Endoscopic third ventriculostomy (ETV) has emerged as an alternative method for CSF diversion when treating obstructive hydrocephalus. There are multiple recommendations on the transcortical ETV entry points, and some are specifically designed to provide a trajectory that avoids displacement to the eloquent periventricular structures. However, the morphology of the ventricular system is highly variable in hydrocephalus, and therefore a single best ETV trajectory may not be applicable to all cases. In the current study, 3 frequently quoted ETV entry points are compared in a cohort of pediatric cases with different degrees of ventriculomegaly.

METHODS The images of 30 consecutive pediatric patients with varying degrees of ventriculomegaly were reviewed. Three-dimensional models were created using radiological analysis of anatomical detail and preoperative MRI scans in order to simulate 3 frequently quoted ETV trajectories for rigid neuroendoscopes. These trajectories were characterized based on the frequency and depth of tissue displacement to structures such as the fornix, caudate nucleus, genu of the internal capsule, and thalamus. The results are stratified based on ventricle size using the frontal horn ratio (FHR).

RESULTS Eloquent areas were displaced in nearly all analyzed entry points (97%–100%). Stratifying the data based on ventricle size revealed that 1) lateral structures were more likely to be displaced in cases of intermediate ventriculomegaly (FHR < 0.4) using all 3 trajectories, whereas 2) the fornix was less likely to be displaced using more posteriorly placed trajectories for severe ventriculomegaly (FHR > 0.4). Allowing for minimal (2.4 mm) tissue displacement, a more posterior entry point was less traumatic for severe ventriculomegaly.

CONCLUSIONS There is no single best ETV trajectory that fully avoids displacement of the eloquent periventricular structures. Larger ventricles require a more posteriorly placed entry point in order to reduce injury to the eloquent structures, and intermediate ventricles would dictate a medial entry point. These results suggest that the optimal entry point should be selected on a case-by-case basis after incorporating ventricle size.
the foramen of Monro in order to access the floor of the third ventricle. These factors depend on the ETV trajectory, which is predefined by the bur hole entry site used. The most frequently described ETV entry sites are either 3 cm lateral to the midline and 1 cm anterior to the coronal suture or located at a point 3 cm lateral to the midline along the coronal suture. Recent morphometric studies recommend placing the bur hole more posteriorly (approximately 1 cm behind the coronal suture and 3 cm away from the midline) in order to grant an atraumatic trajectory through the foramen of Monro that is aimed straight at the floor of the third ventricle. However, the ventricle dimensions in hydrocephalus are highly variable, which translates into diverse anatomical relationships between the floor of the third ventricle and the foramen of Monro. This observation is reinforced by the broad data range reported for the individual entry points of atraumatic trajectories. It is therefore likely that there is no “single best” ETV trajectory that avoids all tissue breaches, and the ETV entry point needs to be adjusted according to the ventricle morphology. To test this hypothesis, we used radiological analysis of anatomical detail to analyze 3 ETV entry points in 30 pediatric cases with different degrees of ventriculomegaly.

Methods

The patients were originally identified and data were collected as part of an ETV audit approved by the Clinical Audit Department of Royal Manchester Children’s Hospital. We created an anonymized database of 30 consecutive pediatric patients between the ages of 6 months and 16 years with varying degrees of ventriculomegaly who underwent treatment for newly diagnosed hydrocephalus. Patients with ipsilateral supratentorial mass lesions were excluded. Preoperative MRI scans were reconstructed, reviewed, and analyzed using the Brainlab iPlan workstation (software version 3.0). This software allows the creation and adjustment of the ETV trajectory in 3 dimensions. We used the “probe view” function to visualize the proximity to the adjacent structures at each point on the planned trajectory, and we could further scrutinize the intersection of this trajectory with key anatomical structures.

Assessment of Ventricle Megaly

We used the frontal horn ratio (FHR) as described by Hahn and Rim to assess the ventricular dimensions. This parameter is calculated as the ratio between the interfrontal distance (maximum distance between the lateral edges of the frontal horns) and the internal diameter of the skull at the same location (Fig. 1D).

