Impact of skull base development on endonasal endoscopic surgical corridors

Clinical article

MATEI A. BANU, M.D., M.S.,¹ AMANCIO GUERRERO-MALDONADO, M.D.,¹
HEATHER J. MCCREA, M.D., PH.D.,¹ VICTOR GARCIA-NAVARRO, M.D.,¹
MARK M. SOUWEIDANE, M.D.,^{1,2} VIJAY K. ANAND, M.D.,³ LINDA HEIER, M.D.,⁵
THEODORE H. SCHWARTZ, M.D.,^{1,3,4} AND JEFFREY P. GREENFIELD, M.D., PH.D.^{1,2}

Departments of ¹Neurological Surgery, ²Pediatrics, ³Otolaryngology—Head and Neck Surgery, ⁴Neurology and Neuroscience, and ⁵Radiology, Weill Cornell Medical College, New York, New York

Object. Scarce morphometric data exist on the developing skull base as a corridor for endonasal endoscopic approaches (EEAs). Furthermore, the impact of skull base lesions on its development has not been assessed. The authors describe a novel set of anatomical parameters characterizing the developmental process as well as the utility of these parameters in preoperative planning and a feasibility assessment of EEAs for neurosurgical treatment of skull base lesions in children.

Methods. Based on specific MRI sequences in 107 pediatric patients (2–16 years of age) without skull base lesions (referred to here as the normal population), 3 sets of anatomical parameters were analyzed according to age group and sex: drilling distance, restriction sites, and working distance parameters. A separate set of patients undergoing EEAs was analyzed in similar fashion to address the impact of skull base lesions on the developmental process.

Results. The volume of the sphenoid sinus significantly increases with age, reaching 6866.4 mm³ in the 14–16 years age group, and directly correlates with the pneumatization type ($r = 0.533$, $p = 0.0001$). The pneumatization process progresses slowly in a temporal-posterior direction, as demonstrated by the growth trend of the sellar width ($r = 0.428$, $p = 0.0001$). Nasal restriction sites do not change significantly with age, with little impact on EEAs. The intercarotid distance is significantly different only in the extreme age groups (3.9 mm, $p = 0.038$), and has an important impact on the transsphenoidal angle and the intracranial dissection limits ($r = 0.443$, $p < 0.0001$). The 14.9° transsphenoidal angle at 2–4 years has a 37.6% significant increase in the 11–13 years age group ($p = 0.001$) and is highly dependent on pneumatization type. Age-dependent differences between working parameters are mostly noted for the extreme age groups, such as the 8.6-mm increase in nare-vomer distance ($p = 0.025$). The nare-sellar distance is the only parameter with significant differences based on sex. Skull base lesions induce a high degree of variance in skull base measurements, delaying development and decreasing parameter values. Skull base parameters are interdependent. Nare-sellar distance can be used to assess global skull base development because it highly correlates with the intercarotid distance in both the normal population and in patients harboring skull base lesions.

Conclusions. Skull base development is a slow, gradual, age-dependent, sex-independent process significantly altering endonasal endoscopic corridors. Preoperative MRI measurements of the pediatric skull base are thus a useful adjunct in choosing the appropriate corridor and in assessing working angles and limits during dissection or reparative surgery. Skull base lesions can significantly impact normal skull base development and age-dependent growth patterns.

(<http://thejns.org/doi/abs/10.3171/2013.10.PEDS13303>)

KEY WORDS • endonasal endoscopic approach • pediatric skull base • magnetic resonance imaging measurements • skull base development • oncology • skull base pathology • sphenoid sinus

Abbreviations used in this paper: EEA = endonasal endoscopic approach; FSE = fast spin echo; HSS = height of the sphenoid sinus; ICA = internal carotid artery; ICD = intercarotid distance; LSS = length of the sphenoid sinus; MaxWiT = maximal width between inferior turbinates; MaxWmT = maximal width between middle turbinates; MaxRZD = maximal reachable zone of the dens; NA = nasal aperture; NDD = nare-dens distance; NSD = nare-sellar distance; NVD = nare-vomer distance; TA = transsphenoidal angle; VCD = vomer-clival distance; VSS = volume of the sphenoid sinus; Wsel = width of the sella turcica; WSS = width of the sphenoid sinus.

THE pediatric skull base undergoes an intricate developmental process. Growth trends vary widely between anatomical regions and across age groups. Skull base compartments evolve continuously in the first 10 years of life, molded by surrounding anatomical structures. Growing temporal and frontal lobes shape the skull base from above.⁶ The pneumatization process of

This article contains some figures that are displayed in color online but in black-and-white in the print edition.

the yet rudimental paranasal sinuses models skull base bone structures from below. Development of the midfacial complex only peaks in late childhood and early adolescence.²⁰ During this process of skull base maturation, intimate relationships arise between ossifying structures and neurovascular anatomy. Pneumatization of the sphenoid sinus is a stepwise process following an established anterior-posterior trend. It directly impacts the course of 2 vital structures, the internal carotid artery (ICA) and the optic nerve. Furthermore, pediatric skull base lesions can significantly alter the local anatomy by delaying or disrupting the developmental process. Tumors obliterating the pneumatizing sinus, impinging on expanding bony and neurovascular structures, or eroding into immature bone alter these developmental patterns. Data about the effect of different pathological entities on the development and maturation of the pediatric skull base are scarce.

Skull base development continuously shifts bony landmarks and changes anatomical corridors commonly used in endonasal endoscopic approaches (EEAs) for skull base lesions.¹⁰ To date, limited characterization of pneumatization and growth patterns has been attempted, however, most measurements found in the literature mainly focus on parameters relevant to sinus surgery. There are few data on age-related changes specifically focused on the EEAs to the skull base that can be used to guide neurosurgeons to choose a particular approach and understand dissection limits based on anatomical constraints. We therefore attempted a comprehensive analysis across the spectrum of EEAs in the entire range of pediatric age groups to help guide these technically challenging surgeries.

Herein we propose a novel set of radioanatomical skull base measurements meant to guide the neurosurgeon during expanded EEAs in the pediatric population. These parameters are designed to assess 3D drilling distances for specific endoscopic corridors and working space for the intracranial approaches. Second, we analyze the main restrictive regions in the pediatric EEA: the nasal aperture (NA) along with the interturbinate distance and the intercarotid distance (ICD).

