Clinical Article

Quantitative Analysis of Developmental Process of Cranial Suture in Korean Infants

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Objective : The purpose of this study was to elucidate the anatomical development of physiologic suture closure processes in infants using three dimensional reconstructed computed tomography (CT).
Methods : A consecutive series of 243 infants under 12 months of age who underwent three dimensional CT were included in this study. Four major cranial sutures (sagittal, coronal, lambdoidal and metopic suture) were classified into four suture closure grades (grade 0=no closure along the whole length, grade 1=partial or intermittent closure, grade 2=complete closure with visible suture line, grade 3=complete fusion (ossification) without visible suture line), and measured for its closure degree (suture closure rates; defined as percentage of the length of closed suture line divided by the total length of suture line).
Results : Suture closure grade under 12 months of age comprised of grade 0 (n=195, 80.2%), grade 1 (n=24, 9.9%) and grade 2 (n=24, 9.9%) in sagittal sutures, whereas in metopic sutures they were grade 0 (n=61, 25.1%), grade 1 (n=167, 68.7%), grade 2 (n=6, 24%) and grade 3 (n=9, 3.7%). Mean suture closure rates under 12 months of age was 58.8% in metopic sutures, followed by coronal (right : 43.8%, left : 41.1%), lambdoidal (right : 27.2%, left : 25.6%) and sagittal sutures (15.6%), respectively.
Conclusion : These quantitative descriptions of cranial suture closure may help understand the process involved in the cranial development of Korean infants.

Key Words : Computed tomography · Cranial suture · Growth and development.

INTRODUCTION

Establishing the timing of normal closure of cranial sutures is important because it can reveal early sutural fusion such as craniosynostosis or late sutural fusion with increased intracranial pressure. Most of the literature on sutural fusion of the skull has been derived from anatomic studies with human skull remains in pre-computed tomography (CT) eras[11,12]. Even in the CT era, extensive analysis of sutural anatomy and ossification process has been mainly confined to the process of synchondroses in the chondrocranium[3,11,23].

Recent advance of three dimensional (3D) CT allows us to examine the skull surface anatomy more extensively than we were able to do with simple skull X-rays or two dimensional (2D) axial brain CT[3,9-11,17,18,20,22,24]. These advances of diagnostic techniques have been mainly utilized as diagnostic tools, surgical planning and follow-up methods for craniosynostosis[10,17,19,22]. Despite recent popular usage of 3D CT, there is paucity of information published pertaining to 3D CT findings of normal developmental stage of cranial sutures in infants. There have been only several reports regarding 3D CT imaging of the timing of physiologic closure of the metopic suture[24], anatomic variation of occipital suture[3] and ossification degree of adult human cranial remains in forensic anthropology[9]. As a result, clinical diagnosis of early sutural fusion using 3D CT has been based on the old reference observed in simple skull X-rays or 2D bone setting brain CT. In additions, most literatures regarding developmental processes of cranial sutures have focused solely on the timing of sutural fusion. There have been no studies that have delineated the process of open suture being closed to the fused suture. It is important to know not only the timing of complete fusion of the cranial sutures, but also the sequential

closure process itself for early diagnosis of skull deformity or for the detection of increased intracranial pressure.

In order to accurately estimate skull development in infants, we need to establish new quantified measurement guidelines, especially for infants under 12 month of age, in whom much of the cranial growth is occurring[4].

Our purpose of this study was to establish new methods for measuring cranial suture development of Korean infants and to chronicle this development to provide 3D CT standards for the patterns and timing of closure of major cranial sutures, so as to provide potentially useful information for assessment of patients with abnormal head configurations.

MATERIALS AND METHODS

Patient selection

We collected a consecutive series of infants under 12 months of age who underwent 3D CT scans for minor head trauma, evaluation for abnormal head configuration, or other medical conditions for two years from January 2007 through December 2008. Of a total 417 cases, patients with definite skull fractures, increased intracranial pressure (e.g. hemorrhage, hydrocephalus, subdural effusion, tumors or cysts), brain atrophy (hypoxic injury, infection or developmental retardation), or other medical conditions being able to affect cranial development (severe systemic illness, congenital anomalies or genetic disorders) were excluded (n=55). All patients with clinical/radiological evidence of craniosynostosis (n=54) or any patient in whom there was a suspicion of craniosynostosis (n=65) were also excluded from the study. Finally, 243 infants who met the above criteria were included in this study.

