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New quantitative patterns of the growing trachea in human fetuses

Michał Szpinda^{1ACDEF}, Marcin Daroszewski^{1ABC}, Anna Szpinda^{1GDE},
Alina Woźniak^{2GDE}, Marcin Wiśniewski^{1GDE}, Celestyna Mila-Kierzenkowska^{2DE},
Mariusz Baumgart^{1DE}, Monika Paruszevska-Achtel^{1GDE}

¹ Department of Normal Anatomy, Ludwik Rydygier Collegium Medicum in Bydgoszcz, The Nicolaus Copernicus University in Torun, Bydgoszcz, Poland

² Department of Medical Biology, Ludwik Rydygier Collegium Medicum in Bydgoszcz, The Nicolaus Copernicus University in Torun, Bydgoszcz, Poland

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Background:

Rapid progress in perinatal medicine has resulted in numerous tracheo-bronchial interventions on fetal and neonatal airways. The present study was performed to compile normative data for tracheal dimensions at varying gestational ages.

Material/Methods:

Using anatomical dissection, digital image analysis (NIS-Elements BR 3.0) and statistical analysis (Wilcoxon signed-rank test, Student's t test, one-way ANOVA, post-hoc Bonferroni test, linear and nonlinear regression analysis) a range of the 4 variables (length in mm, middle external transverse diameter in mm, proximal internal cross-sectional area in mm², internal volume in mm³) for the trachea in 73 spontaneously aborted human fetuses (39 male, 34 female) aged 14–25 weeks was examined.

Results:

No significant male-female differences were found ($P > 0.05$). The length ranged from 10.37 ± 2.15 to 26.54 ± 0.26 mm as $y = -65.098 + 28.796 \times \ln(\text{Age}) \pm 1.794$ ($R^2 = 0.82$). The middle external transverse diameter varied from 2.53 ± 0.09 to 5.09 ± 0.42 mm with the model $y = -11.020 + 5.049 \times \ln(\text{Age}) \pm 0.330$ ($R^2 = 0.81$). The trachea indicated a proportional evolution because the middle external transverse diameter-to-length ratio was stable (0.23 ± 0.03). The proximal internal cross-sectional area rose from 1.46 ± 0.04 to 5.76 ± 1.04 mm² as $y = -3.562 + 0.352 \times \text{Age} \pm 0.519$ ($R^2 = 0.76$). The internal volumetric growth from 11.89 ± 2.49 to 119.63 ± 4.95 mm³ generated the function $y = -135.248 + 9.919 \times \text{Age} \pm 10.478$ ($R^2 = 0.86$).

Conclusions:

The growth in both length and middle external transverse diameter of the trachea follows logarithmic functions, whereas growth of both its proximal internal cross-sectional area and internal volume follow linear functions. The length and middle external transverse diameter of the trachea develop proportionally to each other. The tracheal dimensions may be helpful in the prenatal diagnosis and monitoring of tracheal malformations and obstructive anomalies of the upper respiratory tract.

Key words:

fetal trachea • length • middle external transverse diameter • proximal internal cross-sectional area • internal volume • regression analysis

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Author's address:

Michał Szpinda, Department of Normal Anatomy, Ludwik Rydygier Collegium Medicum in Bydgoszcz, Karłowicza 24 St., Bydgoszcz 85-092, Poland, e-mail: kizanat@cm.umk.pl

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BACKGROUND

The quantitative anatomy of the growing trachea in human fetuses is still far from completed. Generally, in fetuses, no attempts at fetal intubations or interventions involving the airways are performed before the gestational age of 24 weeks. Although *in-utero* surgery, being still experimental in most centers, is performed from 18 weeks, the placenta acts as the fetus' cardiopulmonary by-pass machine, thereby negating a need for manipulation or cannulation of the airways. However, numerical data on fetal tracheas are relevant in prenatal surgery involving the tracheo-bronchial tree [1,2]. Studies on tracheal obstruction in the treatment of congenital diaphragmatic hernias [3,4] included fetuses at the age of 20 weeks and older. Previous observations on fetuses with laryngeal atresia [5–9] proved that the tracheal diameter in affected fetuses was considerably increased as compared with that in normal fetuses at the same age.

To date, the relationship between tracheal variables (length, external and internal diameters) and gestational age has been expressed only by linear functions [10–13]. Of note, few studies have focused on internal cross-sectional area [14–16] and contained volume [15,16] of the trachea, assessed on chest CT scans in children, adolescents and adults, but with no detailed growth curves.

In order to supplement fragmentary information on tracheal dimensions in human fetuses, our objectives were to examine:

- age-specific reference intervals for length, middle external transverse diameter, proximal internal cross-sectional area, and internal volume of the trachea at varying gestational ages;

- the relative growth of the trachea;
- the growth curves for the parameters studied.

MATERIAL AND METHODS

The study was carried out on 73 human fetuses of both sexes (39 male, 34 female) of Caucasian origin, which had been derived from spontaneous abortions or stillbirths in the years 1989–2001. The sample included fetuses that had been the outcome of causes of intra-uterine growth restriction. Legal and ethical considerations were consistent with the rules of the University Research Ethics Committee (KB 189/2011). On macroscopic examination both external and internal anatomical malformations were ruled out in all the included specimens, so the sample examined could have been considered as normal. In no case was the cause of fetal death related to congenital cardiovascular or laryngo-tracheal anomalies. The sample included fetuses that were the outcome of causes of placental insufficiency. The gestational age varied from 14 to 25 weeks (Table 1). The fetal ages were accurately established on the basis of the following criteria: 1) gestational age based on measurements of the crown-rump length [17]; 2) known date of the beginning of the last maternal menstrual period; and 3) a combination of abdominal circumference, femur length and biparietal diameter known by early second-trimester ultrasound scan [8].

