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## Assessment of Foetal Age on the Basis of the Selected Dimensions of the Thorax

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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.** The correct definition of foetal age is a substantial problem in forensic medicine, gynaecology, obstetrics and anthropology.

**Objectives.** The goal of the study was the mathematical assessment of the foetal age with the use of thorax selected dimensions.

**Material and Methods.** The material consisted of 110 fetuses aged 4–7 months of foetal life, including 50 females in the CRL range: 80–233 mm. The following methods were incorporated: preparation, anthropological, image digital acquisition, Image J computer system measurements and statistical analysis. For each foetus the following sizes were taken: crump-rump length – CRL (*v-tub*), total body length – *v-pl* as well as brachial circumference – BC, thoracic circumference – TC and clavicular length – CLA.

**Results.** Six monofunctional mathematical models were elaborated: Bertalanffy growth curve, three Gompertz function based models and two exponential models to assess examined parameters increase along with *t* age. Model no. 3 for Gompertz function revealed the biggest consistency with *v-pl* measurements for every determination ratio  $R^2 = 0.9944$  for exponential model  $R^2 = 0.9917$ . Multiple regression analysis was used to elaborate mathematical formula to assess the foetal age (determination factor  $R^2 = 0.9997$ ) with BC, TC parameters.

**Conclusions.** Examined parameters BC and TC were found useful in foetal age assessment in the evaluated age range. Elaborated mathematical model can be applied in clinical practice e.g. in foetal age ultrasound determination (Adv Clin Exp Med 2014, 23, 5, 805–811).

**Key words:** human foetus, thorax, growth curve, gestational age.

Foetal age determination is an important clinical problem. Observations of foetal biological development incorporate the evaluation method based on foetal body size comparison with adequate standards. Body size classical meters are body length *v-pl* and crump-rump length CRL [1, 2]. Ultrasound measurements techniques which were introduced in the 70s and the 80s were cutting-edge technique in foetal age and size evaluation. They are safe both for the foetus and mother and provided standards based on object examination materials carried out on naturally delivered babies who, in accordance with paediatric criteria, were healthy and normally developed [3]. Available literature presents new foetometric parameters allowing us to assess the foetal age and among

them are: cerebellum transverse dimension, long bones lengths, head, abdomen and thorax circumferences, foot length [4]. The results of ultrasound examinations are predominant. Autopsical examinations have been carried out by the following authors: Woźniak et al. [4–6], Gray and Gardner [7] as well as Barregi et al. [8]. Fong et al. [9] conducted a prospective cross-sectional ultrasound study of foetal thorax growth during normal pregnancy. Foetal thorax circumferences were measured in 100 normal pregnancies from 13 to 41 gestation weeks. The authors constructed nomograms of thorax circumference vs gestational age and femur length. Data from 18 cases of risk of pulmonary hypoplasia indicated that foetal thorax circumference measurement may prove useful in the

antenatal prediction of lethal or clinically severe pulmonary hypoplasia. Also, with the use of new methods- three- (3D) and four-dimensions (4D) ultrasound examinations, foetal thorax dimensions applicability was assessed in developmental lesions aspect. By thorax volume examinations, Achiron et al. [10], in ultrasound tests, identified the following anomalies: diaphragmatic hernia, lung dysplasia, skeletal dysplasia with small thorax/thanatophoric dysplasia, abnormal situs, hydrothorax and esophageal atresia. Britto et al. [11] studied the relation between total area of the lung and thoracic circumference (TC) ratio by three-dimensional (3D) ultrasonography, applying new anatomical landmarks as the foetal aorta and inferior angle of the scapulae. The survey comprised 56 uncomplicated pregnancies between 24 and 32 weeks of gestation. Polynomial regressions were used to evaluate the correlation between TC and gestational age as well as TC and estimated foetal weight. A simple linear regression was used to evaluate the correlation between lung total area and thoracic total area and gestational age. The intraclass correlation coefficient was used to assess the intra and inter observer variability. Measurement of foetal TC and the relationship between total area of the lung as well as TC by 3D ultrasound examination were found to apply new anatomical landmarks and show good reproducibility allowing a new assessment of thoracic and pulmonary growth. Regardless the methods (cross-sectional study or ultrasound method), foetal metric examination are useful not only in anomalies detection but also in foetal growth regularity and foetal hypotrophy diagnostics [12]. The goal of the survey was foetal age assessment mathematical model elaboration on the basis of thorax selected dimensions.

