ORIGINAL PAPERS

Adv Clin Exp Med 2014, **23**, 3, 327–342
ISSN 1899–5276

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Assessment of Growth Dynamics of Human Cranium Middle Fossa in Foetal Period

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A – research concept and design; **B** – collection and/or assembly of data; **C** – data analysis and interpretation; **D** – writing the article; **E** – critical revision of the article; **F** – final approval of article; **G** – other

Abstract

Background. Available literature analysis demonstrated smallness of studies of cranial base.

Objectives. The goal of the study was to analyse the medial fossa of the human cranium in the foetal period against other fossae.

Material and Methods. Survey material consisted of 110 human foetuses at a morphological age of 16–28 weeks of foetal life, CRL 98–220 mm. Anthropological, preparation method, reverse method and statistical analysis were utilized. The survey incorporated the following computer programmes: Renishaw, TraceSurf, AutoCAD, CATIA. The reverse method seems especially interesting (impression with polysiloxane (silicone elastomer of high adhesive power used in dentistry) with 18 D 4823 activator. Elicited impression accurately reflected complex shape of cranium base.

Results. On assessing the relative rate of cranium medial fossa, the rate was found to be stable (linear model) for the whole of the analysed period and is 0.19%/week, which stands for the gradual and steady growth of the middle fossa in relation to the whole of the cranium base. At the same time, from the 16th till 28th week of foetal life, relative volume of the cranium middle fossa increases more intensively than cranium anterior fossa, whereas the cranium middle fossa volume as compared with the cranium posterior fossa is definitely slower. In the analysed period, the growth rate of the cranium base middle fossa was bigger in the 4th and 5th weeks than in the 6th and 7th weeks of foetal life. The investigations revealed cranium base asymmetry of the left side. Furthermore, the anterior fossae volume on the left side is significantly bigger than the one of the fossae on the right side.

Conclusions. Volume growth rate is more intensive in the 4th and 5th than in the 6th and 7th weeks of foetal life. In the examined period, the relative growth rate of cranium base middle fossa is 0.19%/week and it is stable – linear model. The study revealed correlations in the form of mathematical models, which enabled foetuses age assessment (**Adv Clin Exp Med 2014, 23, 3, 327–342**).

Key words: middle fossa, cranium base, volume, human foetus.

Cranium base is still a "no man's land"; however, it plays an important role in the development process of the cranium. Fredie [13] describes three stages of cranium development: mesenchymal (desmocranium), chondral (chondocranium) and osseous (ostocranium). He defined the cranium base as a boundary line structure which adapts to the brain and facial cranium. He found the increase of the cranium anterior base to be completed earlier than that of the posterior one. Blechschmidt [4] reports that the cranium base grows more intensively from the very beginning and it becomes thicker and more resistant to nervous tissue development in comparison with cranium vault structures. The author introduces the notion of "meningeal bands" fixed to the capsule base (cranium base) embracing and shaping the brain. In his opinion, devoid of "meningeal bands", the brain would develop into two ideal hemispheres. The cranium base and vault increase at the osseous stage is based on

Enlow's [10] principles of skeletal growth (superstructure and resorption), which cause cortex drifting and replacement processes. The author states that cranium base growth process is hard to define and evaluate as these two phenomena may take place simultaneously in two opposite directions.

Width increase results from the replacement in petrooccipital articulation and posteriomastoid suture. Fossa length increase is favoured by anterior and posterior intraoccipital articulations with sphenooccipital articulations and Björk [3] posteriomastoid suture. Cranium middle fossa length increases in the sphenoid and petrosquamous sutures. As indicated by Björk [3], posterior dislocation proceeding towards frontal bones in the main direction of temporal bones growth. Cranium middle fossa growth takes place after cranium anterior fossa increase completion and lasts several years. Ford [11] found that cranium base anterior (prechordal) part increases six-sevenfold (linearly) against the posterior (chordal) one which grows only four-fivefold. In order to compensate this slow growth, cranium base angles between cranium prechordal and chordal bases get flattened. Sikora [38] stated that a foetal head width-length index increases gradually until the 3rd month of foetal life (head width increases faster), from the 3rd till the 6th month, the index decreases (head length increases faster) and from the 6th month until the moment of birth, the index is constant (head width and length increases are equable. In his paper, the author points at the index estimative character. Malinowski's survey [26] performed on 150 foetuses deals with the same problem. In his study, Malinowski made width and length traditional measurements defining foetal head indices. His observations revealed that the biggest gains of the foetal cranium width and length happened in the 4th, 5th and 9th months of pregnancy.

Levin et al. [25] detected the progressive growth of the cranium anterior base length in comparison with its posterior part. He also observed a general tendency of cranium base angle, which appeared more and more obtuse along with foetal age. In accordance with his observations, the biggest rate of examined structures growth was indicated in the 4th and 5th months of foetal life. Kvinnsland [21] found that the cranium anterior base development is more active than that of the cranium posterior base. Saggital and occipital element of the cranium base revealed stability during the foetal period, whereas the saggital and ethmoidal part of cranium base angles increased in this period. Kędzia [18], in her paper, demonstrated a strict connection between the dura mater processes and brain and cranium base development. Lee et al. [23] proved that the cranium anterior fossa grows anteriorly. They demonstrated proportional growth of cranium all fossae based on angles with S angular point (sella center). Anterior fossa angle was relatively stable and amounted to 107.4–112.5°. Middle fossa angle increased, whereas posterior fossa angle decreased. In the authors' opinion, cranium base particular fossae angles are keys to normal development assessment of the cranium base.

Derkowski [9] pointed to the irregular growth of cranium anterior fossa. In his opinion, anterior fossa angle decreases and middle fossa angle increases. Progressive growth observed in the 2nd trimester is gradual and the anterior fossa angle changes slightly. What is important, from the 4th till the 7th month of foetal life, the cranium base increases preserving the symmetry in regard to the body median plane. Kędzia et al. [19] demonstrated the sexual dimorphism in the area of cranium anterior fossa on the basis of: anterior fossa angle-bigger in male foetuses as well as ethmoid bone crista galli height – bigger in female foetuses. Sławiński [37] examined the growth parameters of the foetal temporal bone in relation to age. Pyramid length increased with age, and its length growth dynamics dominated width increase. In turn, temporal bone pyramid angle enclosed between long axis and squama decreased with foetal age. The author did not find any other statistically significant differences in regard to side or sex.

Roelfsema et al. [31] pointed at a statistically significant increase of cranium anterior and posterior fossae lengths at cranium base angle slight but visible flexion by 6°. In their survey, they observed a bigger increase of foetal cranium posterior fossa length in relation to the cranium base anterior angle. In the authors' opinion, the more distinct increase of cranium posterior fossa length in relation to the anterior fossa length resulted from the influence of brain development process. Jeffery [17], on the basis of high resolution MRI, observed a twofold higher rate of cranium anterior fossa growth than cranium posterior fossa increase as well as posterior fossa width exceeding its length. In our own surveys, preliminary metrological analysis of cranium base fossae (2009) revealed that cranium middle fossae volume was significantly bigger than the volume of other fossae. Besides, no statistically significant asymmetry was found in relation to all sizes of middle and anterior fossae on the left and right sides or any significant sexual dimorphism of cranium base sizes. Ultrasound examinations are the most popular diagnostic and measurement method presented in literature: Biasio et al. [2], Chitkara et al. [7], Campbell [6], Hata et al. 1989 [14], Hoftbauer et al. [15]. However, not very many papers describe cranium base geometry; usually, the evaluation concentrates on cranium base fossae contents as well as foetus external parameters or long bones. Ultrasound examination usually evaluates: biparietal size, v-tub length, femoral bone length, foetus abdominal circumference, thorax and cerebellum transverse size.