All specimens had been immersed in 10% neutral buffered formalin solution for 12–24 months for preservation, and then dissected under 10-fold magnification using a stereoscope with Huygens ocular (Figure 1). We could not have used perfusion fixation instead of immersion fixation with 10% formalin because the arterial bed of the fetuses from

Table 1. Distribution of fetuses studied.

Fetal age		Crown-rump length (mm)				Number	Sex	
Months	Weeks (Hbd-life)	Mean	SD	Min.	Max.		Male	Female
4	14	79.5	4.3	76.0	81.0	2	1	1
	15	89.3	6.4	84.0	93.0	1	1	0
	16	103.1	6.3	96.0	108.0	2	1	1
5	17	114.0	7.3	110.0	123.0	9	5	4
	18	129.5	6.8	124.0	136.0	10	5	5
	19	141.9	5.9	138.0	149.0	7	4	3
	20	155.0	5.2	152.0	162.0	13	7	6
6	21	166.4	4.9	165.0	174.0	11	6	5
	22	178.9	7.2	175.0	185.0	5	2	3
	23	192.9	7.2	187.0	195.0	6	3	3
	24	201.4	4.2	199.0	204.0	5	3	2
7	25	214.8	4.7	212.0	217.0	2	1	1
Total						73	39	34

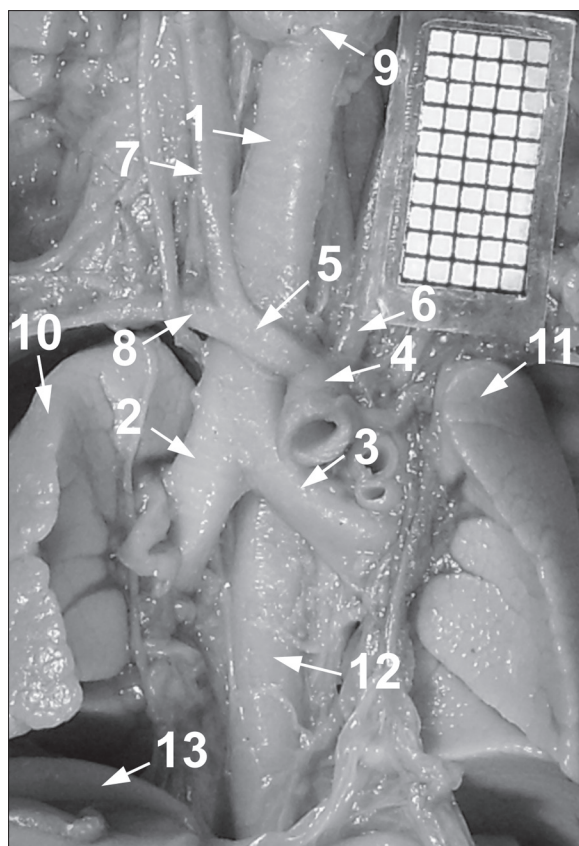


Figure 1. Topography of the trachea and main bronchi in a female fetus aged 19 weeks: 1 – trachea, 2 – right main bronchus, 3 – left main bronchus, 4 – ascending aorta, 5 – brachiocephalic trunk, 6 – left common carotid artery, 7 – right common carotid artery, 8 – right subclavian artery, 9 – larynx, 10 – right lung, 11 – left lung, 12 – esophagus, 13 – abdominal diaphragm.

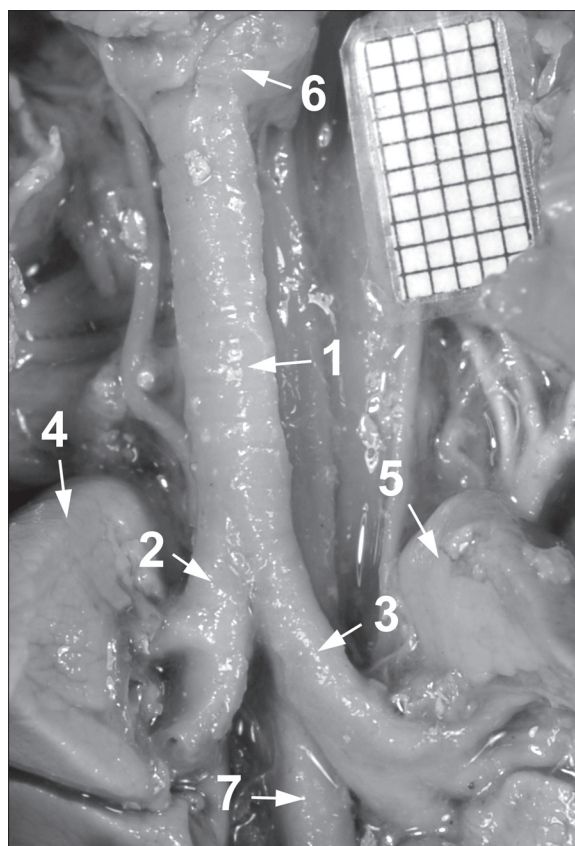


Figure 2. The trachea and main bronchi in a female fetus aged 20 weeks: 1 – trachea, 2 – right main bronchus, 3 – left main bronchus, 4 – right lung, 5 – left lung, 6 – larynx, 7 – esophagus.

