Breathing through a straw: fact or fiction?

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Abstract

INTRODUCTION: For pediatric patients on the intensive care who are mechanically ventilated, it is of major importance that extubation is performed at the right moment. This is because extubation failure is independently associated with a five-fold increased risk of complications and mortality in pediatric patients. It would be an advantage to determine whether the patient is capable of spontaneous breathing, before extubation is performed. A solution could be to first let a patient breathe spontaneously through the ETT, when disconnected from the mechanical ventilator.
OBJECTIVE: The aim of this study is to quantify the WOBimp during spontaneous breathing through a pediatric endotracheal tube.
METHOD: A set-up with a test lung consisting of a cylindrical stepper motor was used to simulate spontaneous breathing. A total of 112 measurements were performed to obtain data to calculate the WOBimp in eleven tubes with different diameters, tubes with a catheter inserted and shortened tubes. At both ends of the tube, a pressure and flow sensor was placed. The collected data was used to calculate the WOBimp.
RESULTS: The WOBimp increases for larger tidal volumes and decreases when larger tube diameters are used. The WOBimp does not exceed the clinically assumed acceptable value of 1.0 J/l, except for the 3.5 mm tube with the largest tidal volume. When compared to standard tube sizes, a significant decrease in WOBimp, ranging from 2.7 % to 32.5%, can be seen in the shortened ETTs. A significant increase in WOBimp can be seen in the tubes in which a catheter was inserted, ranging from 89.0% to 291.5% for the 3.0 and 3.5 mm tubes and from 19.5% to 95.3% for the other tubes.
CONCLUSION: The WOBimp does not exceed the clinically assumed acceptable value of 1.0 J/l, except for the 3.5 mm tube with the largest tidal volume. When compared to standard tube sizes, a significant decrease in the WOBimp is seen when the tubes are shortened and a significant increase in WOBimp can be seen in the tubes in which a catheter was inserted.
RECOMMENDATIONS: Further research is needed to validate the reference value of 1.0 J/l for the maximum WOBimp. This research should eventually also be performed in an in vivo setting to determine an appropriate maximum for WOBimp.

Preface

This report is the result of a multidisciplinary assignment at the University of Twente to acquire a Bachelors degree in Technical Medicine. This project gave us the opportunity to apply the knowledge obtained during the bachelor program in a practical assignment. During the past ten weeks, we have been working on a problem proposed by the Universitair Medisch Centrum Groningen, where we did measurements for two weeks. We obtained the data using Polybench® and analyzed this data using Matlab® and SPSS®. During the past ten weeks we have learned a lot about how to set up and perform a scientific research.

We would like to thank our supervisors for introducing us to the problem, their guidance and their feedback on our research proposal and the concept of this final report. We thank Dr. de Jongh for sharing his knowledge with us and giving us feedback on the analysis and representation of our results. We thank Dr. Kneyber and Drs. Blokpoel for explaining how to work with the test lung and Arduino® motherboard, their help with problems we encountered and providing us a decent workspace. We thank Alette Koopman for teaching us some basic Matlab® skills and help us analyzing our data with a proper script. We thank Jefta van Dijk for his enthusiasm, patience and checking in on us from time to time. Last but not least, we want to thank Michelle van der Stoel for guiding our process during the assignment.

We hope you will enjoy reading our report,
Ruby Egging, Desi ter Woerds, Myrthe van Merkerk and Jill Hanegraaf

Contents

1 Introduction

The respiratory system is one of the most vital systems in our body.[1] The process of inspiration and expiration mainly depends on the difference between atmospherical pressure (P_{atm}), the pressure in the intrapleural cavity (P_{pl}) and the alveolar pressure (P_a). The lungs have a tendency to collapse because of their elastic recoil. The thoracic wall also has such an elastic recoil but it tends to expand. This interaction occurs through the intrapleural space and this results in negative intrapleural pressure. This negative intrapleural pressure keeps the lungs expanded. The transpulmonary pressure consists of the difference between the P_{pl} and the P_a in the following way: $P_{tp} = P_a - P_{pl}$. In static condition the P_a is set to zero, so the transpulmonary pressure is equal to the negative intrapleural pressure, $P_{tp} = -P_{pl}$. The P_{pl} is about 5 cmH_2O in a healthy person.[2]

The lungs can change the pressure inside the lungs by expanding the volume of the lungs, this relation is described by Boyles Law, $P_1 * V_1 = P_2 * V_2$. The muscles that contract to induce inspiration will expand the chest and increase the elastic recoil so the P_{pl} will become more negative. The change in volume of the lungs is mainly a result of diaphragm contraction. This change in volume and decrease in P_{pl} will result in an airflow into the lungs. After the inspiration follows the expiration. At the end of an expiration, not all the air has left the lungs. The remaining volume is called the functional residual capacity (FRC).[2]

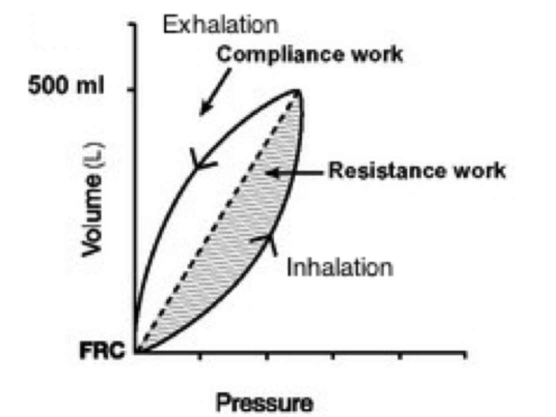

Figure 1: Pressure-volume curve of healthy lungs. V_t is the tidal volume and P_{pl} is the peak inspiratory pressure, the highest level of pressure applied during inhalation.[3]

The relation between pressure and volume can be shown in a pressure-volume curve of the lungs (Figure 1). Hysteresis is the difference between the inflation path and the deflation path, which exists because of the airway resistance. The slope of the curve represents the compliance of the lungs and shows the ability of the lung to expand and stretch. The total compliance is found by adding the lung compliance to the chest wall compliance.[2]

In case a patient is dealing with fibrosis, the lung tissue is abnormally stiff and the force required to get a volume change is abnormally large. The static P/V curve will be very flat in this case and the compliance can be unusually low. A steep P/V curve is the result of a high compliance and can occur when a patient is dealing with emphysema, where much lung parenchyma is lost.[4]

Therefore, a change in compliance of the lungs in pathophysiological conditions can result in breathing problems. Most children who need mechanical ventilation are children with respiratory tract infections and children who need postoperative mechanical ventilation. Infants and young children need mechanical support more often than adults. The airway of pediatric patients is relatively smaller in diameter, and shorter in length. A smaller diameter markedly increases the resistance. Compared to adults, infants and young children spend relatively more energy on their breathing mechanism. This can cause diaphragmatic fatigue and slow down recovery of the patient.[4,5]

1.1 Work of Breathing

The work of breathing, referred to as WOB, is the work needed for inspiration and expiration. The WOB is mostly needed for inspiration and is performed by inspiratory muscles. Expiration in healthy lungs is a passive process and happens just by relaxing the muscles of inspiration. The energy stored in the elastic recoil of the lungs is enough to attend a normal expiration and results in an airflow out of the lungs. If this energy is not sufficient for an entire expiration, the accessory muscles of expiration will help. Some of this work is needed to overcome frictional resistance to flow. Another part is used to deform elastic tissues and is stored as potential energy. The total WOB for a patient who is mechanical ventilated, consists of the physiologic WOB, in combination with the additional work caused by the disease process and resistance caused by the endotracheal tube (ETT). The additional work needed for the ventilator circuit and ETT is also known as the imposed work of breathing (WOBimp). It is important that the WOBimp is not too exhausting for the patient, because this can cause apnea and slow the recovery process.[6]

Work is the physical concept where a force is performed for a given distance, this is described by the following equation:[7]

$$W = force * distance = F * \Delta x \tag{1}$$

Applied to the respiratory system, work is expressed by pressure (force divided by area) and change of volume in the lungs. The WOB is given by the following equation:[7]

$$WOB = P * \Delta V \tag{2}$$

The total WOB is a sum of the work caused by compliance, airway resistance, tissue resistance and inertia:[7]

$$W_{tot} = W_{compl} + W_{aw} + W_{tissue} + W_{inertia} \tag{3}$$

The physiological WOB in preterm and full-term infants ranges between 0.02 and 0.2 J/l and for healthy children and adolescents between 0.3 and 0.6 J/l.[8] The WOBimp is added to the physiological WOB.

