Dystonia is a heterogeneous movement disorder characterized by repetitive movements and/or postures that are caused by sustained or intermittent muscle contractions. There are both known and idiopathic causes for this disorder, with classification determined by clinical phenotype and underlying etiology (e.g., inherited, secondary to a structural nervous system abnormality, etc.). The classification of childhood movement disorders is further complicated by the frequent coexistence of multiple impairments in the same patient. These overlapping features also contribute to difficulties in treatment.

Pharmacotherapy is the mainstay of treatment in children with generalized dystonia, but often provides inconsistent clinical benefit and is associated with significant side effects. In instances of refractory disease, there are neurosurgical options such as ablation or deep brain stimulation (DBS) of the internal globus pallidus (GPI) as a treatment for pediatric dystonia, and to elucidate substrates underlying clinical outcome using state-of-the-art neuroimaging techniques.

OBJECTIVE The objective of this study was to report the authors’ experience with DBS of the internal globus pallidus (GPI) as a treatment for pediatric dystonia, and to elucidate substrates underlying clinical outcome using state-of-the-art neuroimaging techniques.

METHODS A retrospective analysis was conducted in 11 pediatric patients (6 girls and 5 boys, mean age 12 ± 4 years) with medically refractory dystonia who underwent GPI-DBS implantation between June 2009 and September 2017. Using pre- and postoperative MRI, volumes of tissue activated were modeled and weighted by clinical outcome to identify brain regions associated with clinical outcome. Functional and structural networks associated with clinical benefits were also determined using large-scale normative data sets.

RESULTS A total of 21 implanted leads were analyzed in 11 patients. The average follow-up duration was 19 ± 20 months (median 5 months). Using a 7-point clinical rating scale, 10 patients showed response to treatment, as defined by scores < 3. The mean improvement in the Burke-Fahn-Marsden Dystonia Rating Scale motor score was 40% ± 23%. The probabilistic map of efficacy showed that the voxel cluster most associated with clinical improvement was located at the posterior aspect of the GPI, comparatively posterior and superior to the coordinates of the classic GPI target. Strong functional and structural connectivity was evident between the probabilistic map and areas such as the precentral and postcentral gyri, parieto-occipital cortex, and brainstem.

CONCLUSIONS This study reported on a series of pediatric patients with dystonia in whom GPI-DBS resulted in variable clinical benefit and described a clinically favorable stimulation site for this cohort, as well as its structural and functional connectivity. This information could be valuable for improving surgical planning, simplifying programming, and further informing disease pathophysiology.

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KEYWORDS connectivity; deep brain stimulation; dystonia; functional neurosurgery; probabilistic mapping
ulation (DBS). The internal globus pallidus (GPI) was proposed as a potential surgical target for dystonia based on the marked reduction in dystonic dyskinesias following pallidal ablation in patients with Parkinson’s disease. In a study including both children and adults, surgical ablation was shown to be significantly less effective in patients with acquired dystonia than with idiopathic or genetic dystonia. In addition, ablation is associated with permanent adverse events, especially when performed bilaterally. Although DBS response in acquired dystonia is more variable, therapeutic benefit has been demonstrated even in adult patients with dystonic cerebral palsy. In part due to this lack of surgical ablation efficacy, as well as the greater flexibility and reversibility of DBS, GPI-DBS is now the gold standard treatment for medically refractory dystonia. Following DBS surgery, the delivered electrical dose requires individual titration to maximize clinical benefit while minimizing side effects. Our limited understanding of the mechanism of action of DBS enforces an empirical approach to device programming, which can be a challenging and lengthy process. A further challenge is that pediatric programming relies on use of the adult dystonia programming algorithm. Because therapeutic benefit in dystonia may take months to become apparent, multiple postoperative DBS programming visits are often required to achieve optimal results.

Methods

Methods now exist to accurately localize DBS electrodes within individual patients and coregister them into an average brain template, permitting group-level analysis. Using computational volume of tissue activated (VTA) modeling, we can approximate the neural substrates being stimulated. These VTAs can then be clinically weighted and analyzed to allow estimation of brain areas or connectivity profiles that correspond to optimal outcome. Prior investigative efforts have employed VTA modeling to characterize the local region of best response to GPI-DBS in patients with idiopathic and genetic dystonia and clinically effective DBS contacts.