Methods

Exclusion Criteria and Age Groups

Institutional review board approval was obtained for this study from Weill Cornell. Patients with ages ranging from 2 to 16 years who had undergone a maxillofacial or head MRI were selected from a prospectively acquired radiological database. We encountered no patients younger than 2 years of age during our first 50 pediatric skull base surgeries, and thus infants up to 2 years were not included in the radioanatomical study. After 16 years the skull base is considered by most reports^{13,16} to have reached the final developmental stage, and this was set as the upper cutoff for our analysis. Patients with conditions that potentially altered normal skull base anatomy were excluded. Among the exclusion criteria were midfacial abnormalities such as maxillary hypoplasia or craniofacial dysmorphic features, congenital anomalies, craniofacial trauma, previous sinonasal surgery, or sinonasal le-

sions. Images were stratified according to age at the time of the scan and sex of the patient.

Five discrete age groups were chosen to track skull base developmental changes: 2–4 years, 5–7 years, 8–10 years, 11–13 years, and 14–16 years. Pediatric patients who underwent EEA for skull base lesions were included in a separate group, which was used for comparison. Only a select subset of measurements, potentially affected by the pathological entity, were analyzed on preoperative MRI scans. The EEA group was further stratified according to lesion type and location, as follows: 1) sellar and parasellar lesions; 2) suprasellar lesions; 3) clival and odontoid lesions; and 4) maxillary/pterygoid together with cribriform/ethmoidal lesions. Maxillary/pterygoid and cribriform/ethmoidal lesions both affect the skull base from below and were thus grouped together.

Radioanatomical Method

A neuroradiologist and an otolaryngologist performed the measurements independently on the PACS (Agfa Healthcare). The 2 measurements obtained independently were averaged, and this was the final value used for the statistical analysis. A method similar to that described previously by Pinheiro-Neto et al.,¹¹ Shah et al.,¹³ and Tatreau et al.¹⁷ was used. Appropriate changes were made to accommodate the switch to MRI scans from the classic CT-based method. To this end, the following sections and sequences were used: sagittal T1-weighted fast spin echo (FSE); axial T1- and T2-weighted FSE; coronal T1- and T2-weighted FSE; axial T2-weighted FLAIR FSE; axial gradient echo; axial diffusion-weighted imaging; and 2-plane T1-weighted FSE post-Gd (Magnevist [gadopentetate dimeglumine], Bayer Pharmaceutical). Sequences were acquired at 5-mm thickness with no skip.

Measurement Parameters

We used 3 main sets of parameters to assess development of the pediatric skull base (Fig. 1). The first set describes the volume and the aeration level of the sphenoid sinus, the main corridor for EEAs, therefore directly assessing drilling distances to access the cranial cavity. The second set looks at the main intranasal and intracranial restriction sites for endoscopic approaches, including the NA, the width between inferior and middle turbinates, the ICD assessed at the level of the cavernous sinus, and the transsphenoidal angle (TA; defined below). The third set depicts total working distances from the nares to different intracranial targets and bony landmarks for both transsphenoidal and expanded EEAs. Maximal distances are measured solely at the level of anatomical corridors that allow endoscopic access without subsequent functional impairment or distortion of local anatomy.

Drilling Distances. The degree of pneumatization of the sphenoid sinus was described on midsagittal scans according to the 4 classic types (conchal, presellar, sellar, and postsellar), as discussed in the literature.^{7,11,13,17} Using the ellipsoid method, volumetric analysis of the sphenoid sinus (volume of the sphenoid sinus [VSS]) was also performed.¹ For this purpose, the width, height, and length of the sphenoid sinus (WSS, HSS, and LSS) were measured

Fig. 1. Drilling (A–E), restriction (F–I), and working (J–N) parameters shown on MRI studies. **A:** Height of the sphenoid sinus. **B:** Length of the sphenoid sinus. **C:** Width of the sphenoid sinus. **D:** A 3D reconstruction of the sphenoid sinus made using axial, coronal, and sagittal MRI sections to depict the ellipsoid method of calculating the volume of the sphenoid sinus. **E:** Sellar width. **F:** Nasal aperture. **G:** Maximal width between middle and inferior turbinates; *right-hand panel* is an enlarged view. **H:** Intercarotid distance at the cavernous sinus. **I:** Transsphenoidal angle. **J:** Nare-sellar distance. **K:** Nare-dens distance. **L:** Maximal reachable zone of the dens. **M:** Nare-vomer distance. **N:** Vomer-clival distance.

on coronal, midsagittal, and axial sequences, respectively, at the widest aerated cut. Length of the sinus was measured in the axial plane from the most inferior point of the vomer to the posterior wall of the aerated sinus area. Maximal height of the aerated portion of the sinus was assessed on midsagittal sections by using a perpendicular line to a plane passing through the anterior floor of the sinus. Width was measured on coronal sections as the maximal diameter of the aerated portion of the sinus. Maximal width of the sella turcica (Wsel) was also measured on coronal sections for better assessment of the lateral drilling limits of the transsellar approach (Fig. 1).

Anatomical Restriction Sites. Three major sites that can potentially restrict endoscopic access in the pediatric population were analyzed separately. The NA was measured as the maximal diameter on the midsagittal section of T1-weighted sequences, from the upper opening to the inferior aspect of the nasal cartilage. Wherever a larger diameter was noted on sagittal sections other than the midsagittal one, that measure was used instead. The maximal width (or aperture) between the middle and inferior turbinates (MaxWmT, MaxWiT) was measured as the widest area between each pair of turbinates on coronal sections. The ICD was obtained as their maximal distance on axial T2 sequences, at the level of the cavernous

sinus. We also assessed the TA, an angle measured between the most anterior point of the nasal cartilage and a tangential line to the cavernous carotids, on the same cut used for ICD measurements (Fig. 1).

Working Distances. The most important landmarks in EEAs are the bony prominences. Distances to potential intracranial targets, defined as the bony landmarks for the different EEAs, were measured. The nare-sellar distance (NSD) is measured as the maximal distance on midsagittal sections from the nare entrance to the sellar floor, the most anterior point of the sellar rostrum; it is the distance required to access the sellar compartment in its most anterior point. The nare-dens distance (NDD) is assessed on midsagittal sections as well, from the same nasal starting point to the most anterior reachable anatomical point of the odontoid that would allow access without distortion of the endonasal anatomy. The maximal reachable zone of the dens (MaxRZD) is measured as the midsagittal distance from the platform of C-2 to the naso-dental line, which is a tangential line to the hard palate connecting the anterior portions of the nasal bones to the dens. The NDD and the MaxRZD are measurements used for approaches accessing the craniocervical junction, a frequent point of skull base lesions in the pediatric population. The nare-vomer distance (NVD) is the longest distance from the

most anterior tip on axial cuts to the most anterior aspect of the vomer in the sellar compartment. The NVD complements the NSD measurement. The vomer-clival distance (VCD), a measurement intended for extended intracranial approaches, is assessed from the keel of the vomer to the clival edge at the prepontine cistern level. The NVD and the VCD are measured on the same axial cut to reduce variation (Fig. 1).

