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**Distances from vocal cords to mid-trachea for optimizing endotracheal tubes depth markers according to gestational age.**

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**Abstract (258 words)**

**Background:** adequate endotracheal tube positioning in preterm infants is complicated by the short length of the airway. Distal markers were designed to help with the insertion of endotracheal tubes at an appropriate depth below the vocal cords. However, those markers are not standardized between manufacturers, each tube size displays only one (sometimes two) marker to provide information for infants of various gestational ages, and indicated distances are often too long for extremely preterm infants.

**Aim:** The study aims to describe vocal cords to mid-tracheal distance for different gestational ages and suggest depth markers adjusted accordingly.

**Methods:** half the tracheal length added to the height of the posterior lamina of the cricoids approximates the distance between vocal cords and mid-trachea. Those dimensions were retrospectively retrieved from a database of laryngo-tracheal measurements obtained during autopsies of fetuses and newborn infants free of upper airway malformations. The equation of correlation between gestational age and distance from vocal cords to mid-trachea was used to calculate those distances for different gestational ages.

**Results:** data were derived from 114 patients. Vocal cords to mid-trachea distance is linearly correlated with gestational age ( $r=.90$ ; distance =  $2.831 + 0.6208 \times$  gestational age). We suggest depth markers at 17.7, 19.0, 20.8, 22.7, 24.6 and 26.4 mm for gestational ages of 24, 26, 29, 32, 35 and 38 weeks respectively, indicated by contrasting colors.

**Conclusions:** the linear relationship between laryngo-tracheal size and gestational age offers the opportunity to revise endotracheal tubes depth markers for the smallest patients. Trials comparing those suggested markers with those currently in use are needed before implementation.

## What is already known?

- The short lengths of the larynx and trachea increase the risk of suboptimal positioning of endotracheal tubes in preterm infants.
- The black lines used for insertion depth markers are not standardized and are unrelated to gestational age.

## What this study adds?

- The distance from vocal cords to mid-trachea increases linearly with gestational age.
- Those distances can be used to design standardized, color-coded depth markers adapted to gestational age, weight, or length.

## MeSH Keywords

Infant, Premature

Equipment Design

Intubation, Intratracheal/\*instrumentation

Larynx

Growth

Safety

## Introduction

Adequate endotracheal tube (ETT) positioning in preterm infants remains difficult as the short length of the airways only allows a limited margin of error. Accordingly, most Canadian neonatal staff reported challenges in estimating the adequate depth of insertion when intubating extremely low birth weight infants.<sup>1</sup> Adverse respiratory outcomes associated with right main bronchial intubation are well recognized by practitioners of neonatal intubation. However, even suboptimal positions within the trachea, below T2 level, are associated with an increase of non-uniform lung aeration and of a combination of air leaks and right upper lobe collapse.<sup>2</sup>

In 1974, Loewe and Thibeault introduced the “black safety line” on ETTs,<sup>3</sup> as well as centimeters markings. In their report, all 28 intubations with the black mark set at the level of vocal cords led to ETTs radiologically positioned at the mid-third of the trachea or slightly above. The authors described depth markers at 22, 24 and 26 mm for 2.5 mm, 3 mm and 3.5 mm inner diameter tubes respectively. They explained that black offered improved contrast compared to other colors. Aiming for the black line is advocated in neonatal resuscitation teaching,<sup>4</sup> and is widely accepted as an adequate method for optimizing ETT position.<sup>1</sup> However, use of the depth marker rather than a weight based formula was associated, in a randomized controlled trial of intubation in preterm infants, with similarly low (40%) rate of satisfactory uncuffed ETT positions.<sup>5</sup>

Over the years, the depth markers have clearly evolved in a non-harmonized way. Distances from ETT tip to marker line vary considerably between brands and even between tubes from the same company: Distances ranging from 15 to 28 mm were reported in uncuffed 2.5mm ETT.<sup>6-9</sup> This variability is a potential cause of hazard when working with different ETT brands<sup>10,11</sup> or in transport. Calls for standardization<sup>7,10</sup> remain unanswered: the latest (2016) European Standards<sup>12</sup> don't require depth markers, don't indicate distances for them when present, and don't address the specificity of markers for neonatal tubes.

Most ETTs support a single depth marker that is supposed to indicate adequate vocal cord to ETT tip distances for all infants intubated with the same size of tube,<sup>3</sup> regardless of gestational age, weight or length. Ideally, multiple markers could indicate intubation depths below the vocal cords according to those parameters. We therefore aimed to calculate specific distances between vocal cords and mid-trachea to provide basis for such new markers.