Assessment of the Conventional ETV Entry Points and Trajectories for Rigid Neuroendoscopes

Our study was designed for rigid neuroendoscopes. Flexible neuroendoscopes provide greater maneuverability and potentially reduce the extent of tissue displacement. However, neuroendoscopy performed using rigid neuroendoscopes is the most widely used modality at this time, and the majority of our existing experience is derived from this technique. Only right-sided trajectories were considered. The coronal suture and the midline were identified in all cases either on the 3D surface reconstruction and/or using planar scan views (Fig. 1A–C). Three entry points were analyzed: 1) the precoronal point, which is 3 cm lateral to the midline along the coronal suture and 1 cm anterior to the coronal suture; 2) the coronal point, which is 3 cm lateral to the midline along the coronal suture; and 3) the posterior coronal point, which is 3 cm lateral to midline and 1 cm posterior to the coronal suture coronal point. These landmarks were clearly distinguished from one another by multiple case series. Furthermore, the concept of identifying different cranio-metric points accurately by relying on the coronal suture is well established in the literature.

FIG. 1. Comparative analysis of ETV trajectories. A: Entry points for the 3 trajectories plotted over a representative 3D surface reconstruction: the precoronal point is 3 cm to midline and 1 cm anterior the coronal suture (1); the coronal point overlies the coronal suture and is 3 cm away from midline (2); and the posterior coronal point is 3 cm to midline and 1 cm behind the coronal suture (3). The arrows indicate the coronal suture that is visible on the 3D reconstruction on both the sagittal (B) and axial (C) views. D: FHR was computed according to the methods of Hahn and Rim as the ratio of the interfrontal distance (a) to the internal diameter of the skull at the same location (b). Figure is available in color online only.
During ETV, the neuroendoscope is passed under direct vision and the eloquent structures are avoided. However, at the stage of third ventricular fenestration, the neuroendoscope is passed beyond the foramen of Monro and the operator loses direct visualization of its surrounding structures, thereby potentially displacing them while accessing the target area. Therefore, the ETV trajectory for a rigid neuroendoscope was simulated as a straight line between the entry points and the ETV fenestration site (the floor of the third ventricle just anterior to the mammillary bodies) (Fig. 2B and C). The depth of the intersection with the anatomical structures was used to simulate the extent of tissue displacement caused by the rigid neuroendoscope. Displacement was categorized as 1) “anterior displacement,” which included displacement to the fornix, or 2) “lateral displacement,” which included displacement to the caudate nucleus, genu of the internal capsule, or thalamus. The diameter of the rigid neuroendoscope was incorporated into our simulations by assigning the trajectory a width of 4.5 mm (Fig. 2B–E). We recorded both the frequency and the depth of tissue displacement (Fig. 3; Tables 1 and 2).

Data Analysis
Cases were stratified based on the ventricle dimensions into groups with FHR > 0.4 (“severe ventriculomegaly”) or FHR < 0.4 (“intermediate ventriculomegaly”). The simulated displacement of the neuronal structures was analyzed for each trajectory using the Student t-test, chi-square test, 1-way ANOVA, or Fisher exact test with the Freeman-Halton modification.

Results
Patient Population
The cohort consisted of 19 male and 11 female patients, the average age was 7.66 ± 4.59 years (range 9 days to 16 years), and various degrees of ventriculomegaly were noted. The most common diagnosis was posterior fossa neoplasm (22 of 30 patients), including medulloblastoma, ependymoma, and meningioma, followed by primary CSF circulation abnormalities (8 of 30 patients).

Stratification of Cases Based on Ventricle Size
The average FHR was 0.38 (range 0.24–0.57), and we empirically stratified the cohort into severe (FHR > 0.4; n = 12) or intermediate ventriculomegaly (FHR < 0.4; n = 18).

Assessment of the Ventricular Entry Points
The results for the frequency and depth of displacement to the eloquent structures are presented in Tables 1 and 2, respectively, and are summarized in Fig. 3. Initial analysis showed that there was no difference between the virtual tissue displacements for each trajectory without stratification by ventricle size (p = 0.09 and p = 0.4 for anterior and lateral displacement, respectively). We found that the anterior and/or lateral periventricular structures were displaced to some extent by all 3 ETV trajectories in 97% to 100% of cases.

We next stratified the results into severe (FHR > 0.4) and intermediate ventriculomegaly (FHR < 0.4), as summarized in Fig. 3 on the scatterplots. The analysis yielded the following results.

