Fellows Column: Servo Pressure Relationship in High-Frequency Jet Ventilation in Neonates

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Introduction:

High-Frequency Jet Ventilation (HFJV) is a form of mechanical ventilation that was first established by Bert Bunnell, ScD, in the late 1900s. The HFJV became FDA approved for use in neonates in 1988. It has been shown to improve oxygenation and ventilation in premature neonates with respiratory distress syndrome, bronchopulmonary dysplasia, or evolving chronic lung disease, as well as in neonates with air leak syndromes. (1-4)

Understanding the principles through which the HFJV works is integral to understanding servo pressure and its variability. First, fresh, inspired gas actively jets down the center of the airway in a laminar fashion. It does so at very high rates, ranging anywhere from 240—660 beats per minute (bpm). By employing high rates, the HFJV utilizes very small tidal volumes, approximating 1mL/kg. The inspired gas travels down the center of the airway in a laminar fashion, where resistance to flow is lowest. In doing so, effective dead space volume becomes reduced, as only a portion of the anatomic dead space is being used. This process represents active inhalation from the HFJV.(5-7)

Following this active process, passively expired gas exits around the circumference of the airway walls in an annular fashion. Exhilation utilizes the path of least resistance, by making use of the "unused" dead space path, around the center of the highly accelerated inspired gas. The cumulative effect facilitates mucociliary clearance in the airways. (5, 7, 8) Exhalation from the HFJV is passive, as demonstrated in Figure 1.

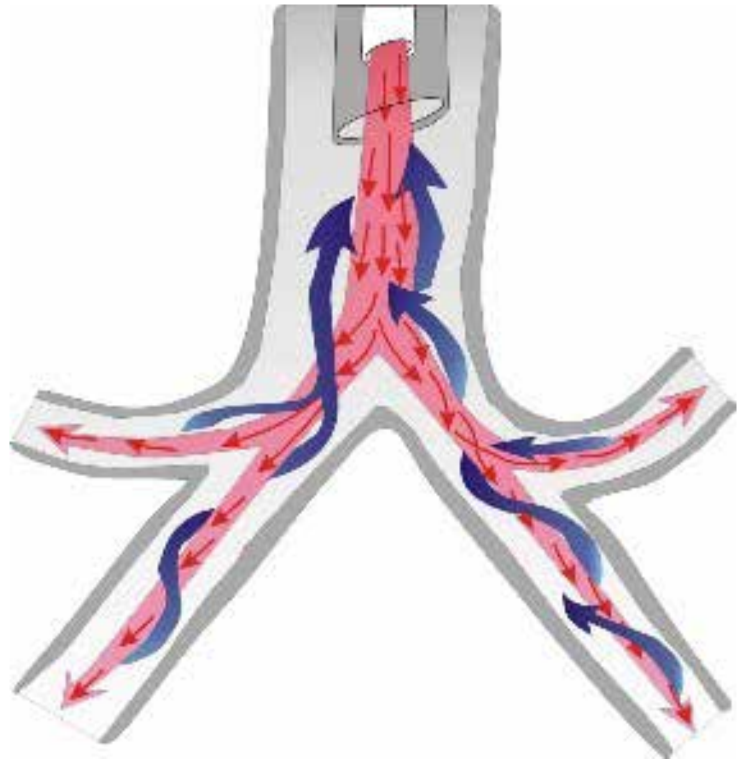

Figure 1: [Adapted from Bunnell, Inc] Accelerated and actively inspired gas travels down the center of the airway in a laminar fashion, as demonstrated in red. Passively expired gas then exits in an annular fashion around the circumference of the airway, as demonstrated in blue.

The advantage of this type of ventilation strategy is threefold. First, the HFJV allows one to effectively ventilate and oxygenate at lower mean airway pressures than that required for conventional ventilation. Second, the use of smaller tidal volumes permits an ability to use higher positive end-expiratory pressure (PEEP) to optimize oxygenation. Higher PEEP use in HFJV has been associated with improving lung compliance and reducing ventilator requirements. Finally, with smaller tidal volumes, lung compliance has less of an influence on gas distribution within the lungs. (7, 9-11). Progressing to the right in figure 2, at higher PEEP, this volume increases further, with a higher risk of ongoing lung injury within the volutrauma zone. In contrast, with HFJV, the smaller tidal volumes at higher rates remain to allow ventilation with ad-