Statistical Analysis

Statistical analysis was performed using SPSS software (version 20.0). Continuous variables are shown as the mean values $\pm$ SD. Categorical values are given as percentages. Measurements are reported as the mean for each age group with the respective 95% CIs. An independent sample 2-tailed test was used to compare means based on sex. One-way ANOVA with unequal variance calculated using a post hoc Tamhane T2 test was used to compare means between age groups. To test how certain measurements impact each other, Pearson and Spearman rho bivariate correlation tests were computed as appropriate. A GLM (general linear model) univariate model was used to analyze the impact of age, sex, and pathological entity on each specific measurement (NSD, NDD, NVD, VCD, MaxWmT, MaxWiT, TA, and ICD). A GLM multivariate model was constructed to determine the overall effect of age group, sex, and lesion location on measurements. Partial eta-squared (η^2) is reported to show the impact of each parameter on the respective measurement (maximal value 1). The MaxWmT and MaxWiT were excluded from the multivariate model because local disease obstructed the measurement for 6 cases. A p value < 0.05 was considered statistically significant.

Results

Patient Cohort

The MRI scans obtained in 107 pediatric patients with no skull base or maxillofacial anomalies were reviewed. Patients were stratified in 5 age groups: 2–4 years ($n = 24$, 22.4%), 5–7 years ($n = 28$, 26.2%), 8–10 years ($n = 21$, 19.6%), 11–13 years ($n = 21$, 19.6%), and 14–16 years ($n = 13$, 12.1%) (Fig. 2 and Table 1). The mean age for the entire cohort was 8.07 ± 0.4 years, with 62 boys (57.9%) and 45 girls (42.1%). Additionally, preoperative MRI scans obtained in 29 patients undergoing EEAs for a variety of skull base lesions were analyzed (Fig. 2 and Table 2). The mean age for the EEA group was 15.9 ± 0.6 years. There were 18 boys (62.1%) and 11 girls (37.9%). These patients were further divided into 3 age groups (11–13 years, $n = 7$; 14–16 years, $n = 11$; and 17–21 years, $n = 11$) and into 4 groups based on the location of the skull base lesion (sellar/parasellar, $n = 16$; suprasellar, $n = 3$; clival and odontoid, $n = 4$; maxillary and ethmoidal, $n = 6$).

The average differences between the 2 independent measurements performed by a neuroradiologist and an otolaryngologist were as follows: NSD ($\Delta = 1.39$ mm), NDD ($\Delta = 5.14$ mm), MaxRZD ($\Delta = 1.91$ mm), NVD ($\Delta = 5.2$ mm), VCD ($\Delta = 4.14$ mm), NA ($\Delta = 1.92$ mm), HSS

Fig. 2. Bar graphs showing general cohort characteristics. **A:** Age groups and sex for the normal pediatric population cohort (107 patients without skull base lesions). **B:** Age groups and sex for the EEA cohort (29 patients with skull base lesions). **C:** Pathological entity and age groups for the EEA cohort. Count = number of patients.

($\Delta = 2.03$ mm), WSS ($\Delta = 1.58$ mm), LSS ($\Delta = 1.56$ mm), ICD ($\Delta = 1.18$ mm), TA ($\Delta = 1.64^\circ$), MaxWmT ($\Delta = 1.78$ mm), MaxWiT ($\Delta = 3.16$ mm), and Wsel ($\Delta = 3.51$ mm). None of these differences were statistically significant. Greater differences were noted in younger age groups,

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TABLE 1: Measurements of drilling, restriction, and working parameters in 107 pediatric patients without skull base lesions*

Measurement	2–4 Yrs	5–7 Yrs	8–10 Yrs	11–13 Yrs	14–16 Yrs
no. of pts	24	28	21	21	13
drilling distances					
HSS	14.2 (11.7–16.7)	17.7 (15.8–19.7)	19.6 (17.9–21.3)	21.2 (19.4–23.0)	22.6 (20.0–25.4)
WSS	12.8 (9.9–15.7)	18.5 (16.1–20.9)	21.5 (19.0–24.1)	23.6 (20.9–26.3)	24.7 (21.4–28.0)
LSS	12.3 (9.5–15.1)	14.6 (12.7–16.5)	18.8 (16.4–21.3)	19 (16.7–21.2)	22.4 (18.1–26.7)
VSS	1618.0 (1108.6–2127.4)	2848.5 (2048.8–3648.2)	4361.5 (3167.7–5555.4)	5172.8 (4104.4–6241.2)	6866.4 (4834.5–8898.3)
Wsel	12.5 (11.4–13.7)	14.4 (12.3–16.6)	14.8 (13.2–16.3)	17.6 (14.6–20.7)	15.6 (12.8–18.4)
restriction sites					
NA	6.7 (6.1–7.3)	8.2 (6.8–9.5)	8.1 (7.1–9.1)	9.3 (8.4–10.2)	8.3 (7.0–9.7)
MaxWiT	5.7 (5.1–6.2)	6.4 (5.1–7.7)	6.3 (5.7–6.8)	5.9 (5.2–6.5)	6.3 (5.2–7.3)
MaxWmT	5.8 (5.3–6.4)	6.4 (5.9–6.9)	7.5 (6.1–8.8)	6.9 (6.1–7.7)	7.0 (6.0–8.1)
ICD	11.3 (9.6–13.1)	12.8 (11.5–14.1)	13.5 (12.3–14.7)	14.1 (12.8–15.5)	15.2 (13.5–16.9)
TA	14.9 (13.3–16.5)	18.2 (16.7–19.7)	20.1 (18.1–22.0)	20.4 (18.5–22.4)	18.6 (16.5–20.7)
working distances					
NSD	63.0 (60.2–65.8)	68.2 (64.8–71.6)	74.4 (71.5–77.3)	76.6 (74.0–79.2)	79.9 (75.5–84.2)
NDD	82.5 (70.1–86.0)	89.4 (86.3–92.5)	94.0 (90.3–97.7)	97.8 (95.2–100.4)	101.8 (96.0–107.6)
MaxRZD	11.4 (9.8–13.1)	11.1 (9.3–13.0)	12.4 (10.3–14.5)	11.8 (9.6–14.0)	13.2 (10.1–16.2)
NVD	46.9 (44.8–49.1)	49.5 (47.0–52.0)	49.0 (47.1–50.8)	50.6 (48.2–53.0)	55.6 (51.2–60.0)
VCD	27.8 (25.5–30.1)	31.8 (30.2–33.4)	32.5 (30.3–34.7)	33.9 (30.9–36.8)	33.9 (31.0–36.8)

* Measurements are reported as distance in millimeters (HSS, WSS, LSS, Wsel, NA, MaxWmT, MaxWiT, ICD, NSD, NDD, MaxRZD, NVD, and VCD), volumes in cubic millimeters (VSS), or angles in degrees (TA), with 95% CIs given in parentheses. Pts = patients.

which was not surprising given the less defined and more complex anatomy ($p = 0.01$).

