization based on the grading originally described by Matsushima and colleagues.\textsuperscript{10,12} Three board-certified, eligible neuroradiologist raters (M.C., N.S.R., and H.N.), who were blinded...
to the study aims, assigned an ASL grade to each patient based on visual grading of signal intensities. The grading scale comprises scores from 1 to 5, indicating the change from the preoperative to postoperative ASL sequences. Score definitions are as follows: 1 = significantly improved perfusion, 2 = slightly improved perfusion, 3 = stable perfusion, 4 = slightly worsened perfusion, and 5 = significantly worsened perfusion. Analysis of ASL grading and angiographic features were done at the hemisphere level.

**Symptom Scoring**

Scoring of symptoms was defined using a scale from 1 to 6 indicating the change from the presenting preoperative frequency of symptoms (1 = daily, 2 = weekly, 3 = monthly, 4 = yearly, 5 = rarely, and 6 = none) to postoperative frequency of symptoms. The change (difference) in score was calculated as the preoperative score minus the postoperative score. For example, a difference in a score of 3 means that the postoperative symptom score change is 3 "less frequent" than the preoperative score, which could be a change from 1 (daily) to 4 (yearly), or from 2 (weekly) to 5 (rarely). Symptom course was analyzed at the patient level.

**Statistical Analysis**

Demographics and symptom scores (pre- and postoperative) were summarized with descriptive analyses, such as frequencies and percentages for categorical variables and medians and IQRs for continuous variables. To test whether the change in the symptom score was significantly different from zero, a one-sample Wilcoxon signed-rank test was used. For evaluating the interrater reliability of ASL grading, a weighted kappa (because each grade is ordinal) was estimated with 95% CIs for each pair of graders. To evaluate the association between ASL grade and symptom improvement, the Spearman correlation was estimated for the ASL grade and the change of symptom score (the Spearman correlation was used because of the skewed distribution of the symptom change score). In this analysis, the ASL grade was based on the grade provided by the majority of the 3 raters, or the average grade from the 3 raters if all raters had assigned different grades.

**Results**

Forty pediatric patients with moyamoya were treated with a revascularization operation. Eighteen patients were excluded because of incomplete MRI or because ASL was not interpretable. Overall, the analysis included a total of 22 patients. Thirteen of these 22 patients had bilateral moyamoya disease and underwent bilateral pial synangiosis. The time interval between operations as well as the decision whether to obtain a 1-year postoperative angiogram was variable because of a gradual change in practice by the pediatric neurosurgeons and/or family requests to reduce the volume of invasive procedures. Most patients underwent bilateral pial synangiosis during the same operation. Eight patients had both ASL sequences and DSA performed postoperatively, whereas 14 patients had only ASL sequences without DSA. There were 14 operative hemispheres in the 8 patients of the ASL+DSA group. The timing of postoperative imaging was also variable but was between 8 and 12 months after surgery.

Of the 22 patients included, 9 were male (41%) and 13 were female (59%). The median patient age at the time of surgery was 6.7 years (IQR 4.6, 11.4). Seventy-three percent of patients had predisposing risk factors for the development of moyamoya and, thus, were considered to have moyamoya syndrome (Table 1). Select patients did have more than one predisposing risk factor. Only 8 patients (36%) had no known predisposing condition. Conditions that were not otherwise specified included Klippel-Flebenger syndrome; posterior fossa anomalies, hemangioma, arterial anomalies, cardiac anomalies, eye anomalies, and sternal cleft and supraumbilical raphe (PHACES) syndrome; and factor V Leiden deficiency. Table 1 also describes the preoperative and postoperative symptoms and stroke rate. Of the 35 hemispheres analyzed, 22 hemispheres (63%) had MRI evidence of acute or chronic stroke preoperatively; 61.9% in the ASL-only group and 64.3% in the ASL+DSA group. The median preoperative Suzuki stage was III.