1.2 Research problem

Up to 64% of the patients on the pediatric intensive care unit need mechanical ventilation for an average period of five to six days. Nowadays the extubation readiness of these patients is based on their clinical appearance. Extubating these pediatric patients at the right moment is of major importance. If extubation fails and the patient is unable to breathe independently, reintubation is needed. Extubation failure is independently associated with a five-fold increased risk of complications and mortality in pediatric patients. On the other hand, prolonged mechanical ventilation is also undesirable. In case of prolonged mechanical ventilation, the dysfunction of the diaphragm and intercostal muscles, due to atrophy, increases more than necessary. Besides this, 50% of unplanned extubations end in success which implies that some patients could be extubated earlier.[9]

Possible consequences of intubation and mechanical ventilation could be infection, hoarseness, injuries to the trachea and vocal chords, significant increase of oxidative stress, increased proteolytic activity and ventilator induced lung injury, particularly barotrauma and atelectrauma.[10,11] In general, children are at higher risk to be injured, compared to adults, because of the narrow internal diameter of pediatric-sized ETT, causing signicant resistance to flow.[12]
Another reason why it is desirable to disconnect a patient from the mechanical ventilator as soon as possible are the high costs. To take care of one patient on the intensive care unit for one day, the costs are in between €2.223,59 and €2.584,28. These costs will decrease drastically when the patient can be detached from the mechanical ventilator.[13]

Taking all these reasons into account, it seems clear that it is very important to extubate a patient at the right moment. It would be an advantage to determine whether the patient is capable of spontaneous breathing, before extubation is performed.

A solution could be to first let a patient breathe spontaneously through the ETT while the mechanical ventilator is disconnected. Doctors nowadays assume that it is not ethical because of the high resistance of the ETT. This resistance is considered higher than the resistance of the trachea itself. To overcome this higher resistance there is more WOB needed. However, this has not been scientifically proven yet.

1.3 Current perspectives

In 2016, a group of Bachelor students did research on this subject by setting up a bench test using a Michigan test lung and writing the software required for analyzing the measurements.[14] The set-up with the Michigan test lung that was used in their bench test had some technical barriers. The Michigan test lung could only generate a negative pressure during inspiration for the tubes with a diameter equal to or less than 3.5 mm. The group recommended a wider scope concerning the diameters of the tubes and tidal volumes. In this bench test another test lung was used; a cylindrical stepper motor.

Comparable studies on the resistance of ETT's in pediatric patients have already been conducted for the past 20 years. Several studies have already led to different methods to compensate for the additional resistance during mechanical ventilation: Pressure Support Ventilation (PSV) and Automatic Tube Compensation (ATC).[11,15]

To correctly compensate for resistance of the tube, the resistance must be known. In 2000, a group of scientists represented this by measuring the resistance of tube diameters from 2.5 to 6.0 mm with different flow rates. They concluded that a smaller diameter or a higher flow rate both increase the resistance over the ETT. Also, shortening the ETT to an appropriate length for clinical use reduced resistance by an average of 22%. However, they did not calculate the WOBimp caused by this resistance.[16]

1.4 Primary objective

The primary goal of this research is to quantify the WOBimp for pediatric patients breathing through an ETT. In this research we focus on the inspiratory calculation of the WOBimp. To represent a patient population from newborn to adolescent, the WOBimp is determined for eleven different tube sizes with four different tidal volumes for each tube. Each tube size corresponds to a specific body weight and inspiration time. A WOBimp beneath 1.0 J/l is considered safe by medical experts for patients to breathe independently through an ETT.

This results in the following main question: Does the inspiratory WOBimp stay beneath the presumed safe value of 1.0 J/l during spontaneous breathing through pediatric ETT's with different diameters and tidal volumes with corresponding inspiration times, measured with a test lung?

1.5 Secondary objective

Nowadays the tubes are often shortened, because doctors assume this will decrease the WOBimp. However, it is still unknown how the tube length actually contributes to the WOBimp. This brings us to the following research question: What is the effect of shortening pediatric ETT's on the WOBimp?

Besides this, it would be interesting to measure the WOBimp in vivo. This could be done using a tracheal catheter, but it is still unknown how much a catheter contributes to the WOBimp. This leads to the following research question: Does adding a catheter into the ETT cause a WOBimp higher than 1.0 J/l?

To predict the results, an analytical approach has been done. These calculated values are compared to the measured values.

2 Research Method

For this research, different tube diameters and tidal volumes were used to simulate a population from newborns to adolescents. The tube sizes match a pediatric patient of a certain age and weight. With this information, the tidal volumes for four values (2.5, 5.0, 7.5, 10.0 ml/kg) were calculated. The different tube lengths and corresponding age, weight and inspiration time are shown in Table 1. For each tube size shown in Table 1 a measurement for all four tidal volumes will be performed. This results in a total of 112 measurements, each consisting of a minimum of 30 simulated breaths.

Table 1: Tube diameters with an approach of corresponding age category and weight.[17,8,18]

Diameter tube (mm)	**Age category**	**Weight (kg)**	**Inspiration time (s)**
3.0	Newborn	5	0.45
3.5	Newborn	7.5	0.45
4.0	Newborn/Infant	10	0.5
4.5	Infant	15	0.5
5.0	Infant	20	0.6
5.5	Small child	25	0.6
6.0	Small child	30	0.75
6.5	Small child/Large child	40	0.75
7.0	Large child	50	0.75
7.5	Large child/Adolescent	60	1.0
8.0	Adolescent/Adult	70	1.0

2.1 Set-up

Spontaneous breathing was simulated with a cylindrical stepper motor driven by an Arduino® motherboard, which represents the test lung in the set-up. One side of the ETT was connected to the test lung. The pressure and flow were measured by two Bicore sensors positioned between the ETT and the stepper motor and at the open end of the ETT. A schematic overview is shown in Figure 2. Bicore 1 was positioned between the test lung and the tube (P_{trach} + $Flow_{trach}$) and Bicore 2 at the open end of the tube (P_{airway} + $Flow_{airway}$). The pressure sensor was placed as close to the tube as possible. The flow sensor was positioned in a way that caused a negative flow during inspiration. This is corrected in Polybench®, resulting in a positive flow during inspiration. We used a Polybench® application to show the pressure and flow realtime. The graphical user interface of this application also showed the tidal volume and inspiration time. The application and graphical user interface from Polybench® can be found in Appendix A. The institutions of the Arduino motherboard were adjusted to achieve the correct tidal volume and inspiration time. The starting position of the cylinder affects the settings required to achieve a certain tidal volume and inspiration time. Therefore, it was not possible to validate standard settings for the test lung.