Radiologic measurement

All CT data were acquired on a 64-detector row CT scanner (Brilliance 64, Philips Medical Systems, Best, the Netherlands) with the following protocol : 120 kVp; 100 mAs; collimation, 16×0.625; rotation time, 0.6 seconds; pitch, 0.683; section thickness, 4 mm; reconstruction increment, 0.5 mm (1.0 mm). The 3D reconstruction was performed on the scanner's workstation using commercially available software (Extended Brilliance Workstation; Philips Medical System, Best, the Netherlands) with reconstruction increment 0.5 mm over 1.0 mm, using a window level of 120 and a length of 255.

Four major cranial sutures (sagittal, coronal, lambdoidal and metopic suture) were examined on the 3D reformatted volume rendering image. The total length of the sagittal suture was measured as the distance from the bregma to the lambda - on the superior view of volume reformations (Fig. 1A), and the total length of the coronal suture was measured from the bregma to the pterion on the lateral view (Fig. 1B). Total length of the lambdoidal suture was measured from the lambda to the asterion on the posterior view (Fig. 1C), and the total length of the metopic suture was measured from the bregma to the glabella on the anterior view (Fig. 1D). If the fontanelle was persistent, the center of each fontanelle was estimated as the end point of each suture. Of the total length of each suture, part of the closed suture line was also measured. For interrupted closures, the lengths of each closed suture line were added up. The term
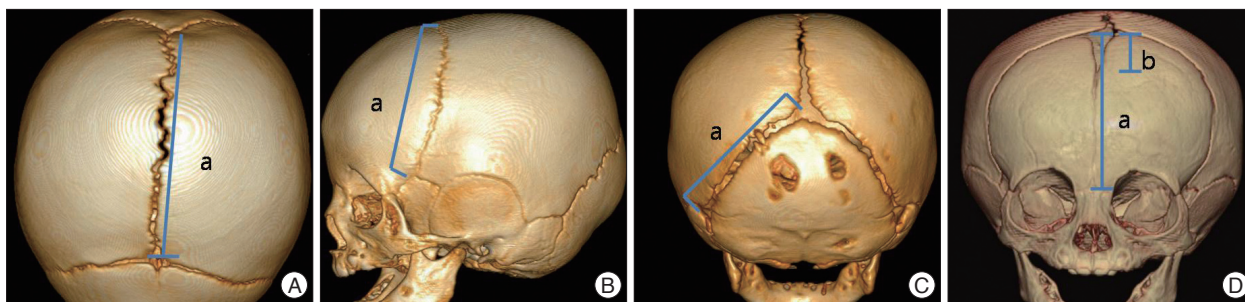

Fig. 1. Length measurement of the cranial suture. A : Total length of sagittal suture in this case is 'a' and length of closed suture line is 0. B : Total length of coronal suture in this case is 'a' and length of closed suture line is also 'a'. C : Total length of lambdoidal suture. D: Total length of metopic suture in this case is 'a' and length of closed suture line is 'a-b'.
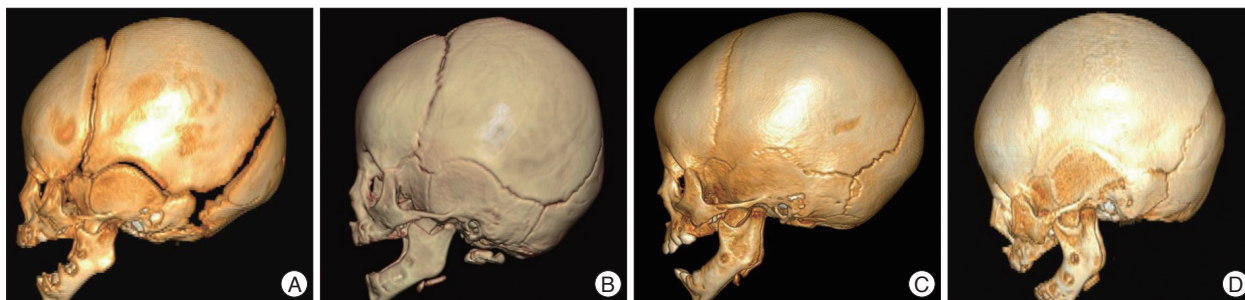

Fig. 2. Suture closure grade in coronal suture. A : Grade 0=no closure along the whole length. B : Grade 1=partial or intermittent closure. C : Grade 2=complete closure (with a visible suture line). D : Grade 3=complete ossification (with no visible trace of the suture line).