**Clinical Outcomes After Pial Synangiosis**

The most common preoperative symptoms were transient ischemic attacks (TIAs), which occurred in 16 patients (73%), followed by headaches (41%). Rarely did patients present with radiographic evidence of disease only without any symptoms (5%). Certain symptoms such as hemiparesis and paresthesias were easily attributable to TIA and were documented as TIA in the patient’s medical record. However, in other instances, symptom classification was less clear and not explicitly stated as TIA in the

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**TABLE 1. Patient demographic and clinical characteristics**

<table>
<thead>
<tr>
<th>Moyamoya risk factors</th>
<th>Overall</th>
<th>ASL</th>
<th>ASL+DSA</th>
</tr>
</thead>
<tbody>
<tr>
<td>N1F1</td>
<td>6 (27.3)</td>
<td>3 (21.4)</td>
<td>3 (37.5)</td>
</tr>
<tr>
<td>Down syndrome</td>
<td>2 (9.1)</td>
<td>1 (7.1)</td>
<td>1 (12.5)</td>
</tr>
<tr>
<td>Sickle cell trait</td>
<td>1 (4.5)</td>
<td>1 (7.1)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Sickle cell disease</td>
<td>3 (13.6)</td>
<td>3 (21.4)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>RT</td>
<td>1 (4.5)</td>
<td>1 (7.1)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Other inherited/NOS</td>
<td>3 (13.6)</td>
<td>3 (21.4)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>None</td>
<td>8 (36.4)</td>
<td>4 (28.6)</td>
<td>4 (50)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Hemisphere level</th>
<th>Overall</th>
<th>ASL</th>
<th>ASL+DSA</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td>8 (36.4)</td>
<td>4 (28.6)</td>
<td>4 (50)</td>
</tr>
</tbody>
</table>

**Note:**

- NF1 = neurofibromatosis type 1; NOS = not otherwise specified; RT = radiation therapy.
- Values represent the number of patients (%) unless indicated otherwise.

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**TABLE 2. Patient demographic and clinical characteristics**

<table>
<thead>
<tr>
<th>Patient level</th>
<th>Overall</th>
<th>ASL</th>
<th>ASL+DSA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preop stroke</td>
<td>22 (62.9)</td>
<td>13 (61.9)</td>
<td>9 (64.3)</td>
</tr>
<tr>
<td>Postop stroke</td>
<td>1 (2.9)</td>
<td>1 (4.8)</td>
<td>0 (0.0)</td>
</tr>
</tbody>
</table>
medical record. Therefore, an additional category of “TIA composite” was created that includes all patients with a diagnosis of TIA as well as patients who presented with weakness, paresthesias, and/or aphasia but who did not have a formal TIA diagnosis. Figure 1 shows the change of clinical outcomes after surgical intervention regardless of the type of postoperative imaging obtained. Overall, in both the ASL-only and ASL+DSA groups, all symptoms significantly improved in frequency after intervention except for seizures, vomiting, lethargy, acute headaches, and other symptoms (n = 1, hallucinations). In both cohorts combined, TIA (p = 0.027), TIA composite (p = 0.0006), chronic headaches (p = 0.035), aphasia (p = 0.019), and weakness (p = 0.00097) all had statistically significant decreases in frequency (a negative symptom score), after surgical intervention, which indicates a positive postoperative symptom score (Table 2 and Fig. 1). In the ASL-only group, the categories of TIA composite and weakness continued to be significantly improved after surgery (p = 0.003 and p = 0.003, respectively); however, no symptom categories in the ASL+DSA group significantly changed (Table 2). The direction of change of symptoms 2 years after surgery was similar to 1 year after surgery, however, the symptoms became less significant (Supplementary Table 1).

Interrater Reliability for ASL Grading
To ensure interpreter reliability, we analyzed ASL grade concordance among the neuroradiologists. Of 35 ASL sequence hemispheres, there were 14 ASL MRI studies for which all 3 neuroradiologists assigned the same ASL grade. Twenty-one postoperative ASLs had 2 of the 3 neuroradiologists assign the same ASL grade. Statistical analysis comparing the ASL grades for each MRI study revealed a weighted kappa of 0.61, 0.60, and 0.51 for the 3 pairs of raters, suggesting that the neuroradiologists had moderate concordance of their reads (Table 3).