## Material and Methods

Research material consisted of 110 fetuses (50 females and 60 males) aged 4–7 months of foetal life in the CRL range: 80–233 mm. The fetuses originated from a specially selected group free from macroscopically detected developmental abnormalities. The following methods were incorporated to the study: preparation and anthropologic methods, image digital acquisition, Image J computer system measurements and statistical analysis. The clavicle was exposed with preparational method. Anthropologic method based on age determination with the use of crump-length length-CRL (CRL or v-tub) by Scammon and Calkins tables [13]. Applying Image J computer system, for each foetus, somatic parameters were taken (crump-rump length – CRL/v-tub, body total length –  $v-pl$ , brachium circumference – BC, thoracic circumference – TC, clavicle length – CLA). The statistics program package STATISTICA v. 9 (StatSoft Inc. Tulsa, USA) was used in the calculations.

## Results

At the first stage of the survey, the correlation between total body length  $v-pl$  (defined in mms) and foetal age (in weeks) was assessed in the length range  $v-pl$  70–460 mm. This correlation was accurately defined ( $R^2 = 0.999727$  – Fig. 1a) with a quadratic polynomial:

$$v-pl = -202 + 25.6 \cdot age - 0.206 \cdot age^2.$$

This model; however, cannot be extrapolated from the examined age range (12–36 hbd). For fetuses younger than 9 weeks,  $v-pl$  length has

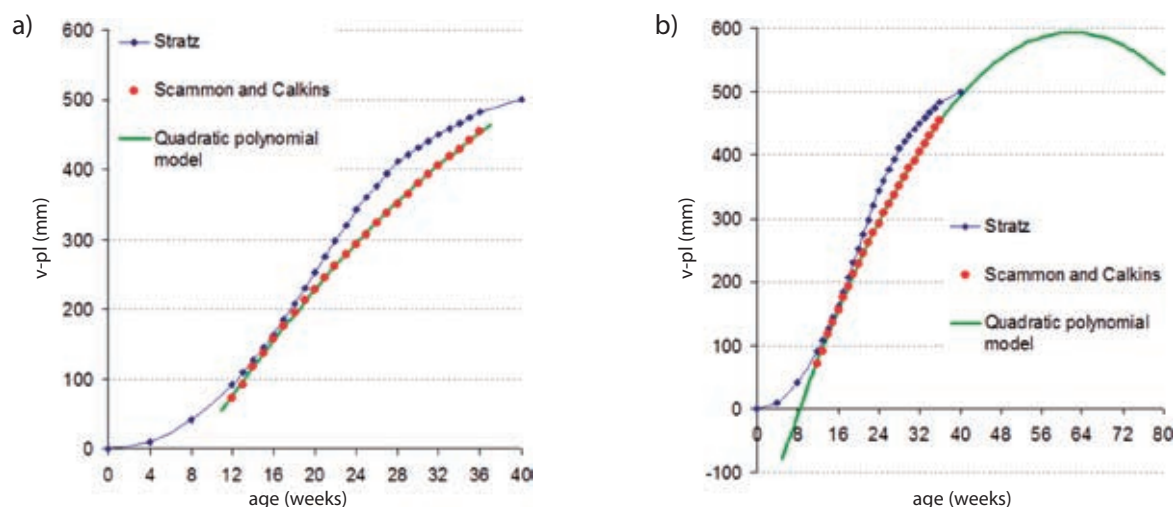


Fig. 1. Foetal body length  $v-pl$  in foetal period according to Stratz [14], Scammon and Calkins [30], own quadratic polynomial (1)

negative values, whereas in infants born after the 63<sup>th</sup> week of foetal life,  $v-pl$  length will decrease (Fig. 1b). Models presented in the paper are devoid of this quality and for  $t = 0$  (week of foetal life), their value amounts to zero.