## Methods

Vocal cords are attached posteriorly to the arytenoid cartilages and anteriorly to a relatively caudal part of the thyroid cartilage.<sup>14</sup> The laryngeal distance between vocal cords

and the trachea is approximated by height of the posterior lamina of the cricoid. Adding half the tracheal length gives the distance between vocal cords and mid-trachea.

Those heights and lengths were retrospectively retrieved from a prospectively collected database. This anonymized database included detailed measurements of laryngeal and tracheal structures obtained from routine autopsies of fetuses and newborn infants, and was analyzed by Fayoux et al.<sup>13</sup> The database has been set in accordance with local legal and ethical considerations. In short, fetuses and infants free of laryngotracheal structures malformation have been studied within 6 hours of death, to avoid tissue retraction. Gestational age was derived from last maternal menstruation or first trimester sonogram. The height of the cricoid's posterior lamina was measured on the midline with a digital caliper (precision 0.02 mm), and tracheal length was defined as the distance between the inferior edge of the cricoid and the inferior part of the carina (measured with divider precise to 0.05 mm). For the present study, data were included when both measurements were available for fetuses/infants weighting more than 399 grams and of gestational age above 21 and below 43 weeks.

Correlations between vocal cords to mid-trachea distance and gestational age, weight or length were evaluated with Statistica (Statsoft-Dell, Tulsa, OK, USA). Equations of correlation were recalculated selecting only infants <2000g, <1000g, <32 weeks GA, <28 weeks GA, < 43 cm or <35 cm and vocal cords to mid-trachea distances were compared with those derived from the main equations.

From those data, we explored possible distances to suggest depth markers at different gestational ages, weight, or length. Vocal cords to mid-trachea distances were calculated for each increment of 1 week in GA in order to choose new markers. A trade-off was sought between finding optimal markers for different gestational ages and limiting the total number of those markers in order to increase their ease of use.

## Results

### *Vocal cords to mid-trachea distance*

One hundred and fourteen sets of measurements fulfilled the inclusion criteria. Distribution according to gestational age, weight or length is depicted in Fig. 1 (Individual data points). The mean weight percentile was  $43 \pm 29\%$ , and 17 percents of the fetuses and infants were small for gestational age, with birthweights below the tenth percentile. Vocal cords to mid-trachea distance was linearly correlated with GA expressed in weeks and decimals ( $r=.90$ ; vocal cords to mid-trachea =  $2.831 + 0.6208 \text{ GA}$ ), weight expressed in grams ( $r=.95$ ; vocal cords to mid-trachea =  $15.8335 + 0.0038 \text{ Weight}$ ), and length in centimeters ( $r=.91$ ; vocal cords to mid-trachea =  $4.5025$  with p values  $<0.0001$ ). Subgroup analyses gave similar data (Table 1).

### *Intubation depth markers*

We suggest using a total of six markers of contrasting colors (Table 2, Fig. 2). Those markers reflect vocal cords to midtracheal distances by 3 weeks of gestational age increases (with the exception of a two weeks step at the lowest gestational ages). The increments between markers is close to 2 mm, sufficient for adequate visualization. Four markers indicating adequate depth for infants up to 33 weeks GA could be depicted on internal diameter 2.5mm ETT. Marks derived for infants between 28 and 37 weeks could be displayed on 3.0mm ETTs and those for newborn above 31 weeks on 3.5mm ETT. Tubes inserted according to such markers for gestational age would have their tip  $0.25 \pm 1.78$  mm above the midtracheal distance (Figure 1A). When using weight or length as references, the ETT tips would be  $1.2 \pm 1$  mm above or  $0.1 \pm 1.8$  mm below the tip, respectively (Figure 1B and C).

**Table 1**

Correlations between vocal cords to midtracheal distance and gestational age (GA), weight and length according to subgroups.