'closed' in this study is a pure radiologic description of the condition in which two or more adjacent bones meet with each other without any patency in their borderline with or without ossification. The term 'fused' in this study means status of ossified suture among closed sutures.

The degree of suture closure was classified into four grades as defined below (Fig. 2).

Suture closure grade

Grade 0=no closure along the whole length

Grade 1=partial or intermittent closure

Grade 2=complete closure (with a visible suture line)

Grade 3=complete fusion with ossification (with no visible trace of the suture line)

Suture closure rates was defined as the percentage of the length of closed suture line divided by the total length of suture line, and was calculated for each suture type.

$$\text{Suture closure rates (\%)} = \frac{\text{length of closed suture line}}{\text{total length of suture line}} \times 100$$

Descriptive statistical analysis of suture closure grade and suture closure rates by age months for each cranial suture was performed with SPSS (SPSS Version 17.0 for Windows, SPSS Inc., Chicago, IL, USA). Analysis of variance and Scheffe multiple comparison test were used to compare the differences between the groups. Multiple t-tests adjusted by the Bonferroni correction (α=0.0167 in sagittal, coronal and lambdoidal suture, α=0.0125 in metopic suture) was also performed.

RESULTS

The median age of the 243 infants was 6 months of age with an interquartile range of 2-9 months. Age distribution by age of months is depicted in Fig. 3. Suture closure grade and suture closure rates under 12 months of age are summarized in Table 1. Most cases had a fully opened sagittal suture (grade 0; n=195, 80.2%) whereas 24 (9.9%) and 24 (9.9%) infants had partially closed (grade 1) or completely closed (grade 2) sagittal suture line, respectively. For coronal sutures, infants with grade 0 was 95 (39.1%) on the right side, 102 (42%) on the left side; grade 1

was 136 (56%) on the right side, 133 (54.7%) on the left side; grade 2 was 12 (4.9%) on the right side, 8 (3.3%) on the left side. For lambdoidal sutures, infants with grade 0 was 157 (64.6%) on the right side, 156 (64.2%) on the left side; grade 1 was 40 (16.5%) on the right side, 46 (18.9%) on the left side; grade 2 was 46 (18.9%) on the right side, 41 (1.9%) on the left side. There was no infant with sutural fusion (suture closure grade 3) in the sagittal, coronal and lambdoidal sutures, whereas 9 (3.7%) metopic sutures were completely obliterated with ossification.

According to the mean suture closure rates, physiologic closure of metopic suture (58.8%) was observed earlier than others, followed by coronal (right : 43.8%, left : 41.1%), lambdoidal (right : 27.2%, left : 25.6%) and sagittal sutures (15.6%) during 12 months of age, respectively (p<0.001).

Fig. 4 shows the process of suture closure in detail by age months. All sagittal sutures were completely patent during the first 4 months in all cases, and began to be partially obliterated from 5 months. At the age of 12 months, the mean suture closure rate was 49.5%. In coronal and lambdoidal sutures, suture closure rates within one month of age were 1.9% and 2.6%, respectively, then progressively increased during one year so that mean suture closure rates at the age of 12 months was 86.8% and 88.9%, respectively. Metopic sutures tended to close faster
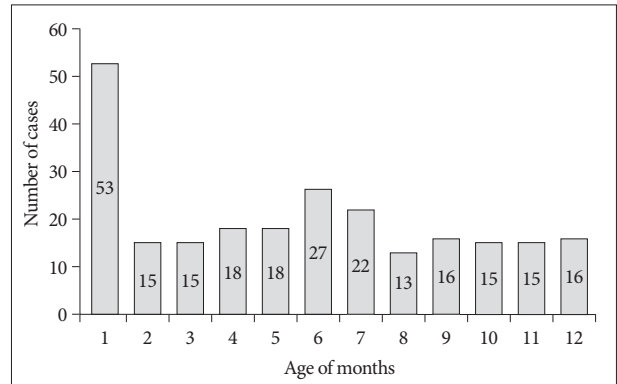

Fig. 3. Graph showing age distribution of the infants. The infants are almot evenly distributed over the different age groups after one month of age.