Then, the study idea based on choosing the best analytical form of the model and estimating the parameters so that the length changes before the 12<sup>th</sup> week preserved the character presented by Stratz [14]. As a very strong positive correlation ( $R > 0.9$ ) is observed between various anatomical structures and foetal age ( $v-pl$ ) – adoption of model one form seems to be well founded – universal mathematical formula for all linear dimensions with parameters different values. This would enable a comparison of measurements results achieved in various research units where the surveys would be carried on different age fetuses. Several mathematical models were taken into account due to the character of  $v-pl$  body length dispersion diagram with  $t$  week of foetal life. There were monofunctional models increasing monotonously, for the age  $t = 0$ , they reaching zero value as well and having inflection point and parameters number not bigger than 3. The functions taken into account were:

- 1) Bertalanffy growth curve (VBGF):

$$y(t) = b_0 \cdot \{1 - \exp[-b_1 \cdot (t - b_2)]\}$$

– Sztencel and Żelawski [28]

- 2) Gompertz function:

$$y(t) = b_0 \cdot \exp\left\{\frac{b_1}{b_2} \cdot [1 - \exp(-b_2 \cdot t)]\right\}$$

- 3) Gompertz function:

$$y(t) = b_0 \cdot \exp\{-\exp[-b_1 \cdot (t - b_2)]\}$$

- 4) Gompertz function:

$$f(t) = b_0 \cdot \exp\left(-\frac{b_1}{b_2}\right) \cdot \exp\left[-\frac{b_1}{b_2} \cdot \exp(-b_2 \cdot t)\right]$$

– Seber and Wild [29]

- 5) Exponential model:

$$y(t) = b_0 \cdot \left[1 - \frac{1}{\left(\frac{t}{b_2}\right)^{b_1} + 1}\right]$$

- 6) Exponential model:

$$y(t) = \exp\left(b_0 + \frac{b_1}{t}\right)$$

Out of the above models, Gompertz function (model 3) – determination factor  $R^2 = 0.9944$  (Fig. 2 a–b) revealed the best adjustment to length  $v-pl$  measurements results. For exponential model (model 6),  $R^2$  value amounted to 0.9917. Table 1 presents these 2 models estimation parameters.

A strong non-linear correlation of thorax analysed dimensions with foetal age determined the basis of interdependence described by Scammon and Calkins (Fig. 3a–c) enabled the formation a mathematical model of foetus based on these sizes. Multiple regression analysis helped to assess parameters values of the model:

$$y = \exp[b_1 \cdot \ln(x_1) + b_2 \cdot \ln(x_2) + b_3 \cdot \ln(x_3)]$$

and finally, the elicited expression enabled foetus age assessment (weeks):

$$\text{Age} = \exp[0,3155 \cdot \ln(BC) + 0,3154 \cdot \ln(TC)]$$

The model did not include clavicle length dimension for which  $b_3$  factor value did not differ significantly from zero ( $p > 0.05$ ). The quality of the proposed mathematical model was proved by a very high value of determination factor:  $R^3 = 0.9997$  as well as by the distribution of results elicited for 110 fetuses (Fig. 4).

