

Technische Geneeskunde; TGO

# **Mechanical power in children mechanically ventilated with high-frequency oscillation ventilation**

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# Abstract

## Introduction

Ventilator-Induced Lung Injury (VILI) is an injury that is caused by mechanical ventilation. The mechanisms causing VILI can be summarised in one variable, the mechanical power (MP). High Frequency Oscillation Ventilation (HFOV) is a technique that could limit the risk of VILI. In contrast to different types of conventional mechanical ventilation (CMV), there are no equations for MP in HFOV available yet. This study's purpose is to determine the MP in HFOV in a mechanical lung model and to evaluate the correlation with different variables (power setting, CDP, frequency, lung compliance and lung resistance) for six different tube sizes.

## Methods

Data of flow, oscillator pressures and lung pressures for different variables were used from a previously conducted Bench Study. The elastic MP ( $MP_{ED}$ ) was calculated in different ways, by multiplying flow and pressure difference (P<sub>osc</sub>-P<sub>lung</sub>) and by taking the integral of the PV-loop. The resistive MP ( $MP_{RD}$ ) was calculated by multiplying the resistance with  $flow^2$ . The results were analysed using multivariable regression analysis.

## Results

Our results include multivariable prediction models and correlations between the different variables and MP for each tube. One tube was left out due to faults in the measurement data. All other results had a significance of  $p < 0.001$ . When using large tubes, the calculated MP was relatively high in comparison with smaller tubes.

## Conclusion

We were able to determine the influence of different parameters on the MP in HFOV. Future trials are needed to determine whether or not the calculated MP in HFOV is a sufficient predictor of VILI.

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# 1 Introduction

Conventional mechanical ventilation (CMV), although indispensable and life-saving in critically ill patients, entails a risk of barotrauma, volutrauma and atelectrauma, due to its associated pressure and volume differences[1, 2, 3, 4]. All these mechanisms, potentially accompanied by biotrauma due to inflammatory responses, can cause Ventilator-Induced Lung Injury (VILI). This is a complex injury with dire consequences such as pulmonary edema, hypoxemia, alveolar collapse or fibrosis. Preventing VILI in patients is thus a must, especially since patients requiring mechanical ventilation could already be suffering from respiratory failure. The use of lung protective ventilation methods are desired to minimize the chance of VILI.

Due to its small pressure differences and low tidal volumes ( $V_t$ ), High Frequency Oscillation Ventilation (HFOV) could be an effective technique in minimizing the risk of VILI. HFOV keeps the lung open with a continuous distending pressure (CDP) and provides high respiratory rates from 5-15 Hz and  $V_t$ s below dead space of around 2 mL/kg using forced in- and expiration[5, 6]. Despite these small volumes, gas exchange is effectuated by indirect ventilation, due to various mechanisms such as turbulent flow[7].

However, it is not yet certain whether HFOV is superior to CMV. This is why HFOV is currently mostly used as a rescue method to protect the lungs, after CMV has failed [8, 9, 10, 11]. The safety and effectiveness of HFOV in adults have been questioned by some big trials[12, 13, 8, 14], although it is not clear whether or not these studies handled the technique the right way[15]. Multiple retrospective observational paediatric studies suggested that the mortality rate was higher using HFOV in comparison with CMV[16, 17]. However, it is not clear whether or not these are confounded by indication, because the methods used to overcome this are missing some important predictors such as PIP, PEEP and FIO<sub>2</sub>[18]. Additionally, the used ventilator strategy might not be optimal, because in previous conducted studies the specific strategy was associated with hemodynamic problems[19]. Also, better outcomes were obtained when the patients' ventilator settings were determined using a different method[20]. Another study suggests that the outcome when using HFOV gives modest short-term improvements, although there is no such evidence for the long-term[21]. There is currently no RCT available in which HFOV is compared to CMV, although there is a RCT launched where, among other things, the use of HFOV is compared with CMV in the case of Paediatric Acute Respiratory Distress Syndrome[22]. Briefly, the superiority of HFOV is not yet proven, although this could be related to the uncertainty concerning the right strategy.

The mechanisms causing VILI can be summarised in one variable, the Mechanical Power (MP), which describes the energy transfer on the lung in joules per minute (J/min)[23]. Since the amount of energy transferred is related to the risk of VILI[34], the MP can be an effective way to determine the safety of HFOV.

The MP during ventilation can be divided in three main parts: elastic dynamic MP ( $MP_{ED}$ ), elastic static MP ( $MP_{ES}$ ) and resistive dynamic MP ( $MP_{RD}$ ), see figure 1[25]. The  $MP_{ED}$  can also be divided into 2 parts: Elastic work due to PEEP ( $MP_{E_{peep}}$ ) and elastic work due to pressure difference (dP) ( $MP_{E_{dP}}$ ). This division is made, because of the assumption that the  $MP_{E_{peep}}$  could contribute less to the total MP than the  $MP_{E_{dP}}$ [26]. The  $MP_{ES}$  can be neglected in the calculation of the total MP, because it only produces work when starting the ventilator to get to the initial setting. After this, there is no change in volume due to PEEP, which results in no work and therefore no MP. The  $MP_{RD}$  is the

power lost over the resistive airways. While using CMV, only the  $MP_{RD}$  during inspiration is taken into account, since the airflow during expiration is seen as natural[23]. In case of HFOV, there is an  $MP_{RD}$  both during inspiration as well as expiration, due to the forced expiration. This part is represented by  $R \dot{V}$ , where R is the resistance of the airways and  $\dot{V}$  the airflow in the lung[27].

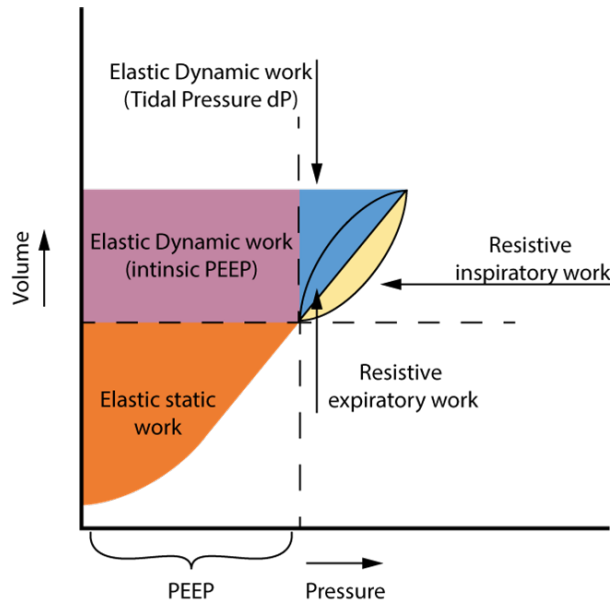


Figure 1: schematic representation of the components of the MP.