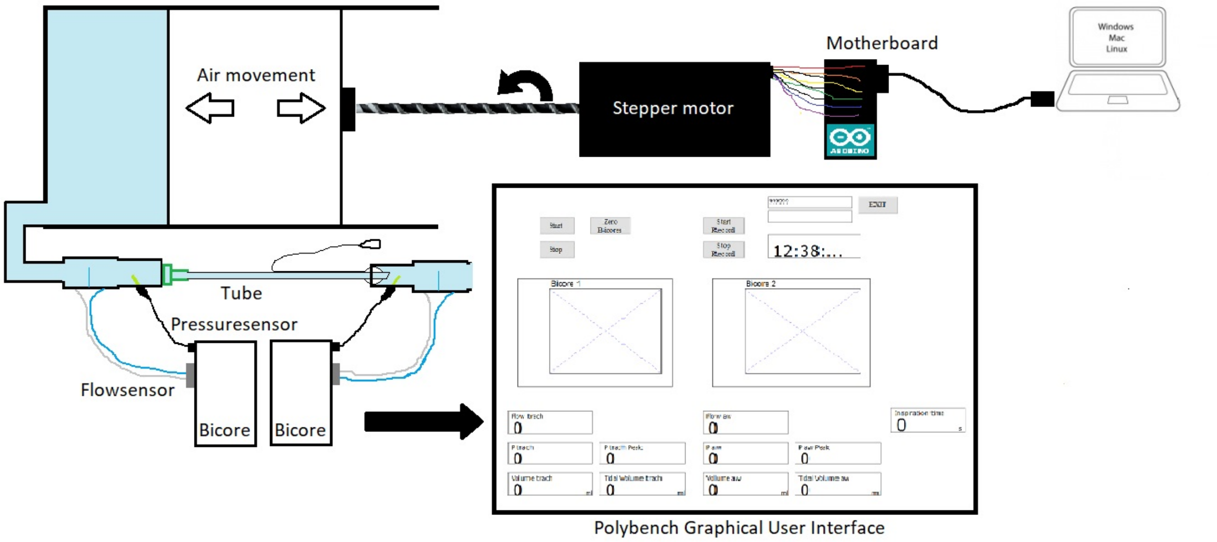

Figure 2: Schematic overview of the set-up

To calibrate the Bicores, the flowsensor which detects the flow at the open end of the ETT, was placed in a paper cup to minimize the flow of the environment through the tube. To achieve the appropriate inspiration time on the graphical user interface while measuring, a threshold value for the flow was used to filter out the time where a negligible amount of volume flows in. This value was set at 300 ml/min for the 3.0 mm ETT and 400 ml/min for the other tubes. The threshold values were not used in the calculations for the WOBimp, so they did not influence the results.

2.2 Materials

- Kimberly-Clark® KimVent Microcuff Endotracheal Tube for Pediatrics (Kimberly-Clark, Roswell, USA) with diameters of 3.0, 3.5, 4.0, 4.5, 5.0, 5.5, 6.0, 6.5, 7.0, 7.5, 8.0 mm;
- 2 Pressure sensors (Applied Biosignals GmbH, Weener, Germany);
- 2 VarFlex® Adult + 2 VarFlex® Neonatal flow sensors (CareFusion, Yorba Linda, USA);
- 2 Bicores with COMport and Bicore USB (Applied Biosignals GmbH, Weener, Germany);
- Cylindrical Stepper Motor driven by an Arduino® Motherboard (Arduino LLC, Ivrea, Italy);
- Polybench® Designer 1.32.0 (Applied Biosignals GmbH, Weener, Germany);
- Matlab® R2015B version 8.6 (The MathWorks, Inc., Natick, Massachusetts, USA);
- IBM Statistical Package for the Social Sciences® software computer program version 25 (IBM Corp., Armonk, NY, USA).

2.3 Shortening tubes

To determine if the length of the tube has considerable influence on the WOB, the tubes were shortened. To determine the appropriate length of the tubes, a formula to calculate the minimum length needed for oral intubation in a patient was used: oral intubation length in mm = age/2 + 12. This formula can only be used until the age of ten. The minimum tube length for older patients will remain equal to the output of the formula for a ten-year-old. The tubes with a diameter of 3.0, 4.0, 5.0, 6.0, 7.0 and 8.0 mm were shortened. It was not possible to shorten the tubes of 7.0 and 8.0 mm to the required length because the inflation mechanism of the cuff could not be cut off. The used lengths after shortening can be found in Table 2. To be able to perform the measurements in a proper way, it is important to keep this mechanism intact so the cuff can be inflated. These tubes are shortened as far as possible.

Table 2: Original tube lengths and tube lengths after shortening

Diameter tube (mm)	**Original tube length (cm)**	**Shortened tube length (cm)**
3.0	16.3	12.0
4.0	19.9	12.5
5.0	23.2	14.0
6.0	26.2	16.0
7.0	28.4	18.0
8.0	31.0	20.0

2.4 Sensor resistance

The air flowing through the ETT also passes the pressure and flow sensors, which have a certain resistance. To determine the influence of the resistance of the pressure and flow sensors, the pressure is measured when sensors are connected on both sides and when only one sensor is connected. Ideally it should give the same results (if the sensors would not have a resistance).

2.5 Analytical calculations

The WOBimp is also theoretically calculated. To do this for one single breath the pressure difference across the ETT has to be determined with the following equation.[2] For an explanation of the symbols, see Appendix B.

$$\Delta P_{ETT} = R * Q \tag{4}$$

With the airway resistance given by:[7]

$$R = \frac{\Delta p}{Q} = \frac{8\mu l}{\pi r^4} \tag{5}$$

And the average flow through the tube follows from:[2]

$$Q = \frac{TV}{t_{inspiration}} \tag{6}$$

These three equations can only be used in case of a laminar flow. To predict if the used flow is laminar or turbulent, the Reynolds numbers have to be calculated with the following equation:[2]

$$Re = \frac{2r\rho\bar{v}}{\mu} \tag{7}$$

The flow is laminar when Re $< \pm$ 2000 and the flow is turbulent when Re $> \pm$ 3000. Between these values the flow is transient.[2] It has to be taken into account that the flow is never completely laminar in lung airways. In these calculations ideal conditions are assumed. It would actually be more accurate if the Rohrer's equation or the Blasius-ito approach was used, but here, a simplified way was used.[19] The WOBimp for one breath is calculated by integrating the pressure difference across the ETT, multiplied with the change in volume.[20]

$$WOBimpforonebreath = \int_0^{TV} \Delta P_{ett} dV \tag{8}$$

The WOBimp for one breath is given in the SI unit Joule but is usually given in Joule per litre. To get the WOBimp in Joule per litre, the WOBimp for 1 breath has to be divided by the tidal volume:

$$WOBimp = \frac{W}{TV} \tag{9}$$

The analytical calculations for WOBimp are executed using inspiration times as used during measurements and with linear increasing inspiration times.

2.6 Data analysis in Matlab®

The data collected by the flow and pressure sensors is stored by Polybench®, to be analyzed using Matlab®. First, the last 30 breaths were separated from the data and the median tidal volume and inspiration time are determined. Second, the volume and pressure are converted to the right unit, cubic meters for volume and Pascal for pressure. After that, the volume will be calculated using the flow and then the WOBimp will be determined by calculating the area under the pressure-volume curve using the Riemann integral. For the full Matlab® script, see Appendix C.

2.7 Statistical analysis

A statistical analysis is conducted, to investigate the significance of a possible difference between the results of the three particular measurements. A one-way ANOVA is used to explore the relations between the WOBimp for ETT's when normally sized, with a catheter or shortened and to obtain the means and standard deviations. Here, the condition of the tube (normally sized, shortened or with a catheter inserted) are factors and the 30 WOBimp values are dependent variables.

3 Results

3.1 Inspiratory WOBimp normal tubes

As can be observed in Figure 3, the WOBimp remains beneath 1.0 J/l for every tube, except for the 3.5 mm tube in combination with the largest tidal volume. The graph represents the WOBimp of four different tidal volumes. These tidal volumes correspond to respectively 2.5, 5.0, 7.5 and 10.0 ml/kg.

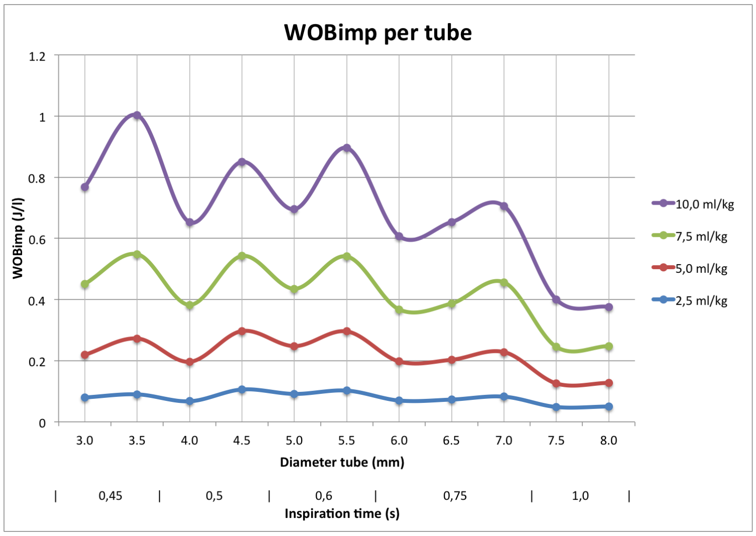

Figure 3: Inspiratory WOBimp in different ETTs

To visualize the results, a continuous line has been drawn, although the measured outcomes can not be considered a linear function of the diameter. It is clear that a larger tidal volume results in a higher WOBimp. The graph has the shape of a wave, with a peak in the 3.5, 4.5, 5.5 and 7.0 mm tubes. Figure 3 shows the most important results to answer the main question.