As previously highlighted, pediatric DBS studies for dystonia are currently lacking in the literature. To our knowledge, none of those studies have performed group-level voxel-wise analyses to identify neural substrates and/or networks associated with clinical benefits. Similarly, a recent meta-analysis reviewed the clinical outcomes in childhood dystonia across subtypes, but did not include imaging findings.

In this paper, we report our experience with GPI-DBS as a treatment for pediatric dystonia, and employ neuroimaging techniques to examine the neural substrates associated with clinical benefits in this patient cohort. This may help guide surgical lead implantation, streamline clinical programming, and inform the pathophysiology of this heterogeneous group of diseases.

Clinical Outcome Measures and Follow-Up

All patients were assessed both pre- and postoperatively by a neurologist specializing in movement disorders. The patients’ charts and videos were retrospectively reviewed and assessed for clinical improvement (by M.A. and L.M.O.). A 7-point Clinical Global Impression scale was used to assess clinical improvement from the preoperative time point to overcome the absence of Burke-Fahn-Marsden Dystonia Rating Scale (BFMDRS) availability in all patients, as has been used previously. Postoperative improvement was graded as follows: 7 = very much worse, 6 = much worse, 5 = minimally worse, 4 = no improvement, 3 = minimally improved, 2 = much improved, 1 = very much improved. Abnormal movements were also graded with the BFMDRS in patients for whom recorded video data were available (8 preoperatively, 9 postoperatively). When available, BFMDRS scores were incorporated into judgment of global improvement.

Neuroimaging Analysis

Retrospective imaging analysis was performed following research ethics board approval from the University Health Network Research Ethics Board.

DBS Lead Localization

Lead localization largely followed the methodology described by Horn and Kühn. Lead-DBS (www.lead-
dbs.org), the pre- and postoperative 3D T1-weighted MR images were rigidly coregistered (http://www.fil.ion.ucl.ac.uk/spm/software/spm12/). Then, the postoperative MRI was nonlinearly warped with “low variance”23 advanced normalization tools (http://stnava.github.io/ANTs/) to Montreal Neurological Institute (MNI) space (MNI152 NLIN 2009b atlas) using the preoperative-to-MNI transforms. Each registration step was visually checked (by A.C.). Following initial prereconstruction, the electrode lead trajectories were manually refined based on the artifact as agreed upon by two trained observers (A.C. and G.J.B.E.), one of whom has experience performing this technique in more than 1000 patients (G.J.B.E.). The post-to pretransforms were corrected for postoperative brain shift using the Lead-DBS subcortical affine transform when required. It has previously been shown that pediatric brains can be successfully normalized to an adult template in children older than 6 years of age.24

VTA Estimation

VTA estimation was conducted in Lead-DBS following the approach described by Horn et al.25 Briefly, the Iso2Mesh toolbox was used to construct a volume conductor model of the DBS electrode and surrounding tissue through creation of a tetrahedral volume mesh. Subcortical gray matter nuclei were defined using the DISTAL atlas,26 and regions devoid of gray matter material were labeled as white matter. Conductivities of 0.33 and 0.14 S/m were used for gray and white matter, respectively. The potential distribution resulting from stimulation as modeled using optimal stimulation settings for each individual patient was then computed using the FieldTrip-SimBio finite element model pipeline and thresholded with a 0.2 V/mm gradient to derive binary VTAs in MNI space.27 Given the small number of patients, all left-sided VTAs were flipped in the midsagittal plane for group-level analysis (n = 21 right-sided VTAs).

Probabilistic Map of Efficacy

Next, a voxel-wise probabilistic map of efficacy was computed in MNI space. A metric of the average clinical improvement at each stimulated voxel was computed by weighting patient VTAs according to improvement (based on the 7-point clinical scale) at the best time point. A frequency map was also computed, which denoted the proportion of VTAs overlapping each voxel. The final probabilistic map of efficacy was calculated by multiplying the average map and the frequency map at each voxel.28 Volume overlap between the positive voxels within this probabilistic map and neighboring structures of interest (as defined by the DISTAL atlas)29 was determined to assess the relationship between clinical outcome and relevant neuroanatomy.