Using CMV, the MP can be calculated using different equations and proves to be a reliable indication of the risk of VILI[23, 25, 28]. There are different approaches for volume controlled and pressure controlled ventilation[25]. In HFOV, pressures measured at the ventilator do not represent pressures in the lung, due to increased damping at high frequencies. Damping occurs due to the combination of resistance and compliance, which is frequency dependent. This damping leads to overestimation of the lung pressures and thereby MP when using pressure measurements at the ventilator, which makes these equations not applicable for HFOV.

The purpose of this study is to describe the influence of different variables (resistance, compliance, power setting [correlates with dP at the ventilator], frequency, CDP) on the MP and its resistive and elastic subcomponents for different ETTs (EndoTrachealTube), using HFOV in a mechanical lung model with paediatric conditions and settings.

## 2 Hypothesis

To test our hypothesis, a simplified model of the respiratory system will be used. A schematic description can be found in figure 2. The  $MP_{ED}$  is represented by the pressure over the test lung, while the  $MP_{RD}$  is represented by the pressure over the resistor. This model can be seen as a first order low-pass filter. The amplitude transfer function for this system is  $jH(f)j = P \frac{1}{1+(f R C 2)^2} = \frac{P_{lung}}{P_{osc}}$ , where  $P_{lung}$  is the pressure over the testlung and  $P_{osc}$  is the pressure over the oscillator. From this function, we hypothesise that a higher frequency, resistance or compliance results in less pressure over the test lung and

therefore in less  $MP_{ED}$ . According to Kirchhoff's law, the input pressure is divided among the components of the circuit, so less  $MP_{ED}$  means more  $MP_{RD}$ .

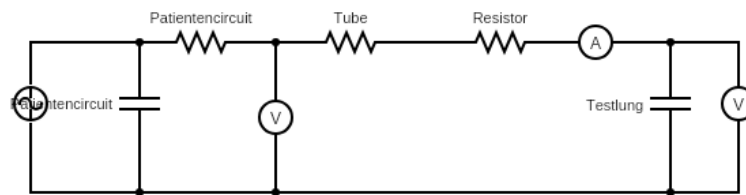


Figure 2: Schematic representation of the lung model.

Because the  $MP_{RD}$  is proportionally divided between the tube and the airway resistance, there will be more MP loss at the tube and therefore the total MP is expected to decrease. However, due to turbulence of the tube and airway resistance will increase. The change of the airway resistance may differ from that of the tube resistance. A higher resistance also means less flow and volume, so it is expected that the resistance has a large influence on the MP. We hypothesise that the power setting and the CDP have a positive correlation with the MP. CDP determines the height of the pressure and not the pressure difference. Therefore we only expect CDP to have an influence on the  $MP_{Epeep}$ , since this is the only component which depends on the pressure level. The power setting directly influences the input dP, and thereby all components of the MP.

### 3 Method

#### Measured data

Data was obtained from a previously conducted Bench test in Universitair Medisch Centrum Groningen (UMCG). The setup is schematically shown in figure 3. The Bench test included a SensorMedics 3100A and 3100B HFOV oscillator (CareFusion, Yorba Linda, CA, USA), connected with an ETT and a linear airway resistance to a test lung made of a 20L rigid glass bottle, filled with water to mimic compliance. Pressure was measured after

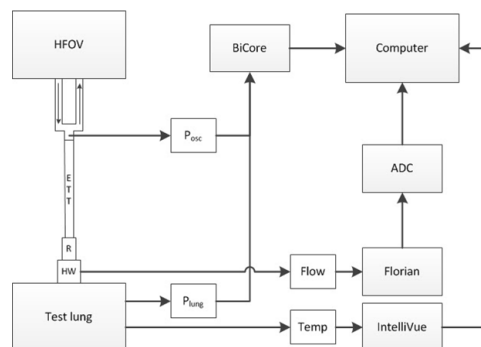


Figure 3: Schematic overview of the Bench test model with the HFOV-ventilator, endotracheal tube (ETT), airway resistance (R), Florian hot-wire (HW) anemometer and the analogue to digital converter. Flow, intra-oscillatory pressure ( $P_{osc}$ ), intrapulmonary pressure ( $P_{lung}$ ), and temperature were recorded. Copied from: Ruben Overduin, Bsc (2018) Vt and Pressure Attenuation during Paediatric HFOV

the oscillator (Posc) and in the lung (Plung) with a BiCore II (Cardinal Health, Quayside, England) and flow ( $V$ ) was measured after the ETT with a Florian hot wire anemometer (Acutronic Medical Systems AG, Hirzal, Switzerland). The flow data was converted with an analogue to digital converter and recorded in Polybench together with the pressures. Flow and pressures were measured for 10 seconds after initialisation of the system by the parameter settings. In total, a combination of six different tube sizes and power settings and three different frequencies, CDPs, resistances and compliances were used. All settings included conditions relevant for clinical practice and can be found in table 1. All measurements were recorded with a sample rate of 200 Hz.

Table 1: Studieprotocol data UMCG

Ventilator	ETT (ID,mm)	Compliantie (mL/cmH2O)	R (cmH2O/L/s)	f (Hz)	P (%)	CDP (cmH2O)	Bias Flow (L/min)	I:E ratio
3100A	3	0.5, 1, 3	0, 50, 200		50			1:2
	4	1, 3, 5			60			
	5	3, 5, 10	5	15				
	6	5, 10, 20	10	25	30			
3100B	7	10, 20, 30	0, 20, 50	15	80	35		
	8	10, 20, 40	0, 5, 20		90			
					100			

ETT = endotracheal tube, ID = internal diameter, C = compliance, R = airway resistance, f = frequency, P = power, CDP = continuous distending pressure, I:E = inspiratory to expiratory ratio. Reproduced from: Ruben Overduin, Bsc (2018) Vt and Pressure Attenuation during Paediatric HFOV.