Roelfsema et al. [31] described foetal cranium base increase with the use of a three-dimensional ultrasound examination. Measurement results proved successful in 69–94% of cases. MRI enables intra cranial structures evaluation and foetal brain development disturbances evaluation (Adamsbaum et al. [1], D'Ecrole et al. [8] Levine et al. [24]).

Mall et al. [27, 28], while constructing biomechanical model of adult cranium with the use of finite-element method, paid special attention to cranium base complex. Elicited model was exposed to virtual forces action and the results were compared with real injury effects.

Frątczak et al. [12] elaborated a foetal cranium computer measurement with the use of finite-elements method. They constructed foetal cranium virtual model on the basis of sectional material embedded in resin samples and exposed to cutting methods. The survey effect was prompt and accurate simulation of foetal cranium stress and recognition of processes leading to perinatal injuries. Recently, large progress has been observed in medicine which enables early diagnosis and treatment of developmental abnormalities during the foetal period. Present prenatal screening is able both to reveal structural defects and to define their character. In the case of foetal abnormalities, reparatory operations are limited. Prenatal surgery is a comparatively new domain and it deals mainly with: hydrocephalus treatment or myalomeningocele closure. Operations are performed either with uterus opening or endoscopically Wysocka [39]. Serlo et al. [34] performed a prenatal assessment of hydrocephalus in 38 foetuses. Foetal hydrocephalus proved to have differentiated aetiology and in 84% of cases, it was connected with other developmental abnormalities. Severe forms of foetal hydrocephalus may be detected with the use of modern ultrasound techniques before the 20th week of pregnancy. In the authors' opinion, the majority of hydrocephalus cases develop slowly in the foetal period. After ultrasound control examinations, hydrocephalus treatment initiated immediately after delivery gives a good or moderate prognosis. Only a minority of foetuses may be potential candidates for intrauterine interventions. Contemporary intrauterine treatment of foetal hydrocephalus is based on ventriculoamniotic valve placement (a shunt serving as a conjunction between foetal brain widened ventricles and amniotic cavity) draining the excess of cerebrospinal fluid to amniotic sac.

Material

The study was carried out on 110 foetuses at a morphologic age of 16–28 weeks of foetal life, in v-tub range 98–220 mm. There were 58 female and 52 male foetuses.

Foetal material originated from the collection of Normal Anatomy Department of Wroclaw Medical University. Foetuses were preserved in formaldehyde solution (concentration hard to define due to the fluid etherial qualities) and in constant concentrations of ethanol and glycerol to minimize formalin toxicity. Scamon's and Calkins [32] tables were used to assess foetuses morphological age with the use of the dependence:

$$\text{age} = 2.23 + \text{v-tub}/7.56+(\text{v-tub}/18.49)^2,$$

when: v-tub – crown-rump length (mm), age (weeks).

Table 1. Quantitative division of foetuses in respect of sex

Age (month)	Sex	Number of foetuses
IV	female	2
	male	2
	total	4
V	female	39
	male	20
	total	59
VI	female	12
	male	21
	total	33
VII	female	5
	male	9
	total	14
Total	female	58
	male	52
	total	110

Methods

The following methods were used: antropological and preparational methods, reverse (impression) method, image computer analysis with the use of Irfan View programme and Scion Image for Windows [33]. Subsequently, the results were subjected to statistical analysis with STATISTICA v. 9 programme. Reverses were made with polysiloxane (silicone elastomer of big adhesiveness used in

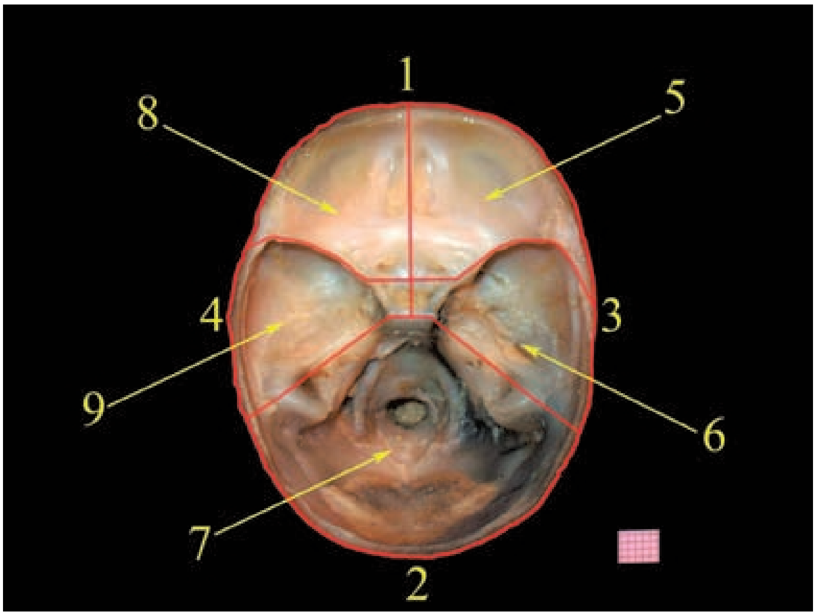

Fig. 1. Material prepared to elicit reverse of female foetus cranium base: 5th month of foetal period, v-tub length 145 mm, down hill projection 1 – front (frontal pole), 2 – back (occipital pole), 3 – right side, 4 – left side, 5 – right anterior fossa of cranium base, 6 – right middle fossa of cranium base, 7 – posterior fossa of cranium base (unpaired), 8 – left anterior fossa of cranium base, 9 – left middle fossa of cranium base. Red line demarcates approximate boundaries of cranium base fossae

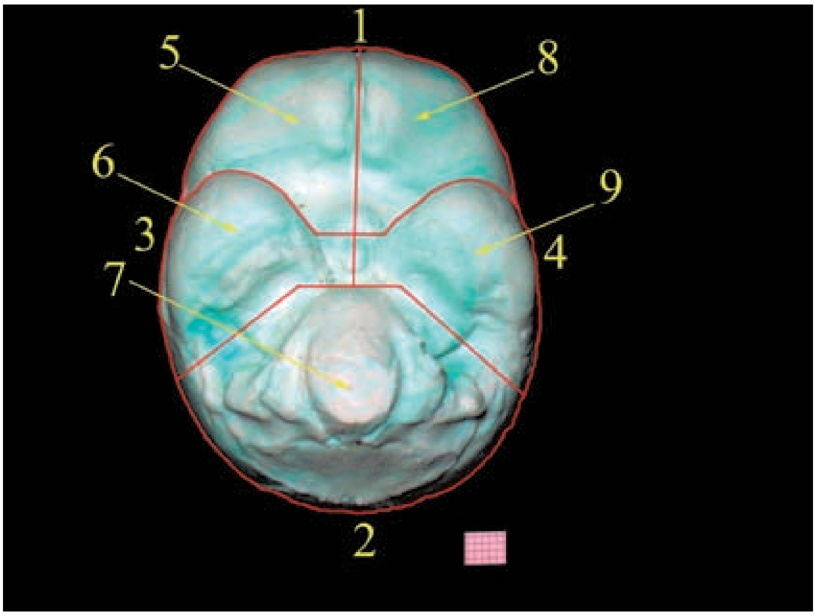

Fig. 2. Reverse of male foetus cranium base, 4th month of foetal life, v-tub length 198 mm 1 – front (frontal pole), 2 – back (occipital pole), 3 – right side, 4 – left side, 5 – reverse of cranium right anterior fossa, 6 – reverse of cranium right middle fossa, 8 – reverse of cranium left anterior fossa, 9 – reverse of cranium left middle fossa, 7 – reverse of cranium posterior fossa (unpaired). Red line demarcates reverses approximate boundaries of cranium base particular fossae