3.2 Measurements with catheter

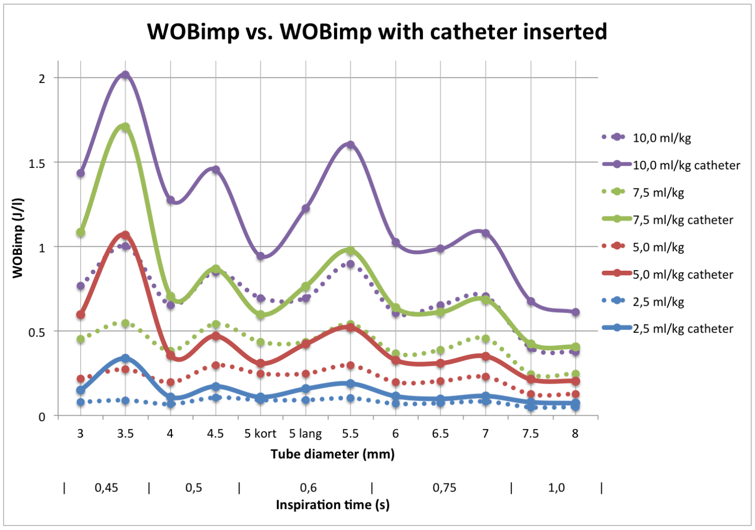

Figure 4: Inspiratory WOBimp in different ETTs, with and without catheter inserted

Figure 4 shows the results obtained during the measurements with a catheter inserted in the tubes compared to the normal tubes. There is a clear increase in the WOBimp for tubes in which a catheter was inserted. As can be seen in Figure 5, the percentual increase is the largest in the 3.0 and 3.5 mm tubes.

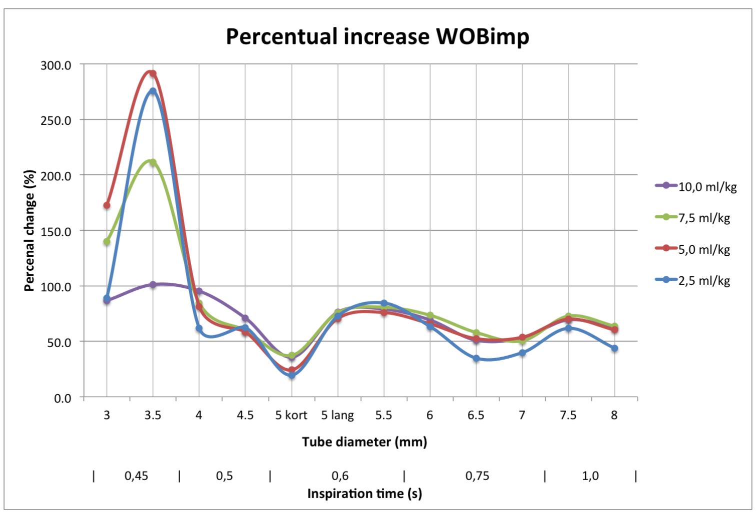

Figure 5: Percentual increase of the WOBimp comparing normally sized tubes with tubes in which a catheter is inserted

3.3 Measurements with shortened tubes

As can be observed in Figure 6, the WOBimp is generally lower in the shortened tubes than in the normal tubes. Table 3 shows the percentual change in WOBimp for the shortened tubes next to the percentual change in tube length. Table 3 shows that the effect of shortening tubes decreases with an increasing tidal volume, except for the 8.0 mm tube.

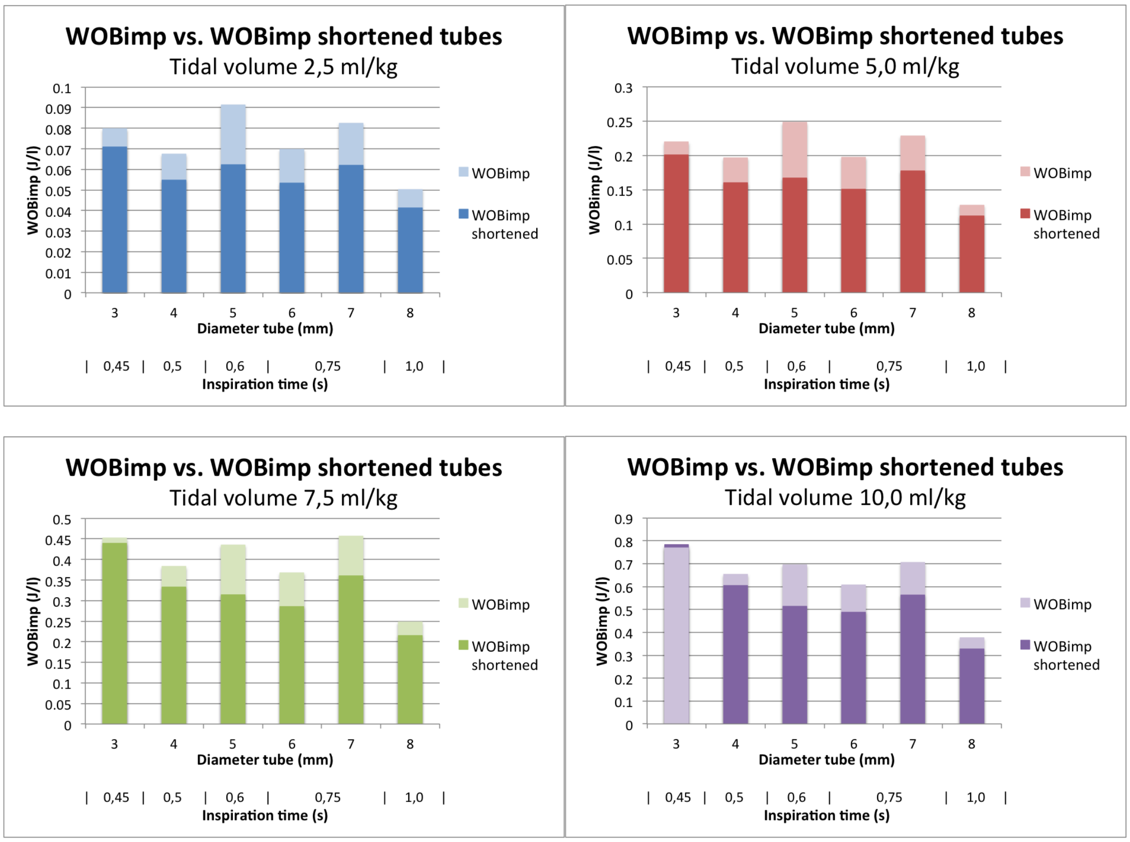

Figure 6: WOBimp of the normal tubes versus WOBimp of the shortened tubes, for different tidal volumes

Table 3: WOBimp for different tube sizes compared to WOBimp for shortened tubes

Diameter tube (mm)	**Tidal volume (ml/kg)**	**WOBimp (J/l)**	**WOBimp shortened (J/l)**	**Change in tube length (%)**	**Change in WOBimp (%)**
3.0	2.5	0.0797	0.0708	26.4	11.2
	5.0	0.2192	0.2001		8.7
	7.5	0.4517	0.4396		2.7
	10.0	0.7689	0.7830		-1.8
4.0	2.5	0.0674	0.0549	37.2	18.5
	5.0	0.1964	0.1598		18.6
	7.5	0.3827	0.3328		13.0
	10.0	0.6530	0.6050		7.4
5.0	2.5	0.0914	0.0621	39.7	32.1
	5.0	0.2477	0.1671		32.5
	7.5	0.4352	0.3146		27.7
	10.0	0.6955	0.5128		26.3
6.0	2.5	0.0697	0.0533	38.9	23.5
	5.0	0.1973	0.1501		23.9
	7.5	0.3675	0.2858		22.2
	10.0	0.6071	0.4889		19.5
7.0	2.5	0.0824	0.0620	36.6	24.8
	5.0	0.2283	0.1769		22.5
	7.5	0.4564	0.3606		21.0
	10.0	0.7054	0.5635		20.1
8.0	2.5	0.0503	0.0411	35.5	18.3
	5.0	0.1275	0.1120		12.2
	7.5	0.2478	0.2153		13.1
	10.0	0.3759	0.3264		13.2

3.4 Analytical calculations

The WOBimp was also calculated with theoretical values. These results provide a rough approximation of reality. Figure 7 shows that the values for the measured WOBimp are much higher than the results of the calculated WOBimp, with a multiplication factor which varies from 2 to 16.