### Mechanical Power

To calculate the MP, the MP was divided into an elastic ( $MP_{ED}$ ) and a resistive ( $MP_{RD}$ ) part. We calculated the  $MP_{ED}$  by taking the integral with respect to  $dV$  of the PV-loop (conventional method) and by using the formula  $MP_{ED} = \int dP$  (direct method), see figure 4. Vt for the PV-loop was obtained by integrating  $V$  with respect to time.  $MP_{EdP}$  was determined using the formula  $MP_{EdP} = (Plung - PEEP) \int V$ .  $MP_{Epeep}$  was then obtained by subtracting  $MP_{EdP}$  from  $MP_{ED}$ .

In order to calculate the  $MP_{RD}$ , either the resistance of, or the pressure difference over the resistor needs to be known. The resistors used are linear and calibrated, so the given resistance was used. To calculate the average  $MP_{RD}$ , the formula  $MP_{RD} = R \int V^2$  was used for each sample during the inspiration and expiration and added together with respect to the inspiration:expiration ratio 1:2.

### Data processing

The MP was calculated using Matlab R2018b (Mathworks, Natick, MA, USA). Due to time differences between the internal clocks during recording of the data, the data was not synchronised. In order to synchronise the data, the onset of the expiration was determined in both the flow and the pressure signals. The pressure signals are shifted according to the sample difference between the expiration in the flow and the pressure. The MP was calculated by taking the mean power of each breath cycle for ten seconds. A summary of the work done in Matlab is visualized in appendix A.

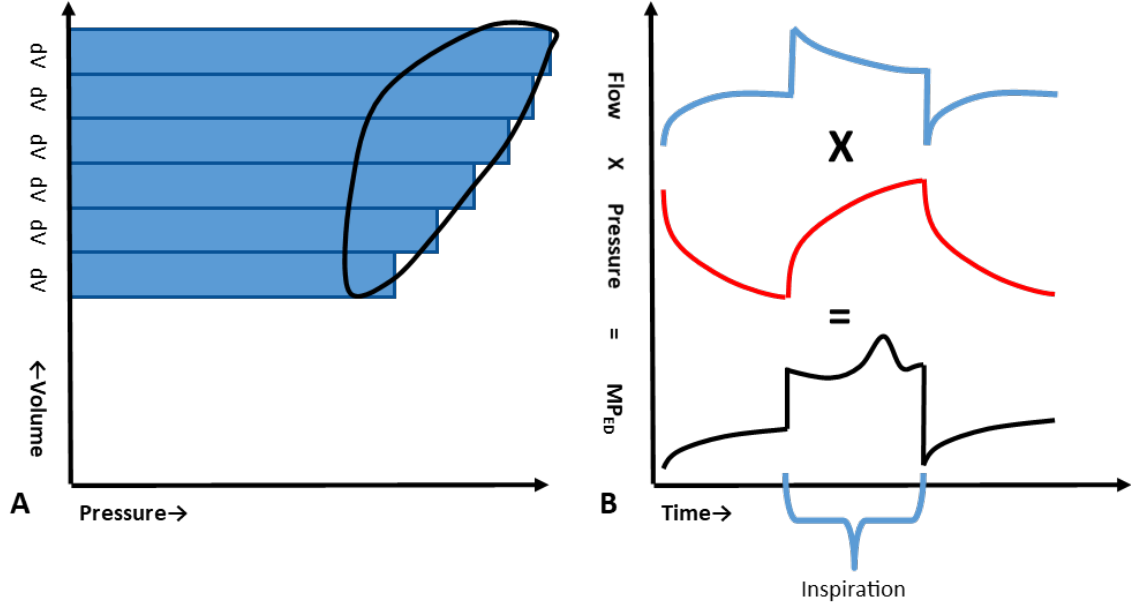


Figure 4: Different methods for calculating MP. Using the conventional method (A), the MP is calculated by taking the sum of the rectangles to estimate the area at the left side of inspiratory P-V-loop. Using the direct method (B), the MP is calculated by multiplying the pressure and the flow during inspiration. A mean value is used to get higher accuracy.

### Statistical Analysis

The statistical analysis was done with IBM SPSS Statistics for Windows, Version 25.0 (IBM Corp., Armonk, NY, USA). First, the results were tested for normality using the one-sample Kolmogorov-Smirnov Test. Since it was not normally distributed, Wilcoxon signed rank tests were used to check for differences between the MP measured at the ventilator and in the lung and for comparing the conventional and direct method for calculation of the MP. The influence of each parameter on the MP was calculated with step-wise multivariable regression analysis with the criteria: probability of variable to enter  $\leq 0.05$ . Because the volume in the lung is given by the solution of a differential equation  $V(t) = A \exp\left(\frac{1}{C} \frac{1}{R} t + \frac{P_{osc}(t)}{C}\right)$ , where A is a constant value, depending on the starting conditions, and the  $MP_{ED}$  is calculated by  $MP(t) = \int_{begininsp}^{endinsp} dV(t) P(t) dt$ , we expect not a pure linear but a logarithmic relationship between the  $MP_{ED}$  and the independent variables. Because the MP is proportional to the square of the transfer function,  $MP \propto \frac{1}{1+f^2} \frac{1}{C^2 R^2}$ , we also expect a more or less  $MP \propto \frac{1}{Var^2}$  relation for resistance, frequency and compliance[29]. For small values, this correlation is not correct, due to value 1 in the denominator. Only correcting R with  $Rt = \frac{1}{R^2}$  showed to have a significant influence.

## 4 Results

A total of 2592 measurements were performed. Measurements with  $C = 30$  and  $C = 40$  mL/cmH<sub>2</sub>O were not performed, due to inability of the test lung to accommodate to these settings. Afterwards, all measurements with ETT 6 were excluded, because of artifacts in the pressure signals. Also pressure measurements with ETT 7 appeared to be unstable,



probably due to reflection of the pressure signal, but are left in. When comparing the 5% trimmed mean and median values between the ETT sizes, it is shown that the MP is larger when using a larger tube (table 2).