Connectomic Analysis

To investigate patterns of functional and structural connectivity associated with clinical benefits, a normative connectomic analysis was performed.29,30 Specifically, the probabilistic map described above was utilized as a

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### TABLE 1. Studies that evaluated DBS in pediatric dystonia*

<table>
<thead>
<tr>
<th>Authors &amp; Year</th>
<th>No. of Pts</th>
<th>Mean Age at Surgery (range), yrs</th>
<th>Mean BFMDRS Motor Score (range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cersosimo et al., 200841</td>
<td>7</td>
<td>13 (9–19)</td>
<td>59 (33–96) 30 (12–66)</td>
</tr>
<tr>
<td>Ghosh et al., 201244</td>
<td>8</td>
<td>14 (8–21)</td>
<td>NR  NR</td>
</tr>
<tr>
<td>Goto et al., 200642</td>
<td>2</td>
<td>18 (15–21)</td>
<td>65 (61–68.5) 1.5 (0–3)</td>
</tr>
<tr>
<td>Jin et al., 201245</td>
<td>1</td>
<td>7</td>
<td>34  3</td>
</tr>
<tr>
<td>Keen et al., 201444</td>
<td>5</td>
<td>11 (8–17)</td>
<td>61 (38.5–102) 52 (34–71)</td>
</tr>
<tr>
<td>Krause et al., 200443</td>
<td>4</td>
<td>17.5 (13–21)</td>
<td>80 (66.5–92) 36 (24.5–49)</td>
</tr>
<tr>
<td>Krause et al., 201546</td>
<td>1</td>
<td>20</td>
<td>44  27</td>
</tr>
<tr>
<td>Krause et al., 201647</td>
<td>8</td>
<td>12.5 (7–17)</td>
<td>45 (16–74.5) 23 (1.5–35.5)</td>
</tr>
<tr>
<td>Kupsch et al., 200348</td>
<td>1</td>
<td>14</td>
<td>34.5  27</td>
</tr>
<tr>
<td>Mehrkens et al., 201049</td>
<td>5</td>
<td>13 (8–16)</td>
<td>NR  NR</td>
</tr>
<tr>
<td>Miyagi &amp; Koike, 201350</td>
<td>2</td>
<td>10 (9–11)</td>
<td>60 (42–78) 76 (63.5–88)</td>
</tr>
<tr>
<td>Olaya et al., 201351</td>
<td>9</td>
<td>16 (6–20)</td>
<td>86 (58–108) 79 (53.3–108)</td>
</tr>
<tr>
<td>Oterdoom et al., 201852</td>
<td>1</td>
<td>9</td>
<td>71  64</td>
</tr>
<tr>
<td>Parr et al., 200753</td>
<td>4</td>
<td>12 (8–14)</td>
<td>83 (66–103) 34 (8–53)</td>
</tr>
<tr>
<td>Petrossian et al., 201344</td>
<td>13</td>
<td>14 (9–17)</td>
<td>40 (12–86) 22 (0–61.5)</td>
</tr>
<tr>
<td>Starr et al., 200455</td>
<td>7</td>
<td>16 (12–18)</td>
<td>64 (34–90) 29 (0–71)</td>
</tr>
<tr>
<td>Tronnier &amp; Fogel, 200056</td>
<td>1</td>
<td>13</td>
<td>77  50.5</td>
</tr>
<tr>
<td>Vidailhet et al., 200557</td>
<td>5</td>
<td>17 (15–19)</td>
<td>38 (25–56) 17 (0–46)</td>
</tr>
<tr>
<td>Zorzi et al., 200558</td>
<td>9</td>
<td>10 (8–15)</td>
<td>57 (44–91) 33 (14–83)</td>
</tr>
</tbody>
</table>

NR = not reported; Pts = patients.

None of these studies included group-level neuroimaging-based inferences.