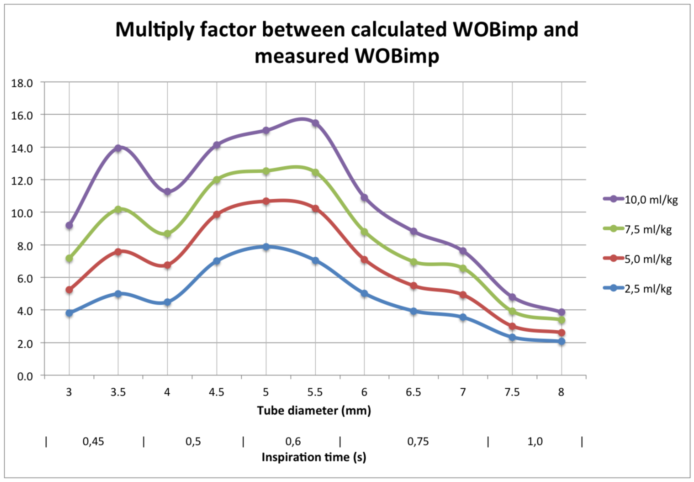

Figure 7: Multiply factor between calculated WOBimp and measured WOBimp

As can be seen in Figure 8, the graph loses the waved shape when linear increasing inspiration times, referred to as IT, are used. The graph shows a decrease of the WOBimp from the smallest tube up to the 5.0 mm ETT, whereafter the WOBimp increases again.

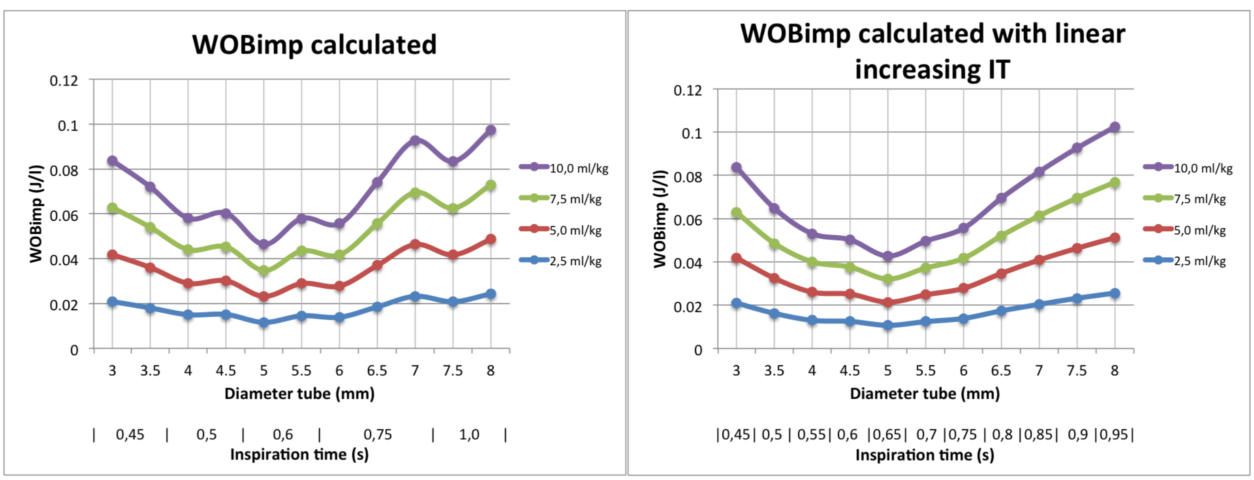

Figure 8: Calculated WOBimp with IT used in the measurements (left) and linear increasing IT (right)

3.5 Statistical analysis

The results of the statistical analysis can be found in Appendix D. The data is described by mean ± standard deviation and the last two columns show the significance. All differences are significant with a significance probability below 5% (P<0,05).

4 Discussion

The results in Figure 3 show that the WOBimp of the normally sized tubes generally stays beneath 1.0 J/l. The WOBimp for the tubes in which a catheter was inserted is significantly higher than the WOBimp for tubes without catheter. The values of the WOBimp with catheter only stays below 1.0 J/l when using a small tidal volume, as can be seen in Figure 4. The results also show that the WOBimp changes significantly when the tubes are shortened.

4.1 Inspiration time

The used inspiration times were given to us by the Pediatric Intensive Care Unit of the UMCG. We used the same inspiration times that were used in previous studies on this subject, to make it possible to compare our results with previous studies.

The wave-like shape of the graph in Figure 3 can be explained by the fact that the same inspiration time was used for two or three consecutive tube sizes while the used tidal volume increases for larger tube sizes. For example, for both the 3.0 and 3.5 mm tubes an inspiration time of 0.45 seconds was used, while the tidal volumes were increased, so it makes sense that the WOBimp becomes higher. If inspiration time and tidal volumes increase in the same proportion, the graph would probably not be wave-like shaped.

For the measurements where a catheter was inserted into the tube, the correct inspiration time could not be reached for the 3.0 and 3.5 mm tubes in the two highest tidal volumes. As can be seen in Figure 5, this results in a relatively lower change in WOBimp than it would have been when the correct inspiration time was used. The 3.0, 3.5 and 4.0 mm tubes with the smaller tidal volumes show a much higher change in WOBimp compared to the larger tubes because the catheter blocks the smaller tubes relatively more.

4.2 Limitations of the set-up

One of the limitations in the set-up is that, for the three smallest tubes, the flow has a long stretched slope at the end of an inspiration. For these tubes the neonatal flow sensor was used. The neonatal flow sensor is very sensitive and is able to detect very small amounts of flow. This could be an explanation for the long stretched slope. Probably, the sensor detected a really small airflow and this makes it look like there is still flow in the tube between the expiration and inspiration. The inspiration time is calculated by detecting the time where air flows in, so the time where just that very small amount of flow is detected will result in a large inspiration time. This inspiration time is not a proper reflection of the real inspiration time, because in this additional time, a negligible amount of volume flows in. To get a more realistic inspiration time, a threshold value was used in Polybench® like described in the method. The inspiration time was calculated again without this threshold value in Matlab® to compare the inspiration times. The inspiration times calculated by Matlab® and Polybench® were very different in the 3.0, 3.5 and 4.0 mm tubes. These were the tubes where the neonatal flow sensor was used, so in all probability the neonatal flow sensor was the limitation here. The WOBimp was calculated both with and without this threshold value. These results were compared and the difference was negligible.