Table 2: 5% trimmed mean and median values of different ETTs

ETT	5% trimmed Mean	N	Std. Deviation	Median
3	7.9	486	4.1	7.3
4	13.0	486	7.7	11.5
5	25.6	486	12.0	25.4
7	62.3	324	48.7	62.6
8	66.5	324	32.6	66.7

### MP corrected for ideal weight

When correcting the MP for ideal weight, it can be concluded that there is a small decrease in the MP/kg when using larger tubes (figure 5). The dispersion between the MP for all different parameters gets also smaller.

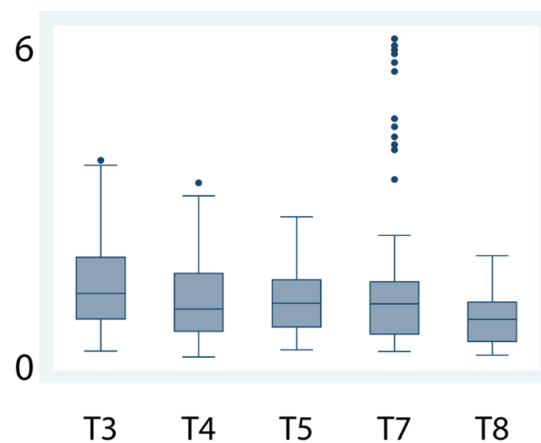


Figure 5: MP/kg for each tube size

### Correlations between variables and MP

From the results, multiple boxplots were made to examine the influence of different parameters on the MP. The boxplot showing the influence of the resistance and compliance can be found in figure 6.

Other boxplots can be found in appendix D. The CDP and power setting appeared to have a positive correlation with the MP, whereas the frequency and resistance mostly have a negative correlation with MP. The influence of the compliance appeared to be minimal.

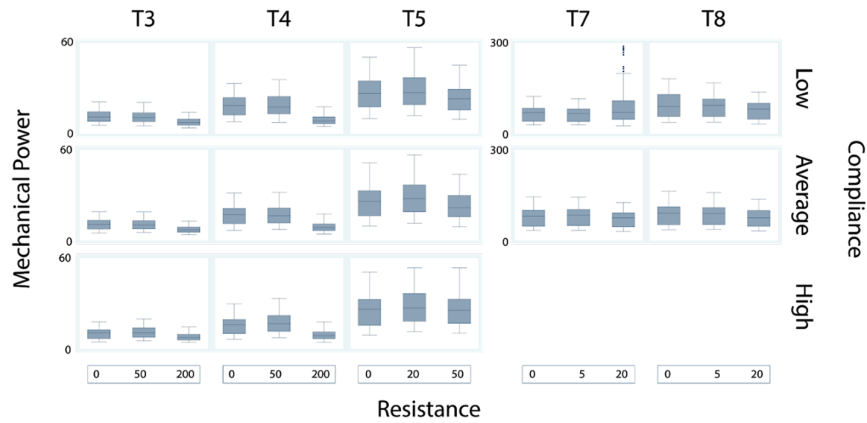


Figure 6: MP for each tube size with different resistances and compliances

### Different MPs

According to the one-sample Kolmogorov-Smirnov Test, the results are not normally distributed ( $p < 0.001$  for all tests). A Wilcoxon Signed Ranks test showed that there is a significant difference between the MP measured at the oscillator and the MP measured in the lung ( $Z = -39.5$ ,  $p < 0.001$ , mean difference = 4.1 [MP<sub>oscillator</sub> - MP<sub>lung</sub>]), see figure 7. It also proved a significant difference between the conventional method and the direct method for the calculation of the MP ( $Z = -39.6$ ,  $p < 0.001$ ), although there is a strong correlation between these methods ( $R^2 = 0.988$ ).

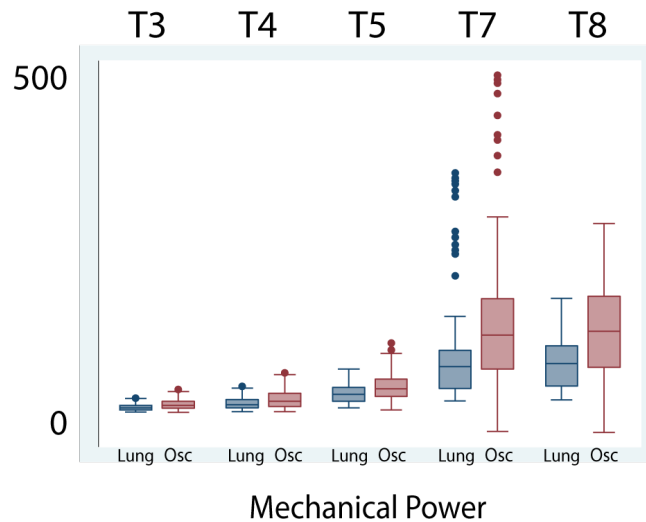


Figure 7: Boxplot of MP calculated at the oscillator and in the lung

### Linear multivariable regression model

Given the data was not normally distributed, stepwise multivariable regression analysis was used to examine the influence of each variable on the MP. The results are shown in table 3.

Table 3: Linear multivariable model predicting MP

ETT	Multivariable prediction model	R <sup>2</sup>	Sig
3	MP = -1.034+0.378*CDP-0.337*f-0.018*R+0.060*Power	0.882	<0.001
4	MP = 4.510+0.620*CDP-0.566*f-0.46*R+0.105*Power-0.340*C	0.854	<0.001
5	MP = -6.904+1.207*CDP-1.113*f-0.40*R+0.196*Power	0.900	<0.001
7	MP = 43.761+3.564*CDP-4.658*f+0.868*R-1.723*C	0.578	<0.001
8	MP = 5.025+3.467*CDP-2.508*f-0.642*R+0.131*Power-0.291*C	0.921	<0.001

When correcting the MP with  $\ln(MP)$  and the resistance with  $Rt = 1=R2$ , the results from table 4 are obtained. Corrections for the other variables did not give better results.