ASL Imaging Correlation With Angiography
There were 14 hemispheres that were assigned a Matsushima grade. These patients were split into 2 groups. The first group had a postoperative angiography Matsushima grade A (n = 7), which correlates with postoperative neovascularization greater than two-thirds of the middle cerebral artery (MCA) territory. The second group had a postoperative angiography Matsushima grade C (n = 7), which correlates with postoperative neovascularization less than one-third of the MCA distribution. No patients demonstrated a postoperative angiography Matsushima grade B (correlating to between one-third and two-thirds
neovascularization of the MCA territory). Analyses were performed to evaluate whether patients who were in the grade A category were different from those in the grade C category in terms of ASL grade (on the scale of 1 = significantly improved perfusion to 5 = significantly worsened perfusion). We found that the ASL grade was significantly different between groups (mean 1.57 vs 2.43, median 2 vs 3, for angiography grade A vs grade C, Wilcoxon signed-rank test p = 0.048), corresponding to the differences observed on DSA. Figure 2 shows an example of preoperative to improved postoperative ASL imaging along with a Matsushima grade A angiogram result.

ASL Imaging Correlation With Clinical Outcomes

While statistical significance was not reached, TIA composite, chronic headaches, lethargy, weakness, aphasia, and vomiting all had positive correlations with grading of postoperative ASL imaging, meaning that improvement in symptoms correlated with an improved visual ASL grade postoperatively. Other categories such as TIAs, acute headaches, seizures, and “other” symptoms did not have a correlation with ASL imaging.

Discussion

Pial synangiosis has become a popular revascularization technique in moyamoya disease, particularly for pediatric patients who show a superior predisposition to developing collaterals with an indirect procedure as opposed to adults. Postoperative surveillance focuses on the evaluation of neangiogenesis in the territory that was revascularized. Although surveillance has traditionally been done with DSA, noninvasive radiographic assessment of cerebral perfusion is a rapidly evolving field of research. In our study, we demonstrate that ASL has potential to be a reasonable alternative to DSA for postoperative monitoring of pediatric patients with moyamoya disease, as all patients in our cohort who underwent pial synangiosis surgery had improvement in symptoms, regardless of whether they had postoperative DSA. Aspirin and hydration were continued, and no patient had additional surgeries regardless of whether patients had DSA that showed good or poor neovascularization. When comparing DSA with ASL, we found that the ASL grade was associated with the DSA Matsushima grade after pial synangiosis. This supports the conclusion that ASL is a potentially effective method of evaluating postoperative revascularization. However, we also showed that the ASL grade was not associated with clinical outcome, which may be in part due to a small sample size. There was a trend toward improved postoperative symptoms correlating with improved perfusion on ASL imaging that did not reach statistical significance.

ASL has been shown to be effective at quantitatively assessing cerebral perfusion in multiple studies. Chng et al. published one of the first studies that compared ASL imaging with DSA. This study examined patients with various intracranial and extracranial stenotic pathologies and found no significant difference in the diagnostic quality between ASL and DSA in both proximal and distal perfusion territories. Other studies have shown that ASL imaging was capable of identifying collateral flow and was even capable of quantitating robust versus poor flow when compared with a DSA control image. ASL has also been compared with the traditional nuclear medicine methods of studying perfusion such as PET and SPECT. Fan et al. compared ASL with PET and demonstrated that it was equally capable of detecting hypoperfusion in the stenotic territories of moyamoya patients but not capable of differentiating mild from severe stenoses. Other studies have concurred and found that ASL had good correlation to the perfusion seen on PET overall but that ASL tends to overestimate cerebral perfusion. Others compared ASL with resting state and acetazolamide-challenged SPECT and found that ASL had a significant correlation to the acetazolamide-challenged perfusion readings on SPECT.