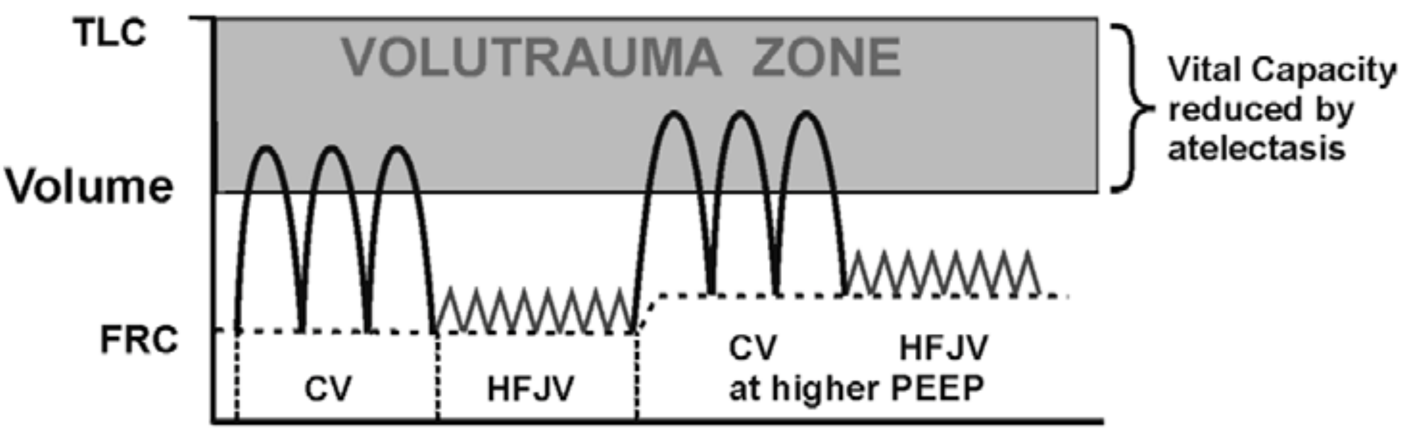

Figure 2: [Adapted from Bunnell, Inc] A conventional lung volume curve is depicted with examples of Conventional Ventilation (CV) and HFJV. As demonstrated from left to right, when ventilating to optimize Functional Residual Capacity (FRC), tidal volumes for CV are high, beyond the limits of physiologic tidal volume (TV) and risking volutrauma and subsequent lung injury, (reaching the limits of Total Lung Capacity (TLC) and reducing vital capacity).