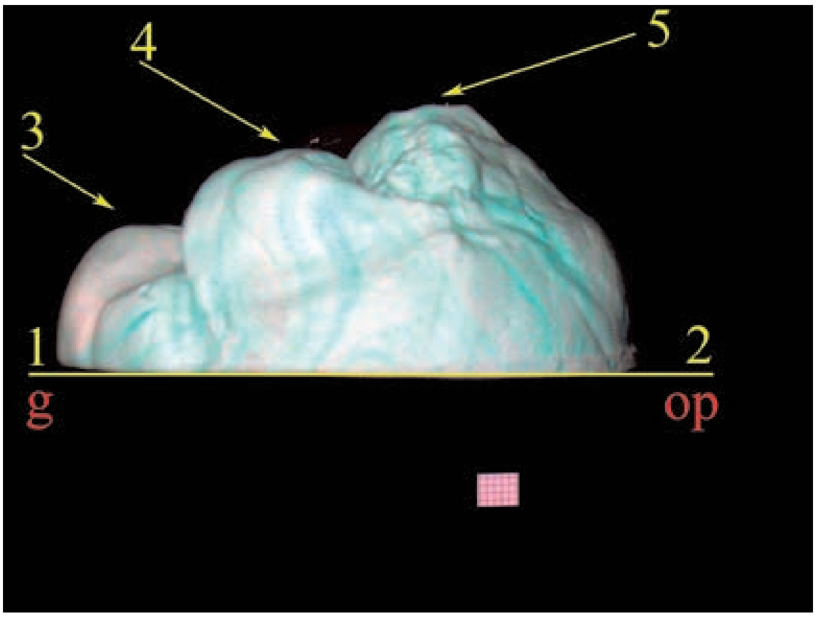

Fig. 3. Reverse of male foetus cranium base, 4th month of foetal life, v-tub length 193 mm, 1 – front (frontal pole), 2 – back (occipital pole), 3 – the lowest point of cranium base right anterior fossa, 4 – the lowest point of cranium base right middle fossa, 5 – the lowest point of cranium base posterior fossa g-op – reverse basic plane (reverse base) based on points g and op

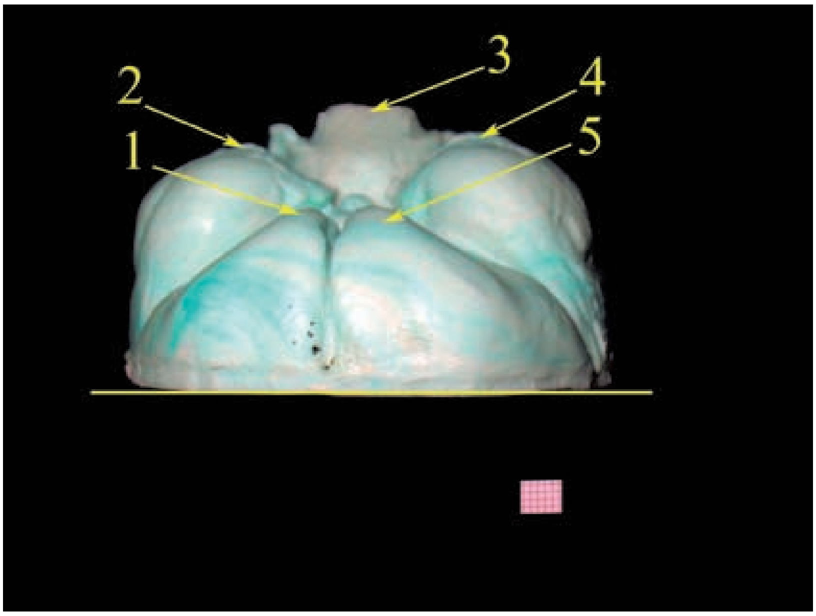

Fig. 4. Reverse of male foetus cranium base, 4th month of foetal life, v-tub length 198 mm, 1 – reverse of cranium left anterior fossa, 2 – reverse of cranium left middle fossa, 3 – reverse of cranium posterior fossa (unpaired), 4 – reverse of cranium right middle fossa, 5 – reverse of cranium right anterior fossa. Yellow line is a basic plane line

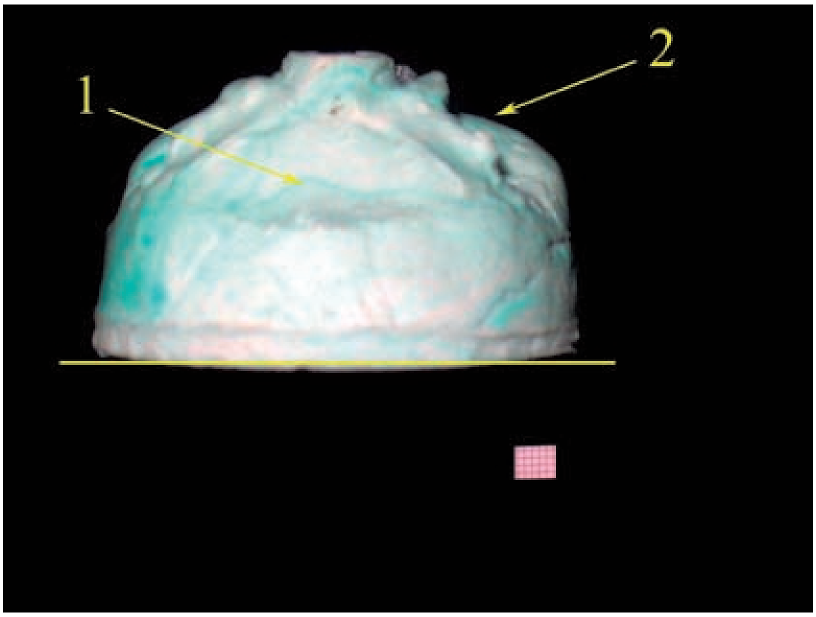

Fig. 5. Reverse of male foetus cranium base, 4th month of foetal life, v-tub length 198 mm, 1 – reverse of cranium posterior fossa (unpaired), 2 – reverse of cranium left middle fossa (fragment). Yellow line is a basic plane line

dentistry) with 18 D 4823 activator which provided adequate accuracy

Elicited reverses were placed in a self-constructed tripod and photographed in five planes with a Canon Power Shot A630 camera with a millimetre scale in the background. JPG format images were rolled in the computer. Particular fossae volumes were defined with triple measurement of liquid extruded by reverses to within ± 1 mL. Reverse sizes of 18 cranium base fossae were turned into a digital representation in the form of a cloud of dots with the use of Cyclone II system – 3D scanner in Institute of Machines Design and Operation, Technical University of Wrocław [22].

Renishaw CYCLONE 2 scanning system is equipped with Wolf&Beck non-contact laser probe enabling the digitalization of geometric data of physical objects as well as the elaboration of computer geometrical models of real objects. They may be used in the reconstruction or modification of objects which do not possess technical documentation in the form of drawings or 3D models. The Cyclone 2 system enables the transformation of geometry of any digital form into a cloud of dots. Renishaw TraceSurf provides further transformation of elicited data. It is used to prepare CAD surface model, which, due to neutral formats record system (DXF, STEP, IGES), enables data export to external software e.g. CAD, FEM. This way available data was processed with Renishaw Tracesurf, which enabled data export to external software (e.g. AutoCAD, CATIA) due to neutral formats record system (DXF, STEP, IGES).