**TABLE 2. Symptom score change based on diagnostic studies at the 1-year follow-up**

<table>
<thead>
<tr>
<th>Variable</th>
<th>All (Mean (SD), Median (IQR))</th>
<th>p Value</th>
<th>ASL (Mean (SD), Median (IQR))</th>
<th>p Value</th>
<th>ASL+DSA (Mean (SD), Median (IQR))</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>TIA</td>
<td>0.55 (1.01), 0 (0, 1)</td>
<td>0.027</td>
<td>0.64 (1.15), 0 (0, 1.75)</td>
<td>0.07</td>
<td>0.38 (0.74), 0 (0, 0.25)</td>
<td>0.37</td>
</tr>
<tr>
<td>TIA composite</td>
<td>1.91 (1.63), 2 (0, 3.75)</td>
<td>0.0006</td>
<td>2.29 (1.59), 2 (1.25, 4)</td>
<td>0.0034</td>
<td>1.25 (1.58), 0.5 (0, 0.25)</td>
<td>0.1</td>
</tr>
<tr>
<td>Seizures</td>
<td>0.18 (0.5), 0 (0, 0)</td>
<td>0.17</td>
<td>0.14 (0.36), 0 (0, 0)</td>
<td>0.35</td>
<td>0.25 (0.71), 0 (0, 0)</td>
<td>&gt;0.99</td>
</tr>
<tr>
<td>Chronic headaches</td>
<td>0.59 (1.14), 0 (0, 0.75)</td>
<td>0.035</td>
<td>0.29 (0.83), 0 (0, 0)</td>
<td>0.37</td>
<td>1.12 (1.46), 0.5 (0, 2)</td>
<td>0.098</td>
</tr>
<tr>
<td>Lethargy</td>
<td>0.27 (0.88), 0 (0, 0)</td>
<td>0.35</td>
<td>0.21 (0.8), 0 (0, 0)</td>
<td>&gt;0.99</td>
<td>0.38 (1.06), 0 (0, 0)</td>
<td>&gt;0.99</td>
</tr>
<tr>
<td>Aphasia</td>
<td>1.05 (1.7), 0 (0, 3)</td>
<td>0.019</td>
<td>1.14 (1.79), 0 (0, 3)</td>
<td>0.06</td>
<td>0.88 (1.64), 0 (0, 0.75)</td>
<td>0.37</td>
</tr>
<tr>
<td>Weakness</td>
<td>1.86 (1.7), 2 (0, 3.75)</td>
<td>0.0007</td>
<td>2.36 (1.6), 2.5 (1.25, 4)</td>
<td>0.0034</td>
<td>1 (1.6), 0 (0, 1.5)</td>
<td>0.18</td>
</tr>
<tr>
<td>Vomiting</td>
<td>0.18 (0.66), 0 (0, 0)</td>
<td>0.37</td>
<td>0.07 (0.27), 0 (0, 0)</td>
<td>&gt;0.99</td>
<td>0.38 (1.06), 0 (0, 0)</td>
<td>&gt;0.99</td>
</tr>
<tr>
<td>Acute headache</td>
<td>0.09 (0.46), 0 (0, 0)</td>
<td>&gt;0.99</td>
<td>0.14 (0.53), 0 (0, 0)</td>
<td>&gt;0.99</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**TABLE 3. Interrater reliability of rater pairs for ASL grading**

<table>
<thead>
<tr>
<th>Raters</th>
<th>Weighted Kappa</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 &amp; 2</td>
<td>0.61</td>
<td>0.44–0.78</td>
</tr>
<tr>
<td>1 &amp; 3</td>
<td>0.60</td>
<td>0.38–0.81</td>
</tr>
<tr>
<td>2 &amp; 3</td>
<td>0.51</td>
<td>0.31–0.70</td>
</tr>
</tbody>
</table>
concluding that ASL imaging could identify at-risk territories for ischemia. Qiao et al. compared ASL imaging with dynamic susceptibility contrast MRI (DSC-MRI) in 15 patients with moyamoya who underwent revascularization surgery and found that ASL was not inferior to DSC-MRI in detecting ischemic areas preoperatively or the reduction in ischemia postoperatively.

In the current study, in patients who had both ASL and DSA postoperatively, we found significant correlation between revascularization seen on DSA and ASL. The visual ASL grades in patients with a DSA Matsushima grade indicating robust neovascularization were significantly better than the ASL grades of patients with a poor Matsushima grade. This finding suggests that ASL can detect a difference in perfusion between patients with successful and those with unsuccessful neovascularization after pial synangiosis. These findings are consistent with previously published results. Quon et al. reviewed the records of 15 pediatric patients who underwent direct bypass surgery for moyamoya and had preoperative and postoperative ASL and DSA. They found that postoperative ASL imaging was able to accurately demonstrate increases in cerebral perfusion in the MCA territory that received the bypass. Interestingly, ASL also detected the decreased perfusion in the lenticulostriate region after the bypass surgery. Lee et al. analyzed ASL utility in a large adult moyamoya population who underwent direct bypass surgery. The authors obtained ASL imaging preoperatively within 1 week of surgery, and 7 months following surgery. They concluded that ASL was able to detect immediate changes in perfusion after the bypass operation when compared with the preoperative imaging, and that the ASL imaging had good agreement with DSA in evaluating collateralization. It should be noted that perfusion changes after direct bypass procedures may be immediate or near immediate compared with perfusion changes that occur after indirect bypass procedures, which can occur gradually over weeks to months. Therefore, studies of ASL after direct and indirect bypass procedures may not be comparable.