Displacement Frequency
Intermediate Ventricleomegaly. The 3 trajectories were associated with displacement frequencies between 44.4% and 66.7% for anterior structures and 94.4% and 88.9% for lateral structures, with no statistical differences between trajectories (Fig. 3; Table 1).
Severe Ventriculomegaly. The displacement frequencies to the anterior structures were significantly less for trajectories through the posterior coronal point (50%) compared with the precoronal (100%) and coronal points (75%; p < 0.05). There was no displacement to the latter structures for any of the trajectories, except for the posterior coronal point in 33% of cases (p < 0.05).

We observed a high frequency of lateral displacement in patients with intermediate ventriculomegaly. On further testing, this proved to be significantly greater than the displacement frequency for the lateral structures in patients with severe ventriculomegaly (0%–33.3% vs 94.4%–88.9%) for all 3 trajectories (p < 0.01). These findings suggest that a more medial entry point would potentially be less traumatic for intermediate ventriculomegaly, as larger ventricles seem to accommodate a more lateral trajectory.

Displacement Depth

Intermediate Ventriculomegaly. The displacement depths are summarized in Table 2. There was no significant difference between trajectories for anterior (p = 0.17) or lateral (p = 0.1) displacement.

Severe Ventriculomegaly. There was a trend toward reduced anterior displacement for the posterior coronal point (p = 0.07) compared with other trajectories. The lateral displacement depth was 1.6 ± 0.73 mm for the posterior coronal point compared with no displacement in the remaining trajectories (p < 0.001).

To further interpret these results, we incorporated the compliance of the neuronal structures to surgical manipulation by introducing a threshold for tissue displacement at the level of the foramen of Monro. We adopted 2.4 mm as the “safe” tissue displacement based on 2 case series.

Table 1. Frequency of tissue displacement to eloquent periventricular structures by the different ETV trajectories in patients with intermediate (FHR < 0.4) or severe (FHR > 0.4) ventriculomegaly

<table>
<thead>
<tr>
<th>Displacement</th>
<th>FHR &lt;0.4 (n = 18)</th>
<th>FHR &gt;0.4 (n = 12)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Precoronal Point</td>
<td>Coronal Point</td>
</tr>
<tr>
<td>Anterior</td>
<td>50%</td>
<td>44.4%</td>
</tr>
<tr>
<td>Lateral</td>
<td>94.4%</td>
<td>94.4%</td>
</tr>
</tbody>
</table>

* Precoronal point: 3 cm lateral to midline and 1 cm anterior to the coronal suture. Coronal point: 3 cm lateral to midline along the coronal suture. Posterior coronal point: 3 cm lateral to midline and 1 cm posterior to the coronal suture. Anterior displacement: displacement to the fornix. Lateral displacement: displacement to the caudate nucleus, genu of internal capsule, or thalamus.

† p < 0.05 (Fisher exact test with the Freeman-Halton modification).
(22 patients total), where ETVs were performed in combination with a biopsy through the same bur hole without procedure-related complications.\textsuperscript{16,25} Our results are summarized in Fig. 3 and Table 3. Direct comparison of the 3 trajectories without incorporating ventricle sizes showed no difference in the adjusted displacement to the anterior (p = 0.36) or lateral structures (p = 0.94). When stratifying for ventriculomegaly, for intermediate ventricles there was no difference in the frequencies of tissue displacement when comparing the precoronal (Fig. 3A and D), coronal (Fig. 3B and E), and posterior coronal points (Fig. 3C and F; anterior displacement, p = 0.44; lateral displacement, p = 0.82). In severe ventriculomegaly, only the posterior coronal point provided a trajectory with no tissue displacement above the threshold for both the anterior and posterior structures (Fig. 3F; Table 3; p < 0.005).

**Discussion**

We tested the applicability of 3 frequently quoted ETV entry points using radiological analyses of anatomical detail in a cohort of 30 consecutive pediatric cases with different degrees of ventriculomegaly. Our results show there is no single best trajectory for a rigid neuroendoscope that avoids any neuronal tissue displacement in every case. For intermediate ventriculomegaly (FHR < 0.4) the lateral periventricular structures were displaced more frequently than in severe ventriculomegaly, which suggests a more medial trajectory for smaller ventricles could potentially be less traumatic. Of the 3 trajectories studied, the posterior coronal entry point (as recommended by Duffner et al.\textsuperscript{6} and Chen and Nakaji\textsuperscript{4}) offered the least amount of tissue displacement for cases with relatively large ventricles (FHR > 0.4).