Drilling Parameters

Assessing the drilling distance through the incompletely pneumatized sphenoid sinus is an important first step during exposure of pediatric EEAs (Fig. 3). Overall, age group significantly influences the volume of the sphenoid sinus ($p = 0.0001$). However, this effect is not powerful (partial $\eta^2 = 0.340$). Moreover, the 95% CI also increases with age, showing larger variations in older age groups. Based on the number of patients in each age group in this study, differences in the volumes of the sphenoid sinus were not statistically significant between adjacent age groups. For instance, the mean volume in the 2–4 years age group, $1618 \text{ mm}^3 \pm 509.4 \text{ mm}^3$, is not significantly different from that found in the 5–7 years age group, $2848.5 \text{ mm}^3 \pm 799.7 \text{ mm}^3$ ($p = 0.364$). However, a statistical difference is reached when compared with the volume in the 8–10 years age group, $4361.5 \text{ mm}^3 \pm 1193.8 \text{ mm}^3$ ($p = 0.002$). Hence, the volume of the sphenoid sinus slowly and steadily increases with age in a linear fashion.

As the sphenoid sinus reaches maturation, higher variability in volume is also noted. This difference in volume is most likely related to changes in the width of the sinus more than the length or the height. Significant differences are observed in WSS at younger ages, the 2–4 years compared with the other age groups, including the adjacent 5–7 years age group ($p = 0.04$). However, the WSS difference between the 5–7 years group and all other older age groups is not statistically significant. For the

HSS and LSS values, the only statistically significant differences are between the extreme age groups; 2–4 years compared with 14–16 years. This further shows that most differences in sphenoid sinus morphological features occur during early childhood and that the sinus expands mostly in a lateral direction without significantly changing the effective drilling distance across age groups. This trend is also reflected in the Wsel. Indeed, Wsel differences are only significant between the 2–4 and 11–13 years age group ($p = 0.007$) (Fig. 3). As expected, Wsel and VSS are significantly correlated, as assessed by the Pearson correlation test ($r = 0.428$, $p = 0.0001$). Changes in pneumatization patterns according to age are statistically significant. Level of pneumatization also correlates with VSS ($r = 0.533$, $p = 0.0001$) and Wsel ($r = 0.289$, $p = 0.002$), showing the interdependence of parameters at the level of the sphenoid sinus.

A small difference was noted in the overall mean volume of the sphenoid sinus in boys ($3988.4 \text{ mm}^3 \pm 373.8 \text{ mm}^3$) compared with the volume in girls ($3673.2 \text{ mm}^3 \pm 441.8 \text{ mm}^3$). However, the difference was not statistically significant ($p = 0.475$). This difference was mainly due to a difference in the width of the sinus as measured on coronal sections; $20.1 \text{ mm} \pm 1 \text{ mm}$ in boys compared with only $18.8 \text{ mm} \pm 1 \text{ mm}$ in girls, similarly not statistically significant ($p = 0.361$). No significant difference according to sex was observed in Wsel or for the 3 pneumatization patterns. A univariate ANOVA model, testing for a combined effect of sex and age group on the volume of the sphenoid sinus, shows no statistically significant impact ($p = 0.307$, partial $\eta^2 = 0.048$, with 1 being the strongest association). However, the same analysis shows

TABLE 2: Specific measurements according to lesion location in 29 pediatric patients with skull base lesions who underwent an EEA*

Location	Pathology	No. of Pts	Age (yrs)	NSD	NDD	NVD	VCD	MaxWmT	MaxWIT	ICD	TA
sellar, parasellar	pituitary adenoma	16	16.4 ± 3.5	68.1 (66.0–70.1)	83.4 (80.7–86.1)	55.6 (52.9–58.3)	28.6 (26.2–31.0)	12.4 (11.0–13.8)	9.8 (8.4–11.2)	15.4 (13.8–17.0)	15.4 (13.8–17.0)
suprasellar	craniopharyngioma	3	12.0 ± 1.7	56.7 (54.9–58.5)	72.0 (68.7–75.4)	49.7 (46.3–53.1)	28.1 (20.7–35.6)	11.9 (10.7–13.2)	9.6 (5.8–13.4)	12.1 (9.7–14.4)	14.7 (9.8–19.6)
clivus, odontoid	germinoma, ependymoma, chordoma, BI	4	16.0 ± 1.9	65.7 (63.5–67.9)	73.9 (66.6–81.3)	48.7 (47.7–49.8)	26.7 (23.1–30.3)	11.6 (8.7–14.5)	11.7 (10.8–12.6)	14.1 (12.1–16.0)	14.7 (13.0–16.3)
maxillary, ethmoidal	JNA, fibrous dysplasia, mucocoele	6	16.5 ± 2.1	68.3 (64.9–71.7)	77.3 (73.7–80.8)	57.8 (51.0–64.7)	26.2 (18.9–33.5)	10.5 (9.4–11.7)	9.0 (7.3–10.7)	15.4 (13.1–17.7)	13.05 (11.4–14.7)

* Measurements reported as distance in millimeters (MaxWmT, ICD, NSD, NDD, and VCD) or angles in degrees (TA), with 95% CIs given in parentheses. Ages are expressed as the mean ± SD. BI = basilar invagination; JNA = juvenile nasopharyngeal angiofibroma.

a significant yet reduced combined effect of age and sex on the Wsel ($p = 0.022$, partial $\eta^2 = 0.110$).

Restriction Parameters

The first limit to an EEA in a child is the NA. Surrounded by cartilaginous structures, it is best visualized on MRI scans. As expected, the NA increases steadily with age ($p = 0.035$). However, the process is slow, as shown by the slope of the NA growth trend (Fig. 4). Differences between age groups are minute and clinically insignificant. The only statistically significant difference is the 2.54-mm increase in NA from 2–4 years to 11–13 years ($p < 0.0001$, Table 1).