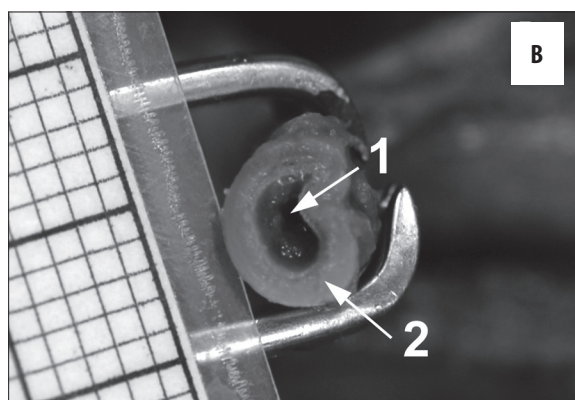
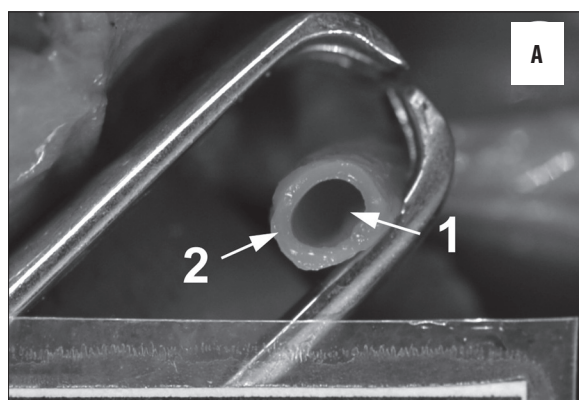


Figure 3. The trachea in cross section at the level of the first tracheal cartilage in a male fetus aged 18 weeks (A), and a female fetus aged 23 weeks (B): 1 – tracheal lumen, 2 – tracheal wall.

our collection had previously been filled with white latex LBS 3060. In each fetus, the trachea *in situ* with a millimeter scale was placed vertically to the optical lens axis, then recorded using a Nikon D200 camera, and digitalized to TIFF images. Next, digital pictures of the trachea (Figure 2) were assessed using digital image analysis (NIS-Elements BR 3.0, Nikon), which semi-automatically estimated the 4

variables: length, middle external transverse diameter, internal (luminal) cross-sectional area, and internal volume of the trachea. At first, both its length and middle external transverse diameter were measured, and after that a tracheal cross-section was taken between the cricoid cartilage and the first tracheal ring (Figure 3). In order to calculate the internal volume of the trachea, the tracheal lumen was

Table 2. The statistical analysis (one-way ANOVA test and post-hoc Bonferroni test) of the morphometric parameters of the fetal trachea.

Fetal age (weeks)	Number of fetuses	Length (mm)	Middle external transverse diameter (mm)		Internal cross-sectional area (mm ²)		Internal volume (mm ³)		
		Mean	SD	Mean	SD	Mean	SD	Mean	SD
14	2	10.37	2.15	2.53	0.09	1.46	0.04	11.89	2.49
15	1	12.24	0.00	2.48	0.00	2.02	0.00	19.61	0.00
16	2	15.12	3.20	2.82	0.20	2.32	0.34	25.09	2.19
17	9	↓ (P<0.05)	3.22	↓ (P<0.05)	0.42	↓ (P<0.05)	0.51	↓ (P<0.05)	7.66
		17.18		3.24		2.54		30.60	
18	10	↓ (P<0.01)	1.41	↓ (P<0.01)	0.36	↓ (P<0.01)	0.43	↓ (P<0.01)	8.86
		18.46		3.65		2.87		45.47	
19	7	↓ (P<0.05)	1.34	↓ (P<0.01)	0.30	↓ (P<0.01)	0.67	↓ (P<0.05)	16.72
		20.94		4.00		3.15		56.59	
20	13	↓ (P<0.05)	2.52	↓ (P<0.05)	0.43	↓ (P<0.01)	0.31	↓ (P<0.01)	11.52
		21.39		4.12		3.48		59.93	
21	11	↓ (P<0.01)	1.96	↓ (P<0.01)	0.38	↓ (P<0.01)	0.73	↓ (P<0.01)	12.31
		21.82		4.26		3.87		69.68	
22	5	↓ (P<0.01)	2.09	↓ (P<0.05)	0.36	↓ (P<0.01)	0.61	↓ (P<0.05)	15.89
		24.39		4.65		4.31		83.54	
23	6	↓ (P<0.05)	2.74	↓ (P<0.05)	0.48	↓ (P<0.05)	0.94	↓ (P<0.05)	18.23
		25.18		4.79		4.63		87.42	
24	5	26.87	1.02	5.05	0.19	5.23	0.78	116.4	23.01
25	2	26.54	0.26	5.09	0.42	5.76	1.04	119.63	4.95

assumed to be uniform in shape along its length. Therefore, the internal volume of the trachea could be described by the following equation:

$$V=S \times l$$

(V = internal volume, S = proximal internal cross-sectional area, l = length of the trachea).

For each fetus the following 5 measurements and calculations of the trachea were performed:

1. length in mm, corresponding to the distance from the superior border of the first tracheal cartilage to the tracheal bifurcation;
2. middle external transverse diameter in mm, measured in mid-length of the trachea;
3. middle external transverse diameter-to-length ratio;
4. proximal internal (luminal) cross-sectional area in mm², traced around the internal border of the first tracheal cartilage;
5. internal (luminal) volume in mm³, calculated by multiplying the proximal internal cross-sectional area by the length.

In order to minimize measurement and observer bias, all the measurements were performed by 1 researcher (M.D). Each measurement was repeated 3 times under the same conditions but at a different time, and the mean of them

was then used. The differences between the repeated measurements, as the intra-observer variation, were evaluated by the Wilcoxon signed-rank test.