In our analysis that could impact outcome include preoperative and postoperative Suzuki stages, idiopathic moyamoya versus syndrome moyamoya, and patient age at the time of surgery. Zhao et al. retrospectively reviewed 209 patients with moyamoya who were treated with indirect bypass methods to delineate prognostic factors associated with successful revascularization and found that patients who presented with cerebral hemorrhage or had a poor status of internal carotid artery collateralization prior to surgery had worse revascularization outcomes. Also of note, younger patients (< 25 years of age) had more success after indirect bypass procedures compared with older patients when presenting with cerebral hemorrhage. Literature has suggested that bypass surgery for revascularization benefits patients with moyamoya regardless of the postoperative radiographic findings. Our data support the use of pial synangiosis as an effective treatment for moyamoya, as all of our patients had significant improvement in the majority of their preoperative symptoms. Riordan et al. followed pediatric patients with moyamoya for 20 years and found that surgical revascularization provided patients with long-term protection from stroke and cerebral ischemia. Yuan et al. reviewed the ability of ASL imaging to evaluate postoperative revascularization volume. In their analysis the authors found that patients who had significant preoperative external carotid artery compensation had lower rates of immediate reperfusion benefit after direct bypass surgery. It is reasonable to assume that some of our patients had significant external carotid artery compensation preoperatively and consequently the imaging showed less profound revascularization, leading to a lower revascularization grade despite the long-term benefit of bypass surgery.

There are several limitations to this study. First, the sample size is small, particularly for evaluating subgroups, so there is limited statistical power for the primary aims and the potential for the results to be influenced by confounders. This is due, in part, to the relatively low prevalence of moyamoya. Many patients were lost to follow-up by 2 years after surgery, making the number of patients in each cohort very small. Also, nearly half of the patients had inadequate MRI studies or uninterpretable ASL images, which demonstrates that improved pediatric MRI acquisition and ASL techniques are needed. Future work including more patients and possibly including multiple patients with moyamoya who underwent revascularization surgery.

**FIG. 2.** A: Example of preoperative ASL imaging showing decreased perfusion to the left MCA territory. B: Postoperative ASL imaging from the same patient showing improved perfusion in the same territory (graded as improved by all 3 neuroradiologists). C: Corresponding angiogram obtained 1 year after surgery showing Matsushima grade A collateralization.
high-volume pediatric centers might be able to success-
fully determine subtle differences that were not revealed
in this study. Second, indirect bypass procedures require
time for revascularization benefit. The average length of
follow-up in this study was 11.1 months. It is possible that
with longer follow-up patients may show clinical improve-
ment that lags behind radiographic results. Finally, ASL
is a relatively new technique that is not used at all centers,
and older ASL sequences are often of poor quality, thus
decreasing the number of eligible patients. Use of quan-
titative ASL calculations and newer, multidelay ASL se-
quences would improve the characterization of perfusion.
However, we opted to perform a visual assessment grading
rather than quantitative calculations, as those methods are
not widely available and are not easily implemented in the
routine clinical realm. The opportunity to use a noninva-
sive, nonionizing, but equally informative method of neu-
rovascular imaging as the postoperative imaging choice
for pediatric patients with moyamoya would potentially
allow for elimination of dependence on DSA with its inva-
sive nature and ionizing radiation.

Conclusions
Noninvasive ASL perfusion imaging had an association
with postoperative DSA neoangiogenesis following pial
synangiosis surgery in children. Both the ASL-only and
ASL+DSA cohorts demonstrated improvement in preop-
erative symptoms after surgery with no significant stroke-
risk differences. Further studies are needed to determine
whether ASL perfusion imaging may replace traditional
invasive angiography.

Acknowledgments
We acknowledge Meghan Connors, BS, for her assistance with
data collection.

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Disclosures
Dr. Fisher: consultant for AstraZeneca and SpringWorks Therapeutics; and support of non–study-related clinical or research effort from AstraZeneca, Array Biopharma, and Exelixis.

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Supplemental Information
Online-Only Content
Supplemental material is available with the online version of the article.

*Supplementary Table 1.* [https://thejns.org/doi/suppl/10.3171/2021.7.PEDS21302](https://thejns.org/doi/suppl/10.3171/2021.7.PEDS21302).

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