The NA can be manipulated to fit the endoscope and the microinstruments; however, the middle and inferior turbinates often restrict access, necessitating resection of part or all of a middle turbinate. Interestingly, our measurements show that the maximal distance between the middle and inferior turbinates does not change significantly with age ($p = 0.088$ and 0.076 , respectively), nor does it change according to sex ($p = 0.124$ and 0.281).

The ICD and TA are important parameters for the neurosurgeon to evaluate preoperatively. The only statistically significant difference in ICD (3.9 mm; from 11.3 mm to 15.2 mm) is noted between the extreme age groups (2–4 years and 14–16 years; $p = 0.038$). Although this small difference seems to be of little clinical relevance, it can directly impact the working angle and the access to more lateral regions of the sellar area. Indeed, significant differences are observed when comparing the TA in younger and older age groups. The 14.9° TA at 2–4 years has a significant increase, of 37.6% ($\Delta TA = 5.6^\circ$), in the 11–13 years age group ($p = 0.001$). After reaching the peak in the 11–13 years group, the angle seems to decrease by almost 2° during the final stages of development in the 14–16 years age group, albeit not by a statistically relevant margin ($p = 0.936$). The ICD seems to be slightly narrower in girls compared with boys (12.96 mm vs 13.34 mm), without the difference being statistically relevant ($p = 0.581$). Differences for the TA based on sex are even smaller. A univariate general linear model testing the combined effect of both age and sex shows that only age has a significant yet limited effect on ICD and TA.

We next investigated if the pneumatization pattern of the sphenoid sinus might predict the ICD and the TA, with potential utility in select cases in which ICD cannot be assessed on preoperative MRI due to invasive lesions. The type of pneumatization significantly influences both the TA and the ICD (Fig. 4). The mean TA in children with sellar sphenoid pneumatization is 7° wider compared with the conchal type ($p < 0.0001$). Similarly, the intercarotid corridor as defined by the ICD parameter is 4.6 mm narrower in the conchal type compared with the sellar type ($p < 0.0001$). The degree of pneumatization of the sphenoid sinus positively correlates with both ICD ($r = 0.431$, $p < 0.0001$) and TA ($r = 0.507$, $p < 0.0001$). There is obvious correlation between the TA and the ICD ($r = 0.443$, $p < 0.0001$). Increased aeration of the sinus induces a degree of expansion of the adjacent bony structures, as demonstrated by the dual increase in VSS and Wsel according to pneumatization type. This further leads to changes in anatomi-

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Fig. 3. Drilling parameters in patients without skull base lesions. **A–E:** Graphs showing growth curves according to age groups. Increments on the y axis denote millimeters for distance (A–C, E) and cubic millimeters for volume (D). **F and G:** Bar graphs showing pneumatization pattern (conchal, presellar, sellar) of the sphenoid sinus based on age and sex.

cal relationships of the overlying neurovascular structures, specifically the ICA. The VSS correlates with both the TA ($r = 0.544$, $p < 0.0001$) and the ICD ($r = 0.433$, $p < 0.0001$). As the sinus expands, distances between structures lying inferiorly and farther away, such as the inferior and middle turbinates, do not change significantly ($r = 0.026$, $p = 0.791$; and $r = 0.169$, $p = 0.082$). This further supports the theory of the posterior and superior direction of the pneumatiza-

tion process,¹² a process that mostly induces changes in the neurovascular structures at the base of the skull.

Working Parameters

The NSD has a relatively steep growth slope in the first 12 years of life, increasing by 11.4 mm ($p < 0.0001$), from 63 mm $\pm$ 2.8 mm (2–4 years) to 74.4 mm $\pm$ 3.4 mm (8–10 years). After 10 years it reaches a plateau, increas-

Fig. 4. Restriction parameters in patients without skull base lesions. **A–E:** Graphs showing growth curves according to age (y axis = millimeters). **F and G:** Bar graphs showing differences in ICD and TA based on pneumatization pattern ($p < 0.0001$ for both parameters). **H:** Scatterplot showing correlation between the TA and the ICD ($r = 0.443$, $p < 0.0001$). In this panel, the increments on x and y axes denote degrees and millimeters, respectively.

ing by only 5.5 mm more ($p = 0.388$) before the completion of the developmental process at 16 years (final NSD = $79.9 \text{ mm} \pm 4.3 \text{ mm}$) (Fig. 5). Furthermore, the NSD seems to be 3.8 mm shorter in girls (69.1 mm), compared with the mean NSD of 72.9 mm measured in boys ($p = 0.04$). These differences according to sex seem to be most prominent in the extreme age groups, with the NSD differing by 5.1 mm in the 2–4 years age group and by 8.36 mm in the 14–16 years age group. A univariate ANOVA shows that the sex of the patient has a statistically significant yet weak effect on NSD ($p = 0.001$, partial $\eta^2 = 0.106$), whereas age has a much more powerful impact ($p < 0.0001$, partial $\eta^2 = 0.452$).

Expanded approaches can access skull base lesions located farther away, anteriorly and posteriorly, from the

sellar region. Working distances become important in defining age groups that are most amenable to specific expanded EEAs such as the transodontoid and transclival approaches. The NDD measures the safest corridor used to access the farthest point of the craniocervical junction. This approach can be further expanded to the platform of C-2 for a complete decompression of the cervical spinal cord and the brainstem in congenital malformations of this region such as basilar invagination. For this expanded approach, a useful measurement is the MaxRZD.

The NDD has an even steeper slope of the age-dependent growth trend compared with the NSD (Fig. 5). There is a 19.2-mm statistically significant difference ($p < 0.0001$) in NDD between the 2–4 years and the 14–16 years age group ($82.5 \text{ mm} \pm 3.5 \text{ mm}$ vs $101.8 \text{ mm} \pm 5.8$

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Fig. 5. Working parameters in patients without skull base lesions. **A–E:** Graphs showing growth curves according to age group. **F and G:** Differences in NSD and NDD based on pneumatization pattern ($p < 0.0001$). **H and I:** Scatterplots showing correlation between NSD and ICD ($H: r = 0.481, p < 0.0001$) and between NSD and TA ($I: r = 0.432, p < 0.0001$).

mm). Significant differences in NDD are not observed at older ages, starting with the 8–10 years age group. Of note, the NDD at 2–4 years (70.1–86 mm) is longer than the NSD reached during adulthood (75.5–84.2 mm). The transodontoid approach is obviously more challenging, regardless of the skull base developmental stage, due to the high distance corridor. Despite being 3.2 mm shorter in girls, the NDD has no sex-dependent statistically significant differences ($p = 0.112$). Interestingly, the largest sex-based difference in NDD (12.8 mm) is noted at 14–16 years (108.7 mm in boys vs 95.9 mm in girls). A univariate ANOVA shows that there is no significant concerted effect of the patient's sex and age on NDD ($p = 0.317$, partial $\eta^2 = 0.047$). The MaxRZD has a much more constant evolution, with differences ranging from 0.3 to 1.7 mm that are not statistically significant, and high variations regardless of age group. This demonstrates that the limiting step in decompression procedures at the craniocervical junction is the access along the NDD.