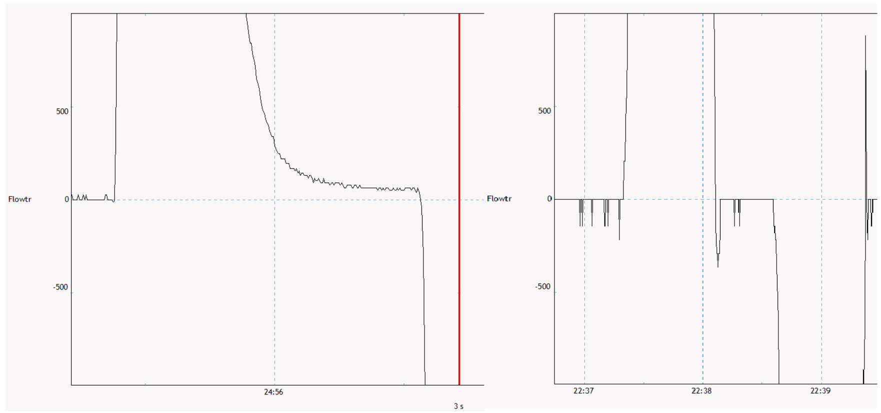

Figure 9: Flowcurve with stretched slope (left) and without stretched slope (right)

The measurements were performed with the pressure sensors as close to the tube as possible, but they could not be placed exactly at the beginning and the end of the tube. This affects the detected pressure.

The settings of the Arduino® motherboard, required to achieve for the correct inspiration times and tidal volumes, are affected by the starting position of the screw, (Figure 2). It influences the pressure at both ends of the tube as well. Because a certain volume has to be pushed through a narrow tube, pressure builds up at the beginning of the tube. This pressure build up is bigger if the starting position is closer to the tube, this is because the same volume is pushed into a smaller space. In the measurements we look at the pressure drop across the tube, so for calculating the WOBimp, it is not a limitation.

The two sensors on each side of the tube also have a certain resistance that influences the pressure difference and thus the WOBimp. Measurements to determine the resistance of these sensors have been conducted, but the starting position was not taken into account. These measurements are useless because the measured pressure can not be compared with the measurements with both sensors, caused by the different starting position. Therefore, it is not possible to compensate for the extra resistance of the sensors in the calculation for the WOBimp. This is a limitation of the set-up. The flow sensor at the end of the endotracheal tube was not used in the calculation for the WOBimp, so it could better be left out of the set-up.

The measurements were performed with dry air at room temperature (20 °C), whereas the air in trachea is humidified and at a higher temperature (32 °C).[21] When the air is humidified and at the temperature of the trachea, it has a larger volume. To compensate for this, the volume can be multiplied by a factor from ATPD to BTPS: Ambient Temperature and Pressure Dry to Body Temperature and Pressure Saturated, given by:

$$factor = \frac{P_A}{P_A - P_B} * \frac{T_A}{T_B} = \frac{760}{760-47} * \frac{273+32}{273+20} = 1.110 \tag{10}$$

This would increase the volume with 11.0%. Temperature and humidity do not only influence the volume, but also the viscosity and density. If humidified air at body temperature would be used, this will result in a higher WOBimp.

The minimum length for oral intubation for the 7.0 and 8.0 mm tubes is lower than the point where they were cut off, it was not possible to shorten them to the required length without removing the inflation mechanism of the cuff. Therefore, the percentual change in tube length is not the same for all tubes. For this reason it is not possible to compare the changes in WOBimp between the different tube sizes.

As mentioned before, the total WOB is caused by multiple factors (equation 3). Our set-up is not completely realistic to human lungs, especially because compliance is not taken into account in this set-up. In physiological conditions, the compliance will cause an extra resistance in the lungs. Especially patients who need to be mechanically ventilated often have a changed compliance and this will affect the WOB. Patients with a lower compliance of their respiratory system will have a higher WOB, so the WOBimp will be of more effect to their respiratory system than to patients with a higher compliance. Besides this, W_{tissue} can not be measured and $W_{inertia}$ can be neglected. Therefore, in this research we only focused on WOBimp, which increases W_{aw}.

The respiratory rate has a big influence on the WOB. If the respiratory minute volume remains the same but the frequency changes, the WOB will be different. This is because the contribution of the elastic forces and the airway resistance are different. Especially the airway resistance has a clear effect on the WOB when increasing the respiratory rate.[4] In our research the respiratory rate is not taken into account. In order to be able to say more about the exact influence of the breathing frequency to the WOB, more research has to be done.

4.3 Theoretically calculated WOB

The measured values for the WOBimp were compared to the theoretically calculated outcomes. The theoretical calculated values assume a completely laminar flow, this assumption will almost always result in lower outcomes. The Reynolds numbers calculated for each tube and tidal volume, can be found in Appendix E. As you can see, the Reynolds numbers often exceed the value of 3000, which means the flow through the tube is turbulent.

4.4 Acceptable WOBimp value

In this study, we stated that a clinically assumed maximum value for the WOBimp is 1.0 J/l. We can not draw any conclusions from this maximum value, thus we can not say whether it is ethical to detach the mechanical ventilator while the patient is still intubated. This value of 1.0 J/l is not scientifically proven yet but is an estimation made by clinical experts. Further research in vivo is needed to determine whether this value is correct and whether this value is different for a healthy person compared to patients with pathological lung conditions.

5 Conclusion

The WOBimp does not exceed the value of 1.0 J/l for all normally sized tubes, except for the 3.5 mm tube at a tidal volume of 10 ml/kg with a median value of 1,003 J/l. When compared to these normally sized tubes, a significant decrease in the WOBimp can be seen in the shortened ETT's, ranging from 2.7 % to 32.5%. Except for the 3.0 mm tube with a tidal volume of 10 ml/kg, where the WOBimp increases with 1.8%. When the 3.0 and 3.5 mm tubes were inserted with a catheter, the WOBimp increases significantly with 89.0% to 291.5%. For the other tubes inserting the catheter caused an increase of the WOBimp ranging from 19.5% to 95.3%.

6 Recommendations

For further research on the WOBimp, adjustments to the set-up should be made to get more reliable results. Ideally, the stepper motor should remember its starting position. This way, the results can be compared more easily and the test lung could be validated with standard settings for a certain tidal volume and inspiration time. To create a better representation of reality, this research should also be conducted with humidified air at body temperature.

A linear increasing inspiration time should be used. The wave-like shape of the graph will probably disappear, giving a better representation of the reality. It would also be better to take compliance into account in the set-up.

The resistance of the sensors should be measured to be able to correct the measured pressure. This resistance could be measured by removing the sensors one by one while the same settings are used. The pressure difference can be found by comparing the two peak pressures, this difference is due to the sensor resistance.

This research showed that the WOBimp through an ETT stays beneath the value of 1.0 J/l. This threshold value is obtained from an expert opinion. However, further research on this value for the maximum WOBimp is necessary to determine if it actually is ethical to let a patient breath through an ETT independently. Further research on this threshold value needs to be performed in vivo.