Table 1. Summary of classification of suture closure grade and mean suture closure rates in 243 infants

| Cranial suture | Suture closure grade (no, %) | | | | Suture closure rates (mean±SD) | p-value* |
	Grade 0	Grade 1	Grade 2	Grade 3		
Sagittal	195, 80.2%	24, 9.9%	24, 9.9%	0, 0%	15.6%±33.6	<0.001
Coronal						<0.001
Right	95, 39.1%	136, 56%	12, 4.9%	0, 0%	43.8%±40.9	
Left	102, 42.0%	133, 54.7%	8, 3.3%	0, 0%	41.1%±41.3	
Lambdoidal						<0.001
Right	157, 64.6%	40, 16.5%	46, 18.9%	0, 0%	27.2%±41.1	
Left	156, 64.2%	46, 18.9%	41, 16.9%	0, 0%	25.6%±39.5	
Metopic	61, 25.1%	167, 68.7%	6, 2.4%	9, 3.7%	58.8%±38.2	<0.001

*Statistical significances were tested by Oneway analysis of variances among the groups. There was no infant with grade 3 closure in the sagittal, coronal and lambdoidal sutures, whereas 9 (3.7%) metopic sutures were completely obliterated with ossification. According to the mean suture closure rates, physiologic closure of the metopic suture (58.8%) was observed earlier than others, followed by coronal (right : 43.8%, left : 41.1%), lambdoidal (right : 27.2%, left : 25.6%), and sagittal sutures (15.6%) during 12 months of age, respectively

than other sutures. Their closure rates were 1.9% within one month of age but at the age of 3 months, about 50% of entire metopic sutures were closed. At the 11 months of age, the mean suture closure rate was 91.5%.

Mean age of patients with suture closure grade 0 was 4.7 months in sagittal sutures, 2.4 (right) and 2.5 (left) months in coronal sutures, 3.7 (both) months in lambdoidal sutures, and 1.2 months
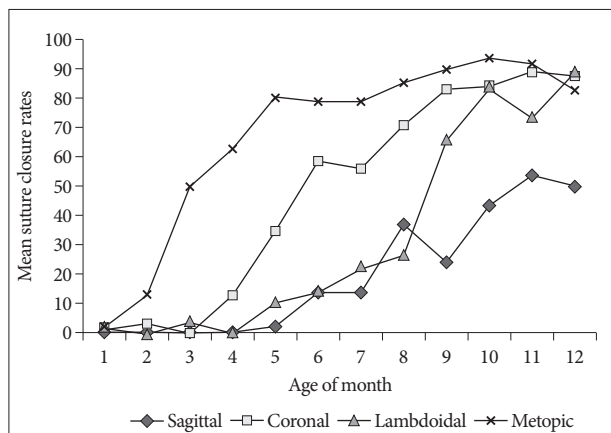

Fig. 4. Differences in mean suture closure rates of major cranial sutures by age of months. Sagittal suture is all completely patent during first 4 month in all cases, then it start to partially obliterated since 5 months. At the age of 12 months, mean suture closure rates is 49.5%. In coronal and lambdoidal suture, suture closure rates within one month of age are 1.9% and 2.6%, respectively, then progressively increased during one year, mean suture closure rates at the age of 12 months is 86.8% and 88.9%, respectively. Suture closure rates of metopic suture are 1.9% within one month of age but at the age of 3 months, about 50% of entire metopic sutures are closed. At the 11 months of age, mean suture closure rates is 91.5%.

in metopic sutures. Mean age of those with grade 1 was 8.8 months in sagittal sutures, 7.6 (right) and 7.8 (left) months in coronal sutures, 7.9 (right) and 8.1 (left) months in lambdoidal sutures, and 7.0 months in metopic sutures. Mean age of those with grade 2 was 10.2 months in sagittal sutures, 8.0 (right) and 9.0 (left) months in coronal sutures, 10.1 (right) and 10.2 (left) months in lambdoidal sutures, and 6.2 months in metopic sutures. There was no grade 3 in sagittal, coronal and lambdoidal sutures. Mean age of those with grade 3 in metopic suture was 9.8 months (Table 2). There were significant differences of mean age of months between the groups of different suture closure grade in all cranial sutures ($p<0.001$). Mean ages in each suture were significantly different between suture closure grade 0 and 1 in all cranial sutures ($p<0.001$). However, difference of mean age in grade 1 and 2 was statistically significant only in lambdoidal sutures ($p<0.001$). In metopic suture, mean ages of grade 2 and 3 were significantly different between the group ($p=0.001$).