All the parameters studied were plotted against fetal age so as to establish their growth. The relative growth of the trachea was expressed as the middle external transverse diameter-to-length ratio. As the first step in the statistical analysis, Student's t test was used to examine the influence of sex on the values of the parameters studied. Of note, the growing fetuses were separated into 12 intervals not equally distributed with respect to gestational age. Because 2 tracheas were included in the gestational ages of 14, 16 and 25 weeks, and even 1 trachea – in the gestational age of 15 weeks, which clearly did not represent adequate samples, the first 3 intervals (14–16 weeks), and the last 2 intervals (24–25 weeks) were separately grouped. Thus, sex differences were tested between the following 9 age groups: 14–16, 17, 18, 19, 20, 21, 22, 23 and 24–25 weeks. Some authors, when faced with this problem, used the graphic Lowess method [18,19], which we have had no experience in. Furthermore, we tested possible sex differences for the whole group, without taking into account the fetal age. In order to test whether the different variables significantly changed with age, the one-way ANOVA test and post-hoc Bonferroni test were used for the 9 groups mentioned above (Table 2). Linear and nonlinear regression analyses were used to derive the curve of best fit for each parameter versus gestational age.

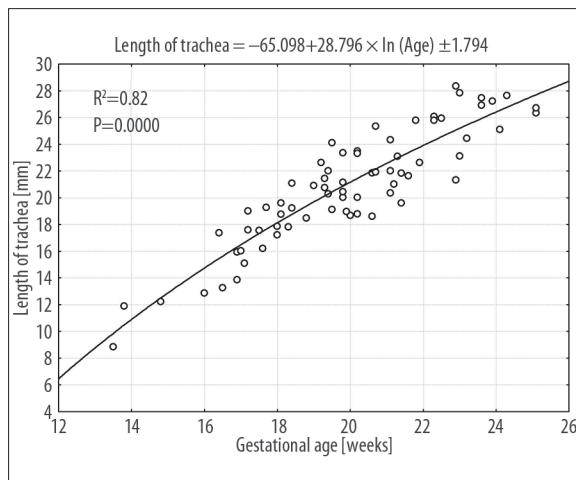


Figure 4. Regression line for tracheal length vs. gestational age.

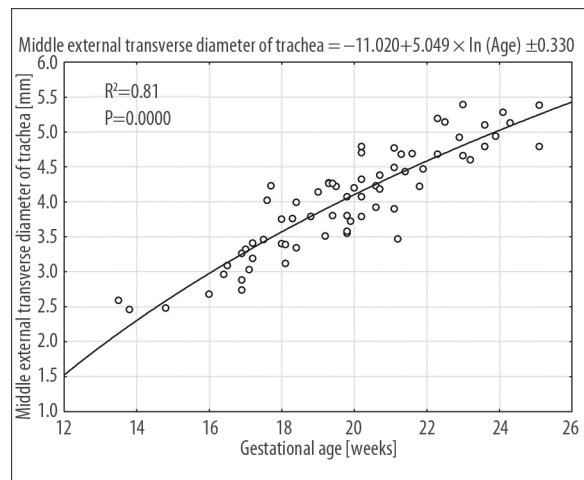


Figure 5. Regression line for middle external transverse diameter of the trachea vs. gestational age.

Table 3. The expected growth velocity for length and middle external transverse diameter of the trachea.

Parameter	Age (weeks)										
	14	15	16	17	18	19	20	21	22	23	24
Length velocity (mm per week)	1.99A	1.86B	1.75C	1.65D	1.56E	1.48F	1.40G	1.34H	1.28I	1.23J	1.18K
Middle external transverse diameter velocity (mm per week)	0.35L	0.33M	0.31N	0.29O	0.27P	0.26Q	0.25R	0.23S	0.22T	0.21U	0.20V

The mean values for length velocity marked by different letters A-K in row differ significantly ($P < 0.05$). The mean values for middle external transverse diameter velocity marked by different letters L-V in row differ significantly ($P < 0.05$).

Coefficients of determination (R^2) between each parameter and fetal age were estimated. Differences were considered significant at $P < 0.05$.

RESULTS

No significant differences were found in the evaluation of intra-observer reproducibility of the tracheal measurements ($P > 0.05$). Since the statistical analysis of tracheal parameters showed no sex differences ($P > 0.05$), the numerical results without regard to sex are given in Table 2. Because of this, the analysis could have been applied to the whole group and the growth for both sexes may also have been considered similar. On the contrary, the growth curves of best fit for the plot for each parameter studied against gestational age were statistically significant ($P = 0.0000$). The values of tracheal length ranged from 10.37 ± 2.15 mm for the 14-week group to 26.54 ± 0.26 mm for the 25-week group. The tracheal length in relation to fetal age in weeks (Figure 4) increased according to the logarithmic function: $y = -65.098 + 28.796 \times \ln(\text{Age}) \pm 1.794$ ($R^2 = 0.82$).

The middle external transverse diameter varied from 2.53 ± 0.09 to 5.09 ± 0.42 mm, being expressed by the logarithmic function (Figure 5) $y = -11.020 + 5.049 \times \ln(\text{Age}) \pm 0.330$ ($R^2 = 0.81$).