To reach the more posterior clival region, the sphenoid sinus and sellar area are transgressed. Thus, we considered it adequate to use 2 complementary measurements for this complex approach: the NVD and the VCD. The NVD does not change dramatically with age; the only peak is reached in the late stages of development (Fig. 5). The only statistically significant differences are between the oldest and youngest age group; 8.6 mm (p

$= 0.025$) between the 2–4 years age group (47 mm $\pm$ 2.2 mm) and the 14–16 years age group (55.6 mm $\pm$ 4.4 mm). The VCD has a similar trend, but reaches a plateau much earlier in the process, at 5–7 years. A significant difference (6.3 mm) is observed between the 2–4 years age group and the last 2 age groups ($p = 0.019$ and 0.028). A univariate ANOVA shows that age plays a significant yet weak role in NVD and VCD (NVD: $p = 0.005$, partial $\eta^2 = 0.141$; VCD: $p = 0.001$, partial $\eta^2 = 0.184$). Small, insignificant sex-dependent differences are observed for both the NVD and the VCD. These measurements indicate a clear developmental pattern of the pediatric skull base. Whereas anterior portions of the skull base continue to expand in the course of the entire childhood, posterior areas finish the growth process earlier.

The Spearman rho nonparametric correlation test indicates that the NSD correlates to some degree with all other working measurements in the group without skull base lesions: NVD ($r = 0.503, p < 0.0001$); VCD ($r = 0.335, p < 0.0001$); and most importantly NDD ($r = 0.862, p < 0.0001$). The proposed working measurements are an interrelated reference system assessing distances in all 3 dimensions. By using the NSD, the neurosurgeon will get an overview of the skull base developmental stage; using the NSD allows one to assess the feasibility of the transphenoidal, transsellar, and other expanded approaches. This is further supported by the significant correlation of

the NSD with the most important restriction parameters: TA ($r = 0.432$, $p < 0.0001$) and ICD ($r = 0.481$, $p < 0.0001$). On the other hand, the NVD and VCD are not significantly interrelated ($r = -0.061$, $p = 0.535$), showing the 2 different and asynchronous growth rates of the anterior and posterior skull base compartments. Moreover, the sphenoid sinus pneumatization type correlates with both the NSD ($r = 0.488$, $p < 0.0001$) and the NDD ($r = 0.443$, $p < 0.0001$).

Although significant, the impact of the pneumatization process on the axial measurements is less important (NVD: $r = 0.242$; VCD: $r = 0.228$). Because the aeration process of the sphenoid sinus progresses superiorly, there is little impact on the anterior-posterior growth pattern of the sella and clivus. Significant differences according to pneumatization pattern are observed only for the midsagittal NSD and NDD. A 13.6-mm difference is observed in the NSD for the conchal sphenoid type compared with the sellar type ($p < 0.0001$). Similarly, the mean NDD for the conchal type is 14 mm shorter than the mean NDD for the sellar pneumatization ($p < 0.0001$). This shows that in younger patients, although the effective drilling distance might be greater, once the exposure portion has been completed the intracranial dissection step might be easier compared with older age groups. With shorter working distances such as the NSD and NDD, better visualization and better access facilitate safer surgery. Figure 6 shows the age-dependent changes in key anatomical areas of the pediatric skull base and the importance of the sphenoid pneumatization process in driving these changes.

Effect of Skull Base Pathological Entities on Development

To test the impact of skull base lesions on the developmental process, we performed the same measurements in a group of patients undergoing EEAs for a variety of

pathological entities of the skull base. Measurements in the group of patients with skull base lesions were significantly different compared with the normal cohort (patients without skull base lesions), regardless of lesion location and age group (Table 2). The mean NSD was shorter by as much as 14.2 mm in patients with clival and odontoid lesions. The NDD differed by as much as 27.9 mm in patients with suprasellar craniopharyngiomas compared with the normal group. The VCD was less affected; it was shorter by only 7.7 mm and mostly changed in patients harboring maxillary and ethmoidal lesions expanding into the cranial cavity. To control for age, we then selected only patients in the 13–16 years age group for the next steps of the statistical analysis. Using a 1-way ANOVA post hoc Tamhane test, significant differences between the normal group and patients undergoing EEAs were observed only for the midsagittal working measurements (NSD and NDD). Expansive suprasellar lesions had the most significant impact, modifying the NSD by 20.9 mm and the NDD by 27.3 mm ($p < 0.0001$). Only sellar lesions significantly modified the axial VCD measurement ($\Delta VCD = 5.1$ mm, $p = 0.001$). As expected, maxillary and ethmoidal lesions did not affect working parameters.

Interestingly, skull base lesions did not significantly alter neurovascular structures and subsequently restriction parameters. Only minor differences were noted in the ICD compared with the normal cohort, mostly in patients with craniopharyngiomas expanding into the cavernous sinus ($p = 0.832$). However, the TA was significantly narrower in sellar ($\Delta TA = 4.5^\circ$, $p = 0.012$) and clival lesions ($\Delta TA = 6.1^\circ$, $p < 0.0001$). Pneumatization patterns were not altered compared with the normal patients in the 13–16 years age group (Fig. 6). We then wanted to verify if the correlations between parameters observed in the nor-

FIG. 6. Axial MRI studies showing age-dependent evolution of the key anatomical areas for EEAs. **Upper:** Cropped and enlarged MRI studies showing representative changes in ICD, TA, NVD, and VCD in the pediatric patient in the 2–16 years age interval. **Lower:** Evolution of the sphenoid pneumatization process based on age, correlating with changes in the restriction and working parameters depicted above. Note the posterior-superior progression of pneumatization and the impact on the anatomy of the 2 ICAs as well as on the main endonasal endoscopic corridors.

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mal cohort were maintained in the group with skull base lesions. Significant correlations were only observed between NSD and ICD (Pearson correlation test, $r = 0.578$; $p = 0.012$) and between NVD and VCD (Pearson correlation test, $r = 0.596$; $p = 0.009$). Nonparametric tests also showed a correlation between NSD and NVD (Spearman rho correlation test, $r = 0.503$; $p = 0.033$).