After entering the data into AutoCAD programme, impressions of dimensional digital models were formed. Then, using the programme

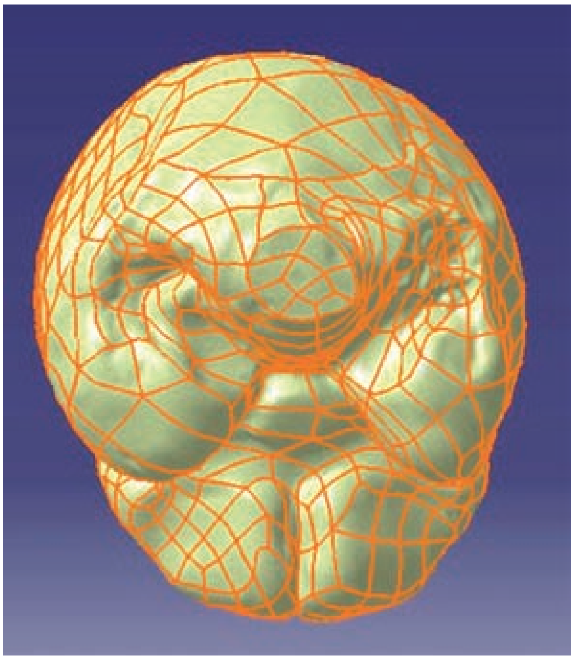

Fig. 6. Superficial digital model of impression elicited with the use of CATIA programme on the basis of cloud of dots formed in Cyclone II system

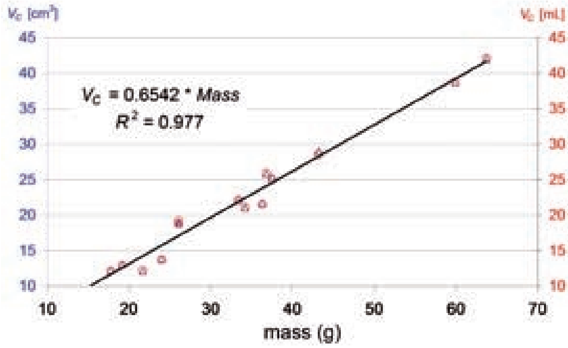

Fig. 7. Diagram of correlation between V_C [cm³] volume calculated on the basis of 3D digital model and impression mass as well as between extruded liquid volume V_C [mL] and impression mass

Presuming the constant density of all reverses, the following formula was elicited:

$$V_C = 0.6542 \times m$$

V_C – fossa volume [cm³];
m – reverse (impression) mass [g].

capabilities, the total volume V_C of the cranial base fossae was calculated as well as the left anterior fossae volume V_{CAL} and the right anterior fossae volume V_{CAR}, left middle fossae volume V_{CML}, right middle fossae volume V_{CMR} as well as posterior fossae volume V_{CP}.

Based on digital models, volumes of 18 impressions were evaluated and compared with volumes defined for the same specimens on the basis of extruded liquid measurements and impression mass weighing with the use of electronic scale. A very strong positive correlation was observed (r > + 0.99) between these results, which allowed us to abandon the more accurate, but time consuming, digital method. The method of weighing the mass of impression was applied. In order to do this, particular fossae were marked in the cranial base impression. Volume measurement based on extruded liquid measurements proved to be the least precise (small repeatability of results, impression mass and extruded liquid volume correlation index $r = 0.998$ against correlation index of the volume assessed on the basis digital model measurement and impression mass which amounted to $r = 0.9999$).

Regarding the remaining 92 impressions, the middle fossae volume was assessed on the basis of the elicited formula (Fig. 7) which represented the correlation between: volume V_C [cm³] calculated on the basis of 3D model, extruded liquid volume V_C [mL] and reverse mass m [g].

Survey Examination

Cranium Middle Fossa V_{FCM}

Middle fossae volume on the left (6033 ± 3995) is bigger than the one on the right (5602 ± 3629) by an average of 431 mm³. The difference is statistically significant ($p < 0{,}001$) (Fig. 8).

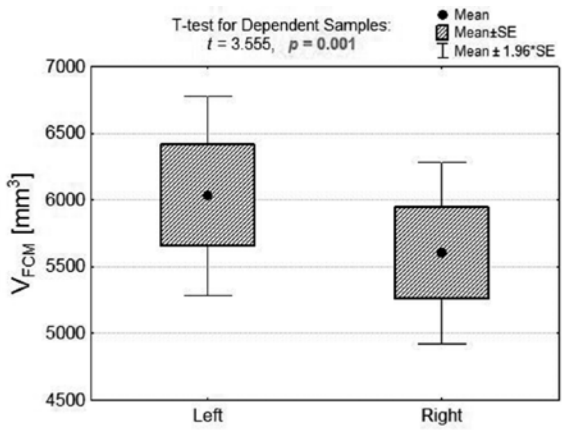

Fig. 8. Comparison of middle fossa volume (V_{FCM} F + V_{FCM} M) [mm³] of examined foetuses on the left and right side and *t*-Student test result for related variables

Taking into consideration non-significantly different width and length for both sides of the foetal cranium middle fossae, the significance of middle fossae volume seems to be mainly determined by their depth. The elicited dependence was described with the following formulas:

$$VFCMR = -4672 + 534{,}6 \times (G2\text{–}MP)$$

$$VFCML = -5260 + 564{,}3 \times (G2\text{–}ML)$$

VFCMR – volume of right middle fossa [mm^3]
V*FCML* – volume of left middle fossa [mm^3]
(*G2–MP*) – depth of right middle fossa [mm]
(*G2–ML*) – depth of left middle fossa [mm]

Relative Rate of Cranium Middle Fossa Volume Increase

The development of geometric sizes in the foetal period were analysed in monthly intervals (4th –7th month) due to small numerousness in the 16th, 27th and 28th month. On comparing the increases of analysed sizes, Scheffe's contrasts test was used with b_{xt} feature-age regression coefficient.

Recognition of the total volume of (left-right) cranium middle fossa V_{CM} and the remaining (anterior and posterior) fossae allowed us to determine undimensional indices, which reveal the relative rate of cranium middle fossa increase in relation both to cranium base growth and other fossae increase – hence the name: relative rate of the growth of middle fossa.

$w_1\,[\%] = \frac{V_{CM}}{V_C} \times 100$ – index of middle fossa total volume part in cranium base fossae total volume

$w_2 = \frac{V_{CM}}{V_{CP}} \times 100$ – index of middle fossa total volume part in anterior fossa total volume

$w_3 = \frac{V_{CM}}{V_{CA}} \times 100$ – index of middle fossa total volume part in posterior fossa total

The part of middle fossa total volume in cranium base fossae total volume amounts to 32.0% in the 16th week and 34.2% in 28th week. The growth rate is 0.19%/week on average. Due to the big differentiation of results, the growth rate may be regarded as constant value (linear model) in the whole analysed period (Fig. 9).

In the period from the 16th–28th week of foetal life, total volume of the middle fossa increases more intensively than anterior fossa total volume. The growth rate of w_2 index is stable and amounts to 1.02%/week (Fig. 10).

W_3 index poorly correlates with foetal age ($p > 0.05$). Middle fossa total volume – posterior fossa volume ratio decreases, which means that the

Table 2. Basic statistics of cranium middle fossa V_{FCM} volume on the left (*L*) and right (*R*)

Age	Foetus sex	$V_{FCM}{}^{L}$ [mm^3] volume			$V_{FCM}{}^{R}$ [mm^3] volume			Matchings
		N	$\bar{x}$	*SD*	*N*	$\bar{x}$	*SD*	*L* vs. *R**
IV	F	2	2168	817	2	1679	559	$t = 0.713$ $p = 0.527$
	M	2	995	218	2	1185	194	
	Σ	4	1582	835	4	1432	445	
V	F	39	4082	1789	39	3846	1556	$t = 3.003$ $p = 0.0039$
	M	20	3964	1977	20	3591	1823	
	Σ	59	4042	1839	59	3760	1640	
VI	F	12	7527	3876	12	7188	3650	$t = 2.497$ $p = 0.0179$
	M	21	10384	4481	21	9365	4033	
	Σ	33	9345	4434	33	8574	3985	
VII	F	5	9425	5774	5	9103	5325	$t = 0.721$ $p = 0.484$
	M	9	7032	2153	9	6692	1746	
	Σ	14	7887	3811	14	7553	3470	
Σ	F	58	5190	3357	58	4916	3156	$t = 3.555$ $p = 0.0006$
	M	52	6974	4450	52	6367	3986	
	Σ	110	6033	3995	110	5602	3629	

N – numerical amount; $\bar{x}$ – attribute arithmetical mean; *SD* – standard deviation.