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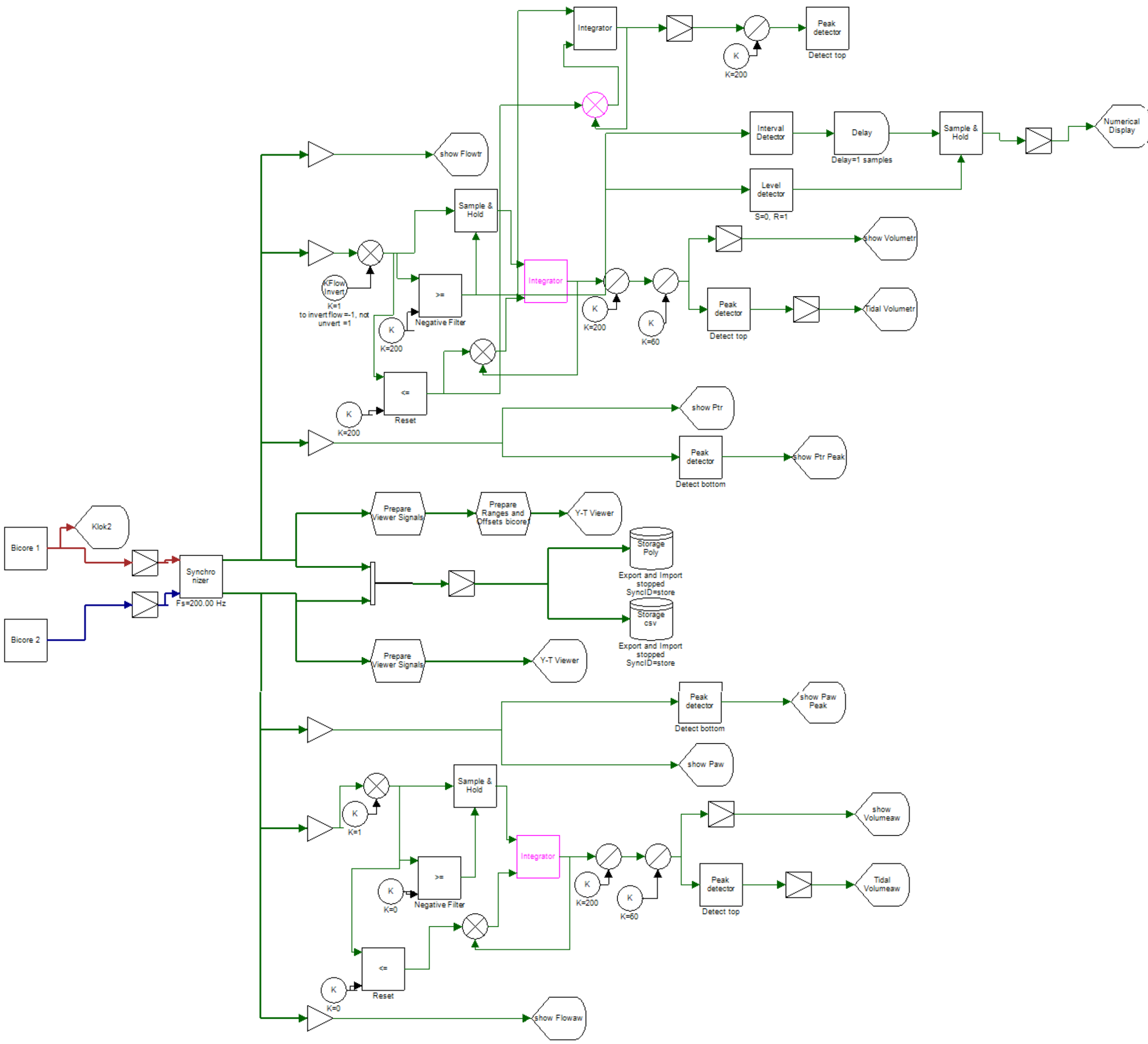
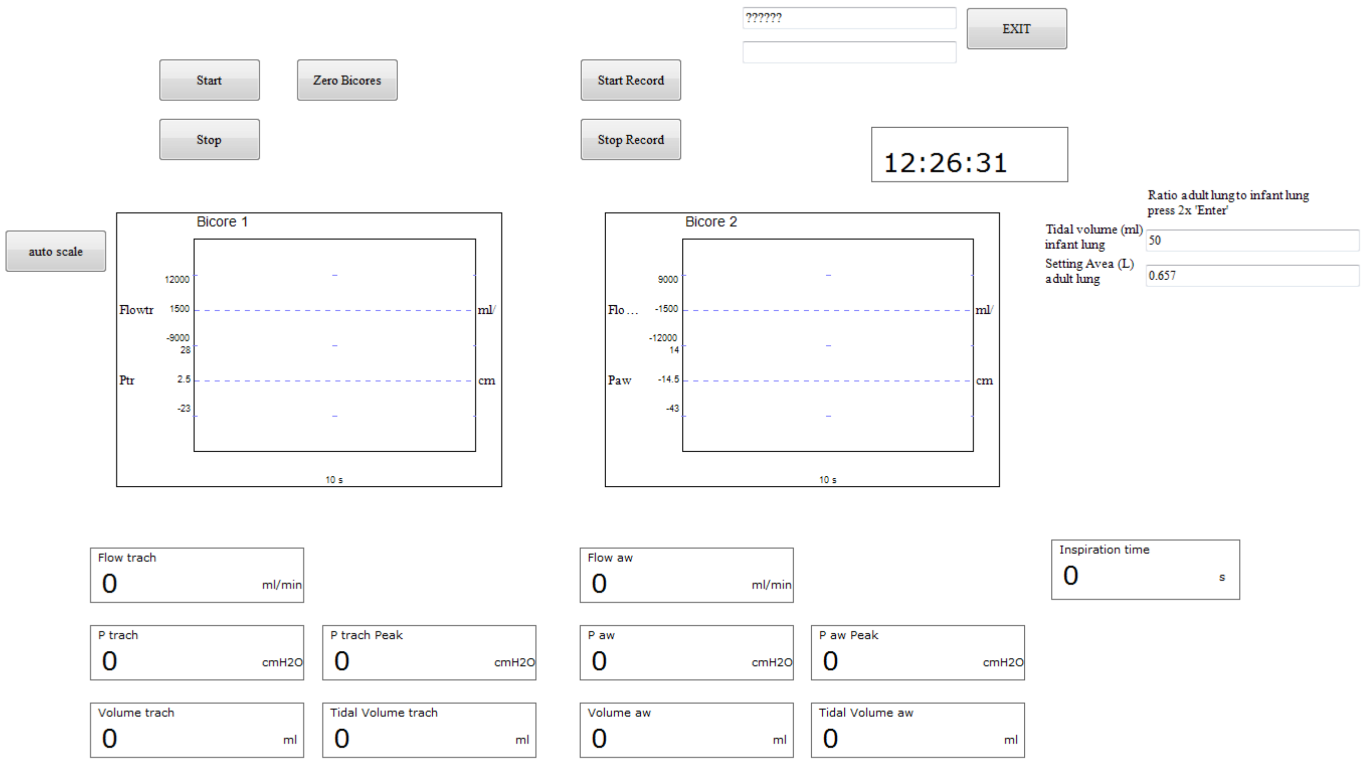
Appendices

A Polybench®

A.1 Polybench® application



A.2 Polybench® graphical user interface



B Symbols

Symbol	Meaning	Unit
l	Length	m
μ	Dynamic viscosity of the gas	Pa*s
r	Radiance	m
ρ	Density of gas	kg/m^3
$\overline{v}$	Velocity of gas	m/s
W	Work	J
P	Pressure	cmH_2O or Pa
F	Force	N
A	Surface	m^2
V	Volume	l or m^3
R	Resistance	$N*s*m^{-5}$
Q	Flow	$l*s^{-1}$
TV	Tidal volume	l
t	Time	s
C	Compliance	$l*cmH_2O^{-1}$