ETV is stratified as a low-risk procedure; however, there are well-recognized complications attributed to injuring the eloquent structures such as the fornix, caudate nucleus, genu of the internal capsule, and thalamus.\textsuperscript{1} These structures are adjacent to the foramen of Monro—the narrowest section of the ETV trajectory—and after passing the neuroendoscope into the third ventricle they are no longer visible to the operator. Therefore, subsequent manipulation of the neuroendoscope during fenestration can displace

TABLE 2. Tissue displacement to eloquent periventricular structures by the different ETV trajectories in patients with intermediate (FHR < 0.4) or severe (FHR > 0.4) ventriculomegaly

<table>
<thead>
<tr>
<th>Displacement Depth (mm)</th>
<th>Precoronal Point</th>
<th>Coronal Point</th>
<th>Coronal Point</th>
<th>Coronal Point</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>FHR &lt;0.4 (n = 18)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anterior</td>
<td>4.27 ± 1.85</td>
<td>2.85 ± 0.96</td>
<td>3.51 ± 1.61</td>
<td>1.07</td>
<td></td>
</tr>
<tr>
<td>Lateral</td>
<td>2.98 ± 1.6</td>
<td>2.64 ± 1.04</td>
<td>3.68 ± 1.52</td>
<td>0.1</td>
<td></td>
</tr>
<tr>
<td>FHR &gt;0.4 (n = 12)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anterior</td>
<td>3.44 ± 1.76</td>
<td>2.75 ± 1.75</td>
<td>1.51 ± 0.39</td>
<td>0.07</td>
<td></td>
</tr>
<tr>
<td>Lateral</td>
<td>None</td>
<td>None</td>
<td>1.6 ± 0.73</td>
<td>&lt;0.001</td>
<td></td>
</tr>
</tbody>
</table>

* ANOVA.

and injure these structures. To minimize this risk, multiple studies recommend an optimal entry point that allows atraumatic passage of the neuroendoscope in order to reach the floor of the third ventricle.\textsuperscript{4,6,14–16} The first set of studies found that the average entry point was approximately 3 cm lateral and 1 cm anterior to the corona l suture.\textsuperscript{19} Other authors proposed a more posterior entry point, averaging approximately 3 cm lateral and 1 cm posterior to the corona l suture.\textsuperscript{4,6} These studies also show that the atraumatic entry point varies considerably between individual cases. The locations range between 12.5 and 18.1 mm to 42.22 and 44.4 mm for the distance from the midline and 16.1 and 30.6 mm anterior to 35.8 and 46.5 mm posterior to the corona l suture.\textsuperscript{4,6} Knaus et al. reported similar variance in the mean optimal ETV entry point in 48 pediatric patients (19.7 ± 26.4 mm posterior to the nasion and 20.5 ± 11.5 mm lateral to the midline).\textsuperscript{13} In parallel to this broad data range, there is significant anatomical variance in ventricular morphology in patients with hydrocephalus, as shown by a series of radiological analyses of anatomical detail.\textsuperscript{4,7,17} Duffner et al. analyzed the MRI appearances of the lateral and third ventricles in patients with hydrocephalus with special consideration to ETV. Their data show highly variable ventricular dimensions: the height and width of the lateral/third ventricle varied 2- to 3-fold, and the distance from the cortex to the lateral ventricle ranged between 5.4 and 34.6 mm.\textsuperscript{6} Gammal et al.\textsuperscript{1} characterized the MRI appearances of patients with normal, atrophic, and hydrocephalic brains. They reported a range of 12 to 30 mm for the corpus callosum–fornix distance compared with 0 to 8 mm for normal and 0 to 15 mm for atrophic brains. The volumes of the third and fourth ventricles in patients with hydrocephalus related to subarachnoid hemorrhage were reported to range up to 6-fold.\textsuperscript{17} This anatomical variability preempts the findings of our study; there is no single universal working trajectory that could be applied to every surgical case given the highly diverse configuration of the periventricular structures.