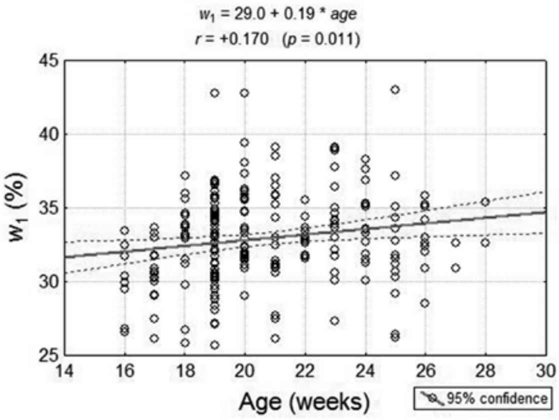

Fig. 9. Correlation diagram of w_1 index (middle fossa volume part in cranium base fossae total volume) with foetal age as well as mathematical model

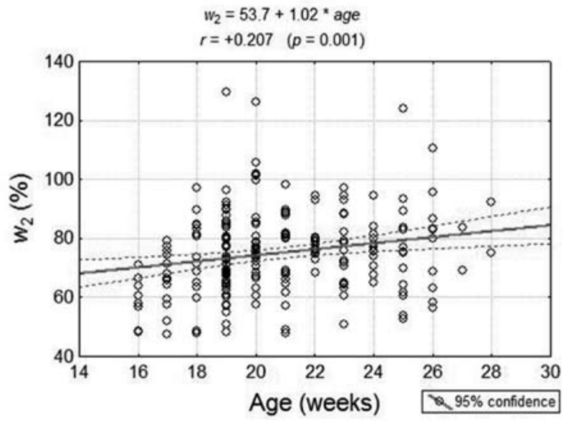

Fig. 10. Correlation diagram of w_2 index (medial fossa volume part in anterior fossa volume) with age as well as mathematical mode

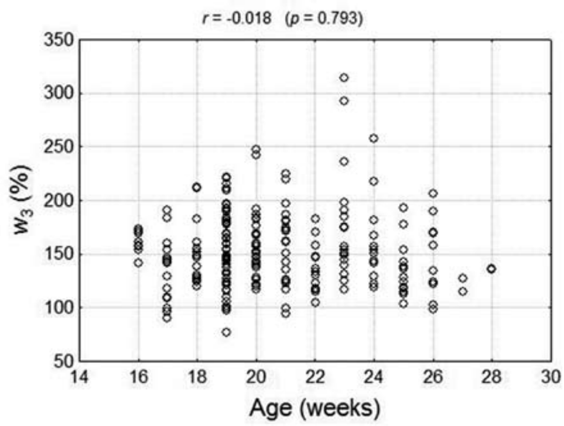

Fig. 11. Correlation diagram of w_3 index middle fossa volume part in posterior fossa volume) with foetal age

increase of the middle fossa volume is slower in comparison with the increase of the posterior fossa volume (Fig. 11).

Values of w_1, w_2 and w_3 indices do not depend on age (Fig. 12).

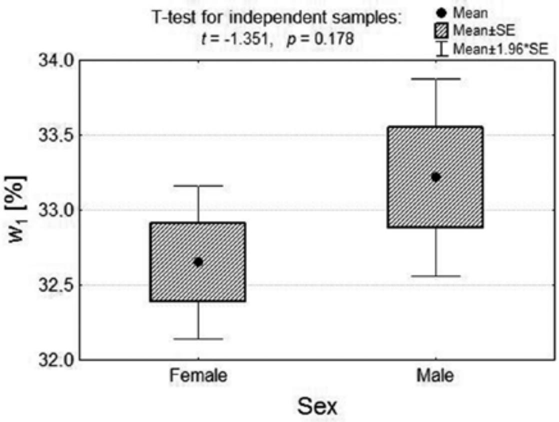

Fig. 12. Comparison of w_1 index of male and female foetuses as well as t-Student test result for non related variables

Anterior Cranial Fossa Volume V_{FCA} [mm^3]

Anterior fossae volume on the left is significantly bigger than the fossae volume on the right ($p < 0.0001$, Fig. 13).

Non-significantly different cranium anterior fossae length and depth on both sides suggest that this is the length which determines the significance of the anterior fossae difference.

Elicited dependence may be represented by the following formula:

$$VFCAP = 485.5 * \exp [0.1202 * (D1-T)]$$

$$VFCAL = 514.7 * \exp [0.1166 * (L1-T)]$$

$VFCAP$ – right anterior fossa volume [mm^3],
$VFCAL$ – left anterior fossa volume [mm^3],
$(D1-T)$ – right anterior fossa length [mm],
$(L1-T)$ – left anterior fossa length [mm],
exp – exponent symbol, record of exponential function with e base being natural log.

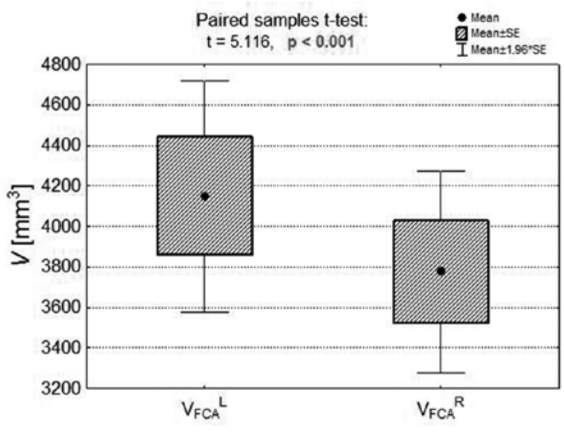

Fig. 13. Comparison of left anterior fossa volume ($VFCAL$) and right anterior fossa volume ($VFCAR$) [mm^3] of examined female and male foetuses and t-Student test result for related variables

Table 3. Basic statistics of anterior cranial fossa volume V_{FCA} on the left (*L*) and right (*R*)

Age	Foetal age	Volume $V_{FCA}{}^{L}$ [mm³]			Volume $V_{FCA}{}^{R}$ [mm³]			Matchings
		N	$\bar{x}$	*SD*	*N*	$\bar{x}$	*SD*	*L* vs. *R**
IV	F	2	1318	431	2	1128	316	$t = 0.792$ $p = 0.486$
	M	2	623	127	2	686	107	
	Σ	4	970	478	4	907	320	
V	F	39	2797	1211	39	2588	1065	$t = 4.090$ $p = 0.0001$
	M	20	2478	1174	20	2292	1119	
	Σ	59	2689	1198	59	2488	1083	
VI	F	12	4748	2598	12	4484	2586	$t = 3.382$ $p = 0.0019$
	M	21	7196	3686	21	6418	3104	
	Σ	33	6306	3499	33	5715	3035	
VII	F	5	7748	5374	5	7352	4541	$t = 2.105$ $p = 0.055$
	M	9	5206	1914	9	4406	841	
	Σ	14	6114	3569	14	5458	2988	
Σ	F	58	3577	2593	58	3341	2396	$t = -5.116$ $p < 0.0001$
	M	52	4784	3407	52	4262	2880	
	Σ	110	4148	3052	110	3776	2664	

N – numerousness; $\bar{x}$ – character arithmetic mean; *SD* – standard deviation.

Conclusions from Statistical Analysis of Middle Fossa Volume in Respect of Other Fossae

The table beneath presents the conclusions from a statistical analysis of the growth rate measurement of the selected parameters of the cranium base middle fossae in respect to other fossae. Conclusions are collected in tabular, textual and figurative forms. Mathematical dependence is applied in the form of a formula.