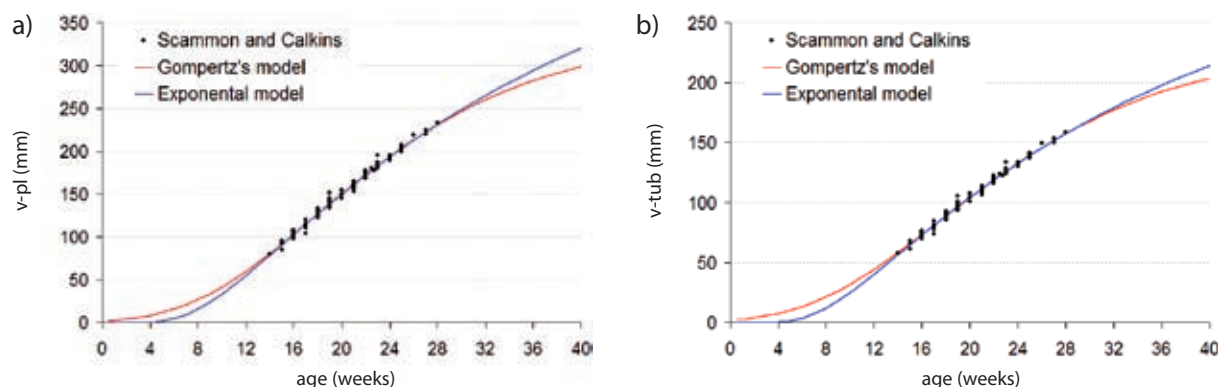
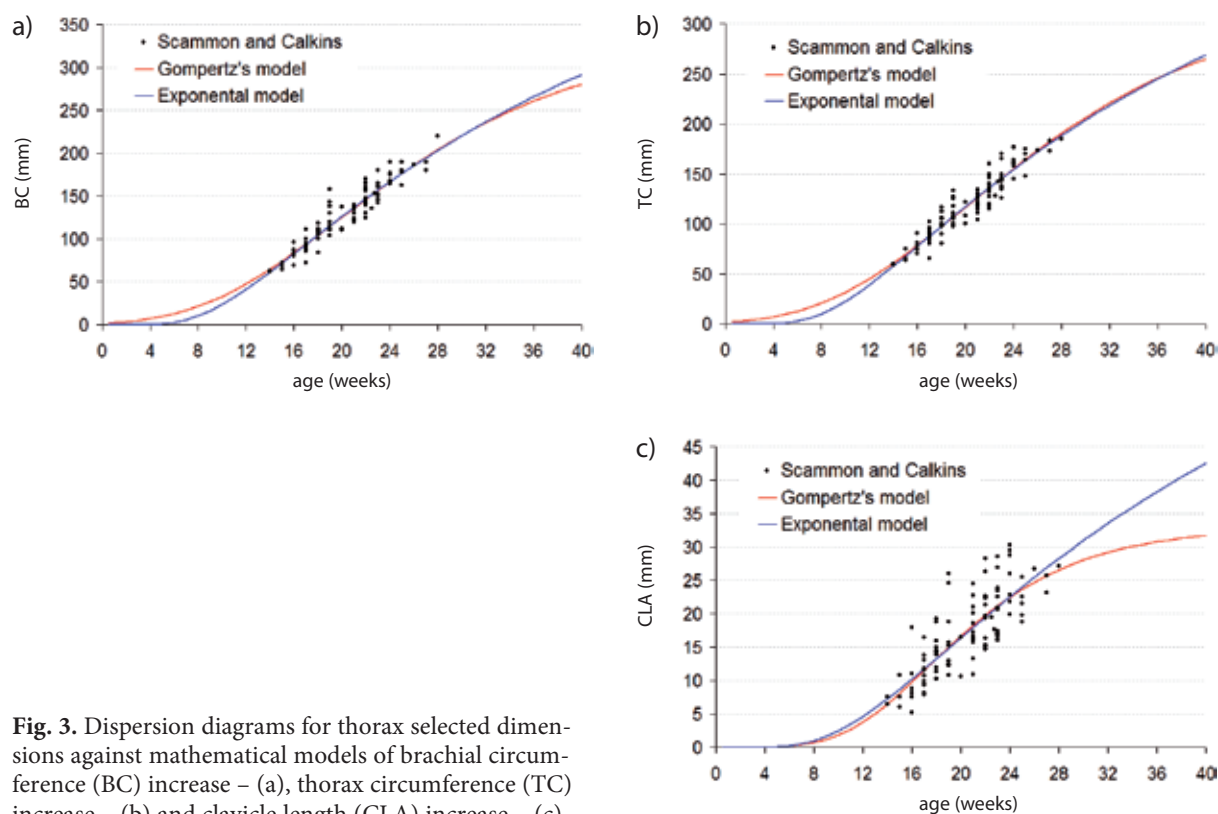


Fig. 2. Correlation diagrams of analysed models: for  $v-pl$  – (a) and for  $v-tub$  (CRL) parameter – (b)

**Table 1.** Parameters of Gompertz growth models and exponential model for selected dimensions of foetal thorax – 12–36 weeks of foetal life [14, 27]

