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## Growth curves for intracranial volume in normal Asian children fortify management of craniosynostosis<sup>☆</sup>

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### ABSTRACT

**Background:** Although the charting of normal intracranial volume (ICV) is fundamental for managing craniosynostosis, Asian norms in this regard are unknown. The purpose of this study was to establish a growth curve for ICVs in a large series of normal Asian children, providing reference values to guide corrective surgery.

**Methods:** A total of 124 normal children (male, 63; female, 61) and 41 children diagnosed with craniosynostoses were analyzed. Patients aged 0–8 years presenting to the emergency room and subjected to computed tomography (CT) for head trauma served as the reference cohort. Axial CT head scan data were obtained from radiographic archives at Jichi Medical University. Imaging was done on a Siemens CT scanner (5-mm slice thickness), using a DICOM viewer to measure ICVs.

**Results:** ICVs were plotted against age, and best-fit logarithmic curves for normal subjects were generated, without and with gender stratification. Male and female growth curves were similar in shape but diverged past the age of 1 year (male > female). ICVs of patients with craniosynostoses were plotted to male and female growth curves by disease subset, revealing the following: sagittal synostosis, near normal (or marginally larger); metopic synostosis, below normal; other non-syndromic synostoses (unilateral, bilateral, and lambdoidal) and Crouzon syndrome, near normal; Apert syndrome, above normal; and Pfeiffer syndrome, variable.

**Conclusion:** ICVs of early childhood were investigated in Asian subjects, creating growth curves that set criteria for timing, planning and goalsetting in surgical correction of craniosynostosis.

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### 1. Introduction

Craniosynostosis alters the morphology of cranial vault, prevents normal cranial growth, and can elevate intracranial pressure over time. Surgical goals in the event of craniosynostosis are to reduce intracranial pressure and to achieve esthetic cranial contours, but the timing of such surgery is open to debate. Although excess intracranial pressure must be avoided, premature surgical

interventions may necessitate secondary revisions. Also, direct attempts to measure intracranial pressure are invasive by design and thus may not be feasible in every case.

Intracranial volume (ICV) is a parameter that can be accurately measured by non-invasive methods, such as computed tomography (CT). ICV correlates with intracranial pressure and may be useful in decisions on appropriate timing of surgery. Few investigators have measured ICV in conjunction with normal growth (Abbott et al., 2000; Kamdar et al., 2009; Sgouros et al., 1999), and none have addressed Asians specifically. Asians are generally less prone to craniosynostosis, compared with Caucasian populations.

The purpose of this study was to establish a standard growth curve for ICV in healthy Asians through large-scale data collection. These growth curves were then extrapolated to Asian patients with craniosynostoses, offering a reference point for needed craniofacial surgery.

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## 2. Material and methods

### 2.1. Patient selection

Children (age range, 0–8 years) presenting at the emergency room of Jichi Medical University Hospital and undergoing CT scans to assess head trauma were eligible for the reference cohort, in the absence of any medical or neurologic disorders. Only those candidates with no significant cranial abnormalities on imaging (124 including 63 males and 61 females) were incorporated in this study. All patients were Japanese and of Asian race. Their ages ranged from 8 days to 8 years.

All patients with craniosynostoses evaluated within the Department of Plastic Surgery at Jichi Medical University from 1996–2010 were analyzed as well (Table 1).

### 2.2. Data acquisition

Normal cranial imaging data (axial CT views) generated during years 2002–2010 were obtained from the radiographic database at Jichi Medical University Hospital. Studies relied on a Siemens CT scanner (5-mm slice thickness; Siemens AG, Munich, Germany).

### 2.3. Intracranial volume measurement and data analysis

A DICOM viewer and software (OsiriX; Pixmeo, Bernex, Switzerland) were used to measure ICVs. The intracranial space was defined as the region extending from vertex (cranially) to first axial image of foramen magnum (caudally).

Regions of interest (ROIs) in each slice were determined by manual delineation. Total ICV was calculated by summing cross-sectional areas of intracranial space across all images (maximum slice thickness, 5 mm).

ICVs of 120 normal subjects were plotted against age (in months). The data were further divided by age (Group A: ≤12 months, Group B: 13–24 months, Group C: 25–36 months, and Group D: >36 months). Data in each group were compared by gender, applying unpaired Student's *t*-test. ICVs of patients with craniosynostoses were then plotted to our growth curves by disease subset.