The concept of “1 trajectory fits all” has been tested by

TABLE 3. Comparative analysis of the frequency of tissue displacement greater than 2.4 mm for the different ETV trajectories

<table>
<thead>
<tr>
<th>Displacement Frequency</th>
<th>Precoronal Point</th>
<th>Coronal Point</th>
<th>Coronal Point</th>
</tr>
</thead>
<tbody>
<tr>
<td>All ventricle sizes</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anterior</td>
<td>50%</td>
<td>33%</td>
<td>30%</td>
</tr>
<tr>
<td>Lateral</td>
<td>33%</td>
<td>40%</td>
<td>40%</td>
</tr>
<tr>
<td>FHR &lt;0.4 (n = 18)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anterior</td>
<td>38.9%</td>
<td>27.8%</td>
<td>50%</td>
</tr>
<tr>
<td>Lateral</td>
<td>55.6%</td>
<td>66.7%</td>
<td>66.7%</td>
</tr>
<tr>
<td>FHR &gt;0.4 (n = 12)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anterior</td>
<td>66.7%</td>
<td>41.7%</td>
<td>0%</td>
</tr>
<tr>
<td>Lateral</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
</tr>
</tbody>
</table>

* Displacement threshold of 2.4 mm.
† p < 0.005 (Fisher exact test with the Freeman-Halton modification).
accessing the ipsilateral anterior horn when using Kocher’s point as the entry point\textsuperscript{21} (which corresponds to the precoronal point in our study). Only a subset (67.5\%) of the ventricular trajectories passed through the frontal horn, and as a result the study recommended small adjustments on a case-by-case basis. Compared with anterior horn ventriculostomy, the ETV has a longer working trajectory, thereby giving rise to a greater degree of cumulative errors, e.g., displacing the eloquent structures. This is in accordance with our results, showing that none of the 3 ETV entry points tested would grant a fully atraumatic trajectory to the floor of the third ventricle.

The translational value of ETV simulations for assessing clinical outcome is traceable in the literature.\textsuperscript{12,13,14} These studies used preoperative computer-assisted planning\textsuperscript{14} or intraoperative neuronavigation\textsuperscript{15} to determine the extent of virtual tissue displacement at the level of the foramen of Monro, which was then correlated with postoperative complication. We adopted the mean tissue displacement of 2.4 mm quoted in these studies, which was associated with no intra- or postoperative complications and an ETV success rate of 86.7\% to 100\%.\textsuperscript{16,17} Displacement values below this threshold are less likely to have clinical consequences, which explains why there is a relatively low complication rate for ETV\textsuperscript{18} despite the high frequency of tissue displacement shown in our study. A suboptimal ETV trajectory, however, can also translate to restricted surgical access and limited visualization, thereby resulting in 1) suboptimal fenestration and consequently stoma failure and 2) intraoperative bleeding from the neurovascular structures, which forces the procedure to be abandoned. The degree of tissue shift appears to be a good indicator of cumulative errors that impact not only the safety but also the success of the procedure. Ultimately, the concept of “individualized” ETV entry points that minimize tissue displacement requires prospective clinical studies for verification. We are in the process of designing these trials using our recently developed operative planning tool.\textsuperscript{24}

Conclusions

Our results show that none of the 3 frequently described ETV trajectories are universally applicable to cases with different degrees of ventriculomegaly. Allowing for a relatively small amount of tissue displacement, the posterior coronal entry point grants the most optimal trajectory for larger ventriculomegaly. However, any degree of tissue displacement may be associated with bleeding or suboptimal visualization, thereby triggering a series of cumulative errors for the procedure. Therefore, ultimately our results suggest individual adjustments should be made to the entry site based on ventricle size in order to optimize procedure safety and success.

References

Disclosure
The authors report no conflicts of interest concerning the materials or methods used in this study or the findings specified in this paper.

Author Contributions
Conception and design: all authors. Acquisition of data: Zador. Analysis and interpretation of data: Zador, Coope. Drafting the article: all authors. Critically revising the article: Zador, Kamaly-Asl. Reviewed submitted version of manuscript: Zador. Approved the final version of the manuscript on behalf of all authors: Zador. Statistical analysis: Zador. Study supervision: Kamaly-Asl.

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