Table 4: Transformed linear multivariable model predicting  $\ln(MP)$ 

ETT	Multivariable prediction model	R <sup>2</sup>	Sig
3	$\ln(MP) = 0.099+0.047*CDP-0.041*f+1286.049*Rt+0.010*Power$	0.960	<0.001
4	$\ln(MP) = 0.262+0.046*CDP-0.041*f+2159.775*Rt+0.012*Power-0.010*C$	0.972	<0.001
5	$\ln(MP) = 1.547+0.047*CDP-0.042*f+88.406*Rt+0.009*Power+0.007*C$	0.952	<0.001
7	$\ln(MP) = 3.377+0.058*CDP-0.068*f+0.003*Power-0.020*C$	0.790	<0.001
8	$\ln(MP) = 2.729+0.056*CDP-0.037*f+3.997*Rt+0.003*Power$	0.931	<0.001

The different parts of the MP (Epeep, EdP and RD), were also predicted with the transformed linear multivariable model, as shown in table 5.

Table 5: Transformed linear multivariable prediction model for the different parts of MP

ETT	Part	Multivariable prediction model	R <sup>2</sup>	Sig
3	Epeep	$\ln(MP) = -1.252+0.074*CDP-0.020*f+1443.606*Rt+0.157*C+0.003*Power$	0.936	<0.001
	EdP	$\ln(MP) = -0.138+0.026*CDP-0.169*f+2957.004*Rt-0.794*C +0.016*Power$	0.945	<0.001
	R.D.	$\ln(MP) = -0.950+0.018*CDP-0.027*f+212.375*Rt+0.029*C +0.019*Power$	0.913	<0.001
4	Epeep	$\ln(MP) = 0.795+0.069*CDP-0.033*f+2202.533*Rt+0.065*C +0.005*Power$	0.956	<0.001
	EdP	$\ln(MP) = -0.428+0.026*CDP-0.178*f+4860.630*Rt-0.537*C +0.017*Power$	0.972	<0.001
	R.D.	$\ln(MP) = -0.715 + 0.021*CDP-0.028*f+1563.564*Rt-0.009*C +0.020*Power$	0.943	<0.001
5	Epeep	$\ln(MP) = 0.702+0.065*CDP-0.037*f+140.545*Rt+0.025*C +0.004*Power$	0.953	<0.001
	EdP	$\ln(MP) = 0.431+0.029*CDP-0.159*f+341.562*Rt-0.237*C +0.016*Power$	0.627	<0.001
	R.D.	$\ln(MP) = 0.511+0.021*CDP-0.031*f-46.841*Rt+0.011*C +0.018*Power$	0.898	<0.001
7	Epeep	$\ln(MP) = 2.771+0.065*CDP-0.047*f-0.008*C$	0.813	<0.001
	EdP	$\ln(MP) = 2.961+0.031*CDP-0.199*f+7.786*Rt-0.084*C +0.013*Power$	0.930	<0.001
	R.D.	$\ln(MP) = 1.134+0.034*CDP-0.074*f-30.560*Rt-0.024*C +0.014*Power$	0.710	<0.001
8	Epeep	$\ln(MP) = 2.137+0.064*CDP-0.017*f+3.686*Rt+0.010*C$	0.914	<0.001
	EdP	$\ln(MP) = 2.483+0.028*CDP-0.171*f+14.513*Rt-0.067*C +0.013*Power$	0.967	<0.001
	R.D.	$\ln(MP) = -0.059+0.036*CDP-0.019*f-17.803*Rt+0.014*Power$	0.911	<0.001

## 5 Discussion

The purpose of this study was to calculate the MP for HFOV and to describe the influence of different variables for different conditions and ventilator settings. We provided prediction models for the total MP and its elastic and resistive components, showed the contribution of each parameter for this MP, compared the two calculating methods and compared the difference in the MP at the ventilator and the lung.

A notable outcome is the higher MP for large ETTs. This could be an explanation for the worse outcomes reported in adult studies, due to the expected relationship between MP and the chance of VILI [15, 23]. From the results of stratification for ideal weight, a small decrease in the MP/kg for larger tubes can be observed. This can be explained by the much lower compliance of the paediatric chest wall, although children have a higher compliance per kg [30]. It is likely that children tolerate much higher MP per kg because of the different structure of the chest wall.

From our data, we derived correlations for each variable with the total MP.

First, these correlations showed that CDP influences the  $MP_{E_{peep}}$  as well as the  $MP_{EdP}$  and the  $MP_{RD}$ . It is known that the CDP is a result of the input power, so it is possible that the CDP is influenced by other variables. This could be an explanation for this correlation between CDP and the  $MP_{EdP}$  and  $MP_{RD}$ . It is also possible that we did not get a pure  $MP_{EdP}$  from our calculations and that there are still some components of the  $MP_{E_{peep}}$  left.

Second, as we expected, we can conclude a positive influence of the power setting on the MP. The power setting is the percentage of total piston displacement, which generates the pressure amplitude and is therefore closely related to the pressure amplitude.  $dP$  is directly related to the MP.

Third, a higher frequency results in a lower MP. The largest occurs with the  $MP_{EdP}$ , as expected. However, higher frequency also results in a lower  $MP_{RD}$ , while we hypothesised higher  $MP_{RD}$  for higher frequencies. A possible explanation for this result is that at higher frequencies the piston cannot reach its maximum amplitude, which results in a lower pressure amplitude at the ventilator and therefore a lower flow rate. This lower flow rate results in a lower  $MP_{RD}$ . It is also possible that a higher frequency results in more leakage in the ventilator, which also affects the pressure amplitude further on in the system.

Fourth, when using small ETTs, a larger resistance results in less MP in all parts. It seems to have a large influence on the flow and thereby on the MP. When using large ETTs, a larger resistance results in a higher  $MP_{RD}$ . The difference in ratio of airway and tube resistance in large ETTs, where the effect of tube resistance is less, could cause this effect.

Fifth, compliance seems to have only little influence on the total MP. However, when comparing the different components of MP, compliance seems to have only a major influence on the  $MP_{EdP}$  and a minor influence on the  $MP_{E_{peep}}$  and  $MP_{RD}$ . This suggests that the compliance has mostly an influence on the distribution of MP, although we were not able to characterise this relationship due to the little differences.