Model	Dimensions $y(t)$ [mm]	N	$\bar{x}$	$b_0$	$b_1$	$b_2$	$R^2$
Gompertz's model (3)	$v-pl$ (Scammon and Calkins)	391	265.0	337.6	0.095	17.795	0.9870
	$v-tub$ (Scammon and Calkins)	210	175.5	232.0	0.091	17.558	0.9870
	BC	110	129.5	334.1	0.086	19.773	0.8919
	TC	110	120.3	321.1	0.083	20.164	0.8903
	CLA	220	17.0	32.9	0.145	17.348	0.6562
Exponential model (6)	$v-pl$ (Scammon and Calkins)	391	265.0	6.526	−30.27		0.9871
	$v-tub$ (Scammon and Calkins)	210	175.5	6.086	−28.74		0.9870
	BC	110	128.9	6.514	−33.55		0.8923
	TC	110	120.3	6.423	−33.17		0.8897
	CLA	220	17.0	4.703	−38.10		0.6524

BC – brachial circumference, TC – thoracic circumference, CLA – clavicle length.

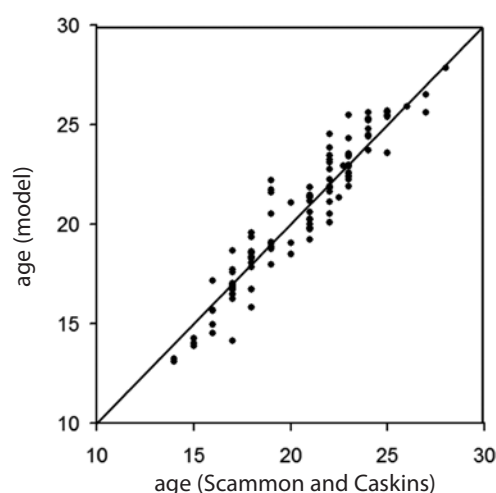


**Fig. 3.** Dispersion diagrams for thorax selected dimensions against mathematical models of brachial circumference (BC) increase – (a), thorax circumference (TC) increase – (b) and clavicle length (CLA) increase – (c)

## Discussion

Foetus biometrics allows us to assess the mathematical relation between gestational age foetus biometric parameters. Usually, this can be done with the use of regression analysis. This method incorporates an independent variable to define the dependant variable. Gestational age is applied as a variable in a nomogram enabling an analysis of

normal growth e.g. of internal organ. In order to apply such nomograms correctly, the doctor should recognize the foetus gestational age. In such situations, morphological features (CRL length, circumferences or long bones lengths) applicability proves very significant not only in the very age definition but also in model formation used to establish the basis for organ growth rate assessment [15]. The first parameter which was evaluated with



**Fig. 4.** Diagrams of age dispersion defined on the basis of Scammon and Calkins tables and age defined with the use of proposed model basing on BC and TC dimensions

ultrasound technique was a biparietal dimension which allows for determining the gestational age to within  $\pm 7$ –11 days and subsequently CRL-crown-rump length with accuracy to within  $\pm 3$ –5 days in fetuses 20–60 mm long [15]. Literature provides new fetometric parameters: head circumference, femoral bone length, abdominal circumference. Age assessment models based on several dimensions or factors are becoming increasingly popular. The relations between somatic parameters and foetal age were determined by cross-sectional analysis in publications of Woźniak et al. [4–6], Barreggi et al. [8], Hadlock et al. [16, 71] and Matsushita et al. [18]. Woźniak et al. [4] introduced a new parameter in foetal age analysis: foetal foot length-width. The material consisted of 158 fetuses aged 13–29 weeks of foetal life, in CRL range: 54–250 mm. In the study, foot length (FL), foot width (WF) were measured as well as ratios: femoral bone/foot length (LF/F ratio) and shank bone/foot length (LF/P ratio). We have found that in the analysed period, foot, femur and shank geometrical sizes are symmetrical and the rate of foot width and length increase as well as this of length-width ratio increase are stable. We created a regression model to assess the foetal age on the basis of the foot length. In turn, in the subsequent paper we described a logarithmic model as the best one to describe bone structure sizes of facial skeleton dependence on foetal age [5]. The material consisted of 112 fetuses aged 4–7 months in the CRL: 83–245 mm. We concluded that the growth rate of the analysed parameters describing facial skeleton morphology was the biggest in the 4<sup>th</sup> and 5<sup>th</sup> month. Woźniak et al. [6] described the mathematical functions used to assess the development of foetal brachial plexus. The most rapid growth was