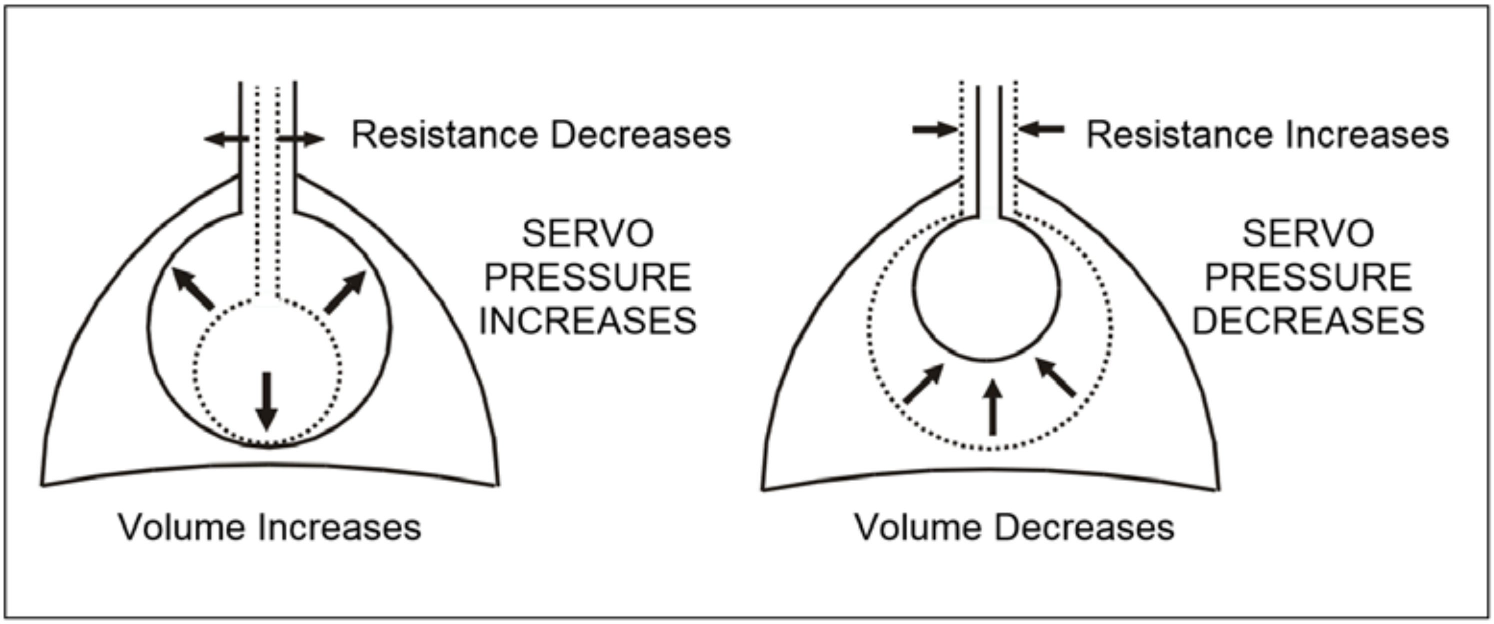

Figure 3: [Adapted from Bunnell, Inc] Servo pressure, as affected by airway resistance and lung volumes. On the left, note that servo pressure increases as airway resistance decreases and/or while compliance is high or lung volumes increase. On the right, note that servo pressure decreases as airway resistance increases and/or while compliance is low or lung volumes decrease.

equate FRC and within a physiologic TV range, allowing us to manipulate PEEP at higher values. With higher PEEP, TV remains within a safe physiologic zone, allowing adequate ventilation as well as optimal oxygenation without risking the volutrauma seen with CV.

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Servo pressure (SP) in HFJV is the driving pressure required to regulate flow. SP automatically rises and falls to ensure that the positive inspiratory pressure (PIP) dialed into the ventilator is delivered, despite changes in a neonate's lung mechanics. In general, increased resistance and decreased compliance generate lower SP. In contrast, decreased resistance and increased compliance generate higher SP. (12) Lung volumes also affect servo pressure, as demonstrated in Figure 3.

Hypothesis:

Servo pressure variability in HFJV has not previously been studied. We attempted to study changes in servo pressures for variable compliance at different pressures and rate settings in a lung model. We predicted that a relationship exists for servo pressure changes at variable settings and variable lung volumes.

Methods:

For this investigation, the HFJV Model 203 was utilized. Lung models with different compliance were predicated by utilizing