* Adapted from Hale et al., 2020.27
<table>
<thead>
<tr>
<th>Variable</th>
<th>Pt No.</th>
<th>Mean ± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td></td>
<td></td>
</tr>
<tr>
<td>M</td>
<td>2</td>
<td>F</td>
</tr>
<tr>
<td>F</td>
<td>4</td>
<td>F</td>
</tr>
<tr>
<td>F</td>
<td>6</td>
<td>M</td>
</tr>
<tr>
<td>M</td>
<td>8</td>
<td>F</td>
</tr>
<tr>
<td>M</td>
<td>10</td>
<td>F</td>
</tr>
<tr>
<td>F</td>
<td>11</td>
<td>M</td>
</tr>
<tr>
<td>Disease etiology</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CP</td>
<td>2</td>
<td>Near-drowning (HII)</td>
</tr>
<tr>
<td>CP</td>
<td>4</td>
<td>CP</td>
</tr>
<tr>
<td>Idiopathic</td>
<td>6</td>
<td>CP</td>
</tr>
<tr>
<td>VPS41 mutation</td>
<td>8</td>
<td>XXX</td>
</tr>
<tr>
<td>Syndrome</td>
<td>9</td>
<td>CP</td>
</tr>
<tr>
<td>Dystonia myoclonus (SGCE-negative)</td>
<td>10</td>
<td>Idiopathic</td>
</tr>
<tr>
<td>Disease duration (yrs)</td>
<td></td>
<td>5 ± 4</td>
</tr>
<tr>
<td>Age at surgery (yrs)</td>
<td></td>
<td>6 ± 4</td>
</tr>
<tr>
<td>Length of follow-up (mos)</td>
<td></td>
<td>5 ± 21</td>
</tr>
<tr>
<td>Postop complications</td>
<td></td>
<td>None</td>
</tr>
<tr>
<td>No. of antidystonia medications: preop/postop</td>
<td></td>
<td>3/2/11/1</td>
</tr>
<tr>
<td>Dominant phenomenology</td>
<td></td>
<td>Limbs &gt; Tr</td>
</tr>
<tr>
<td>BFMDRS motor score</td>
<td></td>
<td>37/34/77</td>
</tr>
<tr>
<td>% improvement</td>
<td></td>
<td>38/53/85</td>
</tr>
<tr>
<td>BFMDRS disability preop/postop</td>
<td></td>
<td>NA/52/95</td>
</tr>
<tr>
<td>Clinical rating score</td>
<td></td>
<td>3/3/3</td>
</tr>
<tr>
<td>DBS settings (average of 2 sides)</td>
<td></td>
<td>4/3/13/6</td>
</tr>
<tr>
<td>Amplitude (V)</td>
<td></td>
<td>4/3.3/3.6</td>
</tr>
<tr>
<td>Mode of stimulation</td>
<td></td>
<td>M/M/M*</td>
</tr>
<tr>
<td>Pulse width (usec)</td>
<td></td>
<td>60/75/60</td>
</tr>
<tr>
<td>Frequency (Hz)</td>
<td></td>
<td>130/125/120</td>
</tr>
</tbody>
</table>
| CP = cerebral palsy; Gen = generalized; HII = hypoxic ischemic injury; I = interleaved; LL = lower limbs; M = monopolar; NA = not available; Tr = Trunk; UL = upper limbs. * Unilateral (right).
weighted seed region in conjunction with two normative data sets derived from large numbers of healthy subjects: a 1000-subject resting-state functional MRI (rsfMRI) data set and a 985-subject diffusion-weighted MRI whole-brain tractography data set. Normative data have been shown to predict clinical outcome in other DBS populations and are often able to provide higher spatial resolution and better signal-to-noise ratios than native patient images. While network integration changes with maturation, it has been shown that connectivity patterns do not change drastically during development, thus validating the use of adult normative data in the context of pediatric patients.

With respect to functional connectomic mapping, a whole-brain, voxel-wise connectivity r-map was obtained on the basis of rsfMRI time course–dependent correlations with the seed. To compute structural connectivity, the whole-brain tractography data set was seeded with the probabilistic map. Streamlines touching the seed were retained and converted to voxel-wise streamline density maps.

The functional and structural connectivity of the probabilistic map were compared to that of the “traditional” GPI-DBS coordinate-based target used for dystonia. The traditional target volume was generated by placing a theoretical DBS electrode in MNI space such that its second most ventral contact was centered on the right-sided GPi coordinates specified by Horn et al. in their probabilistic atlas of DBS targets. The mean voltage settings of the cohort (C+1–3 V) were then modeled as described above to approximate a typical GPI-DBS VTA. The functional and structural networks associated with this volume were determined as detailed for the patients above.