Due to the limited number of cases in each lesion group, these results cannot be widely extrapolated. The 2D and 3D scatterplots (Fig. 6) give an overview of how each lesion type impedes the normal skull base development, inducing large variations in skull base measurements. Regardless of lesion location, age group, or pneumatization type, the NSD, NDD, and TA values are clearly lower than those in the normal population. A lesser effect is seen on axial working measurements or ICD. Frequently, skull base lesions alter measurements not only by delaying the normal growth process but also by masking bony landmarks in the sphenoid sinus on MRI. In such cases, the above-mentioned linear correlations between different parameters can be used to predict the ones that cannot be obtained on preoperative imaging. One such measurement is the NSD, which can be used as a general reference parameter predicting the overall developmental stage of the skull base. Based on the scatterplots in Fig. 7, one would expect children with skull base lesions to have narrower working corridors compared with a child without such lesions (small TA), but also to have lesions that are closer to the NA (small NSD/NDD). However, due to the large lesion-dependent variations, prediction models should only be used to better understand the local anatomy and plan the endoscopic approach.

Discussion

Although rare, skull base tumors in children can be particularly destructive by transgressing growth centers and delaying or irreversibly affecting the developmental process.¹⁹ Early resection of such lesions is important, independent of decisions made for disease control, to reset the growth process.⁵ These lesions in the pediatric skull base can lead to severe functional impairment.^{2,19} However, the unique anatomical features of the growing pediatric skull base frequently impede surgical access to local pathological entities.^{5,10,18,19} Incompletely aerated sinuses or the shallow anterior anterior fossa can hinder anterior transfacial approaches.^{18,19}

The EEAs not only provide better visualization but are also much more adaptable to these anatomical constraints. Endoscopic corridors can safely and effectively reach lesions not amenable to open routes,¹⁰ and with much less cosmetic disfigurement and fewer of the risks inherently associated with craniofacial approaches. Feasibility of these approaches in children has been demonstrated.^{4,8,9} However, successful EEA surgery requires an adequate working space for the endoscope as well as the instruments. Hesitations and questions have been raised regarding the feasibility of performing EEAs in pediatric patients, given the smaller working space compared with adults. For this reason, developmental parameters specifically applicable to EEA work must be established

and analyzed. The developmental progression of the skull base is important to appreciate across all childhood age groups,⁵ and some of the parameters can be adapted to guide transsellar and expanded endoscopic approaches around these growth centers. Areas restricting endoscope passage and safety borders of intracranial dissection, based on local neurovascular structures, change continuously during childhood.¹⁰ Furthermore, skull base structures are clustered together in the early stages of development, and neurosurgeons must adapt their approach to the lesion, its location, and restrictions imposed by age.

In this study we analyzed developmental patterns of the pediatric skull base and the impact on EEA. As neurosurgeons venture past the sellar area, new reference systems are necessary to help practitioners who are using EEAs navigate around the tightly packed neurovascular elements at the extremes of the ventral and dorsal skull base. Starting as early as 2 years, the pneumatization process of the sphenoid sinus is the primary (but not the sole) driving force behind skull base changes pertaining to EEAs.¹⁷ Gradual aeration of the sphenoid sinus affects not only the transsphenoidal corridor but also posteriorly expanded intracranial approaches reaching the cavernous sinus or the clivus. Scuderi et al.¹² and Tatreau et al.¹⁷ show that the pneumatization pattern follows a strict inferior-to-superior and lateral direction. Our volumetric studies using MRI cuts [slices] in all 3 dimensions (coronal, midsagittal, and axial) further support this observation and demonstrate that aeration occurs at a relatively slow pace. Concomitant changes in sphenoid and sellar width are noted, gradually opening endoscopic routes to the parasellar region in older age groups (Fig. 8). Aeration of the sphenoid sinus is the direct determinant of the drilling distance and can help establish the best entry point to access the skull base. Significant volumetric and width changes at the sphenoid-sellar level occur slowly and, based on the sample sizes in this study, reach statistical significance compared with the starting infant ages during early adolescence, at approximately the 11- to 13-year time frame. Patients can thus be roughly divided into 2 main surgical groups: before 11 years, when more drilling is required, and after the 11- to 13-year limit, when access to the parasellar area is more easily obtained due to the lateral aeration.

With this understanding, it should be emphasized that safe drilling can be achieved through the soft immature bone regardless of pneumatization level, especially when accessing lesions in the midline.³ Thus, we consider pneumatization type to be a relative age-dependent limitation for EEAs in children. The more important role of measurements and patterns analyzing pneumatization is to assess the impact on the intracranial neurovascular structures such as the ICD and to predict the safest working angles for the intradural dissection steps. As air enters the posterior and superior portions of the sphenoid sinus, gradually extending laterally, the expanding dorsal bony structures modify the anatomical relationships of the carotid canal.² Conchal pneumatization indicates a narrow intercarotid corridor and a tight working angle regardless of age group. Differences in ICD can be as high as 5 mm, and the TA is almost 7° wider in children with complete pneumatiza-

Fig. 7. Effects of pathological entities on skull base development and parameters. **A–D:** The 2D and 3D scatterplots depict differences in the main restriction and working parameters (TA and NSD) based on age group (A and C) and pneumatization pattern (B and D) between the normal population and patients harboring skull base lesions. A third dimension, sex, is also depicted for the NSD to show that skull base pathology attenuates sex-dependent differences as well as age- and pneumatization-dependent differences in NSD. Schematic drawings of the pediatric skull reflect the impact of clival and sellar/parasellar tumors on the lateral dissection limits (TA, upper right) as well as the effect of suprasellar lesions on the working distances (NSD, center right). **E:** Bar graph showing differences in pneumatization patterns between the normal population and patients with skull base lesions. Copyright Jeffrey P. Greenfield. Published with permission.

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FIG. 8. Age-dependent, pneumatization-induced changes in endonasal endoscopic corridors. Age-dependent differences in VSS are mostly related to changes in the WSS. Significant differences are observed in WSS in younger age groups, specifically the 2–4 years group compared with the other age groups ($p = 0.04$). Furthermore, differences in Wsel are only significant between the 2–4 and 11–13 years age groups ($p = 0.007$). This further shows that most differences in sphenoid sinus morphological features occur during early childhood and that the sinus aeration is a gradual, modular process mostly expanding in a temporal direction without significantly changing the effective drilling distance across age groups. A schematic drawing of the sphenoid sinus depicts the lateral aeration, with limited impact on the drilling step of EEA but significantly affecting the ICD and implicitly the restriction parameters during the intracranial dissection step. Furthermore, as pneumatization extends laterally, new parasellar corridors become available. Pneumatization patterns are a relative limitation in pediatric EEA because the cancellous bone can be easily drilled down. However, restriction parameters impose absolute limitations and are directly affected by the pneumatization process. Copyright Jeffrey P. Greenfield. Published with permission.

tion. These findings differ from those reported by Tatreau et al.,¹⁷ who report no statistically significant difference of the cavernous ICD between patients 9–10 years of age and older. Furthermore, they observed no difference in ICD at the superior clivus after 24 months, concluding that pneumatization of the sphenoid sinus does not significantly impact ICD.