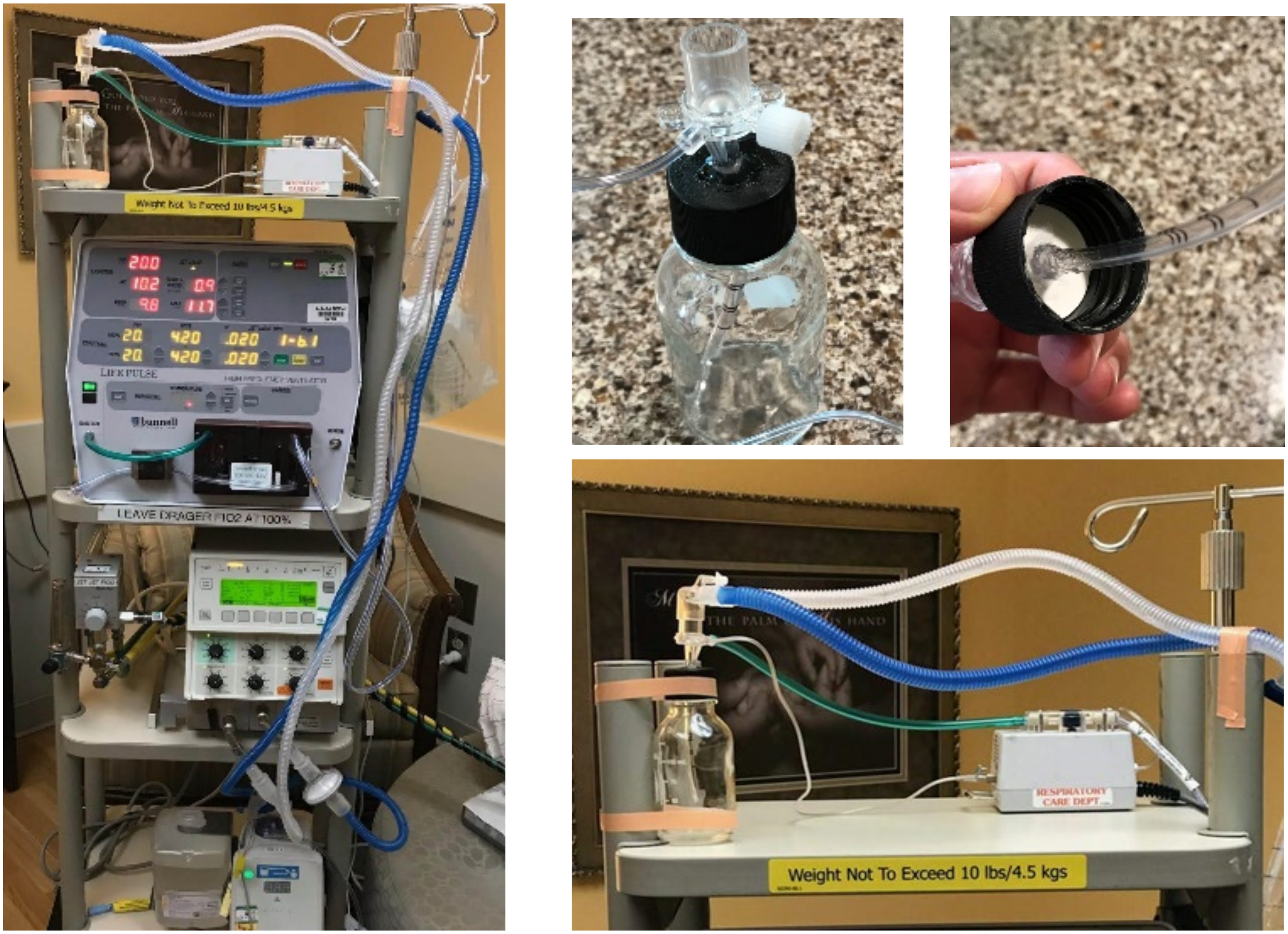


Figure 4: From left to right in a clockwise direction (a-d): A. HFJV connected to test lung model predicated by a glass bottle, via ETT and ETT adapter. B. Test lung with bottle cap sealed to ETT and connected via ETT adapter. C. Silicone gel dried in inside of bottle cap to ETT to ensure no air leak in the system. D. Test lung connected via ETT adapter to tubing attached to HFJV.

sealed glass bottles at different volumes (150 mL and 500 mL volumes). Each glass bottle represented a different lung volume. For this study, it was presumed that higher lung volumes contributed to increasing compliance for each lung model. 4mm holes were drilled into the bottle caps of each glass container. A 3.5-mm endotracheal tube (ETT) was sealed into the bottle cap using silicone gel, which, once dried, guaranteed no air leak. The ETT was then connected to the ETT adapter and subsequently connected to HFJV. See Figure 4. HFJV settings were adjusted, and subsequent SP recorded for each test lung model at 150 mL and 500 mL. Settings used included PEEP of 10-15, PIP from 20-40 at intervals of 4, rates at 240, 300, 360, 400 and 420, and with a fixed inspiratory time of 0.020 seconds.

Additionally, Inspiratory-to-expiratory ratio (I:E ratio), change in pressure (Delta-P), and mean airway pressure (MAP) were also recorded. Data sets were mapped in graphical form using Statistica® Software Technology. Data were modeled to predict SP at each of the settings.

Results:

At the 150 mL lung volume, representative of lower lung compliance, when PEEP and rate were fixed, incremental increases in

PEEP: **10 – 15** *(10, 11, 12, 13, 14, 15)*	**PIP:** **20 - 40** *(20, 24, 28, 32, 36, 40)*	**Rate:** **240 – 420** *(240, 300, 360, 400, 420)*	**I-time** **(0.02 *sec*)**	**SERVO PRESSURE**	***P*-value**
Fixed	Fixed	Incremental increase	Fixed	1 – 4.2	0.88
Fixed	Incremental increase	Fixed	Fixed	**0.9 – 4.7**	**<0.0001**
Incremental increase	Fixed	Fixed	Fixed	**1.1 – 4.3**	**<0.00001**

Figure 5: As depicted in the table above, each measured parameter from the HFJV is listed with its subsequent SP, i-time, and p-values for 150 mL lung volume. Note the increasing statistical significance that increases in PIP and PEEP have on SP

PEEP: **10 – 15** *(10, 11, 12, 13, 14, 15)*	**PIP:** **20 - 40** *(20, 24, 28, 32, 36, 40)*	**Rate:** **240 – 420** *(240, 300, 360, 400, 420)*	**I-time** **(0.02 *sec*)**	**SERVO PRESSURE**	***P*-value**
Fixed	Fixed	Incremental increase	Fixed	1.8 – 8.5	0.88
Fixed	Incremental increase	Fixed	Fixed	**2.1 – 9.2**	**<0.0001**
Incremental increase	Fixed	Fixed	Fixed	**1.9 – 8.6**	**<0.00001**

Figure 6: As depicted in the table above, each measured parameter from the HFJV is listed with its subsequent SP, i-time, and p-values for 500 mL lung volume. Note the increasing statistical significance that increases in PIP and PEEP have on SP.