Volume of Cranium Base Right Middle Fossa V_{FCMR} [mm³]

In the 4th and 5th months, the right middle fossa volume growth rate is bigger than in the 6th and 7th months. It is confirmed by the values of linear regression ratios b_{Xt} presented in Table 4 (volume monthly increases) as well as the shape of mathematical model fitting curve (Fig. 14)

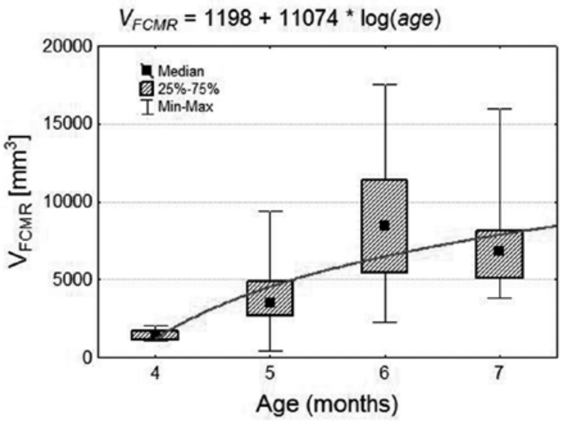

Fig. 14. Volume of cranium base right middle fossa in age monthly classes and adjusted logarithmic model

Volume of Cranium Base Left Middle Fossa V_{FCML} [mm³]

In the 4th and 5th months, the growth rate of left middle fossa volume is bigger in the 6th and 7th months. This is confirmed by the values of linear regression ratios b_{Xt} in Table 5 (volume monthly increases) as well as the shape of fitted mathematical model curve (Fig. 15).

Table 4. Basic statistics of foetal age (t) and X size: V_{FCMR} in four age classes as well as linear correlation indices and parameters of regression straight line $Y = a + b \times X$

Class	Sex	N	$\bar{t}$	S_t	$\bar{x}$	x_{min}	x_{max}	S_x	$r_{X,t}$	$b_{X,t}$	$a_{X,t}$
IV	F	2	110	1	9191	7942	10439	1766.3	1.000	1248.95	−128194.0
	M	2	108	1	5086	4481	5691	855.5	1.000	604.94	−60247.9
	F+M	4	109	2	7138	4481	10439	2626.7	0.926	1489.60	−155227.8
V	F	39	129	8	16479	2779	26952	5690.3	0.567	424.05	−38418.8
	M	20	130	8	14399	5436	38109	7395.4	0.399	392.47	−36719.8
	F+M	59	130	8	15774	2779	38109	6333.8	0.483	406.05	−36902.3
VI	F	12	154	9	27877	9569	44109	9987.2	0.189	220.48	−6131.0
	M	21	153	8	32169	13826	49575	10432.6	0.584	732.02	−80074.3
	F+M	33	154	8	30609	9569	49575	10329.9	0.424	528.23	−50563.5
VII	F	5	179	8	29979	14052	48543	15503.8	−0.242	−464.33	113279.6
	M	9	175	5	31425	22292	45325	7689.3	0.591	882.53	−122625.5
	F+M	14	176	6	30909	14052	48543	10529.1	0.049	79.24	16939.2

N – numerousness; $\bar{t}$ – foetus mean age (day); S_t – foetal age standard deviation; $\bar{x}$ – character arithmetic mean; $S(x)$ – character standard deviation; x_{min} – character minimum value; x_{max} – character maximum value; $r_{x,t}$ - character and foetal age (day) correlation index; $b_{x,t}$ – character and foetal age (day) regression index; $a_{X,t}$ – abscissa in regression model

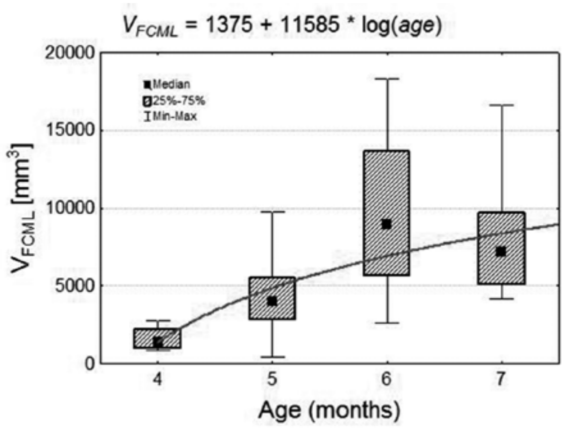

Fig. 15. Volume of cranium base left middle fossa in monthly age classes and fitted logarithmic model

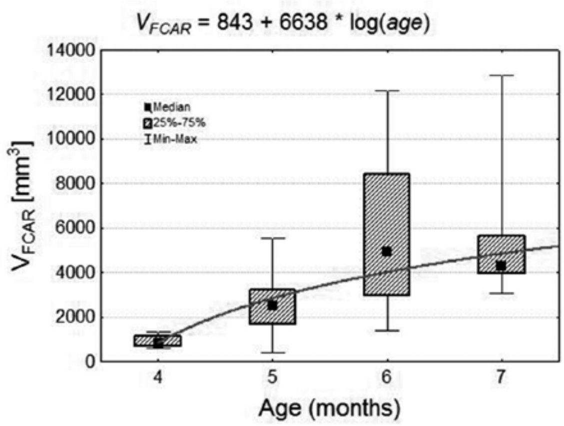

Fig. 16. Volume of cranium base right fossa in monthly age classes and fitted log model

Volume of Cranium Base Right Anterior Fossa V_{FCAR} [mm³]

In the 4th and 5th months, the growth rate of right anterior fossa volume is bigger than in 6th and 7th months. This is proved by the values of linear regression b_{Xt} ratios values in Table 6 (volume monthly gains) as well as fitted mathematical model curve shape (Fig. 16).

Volume of Cranium Base Left Fossa V_{FCAL} [mm³]

In the 4th and 5th months, the volume growth rate of the anterior middle fossa was bigger than in the 6th and 7th months. This is confirmed by the values of linear regression ratios b_{Xt} presented in Table 7 (volume monthly increases) as well as the shape of the fitted mathematical model curve (Fig. 17).

Table 5. Basic statistics of foetal age (t) and X size: V_{FCML} in four age classes as well as linear correlation ratios and regression straight line parameters $Y = a + b \times X$

Class	Sex	N	$\bar{t}$	S_t	$\bar{x}$	x_{min}	x_{max}	S_x	$r_{X,t}$	$b_{X,t}$	$a_{X,t}$
IV	F	2	110	1	6637	5573	7701	1504.9	1.000	1064.16	−110420.3
	M	2	108	1	4266	3038	5493	1736.3	1.000	1227.74	−128330.3
	F + M	4	109	2	5451	3038	7701	1906.4	0.999	1165.85	−121626.0
V	F	39	129	8	12418	2950	18567	4119.3	0.552	298.78	−26263.3
	M	20	130	8	9628	3713	19007	3497.0	0.377	175.37	−13214.3
	F + M	59	130	8	11472	2950	19007	4110.7	0.456	248.78	−20801.8
VI	F	12	154	9	19758	9556	31978	6454.5	0.072	54.49	11351.9
	M	21	153	8	24701	8088	37387	8876.2	0.395	421.25	−39890.2
	F + M	33	154	8	22904	8088	37387	8330.4	0.268	269.50	−18510.0
VII	F	5	179	8	23368	8289	38640	13002.7	−0.111	−178.13	55324.2
	M	9	175	5	22333	16349	27785	3571.7	0.299	207.48	−13882.8
	F + M	14	176	6	22703	8289	38640	7754.8	0.021	24.82	18327.2

Table 6. Basic statistics of foetal age (t) and X size: V_{FCAR} in four age classes as well as linear correlation ratios and parameters of regression line $Y = a + b \times X$