Pneumatization patterns generally correlate with age group,⁷ although certain exceptions are possible (Fig. 3). Hence, expanded endoscopic approaches passing between the ICAs, such as the transcavernous approach, are much safer in older age groups or in patients who have reached complete pneumatization of the sphenoid. Patients with sellar pneumatization patterns are also the best candidates for laterally expanded sellar approaches, because the working TA is much wider, providing more freedom of movement and dissection. However, a prohibitive ICD has been reported to be less than 10 mm,²¹ and our measurements show that the narrowest intercarotid corridor is 11.3 mm in the 2–4 years age group. The ICD, TA, and pneumatization correlations can be best used to establish working space and lateral resection limits instead of simple assessment of feasibility. Predictions of ICD and TA based on pneumatization level can be used when direct measurements of the restriction parameters are not feasible due to tumor obstruction on MRI studies, a common scenario.

Inferior restriction points are the NA as well as the middle and inferior turbinates. The NA was wider than the 3-mm limit reported in the literature,¹⁷ mostly due to the MRI-based measurements, which are able to determine borders of cartilaginous structures more accurately. According to our findings, because it does not change significantly across age groups, the NA does not constitute a real restriction point even for expanded approaches. We were able to perform expanded EEAs safely, both anteriorly and posteriorly, in all age groups without the need for facial degloving and sublabial approaches. The maximal distance between the nasal turbinates is also fairly constant across age groups, with high individual variability. Decisions regarding the resection of the middle turbinate have to be made on a case-by-case basis, depending less on age group and more on the intracranial approach and on the specific anatomical characteristics. Because pneumatization progresses in a superior direction, there is little impact on the bony structures located below the sphenoid sinus. No predictions can be made regarding this bony restriction point based on aeration pattern.

After establishing feasibility based on restriction points and drilling distances for corridor exposure, working distances will provide the best assessment during the intradural dissection step. Development of the skull base has been proven to be asynchronous and asymmetrical.^{14,15} As growth of the midfacies accelerates in late childhood,¹ midsagittal craniocaudal expansion of the skull base also accelerates. However, we show that the dorsal portions have a more rapid development and reach maturation earlier, at 5–7 years, compared with the more anterior compartments of the cranial base. Measurements and opportunity windows for specific expanded approaches are continuously and rapidly changing during childhood. The NSD, a working measurement with a steep age- and sex-

dependent increase, is most useful for transsphenoidal sellar approaches and anteriorly expanded approaches. These are the most frequently used EEAs in the pediatric population, because a common lesion is craniopharyngioma of the sellar and suprasellar region. The NDD has a similar rapid growth trend and aids in assessment of corridors to the craniocervical junction, a common site for congenital anomalies such as basilar invagination encountered independently or in conjunction with a common pediatric anomaly, the Chiari malformation.

All working measurements, sagittal and axial, are interdependent and are correlated to some degree to the level of pneumatization. However, although the pneumatization process advances slowly, distances to intracranial targets increase rapidly. Although corridor exposure is more difficult in young children due to longer drilling distances and narrower working spaces, specific targets are easier to access in early childhood. Better visualization and access may provide superior resection conditions in the young age groups.

Skull base tumors frequently invade adjacent structures and erode into the immature cancellous bone. Obliteration of the sphenoid sinus and interference with the normal pneumatization process will lead to significant delays in skull base development. Although the parameters we describe can be applied based on age group to patients undergoing EEAs, caution must be taken. We show in this study that in a select group of children with skull base lesions the normal anatomical development is frequently altered. Although the NSD is not as strongly correlated to the other measurements as in the normal population, it can still be used to obtain an overview of the skull base developmental stage and largely assess restriction parameters, specifically the ICD. However, when performing EEAs in children harboring aggressive skull base tumors, the neurosurgeon should always expect narrower corridors and shorter working distances.

Conclusions

Development of the pediatric skull base is an intricate, asymmetrical process affecting bony and neurovascular structures, with direct impact on EEA corridors. Pneumatization of the sphenoid sinus is one of the main driving forces of the developmental process influencing drilling, restriction parameters, and working parameters alike. Establishing pneumatization patterns, restriction areas, and maximal distances of reachable targets according to age can help guide preoperative choices of sinus corridors and intracranial approaches. Surgical indications based not only on pathological entity but also on skull base developmental stage will potentially increase the safety of EEAs in children. However, invasive and eroding skull base lesions can significantly delay growth of bony structures and affect measurements. Thus MRI measurements rather than age should guide preoperative planning. Our MRI skull base parameters are highly interdependent and correlate with the pneumatization pattern of the sphenoid sinus. Predictive models based on these interdependent parameters will help establish corridors and working space in the intracranial cavity even

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in those cases in which a lesion impedes preoperative radioanatomical measurements.

Disclosure

Dr. Souweidane is a consultant for Aesculap, and Dr. Schwartz oversees a non-study related clinical or research effort supported by Karl Storz and Visionsense.

Author contributions to the study and manuscript preparation include the following. Conception and design: Greenfield, Banu, Souweidane, Anand, Heier, Schwartz. Acquisition of data: Banu, Guerrero-Maldonado, McCrea, Garcia-Navarro, Heier. Analysis and interpretation of data: Greenfield, Banu, Guerrero-Maldonado, McCrea, Garcia-Navarro, Schwartz. Drafting the article: Banu, Guerrero-Maldonado, McCrea. Critically revising the article: all authors. Reviewed submitted version of manuscript: all authors. Approved the final version of the manuscript on behalf of all authors: Greenfield. Statistical analysis: Banu. Study supervision: Souweidane.

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Manuscript submitted June 14, 2013.

Accepted October 29, 2013.

Portions of this work were presented in abstract form at the AANS Annual Meeting, held in New Orleans, Louisiana, in April 2013.

Please include this information when citing this paper: published online December 6, 2013; DOI: 10.3171/2013.10.PEDS13303.

Address correspondence to: Jeffrey P. Greenfield, M.D., Ph.D., Department of Neurological Surgery, Weill Cornell Medical College, 525 E. 68th St., Box 99, New York, NY 10065. email: jgreenf@med.cornell.edu.