PIP led to increasing SP ranging from 0.9 – 4.7, which reached statistical significance (p = <0.0001). When rate and PIP were fixed, incremental increases in PEEP led to further significant ranges in SP from 1.1 – 4.3 (p = <0.00001). However, when PEEP and PIP were fixed, incremental increases in rate led to only modest changes in SP that were not statistically significant (p = 0.88). See Figure 5.

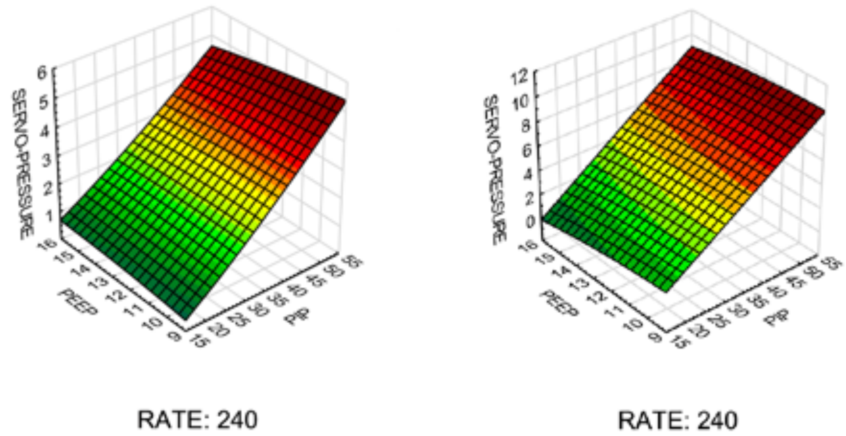
At the 500 mL lung volume, representative of higher lung compliance, when PEEP and rate were fixed, incremental increases in PIP led to increasing SP ranging from 2.1 – 9.2, which reached statistical significance (p = <0.0001). When rate and PIP were fixed, incremental increases in PEEP led to further significant ranges in SP from 1.9 – 8.6 (p = <0.00001). However, when PEEP and PIP were fixed, incremental increases in rate led to only modest changes in SP that were not statistically significant (p = 0.88). See Figure 6.

Furthermore, when datasets were mapped out into graphical form, using Statistica® Software Technology, planar 3-Dimensional graphs were formulated, each categorized by rate, with SP depicted for the variable PIP and PEEP. Note that the x-axis represents PIP, the y-axis represents PEEP, and SP are depicted on the z-axis. See Figure 7 –11 for summary graphs representing lung volumes comparing 150 mL and 500 mL, respectively. Also note the change in colors on each graph as they represent changes in quantitative SP values, for each variable PIP and PEEP setting.

In addition to mapping out datasets in graphical form, a quantitative relationship was calculated based on the relationship changes for servo pressure at each of the settings tested. This resultant calculation for servo pressure was generated for each dataset and shown above each summary graph, in Figures 7 – 11.

$$\textbf{Servo-Pressure (150mL)} = -2.7602 + 0.1281x + 0.228y + 0.0004x^2 - 0.0038xy - 0.0051y^2$$

$$\textbf{Servo-Pressure (500mL)} = -2.2726 + 0.2007x + 0.1925y - 3.4265^{E\text{-}5}x^2 + 0.002xy +$$