**Results**

**Patients**

Eleven pediatric patients with refractory dystonia (2 with genetically determined dystonia, 7 with acquired, and 2 with idiopathic) were treated with GPI-DBS between June 2009 and September 2017. Table 2 features patient demographics, disease etiology, and clinical outcomes. Ten of the 11 patients received bilateral lead implantation, while 1 patient with XXX syndrome had only a single implanted lead (21 total implanted leads). The mean (± SD) age at surgery was 12 ± 4 years, with a mean follow-up of 19 ± 21 months until last follow-up (time point of recorded optimal benefit). Ten (91%) of 11 patients showed response to DBS, as defined by a score of 3 or less on the 7-point postoperative rating scale. The patient who showed no clinical improvement (patient 5) developed status dystonicus immediately postoperatively in the absence of electrical stimulation; these symptoms improved over time following treatment with intrathecal baclofen and multiple oral medications. There were no stimulation-induced adverse events in any patient. Patient 2 showed clinical improvement but, due to subsequent infection of the DBS device, required removal of the system after 6 months of stimulation.

**Electrode Locations and VTA**

Once registered to standard MNI space, active electrode contacts were noted to be centered around the posterodorsal GPi (Fig. 1). There was overlap in the distribution of active contacts of patients with better clinical...
outcomes and those experiencing little benefit. The mean distance from the active contact to the nearest voxel in the primary motor GPi\textsuperscript{36} was 2.8 ± 1.9 mm (Table 3).

### Probabilistic Mapping and Connectivity Patterns

The probabilistic map of efficacy showed that the voxel cluster most associated with clinical improvement was located at the posterior aspect of the GPi. The top 50\% of voxels by voxel value were centered on the following MNI coordinates: x = 23.7, y = -9.4, z = -3.7. These were posterior and somewhat superior to the center-of-gravity coordinates of the “classic” GPi target as defined by Horn et al.\textsuperscript{36} (x = 22.4, y = -5.6, z = -5.0; Fig. 2). The top 50\% of probabilistic map voxels showed considerable overlap with the GPi proper (59.3% overlap); specifically, the greatest overlap was observed with the premotor (12.8\%) and primary motor (11.7\%) territories. A substantial portion of the map (29.8\%) encroached on the globus pallidus pars externa (GPe), while the remainder of the voxels (10.8\%) putatively fell within the neighboring white matter (Fig. 3).

As determined by normative connectomic analysis, the pediatric probabilistic map of efficacy showed broad similarities in terms of functional connectivity with the classic dystonic GPi target as defined by Horn et al.\textsuperscript{36} Specifically, both seeds demonstrated strong positive correlations to the insular cortex, central and precentral gyri, pallidum, putamen, brainstem, and cerebellum (Fig. 4A and B). Regions functionally negatively correlated with both seeds included the posterior parietal lobe, occipital lobe, and temporal lobes. However, there were also differences between the probabilistic map and the classic target. In particular, the middle frontal gyrus as well as the posterior parietal and occipital region were more strongly negatively correlated with the pediatric probabilistic map, while aspects of the temporal lobe and ventromedial prefrontal cortex were more strongly positively correlated with the conventional GPi target.
With regard to structural connectivity, similarities were again noted between the pediatric probabilistic map and the conventional GPi-DBS target. High structural connectivity, as denoted by streamline density, was noted between both seeds and areas including the precentral and postcentral gyri, parietooccipital region, and brainstem (Fig. 4C and D). Overall, these areas demonstrated greater streamline density with respect to the probabilistic map.

### Discussion

In this cohort of pediatric dystonia cases, we showed that VTA-based probabilistic mapping suggests a convergence of DBS-induced clinical benefits within the posterior aspect of the GPi. There was an associated functional and structural connectomic pattern associated with this site, showing both similarities and differences with respect to the conventional coordinate-based target.

A recent meta-analysis found that 88.2% of children with an inherited dystonia showed clinically significant (>20% improvement in motor score) response to DBS. However, dystonic children with cerebral palsy—one of the most frequent causes of childhood dystonia—responded poorly (median 11.1% motor improvement). As such, any insight that could aid in improving treatment response for this often severely debilitated patient population is important. Younger age of onset and acquired dystonia are known predictors of poor treatment response, factors that affected much of our patient population. A systematic review of DBS in pediatric dystonia showed a mean (± SD) 43.7% ± 31% improvement in BFMDRS score, regardless of dystonia type. Consistent with the current literature, our 6 patients with available pre- and postoperative BFM-DRS motor scores demonstrated a mean 40% ± 23% motor response to DBS. Despite inherent predictors of poor outcome, 10 of our patients showed response to DBS using the 7-point scale.