When comparing the calculated MP from the test lung with the MP calculated at the ventilator, it is obvious that the measurements at the ventilator cannot be used to give an indication for the MP which is transferred to the lung. As predicted, there is a signifi-

cant difference between both methods for MP calculation. This means that unlike in CMV, pressures measured at the ventilator can not be used for the calculation of the MP.

In our theoretical approach we used the transfer function to estimate the MP of the lung, based on the MP of the oscillator. In this function we used the tube resistance, which was calculated by dividing peak dP by peak flows. Due to turbulent flow and leakage however, it is difficult to calculate this resistance precisely. This means the estimation of MP with the transfer function is likely to deviate from the actual MP. A further elaboration of the theoretical approach can be found in appendix B.

The  $MP_{ED}$  was calculated using a conventional and a direct method. Because the conventional method is most commonly used, the MP calculated by this method was used in the statistical analysis[25, 31]. However, the direct method might give a more accurate outcome. The conventional method uses an extra step in which the volume is calculated by taking the cumulative integral of the flow. By doing this, the volume signal is shortened, because the value of one volume sample is determined by the integration of two samples of the flow signal. This shortening makes the volume signal slightly different from reality. The second method, on the other hand, does not involve an extra integration step and calculates the MP directly from the flow signal, which makes it the method of choice in the case of a low sample rate.

From the results of the measurements we were able to make a linear multivariable regression model. We made an application for clinical use (see appendix C) that shows a good reflection of the MP when using realistic input parameters.

When comparing the MP values using adult ETT sizes to previously measured MPs in CMV, we can conclude that the mean and median values of the MP are much higher in HFOV than in CMV. A study which used ICU data of previously conducted studies reports a median MP of 22.5 J/min in adults, whereas our reported median by adult tube sizes (ETT 8) is 66.7 J/min [25]. This is much higher, but also includes unrealistic settings of the ventilator, which makes it difficult to compare the median values of MP in HFOV with CMV. Furthermore, both an animal study and a clinical study reported a significant higher survival rate when the MP at day one is below 12 J/min [32, 33]. It is not known yet whether or not this value holds when using HFOV. None of these studies included paediatric patients, which makes it uncertain whether or not these outcomes are usable when ventilating children.

In order to obtain our results, we made some assumptions. When calculating the  $MP_{RD}$  for example, we used the calibrated resistor values. Due to the turbulent flow ( $Re > 10000$ ) however, these values underestimate the real resistance, which results in an underestimation of the mechanical power. Given the absence of a pressure measurement between the tube and the resistor, there was no easy method to calculate the actual resistance. However, in clinical practice the total resistance and compliance are always estimated, so this error should have no large effect on the clinical usage of the MP.

Also the used data was initially not synchronised, which means the same sample number of different measured variables did not match the same point in time. Since corresponding time frames are essential for calculating the MP, we made an approximated synchronisation of all the variables by searching the start of expiration for each breath. Unfortunately, there is no way to be sure this onset is 100% correct and thus flows and pressures are not

‘matched’ entirely well. This could lead to MP outcomes that differ slightly from the actual MP.

During the calculations, we assumed there was no loss of flow due to other compliances in the system. This is probably not entirely true though, since energy loss is a common phenomenon in any system. However, this energy loss is very small and can therefore negligible.

Since this study is performed as a bench test study, it has some limitations. This is the case due to the absence of various dynamic processes normally happening in the lung, for example resonance of the body and the influence of surfactant. These processes cannot be induced in a rigid glass bottle, which simulates a static compliance. More dynamic lung models, for example the Michigan Test Lung, could not be used because the high frequency would induce too much resonance and thereby failure of the system. However, by using this bench test we were able to measure the pressure in the lung for different circumstances which is not possible in children or animals. Thereby this study gives very valuable information that could otherwise not be obtained.

In our calculations, the pressure and compliance of the lung and the added resistance were known, which is why it was possible to determine the mechanical power in multiple ways. In practice however, these values for a patient are not available or easily measurable and have to be estimated.

Another limitation of this study is the occurrence of some inaccurate measurements due to capping of the flow sensor at high flows. To overcome this problem, we used other data collected with the same bench model, in which another flow sensor was used. The pressure sensor was also placed on a different location in the test lung compared to the original measurements. Although this might result in some inconsistencies, the inaccuracy due to these inconsistencies is probably a lot less than when using the first inaccurate measurements.

Recently, there were some doubts whether the MP gives a good indication for the chance of VILI[27]. The concept of MP implies a positive linear relationship between MP and PEEP ( $CDP^{-1/2}$  dP), although some trials showed that a higher PEEP is associated with improved survival in the case of ARDS[4]. This is also confirmed by an animal study, in which the parts of ventilation represented by  $MPE_{peep}$  appeared to be less harmful than the parts represented by  $MP_{ED}$ [26]. It is also not clear yet which subcomponent of the MP, elastic or resistive, has the greatest correlation with VILI[34]. Therefore the elastic and resistive MPs were calculated separately in anticipation of possible future insights on the distribution of the MP. Furthermore, it is known that strain has a large impact on VILI[35]. Four-dimensional computed tomography shows that HFOV gives less strain on the lung than CMV, which suggests that the  $MP_{ED}$  is less in HFOV[36]. This means that the  $MP_{RD}$  must be larger for the same power input. However, this MP loss could also take place in the tube, instead of in the conducting airways, which makes it difficult to determine the influence of the separate parts of MP on the chance of VILI.

## **6 Conclusion**

In this study, we were able to determine the influence of different parameters on the MP in HFOV, using a multivariable regression model. We can conclude that MP rises for bigger tube size and higher power settings, the latter especially in smaller tubes. MP declines for higher frequencies whereas compliance has only little effect. MP in HFOV appears to be higher than in CMV, although this holds only for adults. We calculated three parts of the MP in anticipation of future insights on the distribution of the MP in these components and further research in the development of VILI due to MP.