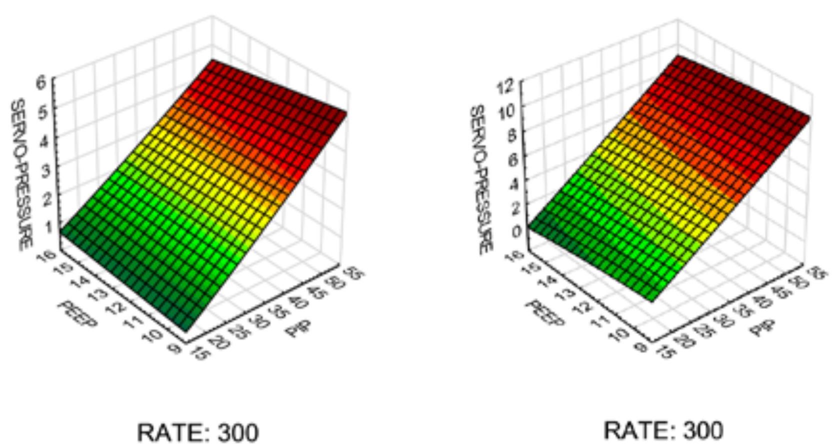


x **= PIP**
y **= PEEP**
z **= Servo Pressure**

Figure 7: 3-Dimensional planar graphs for lung volumes at 150 mL (left) compared to 500 mL (right) for Rate at 240 bpm. Note the quantitative calculation for SP generated based on these results.

$$\textbf{Servo-Pressure (150mL)} = -2.2041 + 0.1439x + 0.1073y + 0.0002x^2 - 0.004xy - 0.0004y^2$$

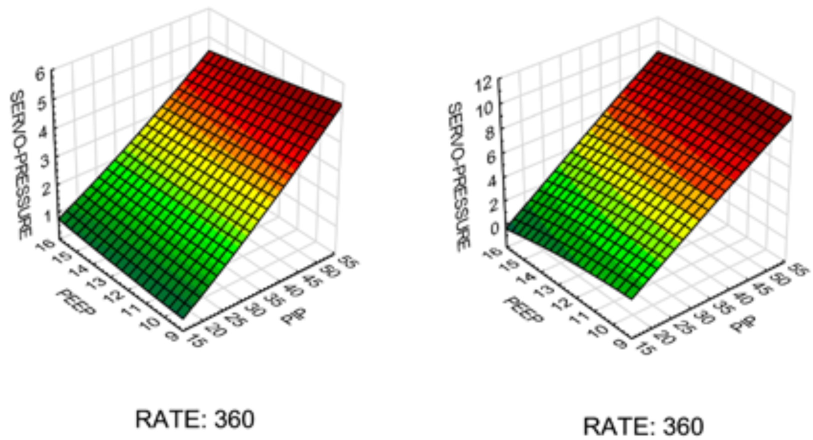
$$\textbf{Servo-Pressure (500mL)} = -1.4741 + 0.2033x + 0.0521y + 0.0002x^2 + 0.0007xy - 0.0101y^2$$



x **= PIP**
y **= PEEP**
z **= Servo Pressure**

Figure 8: 3-Dimensional planar graphs for lung volumes at 150 mL (left) compared to 500 mL (right) for Rate at 300 bpm. Note the quantitative calculation for SP generated based on these results.

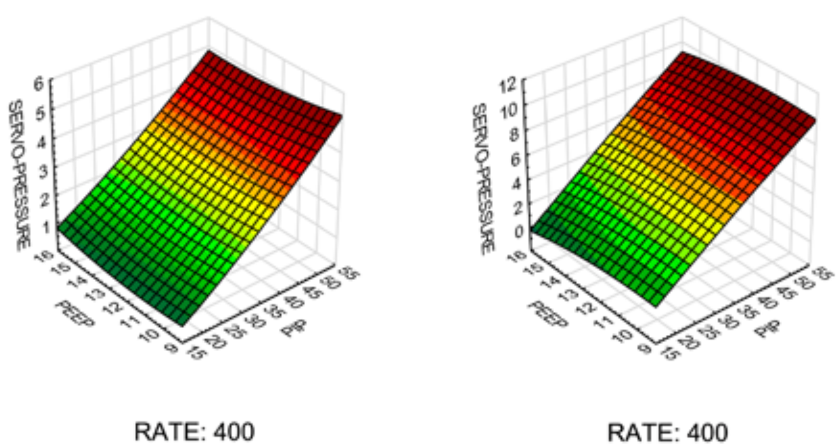
Servo-Pressure (150mL) = $-1.7579 + 0.132x + 0.0587y + 0.0004x^2 - 0.004xy + 0.0018y^2$
Servo-Pressure (500mL) = $-2.981 + 0.2115x + 0.2956y - 0.0003x^2 + 0.0029xy - 0.0232y^2$



x = PIP
y = PEEP
z = Servo Pressure

Figure 9: 3-Dimensional planar graphs for lung volumes at 150 mL (left) compared to 500 mL (right) for Rate at 360 bpm. Note the quantitative calculation for SP generated based on these results.