	Subgroup	N	Linear correlation equations:	R	95% Confidence intervals	
			Vocal cords to midtracheal distance		First factor	Second factor
<b>GA</b>	All	114	= 2.831 + (0.621 * GA)	0.90	(1.029; 4.633)	(0.564; 0.678)
	<32 weeks	64	= 3.599 + (0.594 * GA)	0.72	(-0.334; 7.533)	(0.448; 0.739)
	<28 weeks	39	= 3.029 + (0.616 * GA)	0.54	(-5.069; 11.126)	(0.297; 0.935)
<b>Weight</b>	All	114	= 15.834 + (3.763 * Weight (kg))	0.95	(15.364; 16.303)	(3.518; 4.007)
	<2000g	76	= 15.064 + (4.550 * Weight (kg))	0.71	(13.831; 16.297)	(3.053; 6.047)
	<1000g	35	= 15.323 + (4.261 * Weight (kg))	0.74	(14.630; 16.016)	(3.680; 4.842)
<b>Length</b>	All	110	= 4.503 + (0.439 * Length (cm))	0.91	(2.981; 6.024)	(0.402; 0.476)
	<43 cm	67	= 8.122 + (0.323 * Length (cm))	0.57	(2.865; 13.379)	(0.155; 0.492)
	<35 cm	33	= 7.808 + (0.335 * Length (cm))	0.53	(1.663; 13.953)	(0.136; 0.533)

**Table 2**

Suggested markers according to gestational age (GA) or weight.

Marker distance (mm)	Colour	GA (weeks)	Weight (g)	Length (cm)
17.7	Magenta	24	499	30.1
19.0	Cyan	26	826	33.0
20.8	Yellow-Orange	29	1316	37.2
22.7	Green	32	1806	41.4
24.6	Red-Orange	35	2296	45.7
26.4	Black	38	2786	49.9

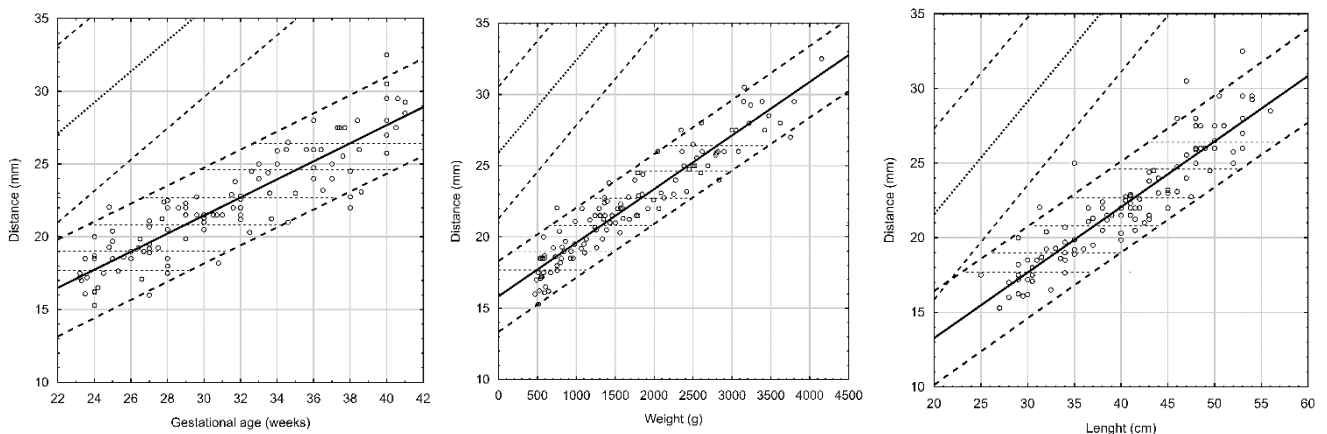


Fig.1 Distances from vocal cords to mid-trachea according to gestational age (dots)(1A), weight (1B) or length (1C). Full and dashed lines: correlation between GA and distance from vocal cords to mid-trachea, with 90% prediction intervals. Horizontal lines: suggested depth markers. Upper left dashed lines: vocal cords to carina distance with 90% prediction intervals.