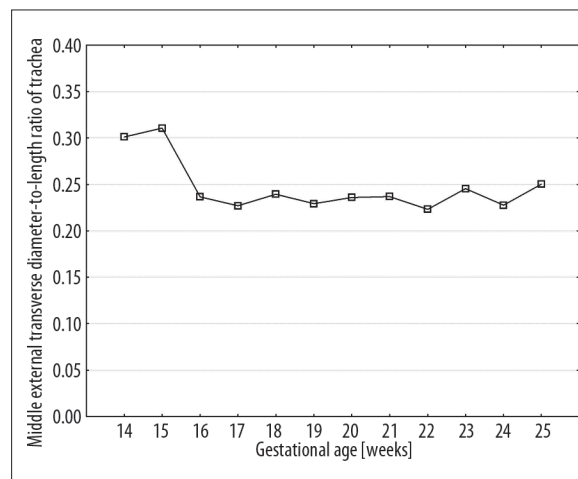


Figure 6. Middle external transverse diameter-to-length ratio of the trachea vs. gestational age.

According to these 2 mathematical models, the growth velocity for both length and middle external transverse diameter of the trachea (Table 3) gradually declined with advanced fetal age ($P < 0.05$). Despite an absolute increase in the values in both middle external transverse diameter and length of the trachea, their relative growth, expressed



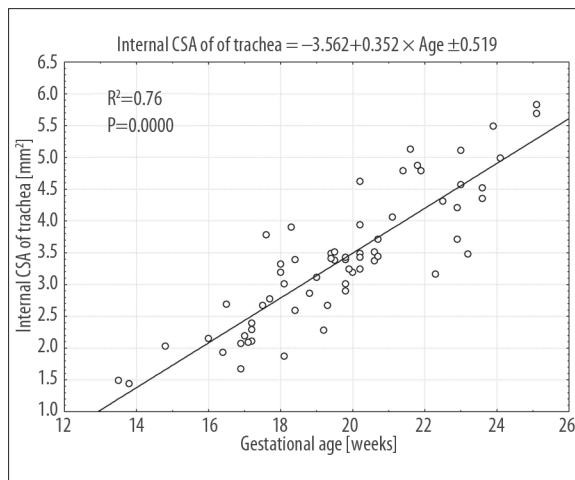


Figure 7. Regression line for proximal internal cross-sectional area of the trachea vs. gestational age.

as the middle external transverse diameter-to-length ratio, was relatively stable (Figure 6) between 16 and 25 weeks of gestation ($P>0.05$) and took the value 0.23 ± 0.03 .

The cross-sectional shape of the tracheas (Figure 3) was almost circular at younger ages (14–18 weeks) and more D-shaped at older ages (21–25 weeks). During the study period, the values of proximal internal cross-sectional area of the trachea ranged from 1.46 ± 0.04 to 5.76 ± 1.04 mm², in accordance with the linear function $y = -3.562 + 0.352 \times \text{Age} \pm 0.519$ ($R^2=0.76$) – (Figure 7).

The values of internal volume of the trachea ranged from 11.89 ± 2.49 mm³ in fetuses aged 14 weeks to 119.63 ± 4.95 mm³ in fetuses aged 25 weeks. The internal volumetric growth of the trachea (Figure 8) generated the linear function $y = -135.248 + 9.919 \times \text{Age} \pm 10.478$ ($R^2=0.86$).

DISCUSSION

The present study describes the normal growth of the trachea in human fetuses aged 14–25 weeks. For anatomists dealing with aborted fetuses the most important information for establishing fetal ages still remains the crown-rump length, being an objective parameter when compared to the known data of the beginning of the last maternal menstrual period [20]. Because of this, we use the crown-rump length to estimate gestational age, yet in clinical practice CRL is only ultrasonographically used to estimate gestational age up to 14 weeks of gestation. Estimation of gestational age beyond that is generally performed using a combination of abdominal circumference, femur length and biparietal diameter [21]. Because the specimens had been fixed in neutral buffered formalin for 12–24 months before quantitative analysis, all the measurements were taken *in situ* to minimize, as much as possible, tissue shrinkage related to formalin fixation. Thus, Daroszewski [22] showed only 0.5–1.0% shrinkage in fetal tracheas *in situ* that had been immersed in 10% neutral buffered formalin solution for 1–2 years. On the contrary, in the study by Chiba et al. [11], which was performed on isolated tracheal segments (from the cricoid cartilage to the carina), as much as 10% shrinkage in fetal human airways after fixation was observed. In

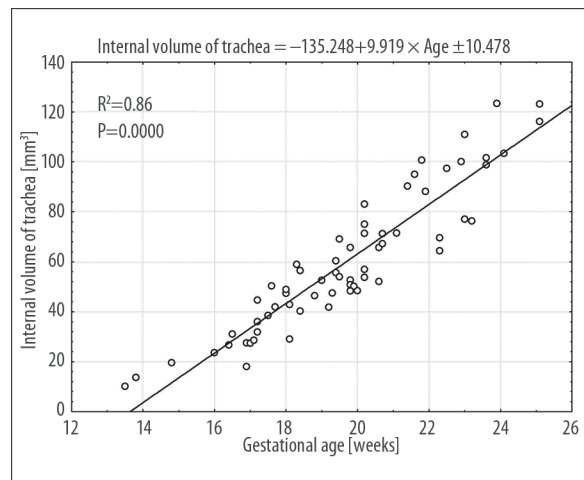


Figure 8. Regression line for internal volume of the trachea vs. gestational age.

our view, both tissue shrinkage and possible artifacts of isolated tracheal segments resulting from formalin fixation were probably more expressed in early fetuses, because immature tracheas are primarily formed of loose connective tissue. Furthermore, the difference between tissue shrinkage concerning tracheal cartilage and pars membranacea may lead to non-proportional changes in sagittal and transverse tracheal dimensions.