Servo-Pressure (150mL) = $-0.722 + 0.103x - 0.2936y + 0.0005x^2 - 0.0022xy + 0.0144y^2$
Servo-Pressure (500mL) = $-5.366 + 0.2344x + 0.5889y - 0.0004x^2 + 0.002xy - 0.0321y^2$

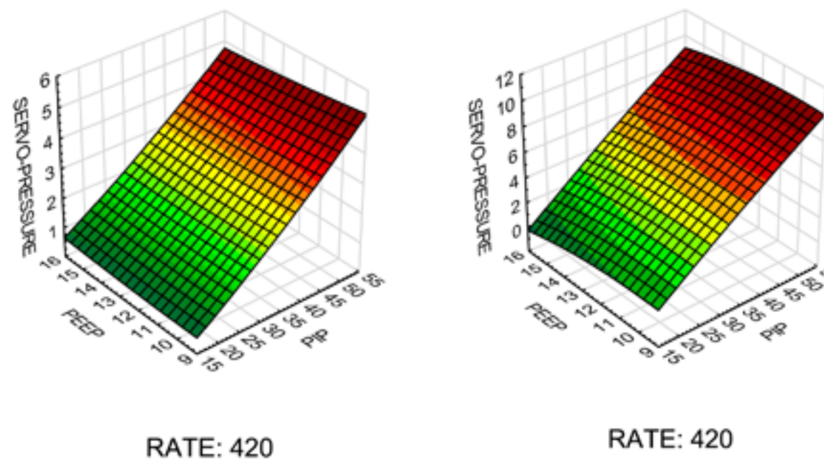


x = PIP
y = PEEP
z = Servo Pressure

Figure 10: 3-Dimensional planar graphs for lung volumes at 150 mL (left) compared to 500 mL (right) for Rate at 400 bpm. Note the quantitative calculation for SP generated based on these results.

Servo-Pressure (150mL) = $-0.7505 + 0.1073x - 0.047y + 0.0004x^2 - 0.0021xy + 0.0037y^2$

Servo-Pressure (500mL) = $-6.0173 + 0.2565x + 0.6429y - 0.0005x^2 + 0.0008xy - 0.0331y^2$



x = PIP
y = PEEP
z = Servo Pressure

Figure 11: 3-Dimensional planar graphs for lung volumes at 150 mL (left) compared to 500 mL (right) for Rate at 420 bpm. Note the quantitative calculation for SP generated based on these results.

Discussion:

High-Frequency Jet Ventilation has been associated with significant improvement in ventilator outcomes when compared with conventional ventilation. (2, 6) In particular, it has been found to improve outcomes when lung disease is characterized by non-homogeneous parenchyma. (13) Although initially used for rescue mode ventilation strategies, HFJV has been shown to be applicable to transport and other scenarios where high-frequency ventilation is indicated. (10, 14, 15) There are certain situations where High-Frequency Jet Ventilation may outperform other oscillatory devices. (7) The evaluation of mean airway pressure, optimizing functional residual capacity is critical to the success of the modality. (3-6) Servo pressure is a method of quantifying High-Frequency Jet mean airway pressure in a way that may be important in defining optimal functional residual capacity.(1, 10-12, 16)

This study confirmed the presence of servo pressure variability. For example, low lung volumes were associated with lower SP. This relationship may potentially be representative of the presumed lower lung compliance at that lung volume. Similarly, high lung volumes were associated with higher SP. This relationship may also be based on presumed higher lung compliance at that higher lung volume. The limitation of this study in making this conclusion, however, is the presumption that larger lung volumes correlated with larger or increased compliance in the system. However, the inherent compliance of a glass bottle remains fixed and is not dynamic. This “static fixture” limits the conclusions we can draw regarding compliance and its relationship with servo pressure. Future directions for a follow-up study may include developing a test lung model with dynamic compliance, rather than a fixed compliance system.

> ***“An integral mathematical relationship does exist to calculate SP’s, which enable adequate ventilation delivery at different lung volumes. This may be applied clinically if SP can be monitored and tracked during the time neonates spend on the HFJV.”***

Another limitation of this study is that airway resistance was a fixed parameter. A 3.5 mm ETT was utilized in carrying out this study, without any applied changes in this airway resistance. Therefore, changes in airway resistance were not studied against SP variability for this study. Future directions for a follow-up study may include changing the size, and hence, the resistance of the ETT while assessing servo pressure variability.