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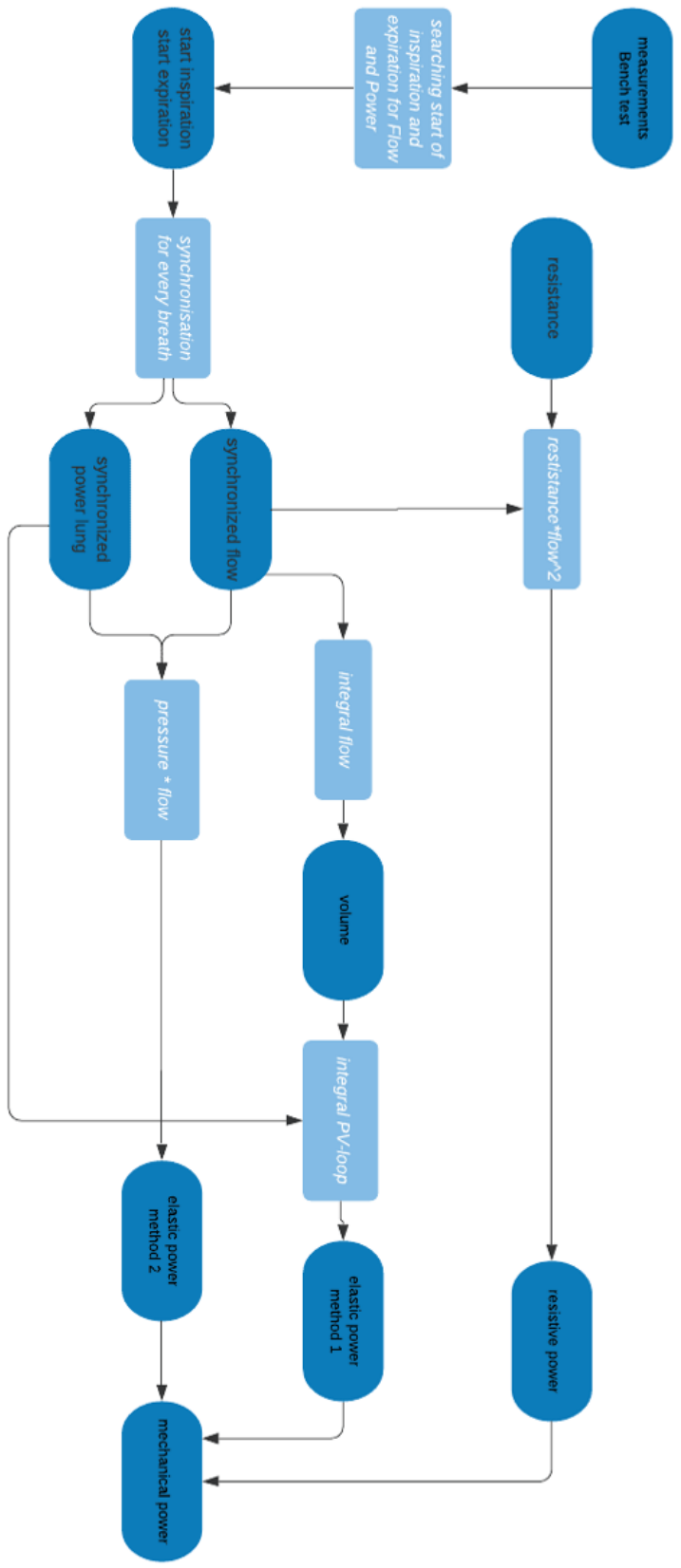
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# Appendices

## A Overview of Matlab code

Figure 8: Overview of the code used in Matlab in order to calculate the MP



## B Theoretical calculation of the MP in HFOV

From figure 2, we derived the amplitude transfer function of Plung/Posc

$$1: |jH(f)| = \frac{1}{1 + (f \cdot R \cdot C)^2}$$

The basic formula describing the MP is given by

$$2: MP = MP_{ED} + MP_{RD} = P_{lung} \cdot V + R \cdot V^2$$

When applying (1) to (2), we can rewrite equation 2 to

$$3: MP = |jH(f)| \cdot P_{osc} \cdot V^0 + R \cdot V^2$$

As can be seen from the formulas, for method (2) you need Plung, which is difficult to measure in real life, while method (3) only uses Posc. In this way, we are able to estimate the pressure in the lung, which makes it possible to directly calculate the MP using pressures measured at the ventilator in clinical practice. However, there are some limitations using this method.

First of all, to correctly estimate the pressure in the lung, the resistance and compliance of the lung needs to be known. These are variables which are always estimated in clinical practice, but can have rather large influence on the calculation of the MP. This holds especially for the resistance, since this is a rather large value compared to the compliance. Furthermore, the resistance used in this formula is an addition of the tube resistance and the airway resistance. Both resistances are not constant when using HFOV, due to turbulence. This makes it difficult to get a realistic estimation of the total resistance.

Second, after comparing the results of the MP when using (3), we get a large difference in comparison with the MP when using (2). This can be explained when looking at the frequency spectrum of the pressure signal. Mostly because of the 1:2 Inspiration : Expiration ratio and of possible artefacts, the pressure signal consists of multiple frequencies (figure 7).

When rewriting the pressure signal as a Fourier series and calculating the MP using (3), we see much smaller differences than when using only the frequency setting. The reported differences between the calculated and measured MP are still rather high, within the testing sample up to 50%, but are much lower than the up to 5000% using only the main frequency in the signal. We were not able to find any systematic deviation between the measured and calculated MP

There are multiple possible explanations for the difference between the MP when using (2), with Plung and (3), with Posc, after correcting for the frequency spectrum. First of all, only the peaks of the frequency spectrum were used in the Fourier series of the signal, because most of the other parts of the frequency spectrum are leakage. This can cause a difference when using the transfer function. Furthermore the signal generated at the ventilator is actually a damped block signal, which is an indication that only looking at