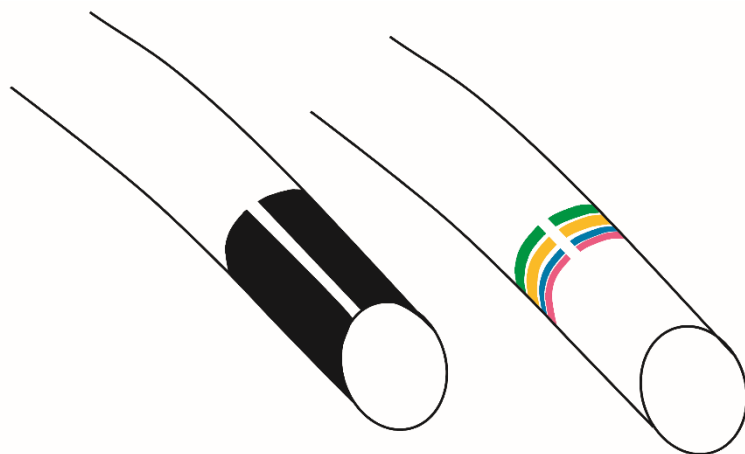


Fig.2 Tip of a 2.5 mm (inner diameter) endotracheal tube. with (starting from tip) depth markers for 23-25 weeks (magenta). 25-27 weeks (cyan). 28-30 weeks (yellow-orange). and 31-33 weeks GA (green). Classical 22 mm depth marker for comparison.

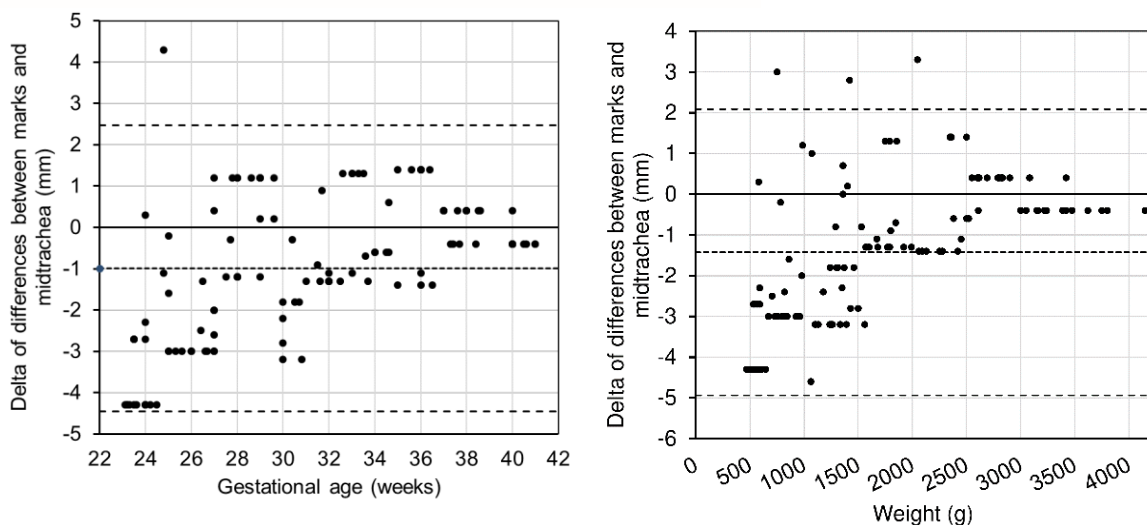


Fig.3 Comparison of proximity to midtracheal level according to suggested or classical markers. Positive numbers indicate classical markers (see text for choice of marker) being closer to the midtracheal level. Negative numbers are in favor of new, suggested markers. 3A. According to gestational age, 3B according to weight. Dashed lines: mean difference, upper and lower limits of agreement.

### Comparison with classical markers

For this comparison, we choose to assign the classical 22 mm marker for infants below 30 weeks or 1000g, the 24mm mark for those below 35 weeks or 2000g and the 26mm line for the older or bigger. Tube size in neonate is usually not chosen according to length, explaining the missing comparison. If tubes are inserted according to our suggested markers rather than classical markers, they would be closer to the midtracheal point by a mean of 1 or 1.4 mm, according to gestational age or weight respectively. The most important differences are found in very preterm and very low birth weight infants. (Figure 3).

### Discussion

As laryngeal growth is linearly correlated with gestational age<sup>13</sup>, using multiple depth markers has the potential to improve ETT positioning before X-ray confirmation. For all gestational ages, suggested markers would lie within a millimeter of the mean mid-tracheal location. However, operators need to remain aware of the variability of laryngeal and tracheal lengths. Importantly, this variability is proportional to gestational age,<sup>13</sup> resulting in more precise estimations at lower GA, when the trachea is the shortest. Additional methods<sup>15</sup> to rapidly

confirm an adequate tube position remain important, as X-rays may be delayed.

Depth markers presented here are derived from the equation using GA, even if the VC-MiTr distance has a slightly better correlation with weight. At birth, the situation where most emergency intubations occur, GA is more readily available than weight. Weights corresponding to those marks are also presented. This could be useful in secondary intubations, even if the non round numbers resulting from this calculation might be less convenient. Importantly, GA derived formula to estimate ETT lip to tip distance give more accurate prediction than those based on weight.<sup>16</sup> Length can rapidly be approximated even at birth, and a specific "Broselow tape"<sup>17</sup> could be devised for preterm infants.