An integral mathematical relationship does exist to calculate SP's, which enable adequate ventilation delivery at different lung volumes. This may be applied clinically if SP can be monitored and tracked during the time neonates spend on the HFJV. For impediments in ventilation or oxygenation, i.e., hypercapnea, RDS, or pneumothorax, SP can be assessed, and variable settings on HFJV can be predicated by utilizing the calculations obtained from this study. (12) However, more extensive clinical studies would first be required to evaluate this calculation and confirm its relationship in vivo.

References:

1. *Pagani G, Rezzonico R, Marini A. Trials of high-frequency jet ventilation in preterm infants with severe respiratory disease. Acta Paediatr Scand. 1985;74(5):681-6.*
2. *Bancalari A, Gerhardt T, Bancalari E, Suguihara C, Hehre D, Reifenberg L, et al. Gas trapping with high-frequency ventilation: jet versus oscillatory ventilation. J Pediatr. 1987;110(4):617-22.*
3. *Carlo WA, Chatburn RL, Martin RJ. Randomized trial of high-frequency jet ventilation versus conventional ventilation in respiratory distress syndrome. J Pediatr. 1987;110(2):275-82.*
4. *Spitzer AR, Butler S, Fox WW. Ventilatory response to combined high frequency jet ventilation and conventional mechanical ventilation for the rescue treatment of severe neonatal lung disease. Pediatric Pulmonology. 1989;7(4):244-50.*
5. *Belaguid A, Guenard H. Variations in flows and pressures during jet ventilation in the infant: a model study. Pediatr Pulmonol. 1994;17(3):183-8.*
6. *Keszler M, Modanlou HD, Brudno DS, Clark FI, Cohen RS, Ryan RM, et al. Multicenter controlled clinical trial of high-frequency jet ventilation in preterm infants with uncomplicated respiratory distress syndrome. Pediatrics. 1997;100(4):593-9.*
7. *Friedlich P, Subramanian N, Sebald M, Noori S, Seri I. Use of high-frequency jet ventilation in neonates with hypoxemia refractory to high-frequency oscillatory ventilation. J Matern Fetal Neonatal Med. 2003;13(6):398-402.*
8. *Musk GC, Polglase GR, Bunnell JB, McLean CJ, Nitsos I, Song Y, et al. High positive end-expiratory pressure during high-frequency jet ventilation improves oxygenation and ventilation in preterm lambs. Pediatr Res. 2011;69(4):319-24.*
9. *Plavka R, Dokoupilova M, Pazderova L, Kopecky P, Sebron V, Zapadlo M, et al. High-frequency jet ventilation improves gas exchange in extremely immature infants with evolving chronic lung disease. Am J Perinatol. 2006;23(8):467-72.*
10. *Bass AL, Gentile MA, Heinz JP, Craig DM, Hamel DS, Cheifetz IM. Setting positive end-expiratory pressure during jet ventilation to replicate the mean airway pressure of oscillatory ventilation. Respir Care. 2007;52(1):50-5.*
11. *Musk GC, Polglase GR, Bunnell JB, Nitsos I, Tingay D, Pillow JJ. A comparison of high-frequency jet ventilation and synchronised intermittent mandatory ventilation in preterm lambs. Pediatric Pulmonology. 2015;50(12):1286-93.*
12. *Patel A, Tong C, Goldstein M. Relationship of Servo Pressure in High Frequency Jet Ventilation in Lung Models with Variable Compliance for Neonates. Pediatrics for the 21st Century; July 22, 2019: American Academy of Pediatrics; 2019.*
13. *Mokra D, Mikusiakova LT, Mikolka P, Kosutova P, Jurcek M, Kolomaznik M, et al. High-Frequency Jet Ventilation against Small-Volume Conventional Mechanical Ventilation in the Rabbit Models of Neonatal Acute Lung Injury. Adv Exp Med Biol. 2016;912:83-93.*
14. *Ethawi YH, Abou Mehrem A, Minski J, Ruth CA, Davis PG. High frequency jet ventilation versus high frequency oscillatory ventilation for pulmonary dysfunction in preterm infants. Cochrane Database Syst Rev. 2016(5):CD010548.*
15. *Mainali ES, Greene C, Rozycki HJ, Gutcher GR. Safety and efficacy of high-frequency jet ventilation in neonatal transport. J Perinatol. 2007;27(10):609-13.*
16. *Musk GC, Polglase GR, Song Y, Pillow JJ. Impact of conventional breath inspiratory time during high-frequency jet ventilation in preterm lambs. Neonatology. 2012;101(4):267-73.*

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