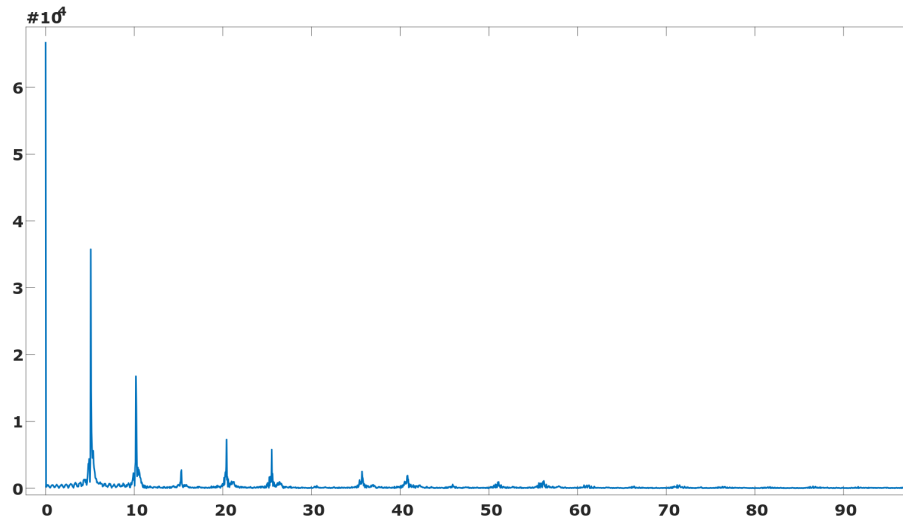


Figure 9: frequency spectrum of the pressure measured at the ventilator at a frequency of 5 Hz

the peaks of the spectrum is probably not enough. Second, the resistance of the tube was estimated using the measurements with zero airway resistance. As stated before, this resistance is not stable, which could explain the difference between the calculation of the MP using the flow and pressure in the lung (2) and using the transfer function (3). However, using an extra pressure sensor at the end of the tube can eliminate the need for an accurate resistance value of the tube, leaving only an estimation of the airway resistance. Third, using the transfer function calculation method in Matlab, the calculated pressures differences in the lung calculated are much smaller than the measured values. This is an indication that the model used is not sufficient for the calculation of the pressures in the lung, probably due to interference or resonance.

## C Application for in the clinic

### Mechanical power in HFOV

Selecteer de juiste ETT:  ▼

Geef een schatting van de luchtweg weerstand (cmH<sub>2</sub>O/L/s):

Geef een schatting van de long compliantie (mL/cmH<sub>2</sub>O):

Voer ventilator instellingen in:

Power (%):

Frequency (Hz):

CDP (cmH<sub>2</sub>O):

Biasflow: 20 (L/min)

I:E ratio: 1:2

**Total mechanical power:**

**7.36 J/min**

**Resistive mechanical power:**

**2.55 J/min**

**Elastic mechanical power:**

**4.81 J/min**

## D Additional boxplots of the results

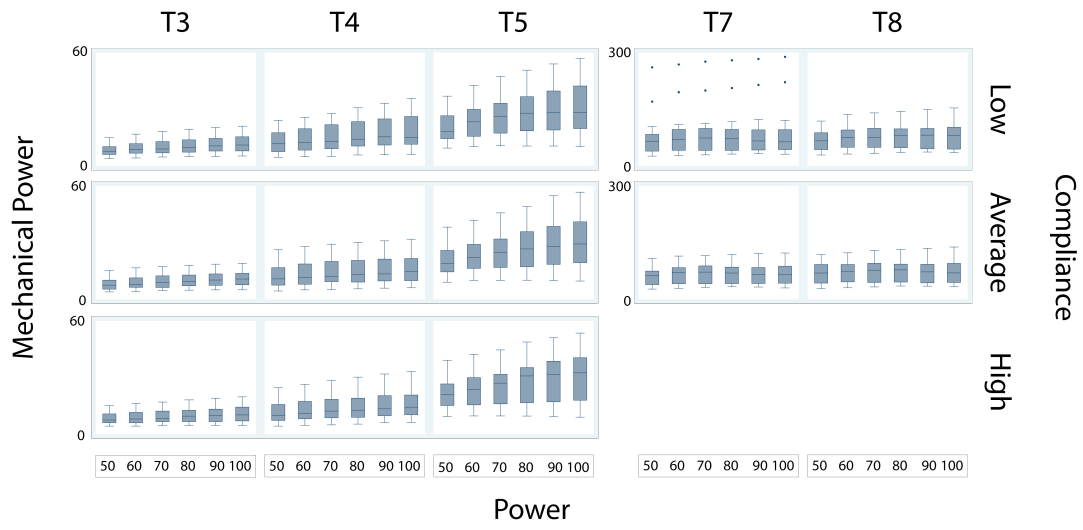


Figure 10: Boxplot of the MP sorted by the power setting

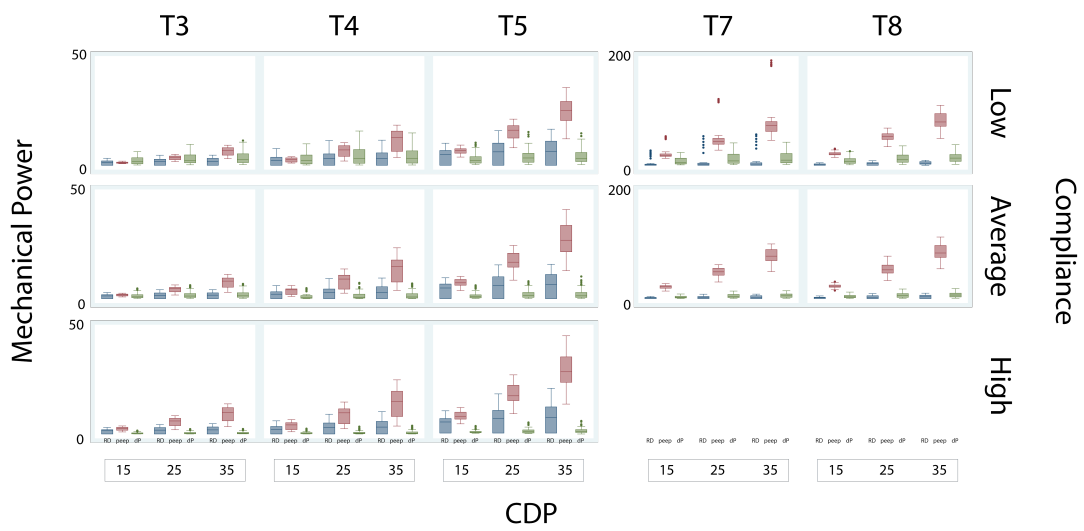


Figure 11: Boxplot of the different parts of MP sorted by CDP