DISCUSSION

Cranial sutures, the fibrous tissues uniting the bones of the skull, are the major sites of bone growth along margins of the cranial bones during cranial development[2]. Premature osseous obliteration of sutures by fusion of bone across the suture site results in craniosynostosis which represent restricted growth perpendicular to the fused suture(s) and compensatory growth in the skull's unfused bony plates, producing abnormal head shapes[5,16]. To facilitate exact diagnosis of craniosynostosis, thorough understanding of cranial suture anatomy and its normal development is required, especially in infants under 12 months of age in which periods of rapid growth of the infant's brain usually occurs[13].

With the introduction of multislice 3D CT, better visualization of skull and suture anatomy can be obtained, leading to early detection of craniosynostosis or positional plagiocephaly[20,24]. It is seen as the gold standard for establishing the diagnosis of craniosynostosis and seems promising for screening and as a follow-up modality, though it needs sedation of and radiation exposure to the patient as a screening tool[3,9,10].

In the past, imaging features of simple skull X-rays and 2D axial CT had been widely used for diagnosis of skull abnormalities. However, simple skull X-ray imaging has many drawbacks, such as its limited angle (e.g. vertex view), overlapping image of left and right structures, limitations in viewing inner structures or the skull base. 2D axial CT scan im-

Table 2. Mean age of months by suture closure grade

Cranial suture	Grade 0	Grade 1	Grade 2	Grade 3	p-value*
	Mean (months)±SD				
Sagittal	4.7±3.3	8.8±2.1	10.2±1.8	-	<0.001
	a[†]	b	b	-	
Coronal					<0.001
Right	2.4±2.1	7.6±2.8	8.0±2.3	-	
	a	b	b	-	
Left	2.5±2.1	7.8±2.6	9.0±2.3	-	
	a	b	b	-	
Lambdoidal					<0.001
Right	3.7±2.5	7.9±2.6	10.1±1.9	-	
	a	b	c	-	
Left	3.7±2.5	8.1±2.4	10.2±2.0	-	
	a	b	c	-	
Metopic	1.2±0.5	7.0±3.0	6.2±1.2	9.8±1.6	<0.001
	a	b	b	c	

There were significant differences of mean age of months between the groups of different suture closure grade in all cranial sutures ($p<0.0001$). Mean ages in each suture were significantly different between suture closure grade 0 and 1 in all cranial sutures. However, difference of mean age in grade 1 and 2 was statistically significant only in lambdoidal sutures. In metopic suture, mean ages of grade 2 and 3 were significantly different between the groups. *Statistical significances were tested by oneway analysis of variances among the groups, [†]The same letters indicate non-significant difference between the groups based on Scheffe multiple comparison test

aging has also several shortcomings in that a short segment fusion can be missed on axial views, and several signs on axial CT previously known as sutural fusion including perisutural ridging and end-to-end morphology proved not to be signs of sutural fusion after 3D CT introduction[20]. Sutural imaging of axial CT delineates more figures, but there is some difficulty in observing the full length of suture according to the scan angle or scan thickness.

Nowadays, technological advances in computer imaging analysis has made possible 3D reconstruction of anatomic structures from contiguous axial CT slices[17,21]. There are almost an unlimited number of ways to reconstruct and view multidetector CT data set including automated or manual creation of multiplanar (MPR), volumetric, and maximum intensity projection images (MIP). With MPR imaging, standard thicker sections (3 mm) of coronal and sagittal images are simple to create and can be reviewed quickly and efficiently[21]. However, volume rendering images seems to be more straightforward than MPR or MIP in infantile head evaluation. Its popularity of 3D volume reformatted CT than axial 2D CT in interpretation of suture anatomy was due in large part to the fact that it excels at showing bone surface anatomy, and it can be manipulated by post acquisition process to optimally visualize the region of interest.