After reviewing the professional literature on tracheal measurements in fetuses [6,8,12,13,23,24], we found little information about length and diameter of the growing trachea. In keeping with other reports [12,23–25], a lack of statistically significant sex differences for the parameters of the fetal trachea was found in this study. In this aspect our results closely corresponded with the professional literature in relation to the tracheal length and diameters obtained in fetuses [12,23] and throughout childhood until the age of 14 years [24–26]. On the other hand, significant male-female differences in tracheal measurements, being greater in males, were presented in adolescents [27], adults [15,24,28], and in children [29].

In the present study, the tracheal length increased from 10.37 ± 2.15 to 26.54 ± 0.26 mm, being greater than that recorded by Kher and Makhani [30] and Harjeet et al. [23]. Our findings demonstrated an increase in external transverse diameter of the trachea in its mid-length from 2.53 ± 0.09 to 5.09 ± 0.42 mm.

Some authors have presented plots showing both the tracheal length and diameters in relation to the crown-rump length [12] or gestational age [13,25]. Although these authors showed neither numerical data nor regression coefficients, their growth curves for both the tracheal length and diameters supported a proportional relationship. According to Kalache et al. [8], a linear relationship was found between the internal tracheal diameter and gestational age in fetuses aged 15–40 weeks, as follows $y = -0.28 + 0.12 \times \text{Age}$ ($R^2=0.66$, $P<0.001$). Of note, in the material under examination, neither the length nor middle external transverse diameter of the trachea formed straight lines on normograms. The best growth models appeared to be the logarithmic functions, as

follows $y = -65.098 + 28.796 \times \ln(\text{Age}) \pm 1.794$ for its length, and $y = -11.020 + 5.049 \times \ln(\text{Age}) \pm 0.330$ for its middle external transverse diameter, thereby providing novel data about their developmental dynamics. The differences between our findings and other studies may be attributed in part to the inter-individual variability and different methods used in measurements. Thus, our results show that, according to the logarithmic functions, the growth velocity for tracheal length and middle external transverse diameter was gradually decreasing (Table 3) with advanced fetal age, from 1.99 to 1.18 mm, and from 0.35 to 0.21 mm, when compared to fetuses at the ages of 14 and 24 weeks, respectively.

As indicated in Figure 6, the trachea revealed a proportional evolution, because the middle external transverse diameter-to-length ratio we calculated showed no significant changes ($P > 0.05$) in its value (0.23 ± 0.03) during the study period. In our view, length and middle external transverse diameter of the trachea increased at all times at the same growth rate, being responsible for little individual variations in growth and specific adult forms of the trachea [12,31,32].

Digital image analysis was an excellent method of determining the internal cross-sectional anatomy of the growing trachea, because the internal tracheal border, both circular and D-shaped, could be accurately traced using a cursor. In the present study, an increase in the values of proximal internal cross-sectional area of the trachea, from 1.46 ± 0.04 to 5.76 ± 1.04 mm², followed the linear function $y = -3.562 + 0.352 \times \text{Age} \pm 0.519$ ($R^2 = 0.76$). A proportional evolution of internal cross-sectional area of the trachea, but with no growth curves, was reported in children and adolescents by Effmann et al. [14] and Griscom and Wohl [15]. According to these authors, CT-derived internal cross-sectional areas ranged from 20 mm² in children aged 4 months to 275 mm² in patients at the age of 18 years [14], and from 28 ± 9 to 230 ± 39 mm² in patients aged 0–20 years [15].

From a stereological point of view, the volume of each object can be determined using Cavalieri's method in a serially sectioned structure as the product of the slice areas and the slice thickness [33,34]. However, in the present study the tracheas were not sliced, so we could not have used Cavalieri's method to estimate the internal volume of the trachea. As the tracheal lumen may have been considered as uniform in shape along its length, the means of estimating the tracheal volume used in the present study was multiplying the length by the proximal internal cross-sectional area. In the material under examination, the tracheal volume varied from 11.89 ± 2.49 to 119.63 ± 4.95 mm³. The regression equation for internal volume of the trachea, modeled as a relationship of gestational age in weeks, was the linear function $y = -135.248 + 9.919 \times \text{Age} \pm 10.478$. Surprisingly, the internal volumetric growth of the trachea did not follow a quadratic function, but the simple linear function turned out to be its best growth model. In our opinion, this fact was probably the consequence of strong growth of tracheal wall thickness (Figure 3), which relatively reduced the tracheal luminal volume. This hypothesis is strengthened by Daroszewski [22], who correlated the tracheal internal volume with the tracheal wall thickness. The mean values of internal volume of the trachea recorded by Griscom and Wohl [15] increased from 1.57 ± 0.67 cm³ at the age of 0–2 years, through 5.67 ± 1.2 cm³ at 6–8 years, and 18.2 ± 2.2 cm³

at 14–16 years, to 30.3 ± 5.9 cm³ at 18–20 years. Kamel et al. [16] reported a wide variation in internal tracheal volume, ranging in men from 18.9 to 53.6 cm³ (35.6 ± 6.8 cm³), and in women from 12.9 to 35.7 cm³ (24.7 ± 6.1 cm³). It is noteworthy that tracheal dimensions were similar in prepubertal boys and girls, and significant differences emerged only at puberty [15]. When boys stopped growing taller, their tracheas at first stopped growing in length, and did so in internal diameter, internal cross-sectional area, and internal volume as late as 2 years afterwards. In men aged 16–20 years, dimensions of the trachea were statistically greater approximately 7% for its length, 14% for its internal transverse diameter, 28% for its internal cross-sectional area, and 44% for its internal volume.