## 3. Results

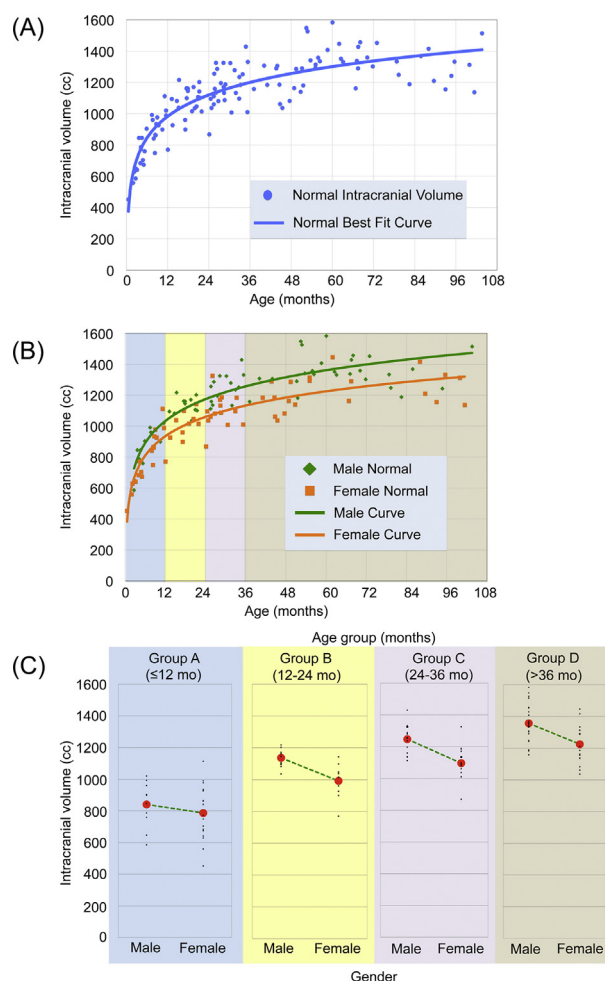
Scatter plots of ICV measurements against age (in months) are shown in Fig. 1A, generating a best-fit logarithmic curve:  $y = 198\ln(x) - 185.54$  ( $R^2 = 0.76843$ ). Best-fit logarithmic curves are shown by male and female gender in Fig. 1B, becoming  $y = 180.26\ln(x) - 128.43$  ( $R^2 = 0.81222$ ) and  $y = 204.15\ln(x) - 171.22$  ( $R^2 = 0.80483$ ), respectively.

All values of  $R^2$  were high, so the curves approximated plotted points quite closely. The data show a doubling of ICV from birth to 260 days of age.

Average ICVs by gender in the four age groups of normal subjects were as follows: Group A, 840.8 cc (male) and 774.1 cc (female); Group B, 1137.1 cc (male) and 991.7 cc (female); Group C, 1247.5 cc (male) and 1096.8 cc (female); and Group D, 1356.7 cc (male) and 1225.6 cc (female) (Fig. 1C). Gender differences in the B, C, and D age groups were statistically significant (B:  $p = 0.00050$ , C:  $p = 0.00045$ , and D:  $p = 0.00028$ ).

ICVs in patients with sagittal synostoses were nearly the same or were marginally above normal (Fig. 2A). In patients with unilateral synostoses, values were near normal (with one exception) (Fig. 2B), and in instances of bilateral or lambdoidal synostosis, values were essentially normal (Fig. 2C and D). ICVs associated with metopic synostoses were below normal (Fig. 2E). In syndromic patients, values were as follows: Crouzon, normal (Fig. 2F); Apert, above normal (Fig. 2G); and Pfeiffer, variable (Fig. 2H).

The Asian ICV growth curve shows the same trend previously documented in other races, although values ran slightly higher after the age of 12 months (Fig. 3).



**Fig. 1. Intracranial volume of normal Asian children.** (A) Scatter plot of normal intracranial volumes by age (in months), with best-fit logarithmic curve of  $y = 198\ln(x) - 185.54$  ( $R^2 = 0.76843$ ). (B) Scatter plot of normal intracranial volumes by age (in months), with best-fit logarithmic curves of  $y = 180.26\ln(x) - 128.43$  ( $R^2 = 0.81222$ ) in male subjects and  $y = 204.15\ln(x) - 171.22$  ( $R^2 = 0.80483$ ) in female subjects. (C) Data plotted incrementally by age as Group A (≤12 mo, blue), Group B (13–24 mo, yellow), Group C (25–36 mo, purple), and Group D (>36 mo, brown) for gender comparisons (unpaired Student's *t*-test applied).

**Table 1**  
Patients with craniosynostosis evaluated in this study.

Craniosynostosis (subsets)	Patient no.		
	Male	Female	Total
<i>Nonsyndromic</i>			
Sagittal	14	4	18
Unicoronal	4	2	6
Bicoronal	2	2	4
Metopic	2	0	2
Lambdoidal	1	0	1
<i>Syndromic</i>			
Crouzon	3	0	3
Apert	1	3	4
Pfeiffer	3	0	3
Total	30	11	41

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