However, there is sparse information about sequential data of normal suture closure in 3D CT imaging. Research about normal developmental process of infantile skull with 3D CT had been carried out only in metopic suture[24] and in occipital suture[3]. Physiologic closure of sagittal, coronal and lambdoidal suture had been analyzed using 3D CT but it was an anthropologic study with adult dry skulls[9]. Therefore, most of the information regarding the timing of suture closure was based on the examination of simple skull X-rays or axial CT scans[8,11,19,23]. It has been reported that normal closure of the suture in 3D CT occurs much earlier than what has been previously described by simple X-rays or axial CTs[23]. Therefore, normal anatomy and development of physiologic suture closure need to be reestablished using the 3D CT. In addition, most reports describing physiologic suture closure observe only the time of completion of suture closure (completely fused sutures, suture closure grade 3). Quantitative degree of closure by age has not been yet fully described, especially for sagittal, coronal and lambdoidal sutures, which usually complete their ossification process at adulthood[14]. Furthermore, there have been no reports to date that studied development of the cranium in Korean infants.

In this article, we described the imaging features of the normal anatomy and development of physiologic suture closure in infants by using 3D CT. Sutural closure does not occur simultaneously along the entire length or depth of the suture[11]. Thus, to quantify the degree of suture development between a patent suture and a completely fused suture, we defined the suture closure grade and suture closure rates to standardize the physiologic process of suture development. As we have already mentioned above, 'closure' in this study did not mean complete ossification, but rather indicated the radiologic closure of the suture line. Hence, the authors attempted to define suture closed degree in details as grade 2 (closed suture), which means radiologic closure of the sutures with a visible suture line, and grade 3 (fused suture) which means histologic completion of ossification without a visible suture line. In the previous literature, the terms 'closure' and 'fusion' have been used being mixed up with each other. The authors suggest that discriminated use of these terms might help describe the sequential process of sutural development more clearly because each term includes different information about cranial suture development.

Except for the metopic sutures in which complete ossification (fusion) of the suture can occur in childhood, physiologic ossification process of the sagittal, coronal and lambdoidal sutures are usually complete in adulthood. In normal infants, therefore, suture closure grade 3 (fused suture) can be observed only in metopic sutures.

In the statistical analysis, proposed suture closure grades and suture closure rates successfully represented age-related and anatomy-related differences of each suture. Although we failed to show statistical significances between suture closure grade 1 and 2 in sagittal, coronal and metopic sutures, dividing suture closure grade into grade 1 and 2 gives us much qualitative information of the developmental process of the cranial sutures. The Tables and Figures demonstrate the above results, and the serial process of development of each suture can be quantitatively provided. Given that the prevalence of human craniosynostosis is different for each suture, it is not surprising that each calvarial suture has different processes of formation in closing sequence and rates[15]. Our study population comprised of the infants less than 12 months of age, and therefore the exact fusion time (suture closure grade 3) of sagittal, coronal and lambdoidal suture could not be conclusive, but, obviously metopic suture fuses much earlier than previous reports[1,6,7,14,16]. According to past literatures in which metopic suture was evaluated with simple X-ray or 2D CT, the physiologic fusion time of the metopic suture varies from before[12], or at the second year of life[6,14], between the second and third year of life[7], up to age 8 years[24]. Our findings of the metopic suture seems to be compatible with other studies that have investigated 3D CT evaluation of the metopic suture[24] in that metopic suture clearly begin to fuse before 12 months of age. To our knowledge, there is no report on the sequential process of physiologic closure in sagittal, coronal and lambdoidal suture in infants and children. In this study, time sequence of the beginning of suture closure was clearly depicted in order; metopic suture first, followed by the coronal suture, lambdoidal suture, and sagittal suture, respectively. Our results showed that the earliest beginning of suture closure was within one month for each suture, except the sagittal suture. In sagittal sutures, the beginning of suture closure before 5 months of age did not occur, thus any evidence of short segment closure in sagittal sutures in these age period should be closely followed up for the possibility of premature fusion.

To allow the study data to represent a normal population, the authors made every effort specially in excluding those with conditions that conceivably might be associated with a developmental abnormality of the skull. It is our hope that the proposed grading system and data in this study would assist understanding of the patterns in the timing of cranial suture closure, and assist in the diagnosis of skull deformities such as craniosynostosis, skull fracture or increased intracranial pressure. Relationship of this grading system with increased intracranial pressure or intelligence should be further evaluated. Racial difference in cranial growth needs to be clarified in the future.

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