Having presented the normal growth of the growing trachea during gestation, we would like to stress the importance of the tracheal measurements, because the reader should be provided with relevant data. Thus, in fetuses, neonates and infants, at the level of the trachea we can expect the following malformations: agenesis, atresia, tracheal stenosis, short trachea, trachiectasis, primary tracheomalacia, tracheal diverticulum, and tracheomegaly. The fetal trachea may be completely absent (agenesis) or considerably underformed (atresia) with no normal continuous airway between the larynx and the lungs. Tracheal agenesis may be found in the VACTERL association (vertebral anomalies, anal atresia, cardiac defects, tracheoesophageal fistula, renal and limb malformations) or TACRD association (cardiac anomalies, radial ray defects, duodenal atresia) [35]. Congenital tracheal stenosis, a fixed narrowing, results from the presence of focal or diffuse complete tracheal cartilage rings [36,37]. Short trachea is composed of a number of cartilage rings reduced to 15 or less compared to the average of 17 rings, with increased frequency in DiGeorge anomaly, some skeletal dysplasias, brevicollis, diaplacental rubella and meningocele [38]. Trachiectasis, a congenital tracheal enlargement, is associated with diseases of elastic fibres and organomegaly [39]. Primary tracheomalacia refers to congenital immaturity of the tracheal cartilage and hypotonia of myoelastic elements [40]. Congenital tracheal diverticulum is thought to be a malformed supernumerary branch of the trachea that is composed of the same elements as the tracheal wall [41]. Tracheomegaly, a dilatation of the trachea, refers to a congenital defect of the elastic and muscle fibres, being often associated with Ehlers-Danlos syndrome [42]. Tracheomegaly also occurs in children with congenital diaphragmatic hernia, who underwent fetoscopic endoluminal tracheal occlusion during gestation [43].

In summary, the present study identifies an increase in dimensions of the trachea with advanced fetal age, providing mathematical formulae of growth curves for its length, middle external transverse diameter, proximal internal cross-sectional area, and internal volume. The present normograms describe tracheal dimensions and improve our knowledge of tracheal quantitative morphology in fixed human fetuses that can be adapted *in vivo* to fetal and neonatal airways. Of all the parameters studied, the most relevant is the tracheal diameter, which may contribute to the prenatal diagnosis and monitoring of the tracheal malformations like agenesis, atresia, tracheal stenosis, short trachea, trachiectasis, primary tracheomalacia, tracheal diverticulum, and tracheomegaly. In turn, the tracheal length may be helpful

in the diagnosis of short trachea. We also believe that all the parameters presented in this study may serve as a useful reference to morphologists teaching growth patterns in human developmental anatomy.

CONCLUSIONS

1. The tracheal parameters do not show sex differences.
2. The growth, both length and middle external transverse diameter, of the trachea follows logarithmic functions, whereas its internal cross-sectional area and internal volume generate linear functions.
3. The length and middle external transverse diameter of the trachea develop proportionally to each other.
4. The tracheal dimensions may be helpful in the prenatal diagnosis and monitoring of tracheal malformations and obstructive anomalies of the upper respiratory tract.

REFERENCES:

1. Wojcicki P, Drozdowski P: In utero surgery – current state of the art: Part I. *Med Sci Monit*, 2010; 16(11): RA237–44
2. Wagner W, Harrison MR: Fetal operations in the head and neck area: current state. *Head Neck*, 2002; 24: 482–90
3. Harrison MR, Keller RL, Hawgood SB et al: A randomized trial of fetal endoscopic tracheal occlusion for severe fetal congenital diaphragmatic hernia. *N Engl J Med*, 2003; 349: 1916–24
4. Jani J, Gratacós E, Greenough A et al: Percutaneous fetal endoscopic tracheal occlusion (FETO) for severe left-sided congenital diaphragmatic hernia. *Clin Obstet Gynecol*, 2005; 48: 910–22
5. Furness ME, Donnelley BW, Lipsitt J: Larynx atresia. *Fetus*, 1991; 1: 1–3
6. Dolkart LA, Reimers FT, Wertheimer IS et al: Prenatal diagnosis of laryngeal atresia. *J Ultrasound Med*, 1992; 11: 496–98
7. Richards DS, Farah LA: Sonographic visualization of the fetal upper airway. *Ultrasound Obstet Gynecol*, 1994; 4: 21–23
8. Kalache KD, Franz M, Chaoui R et al: Ultrasound measurements of the diameter of the fetal trachea, larynx and pharynx throughout gestation: applicability to prenatal diagnosis of obstructive anomalies of the upper respiratory-digestive tract. *Prenat Diagn*, 1999; 19: 211–18
9. Kohl T, Hering R, Bauriedel G et al: Fetoscopic and ultrasound-guided decompression of the fetal trachea in a human fetus with Fraser syndrome and congenital high airway obstruction syndrome (CHAOS) from laryngeal atresia. *Ultrasound Obstet Gynecol*, 2006; 27: 84–88
10. Wailoo MP, Emery JL: Normal growth and development of the trachea. *Thorax*, 1982; 37: 584–87
11. Chiba T, Albanese CT, Farmer DL et al: Balloon tracheal occlusion for congenital diaphragmatic hernia: experimental studies. *J Pediatr Surg*, 2000; 35: 1566–70
12. Adamiec E, Dzieciolowska-Baran E, Czerwiński F et al: Prenatal development of the human trachea. *Folia Morphol*, 2002; 61: 123–25
13. Fayoux P, Marciniak B, Devisme L et al: Prenatal and early postnatal morphogenesis and growth of human laryngotracheal structures. *J Anat*, 2008; 213: 86–92
14. Effmann EL, Fram EK, Vock P et al: Tracheal cross-sectional area in children: CT determination. *Radiology*, 1983; 149: 137–40
15. Griscom NT, Wohl ME: Dimensions of the growing trachea related to age and gender. *Am J Roentgenol*, 1986; 146: 233–37
16. Kamel KS, Lau G, Stringer MD: *In vivo* and *in vitro* morphometry of the human trachea. *Clin Anat*, 2009; 22: 571–79
17. Iffy L, Jakobovits A, Westlake W et al: Early intrauterine development: I. The rate of growth of Caucasian embryos and fetuses between the 6th and 20th weeks of gestation. *Pediatrics*, 1975; 56: 173–86
18. Rissech C, García M, Malgosa A: Sex and age diagnosis by ischium morphometric analysis. *Forensic Sci Int*, 2003; 135: 188–96
19. Rissech C, Schaefer M, Malgosa A: Development of the femur-implications for age and sex determination. *Forensic Sci Int*, 2008; 180: 1–9
20. Szpinda M: Morphometric study of the great arteries of the thorax in human fetuses (in Polish). Habilitation thesis. Bydgoszcz: CM UMK; 2006; 1–143
21. Achiron R, Zimand S, Hegesh J et al: Fetal aortic arch measurements between 14 and 38 weeks' gestation: in utero ultrasonographic study. *Ultrasound Obstet Gynecol*, 2000; 15: 226–30
22. Daroszewski M: Morphometric study of the trachea and main bronchi in human fetuses. Doctoral thesis. Torun, 2011; 1–171 [in Polish]
23. Harjeet J, Sahni D, Batra YK et al: Anatomical dimensions of trachea, main bronchi, subcarinal and bronchial angles in fetuses measured *ex vivo*. *Paediatr Anaesth*, 2008; 18: 1029–34
24. Jit H, Jit I: Dimensions and shape of the trachea in the neonates, children and adults in northwest India. *Indian J Med Res*, 2000; 112: 27–33
25. Menu Y, Lallemand D: Determination of the normal transverse diameter of the trachea in childhood. *Ann Radiol*, 1981; 24: 73–75
26. Fayoux P, Devisme L, Merrot O et al: Determination of endotracheal tube size in a perinatal population: an anatomical and experimental study. *Anesthesiology*, 2006; 104: 954–60
27. Hamill PV, Drizd TA, Johnson CL et al: Physical growth: National Center for Health Statistics Percentiles. *Am J Clin Nutr*, 1979; 32: 607–29
28. Randestad A, Lindholm CE, Fabian P: Dimensions of the cricoid cartilage and the trachea. *Laryngoscope*, 2000; 110: 1957–61
29. Pagtakhan AD, Bjelland JC, Landau LI et al: Sex differences in growth patterns of the airways and lung parenchyma in children. *J Appl Physiol*, 1984; 56: 1204–10
30. Kher GA, Makhani JS: A preliminary study of the lengths of the two main bronchi and angle at the carina. *J Indian Med Assoc*, 1960; 34: 262–65
31. Randestad A, Lindholm CE, Fabian P: Dimensions of the cricoid cartilage and the trachea. *Laryngoscope*, 2000; 110: 1957–61
32. Standring S (ed.): *Gray's Anatomy. The Anatomical Basis of Clinical Practice*. Edinburgh: Elsevier, 2008; 1086–89
33. Gundersen HJ, Bendtsen TF, Korbo L et al: Some new, simple and efficient stereological methods and their use in pathological research and diagnosis. *APMIS*, 1988; 96: 379–94
34. Mouton PR: *Principles and practices of unbiased stereology. An introduction for bioscientist*. Baltimore: John Hopkins University Press, 2002; 1–214
35. Fraser N, Stewart RJ, Grant J et al: Tracheal agenesis with unique anatomy. *J Pediatr Surg*, 2005; 40: E7–10
36. Phipps LM, Raymond JA, Angeletti TA: Congenital tracheal stenosis. *Crit Care Nurse*, 2006; 26: 60–69
37. Chowdhury O, Greenough A: Neonatal ventilatory techniques – which are best for infants born at term? *Arch Med Sci*, 2011; 7(3): 381–87
38. de Priester JA, Vos GD, van Waardenburg DA et al: Congenitally short trachea with compression of the left mainstem bronchus: MRI findings. *Pediatr Radiol*, 1998; 28: 342–43
39. Saxena AK: Congenital anomalies of soft tissues: birth defects depending on tissue engineering solutions and present advances in regenerative medicine. *Tissue Eng Part B Rev*, 2010; 16(5): 455–66
40. Webb EM, Elicker BM, Webb WR: Using CT to Diagnose Nonneoplastic Tracheal Abnormalities: Appearance of the Tracheal Wall. *Am J Roentgenol*, 2000; 174(5): 1315–21
41. Restrepo S, Villamil MA, Rojas IC et al: Association of two respiratory congenital anomalies: tracheal diverticulum and cystic adenomatoid malformation of the lung. *Pediatr Radiol*, 2004; 34: 263–66
42. Kim MY, Kim EJ, Min BW et al: Anesthetic experience of a patient with tracheomegaly – a case report. *Korean J Anesthesiol*, 2010; 58(2): 197–201
43. Breyssem L, Debeer A, Claus F et al: Cross-sectional Study of Tracheomegaly in Children after Fetal Tracheal Occlusion for Severe Congenital Diaphragmatic Hernia. *Radiology*, 2010; 257: 226–32