Inaccurate lead placement is a reported cause of therapeutic failure for DBS in dystonia, highlighting the
importance of precise surgical targeting. As defined by probabilistic mapping, the optimal stimulation site in our cohort was lateral and superior to the widely described surgical target. While in theory the electrodes are surgically inserted in similar places, individualized programming empirically drives the stimulation. This, at least in part, accounts for the differences between our hotspot—based upon clinically weighted VTA locations—and the location of active contacts described by Horn et al. In 20 adult patients with DBS-responsive cervical dystonia, an acute stimulation challenge produced maximum response with stimulation around the lamina medullaris, between the posteroventral GPi and GPe. In agreement with the adult literature, a stimulation volume encompassing both the ventroposterior pallidal region and adjacent subpallidal white matter appears to result in stronger clinical benefit in our cohort. It has been proposed that DBS may preferentially affect axons, perhaps explaining why our site of probabilistic clinical benefit encroached on the adjacent white matter. Connectomic analysis of this probabilistic map, moreover, indicated its dense interconnectedness with primary motor, premotor, and somatosensory cortical regions, underscoring the importance of relationships between subcortical DBS targets and relevant cortical regions.

This work has potential applications for the refinement of surgical targeting and postoperative optimization of DBS therapy for pediatric dystonia. While preliminary, the probabilistic hotspot and connectomic signature described here present an opportunity for guiding future electrode placements and DBS programming. The zone of optimal activation and its associated functional and structural connectivity patterns could be transformed into native patients and used in conjunction with pre- and postoperative imaging. An example of such an experimental method has already been performed on at least 1 adult patient with essential tremor. Eventual clinical applications would require larger sample sizes (likely by means of multicenter collaboration) and the adoption of more refined methods, such as robust statistical analysis and perhaps machine learning, to identify the substrates of efficacious outcome. This approach would enable information from retrospective cases to effectively inform future intervention.

The present study has several limitations. Although, to our knowledge, it is the largest study making neuroimaging inferences in pediatric patients with dystonia, it remains exploratory given its small sample size and retrospective character. In addition, we were unable to rigorously quantify or validate these findings due to the small sample size. Furthermore, the etiology of our patients’ underlying disease was heterogeneous. Lastly, we employed large-scale normative data sets for our connectomic analysis; while these may differ somewhat from the native connectivity of pediatric dystonia patients, they have previously been shown to be informative in many other diseases, including Parkinson’s disease and dementia.

Conclusions

DBS for pediatric dystonia is a complex treatment heightened by multiple sources of variability, including heterogeneous disease etiologies and variance in surgical lead placement and postoperative programming. This treatment demands a multidisciplinary team and months of pre- and postinsertion management. Patients affected by this devastating disease have few other treatment options. We reported on 11 cases of pediatric dystonia in which GPi-DBS was used to overall good effect, describing a clinically favorable stimulation site and its structural and functional connectivity signature. These results may provide valuable insights into improving surgical planning, facilitating programming, and informing disease pathophysiology.

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References


Disclosures
Dr. Oliveira reports receiving funding for travel from Medtronic. Dr. Kalia reports being a consultant to Medtronic. Dr. Lozano reports being a consultant to Boston Scientific, Medtronic, Abbott, and Insightec; and being an employee of Functional Neuromodulation. Dr. Fasano reports being a consultant to and receiving honoraria from, Abbott, Boston Scientific, and Medtronic.

Author Contributions
Conception and design: Fasano, Coblentz, Elias, Boutet, Widjaja, Lozano. Acquisition of data: Coblentz, Elias, Boutet, Algarni, Oliveira, Ibrahim, Lozano. Analysis and interpretation of data: Coblentz, Elias, Boutet, German, Algarni, Oliveira, Neudorfer. Drafting the article: Coblentz. Critically revising the article: Fasano, Elias, Boutet, German, Neudorfer, Widjaja, Ibrahim, Kalia, Lozano. Reviewed submitted version of manuscript: Fasano, Elias, Boutet, Kalia. Approved the final version of the manuscript on behalf of all authors: Fasano. Administrative/technical/material support: Jain. Study supervision: Fasano.

Supplemental Information
Previous Presentations
Portions of this work were presented in abstract form on May 3, 2019, at the Society for Pediatric Radiology conference in San Francisco, California.

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