C Matlab® script

```
clear all

% The data must be obtained from the Current Folder.
% Change the filename to the corresponding filename in the Current
Folder:
filename='20171208_125949.rawDataCsv.csv';
M=dlmread(filename,',',1,2);
Inspirationtime=M(:,2);
Flowtr=M(:,4);
Ptr=M(:,5);
Paw=M(:,7);

% Find the number of peaks/breaths in the data
[pks,locs]=findpeaks(Flowtr,'MinPeakHeight',300,'MinPeakDistance',500);
cycles=diff(locs); % length of all the seperate cycles (in number of
samples)
medianCycle=median(cycles); % average length (in samples) of 1
breath/cycle

% Define the samples that contain the last 30 cycles.
thirtycycles1=30*medianCycle; % the number of samples in 30 cycles
thirtycycles=round(thirtycycles1,0); % round the number of samples to a
whole number
totalsamples=size(Ptr,1); % the total number of samples in the data
firstrange=totalsamples-thirtycycles; % the first cut-off point when
analyzing only the last 30 cycles

% Cutt-off until the last 30 breaths/cycles for all further used data
Pt=Ptr(firstrange:totalsamples);
Pa=Paw(firstrange:totalsamples);
Flowt=Flowtr(firstrange:totalsamples);
Inspirationt=Inspirationtime(firstrange:totalsamples);

% Inspiration time calculated by Polybench
Inspirationtime2=Inspirationt(Inspirationt>0.3);
medianITpolybench=median(Inspirationtime2) % average inspiration time

% Pressure difference between Ptr en Paw in cmH2O and converted to
Pascal
dPcmH2O=Pt-Pa;
dP=dPcmH2O*98.06;

% Calculate the amount of samples in one breath for all 30 breaths
aantalsamples=zeros(thirtycycles,1);
for s=2:thirtycycles;
    if Flowt(s)<=0;
        aantalsamples(s)=0;
    elseif Flowt(s)>0;
        aantalsamples(s)= 1 + aantalsamples(s-1);
    end
end
```

```
% Inspiration time calculated by amount of samples per breath
ITinsamples=findpeaks(aantalsamples,'MinPeakDistance',500);
ITinsec=ITinsamples/200;
medianITmatlab=median(ITinsec)

% Calculate volume during inspiration by area under the flowcurve
Flowt1=(Flowt/60); % flow from ml/min to ml/sec
VolumeIN=zeros(thirtycycles,1);
for s=2:thirtycycles; % Loop taken for the number of samples of the
last 30 breaths/cycles
    if Flowt1(s)<=0;
        VolumeIN(s)=0;
    elseif Flowt1(s)>0;
        VolumeIN(s)= ((Flowt1(s)+Flowt1(s-1))/2)*(1/200) + VolumeIN(s-
1);
    end
end
TidalVolume=findpeaks(VolumeIN,'MinPeakDistance',500);
medianTV=median(TidalVolume)

% Volume from ml to m^3
Volumetrm3=VolumeIN/1000000;

% Calculate a Riemannsom for the pressure difference over the Volume in
the trachea:
sWOB=zeros(thirtycycles,1);
for s = 2:thirtycycles; % Loop taken for the number of samples of the
last 30 breaths/cycles
   if Flowt(s)<=0;
       sWOB(s)=0;
   elseif Flowt(s)>0;
       sWOB(s)=(((dP(s)+dP(s-1))/2)*(Volumetrm3(s)-Volumetrm3(s-
1))+sWOB(s-1)); % integrating using the Riemannsom
   end
end

% Filter all WOB below 0, which is 1 sample per breath
sWOB(sWOB<0)=0;
% Find the 30 peaks in the summed WOBimp to calculate the WOBimp per
breath
peaks=findpeaks(sWOB,'MinPeakDistance',500);
% The peaks need to be devided by the number of peaks (should always be
30)
aantalteugen=size(peaks);
% The median of the peaks
medianWOB=median(peaks);
%Tidal volume from ml to liters
TV=medianTV/1000;
% Divide the WOBimp by the tidal volume
medianWOBimp=medianWOB/TV % Divide by the tidal volume, to get the Work
of Breathing in Joule per litre
```

D Statistical analysis

Diameter tube (mm)	Tidal volume (ml/kg)	Main measurements (mean ± SD)	Shortened tubes (mean ± SD)	Catheter (mean ± SD)	Significance shortened vs. main	Significance catheter vs. main
3.0	2.5	0.079 ± 0.001	0.071 ± 0.001	0.149 ± 0.002	0.000	0.000
	5.0	0.218 ± 0.003	0.200 ± 0.003	0.597 ± 0.007	0.000	0.000
	7.5	0.455 ± 0.005	0.439 ± 0.004	1.080 ± 0.014	0.000	0.000
	10.0	0.766 ± 0.011	0.780 ± 0.010	1.434 ± 0.010	0.000	0.000
3.5	2.5	0.0902 ± 0.0012	-	0.337 ± 0.005	0.000	0.000
	5.0	0.273 ± 0.003	-	1.069 ± 0.015	0.000	0.000
	7.5	0.546 ± 0.006	-	1.701 ± 0.012	0.000	0.000
	10.0	1.002 ± 0.013	-	2.018 ± 0.017	0.000	0.000
4.0	2.5	0.067 ± 0.001	0.055 ± 0.001	0.109 ± 0.001	0.000	0.000
	5.0	0.196 ± 0.003	0.160 ± 0.002	0.354 ± 0.011	0.000	0.000
	7.5	0.382 ± 0.005	0.333 ± 0.005	0.705 ± 0.008	0.000	0.000
	10.0	0.653 ± 0.007	0.780 ± 0.010	1.274 ± 0.015	0.000	0.000
4.5	2.5	0.106 ± 0.001	-	0.172 ± 0.002	0.000	0.000
	5.0	0.297 ± 0.004	-	0.469 ± 0.005	0.000	0.000
	7.5	0.543 ± 0.007	-	0.689 ± 0.010	0.000	0.000
	10.0	0.850 ± 0.010	-	1.456 ± 0.014	0.000	0.000
5.0	2.5	0.091 ± 0.001	0.062 ± 0.001	0.158 ± 0.001	0.000	0.000
	5.0	0.247 ± 0.002	0.170 ± 0.000	0.423 ± 0.003	0.000	0.000
	7.5	0.435 ± 0.004	0.315 ± 0.002	0.765 ± 0.005	0.000	0.000
	10.0	0.698 ± 0.007	0.513 ± 0.003	1.226 ± 0.008	0.000	0.000
5.5	2.5	0.102 ± 0.001	-	0.189 ± 0.001	0.000	0.000
	5.0	0.296 ± 0.003	-	0.521 ± 0.007	0.000	0.000
	7.5	0.542 ± 0.005	-	0.978 ± 0.009	0.000	0.000
	10.0	0.896 ± 0.008	-	1.604 ± 0.012	0.000	0.000
6.0	2.5	0.070 ± 0.001	0.053 ± 0.002	0.114 ± 0.001	0.000	0.000
	5.0	0.197 ± 0.002	0.150 ± 0.001	0.327 ± 0.002	0.000	0.000
	7.5	0.368 ± 0.004	0.285 ± 0.004	0.637 ± 0.006	0.000	0.000
	10.0	0.605 ± 0.007	0.490 ± 0.005	1.026 ± 0.008	0.000	0.000
6.5	2.5	0.072 ± 0.001	-	0.096 ± 0.016	0.000	0.000
	5.0	0.203 ± 0.002	-	0.310 ± 0.002	0.000	0.000
	7.5	0.387 ± 0.003	-	0.611 ± 0.003	0.000	0.000
	10.0	0.653 ± 0.006	-	0.986 ± 0.105	0.000	0.000
7.0	2.5	0.082 ± 0.001	0.062 ± 0.001	0.115 ± 0.001	0.000	0.000
	5.0	0.228 ± 0.002	0.177 ± 0.002	0.351 ± 0.004	0.000	0.000
	7.5	0.457 ± 0.004	0.360 ± 0.004	0.687 ± 0.005	0.000	0.000
	10.0	0.705 ± 0.006	0.563 ± 0.006	1.081 ± 0.010	0.000	0.000
7.5	2.5	0.048 ± 0.001	-	0.079 ± 0.001	0.000	0.000
	5.0	0.125 ± 0.001	-	0.231 ± 0.002	0.000	0.000
	7.5	0.245 ± 0.002	-	0.423 ± 0.004	0.000	0.000
	10.0	0.400 ± 0.003	-	0.678 ± 0.006	0.000	0.000
8.0	2.5	0.050 ± 0.001	0.041 ± 0.001	0.072 ± 0.001	0.000	0.000
	5.0	0.127 ± 0.002	0.112 ± 0.001	0.204 ± 0.002	0.000	0.000
	7.5	0.248 ± 0.003	0.216 ± 0.002	0.406 ± 0.003	0.000	0.000
	10.0	0.376 ± 0.003	0.326 ± 0.003	0.610 ± 0.004	0.000	0.000

E Reynolds number

Diameter (mm)	Tidal Volume (ml)	Reynolds number
3.0	12.5	773
	25	1547
	37.5	2320
	50	3093
3.5	18.75	994
	37.5	1989
	56.25	2983
	75	3977
4.0	25	1044
	50	2088
	75	3132
	100	4176
4.5	37,5	1392
	75	2784
	112,5	4176
	150	5568
5.0	50	1392
	100	2784
	150	4176
	200	5568
5.5	62,5	1740
	125	3480
	187,5	5220
	250	6960
6.0	75	1392
	150	2784
	225	4176
	300	5568
6.5	100	1856
	200	3712
	300	5568
	400	7424
7.0	100	1989
	200	3977
	300	5966
	400	7955
7.5	150	1790
	300	3580
	450	5369
	600	7159
8.0	175	1827
	350	3654
	525	5481
	700	7308