observed between the 14<sup>th</sup> and 18<sup>th</sup> week, and the slowest one between the 24<sup>th</sup> and 28<sup>th</sup> week. Four formulas were used in the mathematical growth model: linear regression, logarithmic function, the von Bertalanffy growth model and the Gompertz curve. The prenatal development of the brachial plexus was not constant as well as the applied mathematical functions which proved useful in describing its growth rate. Barreggi et al. [8] carried on longitudinal measurement of foetal limbs and allometric analysis in 58 fetuses between 8<sup>th</sup>–14<sup>th</sup> week in CRL range: 38–116 mm. The created models were found very useful in determining the foetal growth. Hadlock et al. [16, 17] in their 2 papers described cross-sectional studies. Foetal abdominal circumference, foetal head circumference and relation to menstrual age in the material of 400 fetuses aged 15–41 weeks were described. Both measurements were clinically important in the assessment of the foetal age. Head circumference values as the function of menstrual age was described with linear cubic function. In turn, Matsushita et al. [18] examined 21 anthropometric measurements of long bones, originating from 122 Japanese fetuses aged 18–40 weeks. Allometric coefficients of total measurement set and length measurements set were described. In many ultrasound surveys, authors observed that foetal age assessment models based on somatic parameters e.g. limbs length may be very useful in diagnosing foetal dwarfism, intrauterine growth restriction, limb malformations, microcephaly, determination of gestational age, archaeological dating as well as forensic applications [19, 20]. With the use of ultrasound examinations of 576 women (16–40 gestation weeks), Chitkara [21] observed foetal thorax circumference variability and formed thorax circumference and thorax length nomogram. This parameter applicability in foetal age estimation has been proved by our own results as well e.g. strong non-linear correlation of thorax analysed dimensions with foetal age. Elaborated mathematical model is of high quality, which is evidenced by a very high determination index  $R^2 = 0.9997$ . The novelty of paper concerns the use brachial circumference as a parameter in objective assessment of foetal age. We hope that the presented measurements will be clinically useful (ultrasound method) in antenatal detection of fetuses at the risk of anomalies characteristic for foetal lungs and chest e.g. pulmonary hypoplasia or spondylothoracic dysplasia as well as intrauterine growth restriction. In his paper, Hadlock et al. [22] demonstrated that models based on more than 1 parameter enabled a more accurate age assessment. They showed that after the 36<sup>th</sup> week, the total measurement of circumferences (head, thorax, femur length) was characteristic for





**Fig. 5.** Normal placenta (left), hypotrophic placenta (right). Photo courtesy of authors

better accuracy and a significant decrease of values of average error, standard deviation or maximum error in comparison with single parameter measurement. In turn, Chervenak et al. [23] found that in the 2<sup>nd</sup> trimester, the head circumference was the best determinant and accessory measurements of abdominal circumference and femoral bone length increased definition accuracy. Literature provides mathematical models of growth elaborated on the basis of ultrasound method measurements. Merz et al. [24] used tangens hyperbolicus whereas Scheuer et al. [25] used linear and logarithmic regression to assess foetal age. Recognition of foetus exact age, on the basis of mathematical models, foetal growth regularity may be

evaluated, which is useful in intrauterine growth restriction diagnostics. The ultrasound method is the accepted standard for foetal growth monitoring. A series of ultrasound measurements can provide a reasonable estimation of foetal gestational age and weight based on individual and composite foetal biometric measurements [26]. Normal placenta as well as intrauterine growth restriction placenta are presented in Fig. 5. Intrauterine growth restriction constitutes a substantial clinical problem in gynecology and obstetrics so available literature stresses the significance of mathematical models in foetal age determination on the basis of foetus biometric parameters which are so easy to be defined with ultrasound methods.

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