In extremely preterm infants, calculated distances for intubation markers are 4.3 mm shorter than the classical 22 mm marks suggested by Loewe and Thibeault.<sup>3</sup> Critically, those are the infants who present the highest risk of requiring an endotracheal tube and where avoiding right main bronchus intubation is more difficult as the tracheal length is limited. Conversely, a 26 mm marking on 3.5 mm ETT represent an adequate distance only for term infants, and will be too long for moderately preterm newborns. This is in keeping with the results of Gill et al RCT comparing intubation according to depth marker or weight based formula where 49% of the preterm infants in the depth marker group had their ETT inserted too distally.<sup>5</sup>

Most studies reporting on ETT insertion focus on lip or nares to tip distances. Data for vocal cords to mid-tracheal distances in preterm infants are limited. Balu and Bustani reported their results in abstract form.<sup>18</sup> They used chest Xrays to evaluate the distance between the middle of the C4 and T2 vertebrae. Those landmarks were used as surrogate for VC end mid-tracheal levels, respectively. In infants below 750g, the population where the classical 6-7-8 rule is often inadequate,<sup>16</sup> their findings are similar to those reported in this study. In heavier infants, they suggest longer distances for mid-trachea (25 mm for 1500 g and 33 mm for 3000 g, vs 21 mm and 27 mm in this study).

This discordance may potentially be explained by variable relationships between laryngeal structures and cervical vertebrae, and again, GA derived formula might perform better.<sup>16</sup> Song and collaborators used computed tomography images to evaluate vocal cords to mid-tracheal distance in pediatric patients.<sup>19</sup> Their equation  $[2 \times \text{age in years}] + 30\text{mm}$  is within 2 mm of the results described here for newborns at 40 weeks (considered as zero year).

The number of colors suggested here is limited to three or four per tube size to improve color discrimination.<sup>20</sup> The succession of bright colors should improve contrast and help with discrimination between the markers. As recommended for the aerospace industry, standardized colors<sup>20</sup> would be imperative to decrease risks previously described.<sup>10,11</sup> While black marks were used to improve contrast in the Seventies, the spectral irradiance of more recent laryngoscopes using LED illumination<sup>15</sup> is now likely to allow adequate perception of other colors. The alternate use of vertical and horizontal stripes, suggested in the Standards<sup>12</sup> to enhance identification of the different sections, would be difficult given the small (1-2mm) increments advocated here.

The high number of measurements covering the whole range of gestational ages and birth weights is important to increase the validity of this study. However, the colored markers suggested here were calculated from fresh anatomical measurements, and were not derived from actual distances obtained during laryngoscopy with secondary X-ray confirmation. Multiple depth markers on ETT should be compared to commonly used patterns before being implemented. Another important comparison would be with other methods of assessment, such as formula,<sup>5</sup> suprasternal palpation, and sonography.<sup>15</sup> End-points for clinical trials should not be limited to radiological position but would need to include procedural and respiratory adverse events. If proven useful, those designs should then be suggested as new, improved standards.

While the very short distances between the suggested depth marker are designed for the

most precise positioning of the ETT, their practicality needs to be tested against potential difficulties at different times of the intubation procedure. The narrow oropharyngeal cavity in the most preterm infants doesn't always allow the visualization of the vocal cords once the tube is in place. Emergency intubation of a preterm infant is stressful for most operators, and the skills to integrate multiples depth markers at that time might be lacking for less experienced practioners.<sup>21</sup> Finally, the tube may be displaced during the removal of the laryngoscope or at time of taping. Even if most of those practical concerns also apply to classical markers, they need to be addressed by the clinical trials evaluating new depth markers.

To our knowledge, this study represents the first attempt to revise tracheal depth markers for neonatal uncuffed ETT since their introduction forty years ago. Optimizing endotracheal tubes for use in extremely preterm infants is important, as the reduced length of their airway makes adequate ETT positioning more difficult. The linear relationship between laryngo-tracheal length and gestational age offers the opportunity to adjust tube markers for the smallest patients.

### **Ethical approval**

The study was approved by the review board of the Centre Hospitalier Régional de Liège.

### **Conflicts of interest Statement**

No conflicts of interest declared

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