Class	Sex	N	$\bar{t}$	S_t	$\bar{x}$	x_{min}	x_{max}	S_x	$r_{X,t}$	$b_{X,t}$	$a_{X,t}$
IV	F	2	110	1	8278	6951	9605	1877.0	1.000	1327.23	−137717.6
	M	2	108	1	5320	3789	6851	2165.5	1.000	1531.25	−160055.1
	F + M	4	109	2	6799	3789	9605	2377.7	0.999	1454.06	−151693.4
V	F	39	129	8	15488	3679	23157	5137.7	0.552	372.65	−32755.9
	M	20	130	8	12008	4630	23706	4361.5	0.377	218.72	−16481.0
	F + M	59	130	8	14308	3679	23706	5126.9	0.456	310.28	−25944.2
VI	F	12	154	9	24642	11919	39883	8050.1	0.072	67.97	14158.2
	M	21	153	8	30808	10088	46630	11070.5	0.395	525.39	−49751.5
	F + M	33	154	8	28566	10088	46630	10389.7	0.268	336.13	−23085.9
VII	F	5	179	8	29145	10339	48192	16217.1	−0.111	−222.16	69001.0
	M	9	175	5	27854	20391	34654	4454.6	0.299	258.77	−17314.8
	F + M	14	176	6	28315	10339	48192	9671.9	0.021	30.96	22857.9

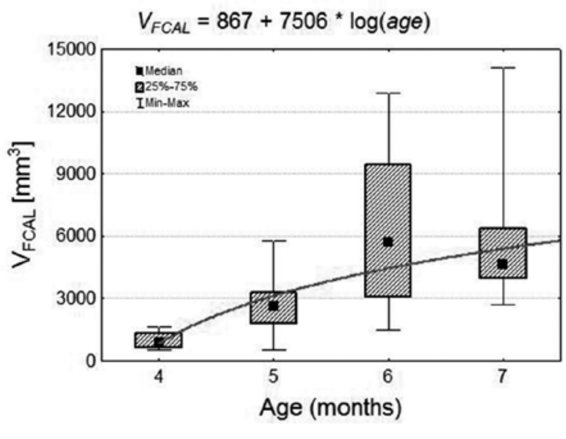

Fig. 17. Volume of cranium base left anterior fossa in age monthly classes and fitted logarithmic model

Table 7. Basic statistics of foetal age (t) an X size: V_{FCAL} in four age classes and four ratios of linear correlation as well as parameters of regression line $Y = a + b \times X$

Class	Sex	N	$\bar{t}$	S_t	$\bar{x}$	x_{min}	x_{max}	S_x	$r_{X,t}$	$b_{X,t}$	$a_{X,t}$
IV	F	2	110	1	34768	28351	41184	9074.5	1.000	6416.64	–671062.2
	M	2	108	1	17874	12735	23013	7267.9	1.000	5139.18	–537158.0
	F + M	4	109	2	26321	12735	41184	11840.2	0.981	7112.44	–748934.8
V	F	39	129	8	51207	6018	84459	17900.1	0.603	1419.08	–132509.1
	M	20	130	8	41188	24199	105051	19214.8	0.265	677.42	–47045.3
	F + M	59	130	8	47811	6018	105051	18808.3	0.457	1140.92	–100199.4
VI	F	12	154	9	86185	38472	136945	27817.2	0.038	122.16	67341.3
	M	21	153	8	110200	41326	190492	41399.7	0.562	2797.70	–318780.2
	F + M	33	154	8	101468	38472	190492	38403.6	0.373	1729.85	–164352.5
VII	F	5	179	8	87831	48464	134595	43018.3	–0.313	–1665.95	386702.0
	M	9	175	5	97281	57547	134585	22582.4	0.487	2134.95	–275385.8
	F + M	14	176	6	93906	48464	134595	30088.4	–0.051	–235.43	135408.3

Volume of Cranium Base Posterior Fossa V_{FCP} [mm³]

In the 4th and 5th months, the increase rate of the posterior fossa volume is bigger than in the 6th and 7th months. This is confirmed by the ratio values of linear regression b_{Xt} in Table 8 (volume monthly increases) as well as the shape of the curve of the fitted mathematical model (Fig. 18).

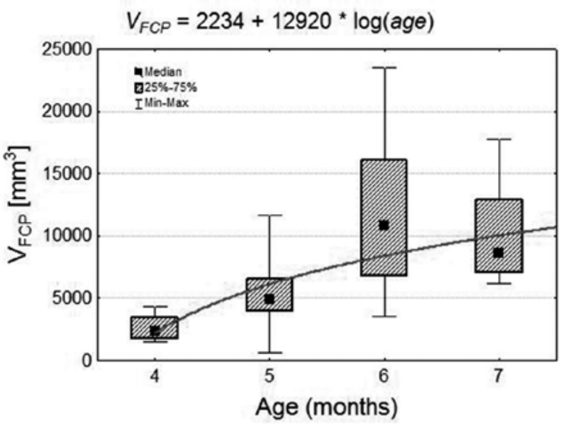

Fig. 18. Volume of cranium base posterior fossa in monthly age classes and fitted logarithmic model

Surveys Results Resumption

In the area of central fossa symmetry in respect to other fossae:

– central fossae volume on the left is bigger than the one on the right by 431 mm³ on average. The difference is statistically significant at the level $p < 0.001$;
– anterior fossae volume on the left side was statistically bigger than the anterior fossae volume on the right side at the level $p < 0.0001$.

As for middle fossa volume growth rate against other fossae:

– In 4th and 5th months, the volume growth rate of particular right and left middle fossae was more intensive than in the 6th and 7th months.
– The growth rate of the relative volume of the middle fossa against the total volume of the cranium base is on average 0.19%/week and is constant (linear model) in the whole of the analysed period:
– In the period the 16th–28th week of foetal life, relative volume of cranial fossa increases more intensively than the total volume of the anterior fossa:
– The growth of the relative volume of the cranium middle fossa against the growth of the volume of the posterior fossa in the analysed period is slower:
– In the 4th and 5th months, the growth rate of the anterior left and right fossae is bigger than in the 6th and 7th months.
– In the 4th and 5th months, the growth rate of posterior fossa volume is bigger than in the 6th and 7th months.

With reference to elicited correlations:

During the survey, some important correlations with foetal somatic measures were elicited.

Table 8. Basic statistics of foetal age (t) and X size: V_{FCP} in four age groups as well as linear correlation ratios and parameters of regression straight $Y = a + b \times X$

Class	Sex	N	$\bar{t}$	S_t	$\bar{x}$	x_{min}	x_{max}	S_x	$r_{X,t}$	$b_{X,t}$	$a_{X,t}$
IV	F	2	110	1	3469	2631	4307	1185	1.000	838.03	–88714.0
	M	2	108	1	1731	1477	1985	359	1.000	253.98	–25698.5
	F + M	4	109	2	2600	1477	4307	1231	0.938	707.39	–74505.0
V	F	39	129	8	5362	622	9577	2046	0.638	171.41	–16828.2
	M	20	130	8	4778	1859	11646	2162	0.347	99.83	–8224.8
	F + M	59	130	8	5164	622	11646	2086	0.526	145.69	–13735.8
VI	F	12	154	9	9383	3498	17890	4342	–0.033	–16.55	11937.2
	M	21	153	8	12975	5220	23482	5484	0.508	334.88	–38372.5
	F + M	33	154	8	11669	3498	23482	5325	0.301	193.32	–18037.5
VII	F	5	179	8	11158	6460	17762	5574	–0.390	–268.80	59381.2
	M	9	175	5	9148	6163	12974	2344	0.672	306.11	–44283.6
	F + M	14	176	6	9866	6163	17762	3733	0.083	47.47	1498.7

They may be of diagnostic (medical visualisation equipment), prognostic or evaluation (morphometric preparation of operative field) importance.

Relationships presented below might prove useful in criminology.

