Is arterial spin labeling relevant in MRI-negative drug-refractory epilepsy?

TO THE EDITOR: We read with a great deal of interest the article by Lam et al.1 (Lam J, Tomaszewski P, Gilbert G, et al. The utility of arterial spin labeling in the presurgical evaluation of poorly defined focal epilepsy in children. J Neurosurg Pediatr. 2021;27[3]:243–252). The authors describe the results of an arterial spin labeling (ASL) study in 25 cases of poorly defined focal epilepsy in children. The paper was intelligently written, providing insights into the role of ASL in MRI-positive and MRI-negative cases in localizing the epileptogenic zone (EZ). ASL was done as part of an exhaustive presurgical evaluation along with MRI, video-electroencephalography, PET, ictal/interictal SPECT, magnetoencephalography, and invasive intracranial recordings. Microvessel density was studied in 12 specimens (8 were pathological and 4 were internal controls). In 11 patients who had undergone surgery, the EZ was proven by good seizure outcome and histopathology.

ASL abnormalities were 85% concordant with MRI, 75% with FDG-PET, and 62.5% with SPECT. Ten of the surgically treated patients were MRI positive, and ASL was concordant qualitatively and quantitatively. Only 1 MRI-negative patient was surgically treated, and in that patient perfusion abnormality was not seen in the quantitative assessment and retrospective quantitative analysis showed perfusion abnormality that was concordant with the EZ. Microvessel density in focal cortical dysplasia was not significantly different from that in internal controls.

Their prospective study is strengthened by comprehensive methodology, histopathology, and long-term seizure outcome. Although ASL perfusion abnormalities were well correlated in MRI-positive cases, ASL did not have a role in localizing the EZ. As the authors hypothesized, this could be a consequence of poor spatial resolution and signal-to-noise ratio.

We appreciate the authors for optimizing the imaging protocol, such as the 3D pseudocontinuous readout protocol to improve spatial resolution,2 post-label delay of 1500 msec3 in these pediatric patients, and quantitative analysis in all cases. Although the authors claim that the study compares the ability of ASL to localize the EZ in MRI-positive versus MRI-negative cases, we believe that the role of ASL in EZ localization in MRI-negative cases is limited, as only 1 MRI-negative case was surgically treated and had evidence of the EZ.

At present, ASL has limited value compared to FDG-PET and SPECT in MRI-negative cases because of poor spatial and temporal resolution and signal-to-noise ratio. FDG-PET and ictal/interictal subtraction SPECT are better correlated with the EZ.4 More prospective studies are required to establish the role of ASL in these difficult cases, especially MRI-negative cases.

Raghu Samala, MCh
Ramesh Doddamani, MCh
Manjari Tripathi, DM
P. Sarat Chandra, MCh
All India Institute of Medical Sciences (AIIMS), New Delhi, India

References

Disclosures
The authors report no conflict of interest.

Correspondence
Ramesh Doddamani: drsdramesh@gmail.com.

INCLUDE WHEN CITING
Published online June 18, 2021; DOI: 10.3171/2021.3.PEDS21139.

Response
We greatly appreciate the authors’ interest and kind, insightful comments regarding our article. Furthermore, we thank them for raising this extremely important question: “Is arterial spin labeling relevant in MRI-negative drug-refractory epilepsy?”
However, before we share our specific perspective and try to best address their question, allow us to correct two misrepresentations from their letter.

First, they wrote that “although ASL perfusion abnormalities were well correlated in MRI-positive cases, ASL did not have a role in localizing the EZ.” This statement is incorrect. In fact, the Surgical Details subsection of our paper’s Results begins, “In all ASL-positive surgical cases, the ASL results contributed to the presurgical hypothesis but were not used to plan the resections.” The ASL findings were discussed as part of the presurgical evaluation, and when they were concordant with other results, they certainly added to the confidence regarding the hypothesized EZ. We believe they meant that the ASL results were not used to plan the resections, which is true, as it would have been inappropriate to use an investigational test to plan the actual resection.

Second, they wrote, “although the authors claim that the study compares the ability of ASL to localize the EZ in MRI-positive versus MRI-negative cases, we believe that the role of ASL in EZ localization in MRI-negative cases is limited, as only 1 MRI-negative case was surgically treated and had evidence of the EZ.” Indeed, our study did not directly address the question regarding the ability of ASL to localize the EZ in MRI-negative versus MRI-positive cases because of unbalanced samples. Although we did compare these two groups, we found that our ASL results for the former were inconclusive because of the few MRI-negative cases tested.

Now, as to their specific question of whether ASL is relevant in MRI-negative drug-resistant epilepsy, to the best of our knowledge, we believe that ASL is not clinically relevant in completely MRI-negative drug-resistant epilepsy. We emphasize “completely MRI negative” because our results showed that ASL perfusion abnormalities may overlap with subtle MRI signal abnormalities that are not directly obvious from the radiological interpretation of MRI. In our early experience so far, we have found that ASL added strength to the possibility that the overlap of subtle ASL/MRI signal abnormalities pointed to genuine epilepsy-causing pathology. Looking forward, more data are required to confirm these early findings in other poorly defined cases. Importantly, these cases still require confirmation from another modality to ascertain clinical significance. In our practice, we rely on PET, SPECT, and magnetoencephalography for the majority of our cases, not ASL. We emphasize that ASL does not, and may never, entirely replace these other very important tests. However, we and other groups are pursuing research efforts to develop its potential in pediatric epilepsy. We also look forward to future methodological advances in terms of data analytics and the establishment of normative variants of such measures in children.

Jack Lam, MSc
Sylvain Baillet, PhD
McConnell Brain Imaging Centre, Montreal Neurological Institute, McGill University, Montréal, QC, Canada
Roy W. R. Dudley, MD, PhD
McGill University Health Centre, Montréal, QC, Canada

INCLUDE WHEN CITING
Published online June 18, 2021; DOI: 10.3171/2021.4.PEDS21142.
©AANS 2021, except where prohibited by US copyright law