– middle fossae volumes (in the range the 4th –7th month):

$$VFCMR = -4672 + 534{,}6 * (G2-MP)$$

$$VFCML = -5260 + 564{,}3 * (G2-ML)$$

$VFCMR$ – right middle fossa volume [mm^3],
$VFCML$ – left middle fossa volume [mm^3],
($G2-MP$) – right middle fossa depth [mm],
($G2-ML$) – left middle fossa depth [mm].

– anterior fossae volume (in the range 4th–7th month):

$$VFCAP = 485.5 * \exp\,[0.1202 * (D1-T)]$$

$$VFCAL = 514.7 * \exp\,[0.1166 * (L1-T)]$$

$VFCAP$ – right anterior fossa volume [mm^3],
$VFCAL$ – left anterior fossa volume [mm^3],
($D1-T$) – right anterior fossa length [mm],
($L1-T$) – left anterior fossa length [mm].

– posterior fossa volume (in the range 4th–7th month):

$$VFCP = 2234 + 12920 * \log\,(age)$$

$$age = 0.672 * \exp\,(0.0002 * VFCP)$$

– undimensional ratios presenting relative rate of middle fossa growth with reference to both cranial base and other fossae (4th–7th month)

$w_1\,[\%] = \frac{V_{CM}}{V_C} \times 100$ – index of the part of middle fossa total volume in cranial base fossae total volume:

$w_2 = \frac{V_{CM}}{V_{CP}} \times 100$ – index of the part of middle fossa total volume in anterior fossa total volume:

$w_3 = \frac{V_{CM}}{V_{CA}} \times 100$ – index of the part of middle fossa total volume in posterior fossa volume

Discussion

The available literature does not provide any materials concerning the middle fossa of the base of foetal cranium. Examined material comprised the group of 110 pairs of middle fossae belonging to the collection of Normal Anatomy Department of Wroclaw Medical University aged 4–7 months of foetal life. The survey incorporated many methods characteristic for medicine, dentistry, mathematics and computer science. The available literature concerning cranial base at the particular foetal age does not include any information of such methodological combinations. The reverse (impression) method seems innovatory, as it has not been applied in neuroanatomical studies. The method presents complicated shape of the examined object with dental accuracy. Besides, reverse method is strictly connected with the possibility of measurement of such a complicated structure like cranium middle fossa or cranium base.

Apart from new methods of investigations, traditional ones were incorporated: preparational method, anthropologic method (taking foetal somatic features sizes) as well as the statistical method used to analyse the results statistically. Earlier investigative techniques of the foetal cranial base region were based on observations, autopsical examinations and traditional linear and angular measurements – Ford [11], Lee SK et al. [23]. Wysocki [40] made measurements of cranial cavity with lead shot and sand, whereas Modrzewska [29] defined the neurocranium volume with millet and rape seeds. However, these methods were characteristic for small accuracy of the measurement. During the development of the human organism, differences in the internal structure appear and the problem of body asymmetry arises. Literature discussing the foetal period touches on the problem of symmetry; however, only some papers concentrate on the cranial base. In 2008, Kędzia et al. [20] assessed the symmetry of cranial base in 77 foetuses aged 10–27 weeks of foetal period. The authors observed a high degree of symmetry maintenance in respect of the body median plane during the developmental period. Sławiński [37] noticed that the height and length of temporal squama in human foetuses did not reveal significant differences in respect to the examined body side and sex. Derkowski [9] observed that in the period from the 4th till 7th month, the cranial base grows preserving symmetry towards the body median plane. While building a mathematical model of the human cranium base fossae in 13 foetuses, Skomra et al. [36] did not describe any asymmetry though they observed a significant difference between the linear sizes of middle fossae on the left and right during the formation of a mathematical model of fossae volume increase in human cranium base. The present data concentrating on the period between the 4th and 7th month of foetal life, middle fossa volume on the left was significantly bigger. It seems that asymmetry is more characteristic for the adult age, whereas symmetry is more characteristic for foetal period. However, at some stage, lateralization of the cranium base parameters takes place. Modrzewska [29] who examined the changes that took place with age in the volume of 214 human skulls defined their pertinence on the basis of detailed inspection. Besides, while measuring their volume, she found a significant difference between females and males in favour of the latter. Regarding adults, Piontek et al. [30], with the use of Manouvier's formula, revealed a significant sexual dimorphism in female and male average volumes of male and female skulls surveyed in Polish population. Malinowski [26], analysing the length and width of 150 foetal crania from the age of 2 months of foetal life till birth, demonstrated the biggest growth of both parameters in the 4th, 5th and 9th month of the foetal period. In 1996, Lee SK et al. assessed X-ray images of foetal crania bases (18th–40th weeks) and observed that the angle of the cranium middle fossa based on pitauitary gland (point S) with its arms designated by zygomatic bone ossification points and temporal bone pyramid ridge increases at the expense of the angle of posterior fossa. Furthermore, the authors established that the anterior fossa angle was relatively stable and the cranium anterior fossa grew centrifugally forwards. In 1997 Błaszczyk [5] observed the biggest dynamics of foetal cranium base posterior fossa growth between the 4th and 5th or between the 5th and 6th month. Later, the development rate slowed down. In Derkowki's opinion [9], foetal cranium middle fossa angle increases at the expense of anterior fossa decreasing angle. The author also pointed to a two and half fold greater depth of cranium middle fossa in the analysed period from the 8th till 27th week. Initially, the irregular increase of the anterior fossa in the 1st trimester becomes steadier in the 2nd trimester. Our results proved that in the 4th and 5th months, the increase rate of particular right and left middle fossae is bigger than in the 6th and 7th months. Furthermore, the relative dynamics of the cranium middle fossa total volume (right + left) growth in reference to the cranium base total volume amounts to 0.19%/week and it is stable in the whole analysed period. It evidences steady growth of the middle fossa in relation to the cranial base. The elicited volume ratios (w_1, w_2, w_3) suggest that in the period from the 16th till 28th week of foetal life, the total volume of the cranium base middle fossa grows faster than volume of the anterior fossa. The growth rate is stable and it correlates with age, whereas the cranium middle fossa volume increase in proportion to the posterior fossa volume growth is less intensive in the analysed period and poorly correlates with age. The survey effects are inclinations of clinical (diagnostic) importance, which may be useful in the assessment of potential operative field in the area of middle fossa. Elicited correlations may be also used in programming medical diagnostic equipment (USG, CT, MR). During the study, in the form of mathematical formulas, the cranium base middle fossae volume was related to its depth. Additionally, cranium base anterior fossae volume depends mainly on their length. Mathematical relations of estimative character were established in the period from the 4th till 7th month. Foetal age assessment is of great importance in neonatology, radiology, obstetrics, neurosurgery, anthropology or crime detection. Elicited results are of cognitive value and may be used in forensic medicine for dead foetus age assessment even if only a cranium fragment is available, e.g. middle fossa. Though imaging equipment is increasingly more advanced, doctors still elicit false data about foetal age. In our earlier studies [35], there were very promising correlations assessing cranium base fossae volume only on the basis of head mass and length up to the formula:

$$V = -15{,}2 + 0{,}025 \cdot mass + 0{,}594 \cdot (g - op)$$

The authors concluded that in the analyzed foetal period, there is asymmetry of cranium base middle fossa in favour of the left side. Volume growth rate in the 4th and 5th months of foetal life is bigger than in the 6th or 7th months. In the observed period, the so-called growth relative rate of cranium base middle fossa is 0.19%/week and it is stable in forming a linear model. Middle fossa growth dynamics is of in-between character among anterior fossa, which grows more slowly, and the posterior fossa, which grows faster. The survey revealed a correlation in the form of mathematical formulas enabling foetal age assessment.

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Conflict of interest: None declared

Received: 25.03.2014
Revised: 29.05.2014
Accepted: 9.06.2014