Measuring the Functional Residual Capacity in Ventilated Neonates

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Abstract

Dr. William Walsh, M.D. and the Division of Neonatology at Vanderbilt Children’s Hospital have an interest in determining the functional residual capacity (FRC) in neonates who are mechanically ventilated. Such information will allow doctors and researchers to optimize ventilator settings so as to prevent shunting or to prevent over oxygenation of neonates coming in at 100% oxygen with air in lungs. Additionally, knowing the FRC will allow physicians to utilize appropriate methods to facilitate breathing in neonates suffering from lung pathologies, and specifically allow physicians to assess the need for extracorporeal membrane oxygenation (ECMO). Due to the critical nature of mechanically ventilated neonates, methods must be simple, non-invasive, and allow free, non-obstructive access to neonates. The proposed device, compatible with both continuous positive airway pressure (CPAP) and mechanical ventilation, consists of a helium sensor, air pump, three-way valve, anesthesia bag in an airtight container, and standard medical tubing. The device, which uses a modified version of the standard helium dilution method, allows for FRC measurements and accounts for the effect of leaks within the system by expressing them as an exponential function of time and measuring the helium concentration at two time points—45 s and 60 s. This estimate of the final helium concentration can then be used in the standard helium dilution equation to calculate the FRC. Testing of the prototype device did not yield reliable results due to what we believe was inadequate gas mixing within the sensing circuit. Thus, the device was instead simulated using a simple, two compartment model. For a circuit volume of 185 ml and a neonate with a FRC of 26.5 ml, and using normal parameters for ventilated neonates, both the concentration of helium in the measuring circuit and oxygen content of the lungs were simulated for multiple leak states. For a neonate with normal ventilation parameters, the oxygen content of the lungs remains at safe levels over the measurement period. To ensure adequate gas mixing, the total volume of the sensing circuit must remain as low as possible without compromising the neonate’s oxygen levels.
Introduction

Functional residual capacity (FRC) of the human lung is the volume remaining in the lungs at resting expiratory level, meaning the volume at the end of normal, not forced exhalation. It is equivalent to the alveolar volume which contains 60-70% of the total lung volume, or more specifically, it is the sum of the residual volume and the expiratory reserve volume. Normal FRC in adults ranges between 1.8 to 3.4 L [1], while estimated FRC in healthy neonates is approximately 25 ml, and is known to be a function of the baby’s total weight.

Determination of the functional residual capacity is most commonly measured by helium dilution method, nitrogen washout technique, or body plethysmography (body box). In healthy subjects all of the above methods show good agreement; however, in obstructive lung disease, helium dilution method and nitrogen washout technique underestimate FRC because they only measure areas of lung that are in communication with the system and do not measure trapped gas. Nevertheless, they are the two most common methods used to measure FRC because they are effectively simpler to perform and much more cost efficient than the body-box.

Helium dilution requires the patient to breathe from a known volume of gas with a known helium concentration. The gas in the lungs dilutes the helium taken in causing the helium concentration to drop. After the gas has had time to equilibrate with the patient’s lungs, the concentration is measured again. The FRC can be calculated using,

\[ FRC = V \left( \frac{C_i}{C_f} - 1 \right) \]
where $C_i$ and $C_f$ are the initial and final helium concentrations, respectively, and $V$ is the initial volume of the closed system. While potentially any gas can be used, helium has some distinct advantages in that it is physiologically inert, and is not absorbed by the blood in any appreciable amount. Additionally, it is relatively common and inexpensive. Standard helium dilution does have a drawback as well, as it requires a closed system. Any leaks, such as those from an uncuffed endotracheal tube, which is used to intubate the neonate, will make the measurement invalid.

The nitrogen washout technique is based on the underlying fact that the unknown functional residual capacity contains about 78% nitrogen and an unknown amount of oxygen and carbon dioxide. Nitrogen in the lungs is consequently “washed out” by breathing in 100% oxygen beginning at the end of exhalation for several minutes. The exhaled volume is then collected until the expired nitrogen concentration falls between 1 and 1.5% by volume. By measuring the volume of nitrogen in the FRC and applying a concentration dilution formula, the FRC volume can be determined [2].

Although neonatal functional residual capacity has successfully been measured using the helium dilution method and the nitrogen washout technique, the methods have seldom been applied to mechanically ventilated neonates who suffer from various lung pathologies and complications. Furthermore, extensive patent searches on the U.S. Patent & Trademark Office database indicate that neither methodologies nor devices that accomplish such have been successfully patented.

The most common admitting diagnosis to the Neonatal Intensive Care Unit (NICU) is respiratory distress, and as such, the two most common methods of rehabilitation from such pathologies are continuous positive airway pressure (CPAP) and mechanical ventilation. CPAP is the application of positive pressure to the airways of the spontaneously breathing patient throughout the respiratory cycle. CPAP maintains inspiratory and expiratory pressures above ambient pressure, which results in an increase in functional residual capacity (FRC), improvement in static lung compliance, and decreased airway resistance in the
infant with unstable lung mechanics. This allows a greater volume change per unit of pressure change (i.e., greater tidal volume for a given pressure change) with subsequent reduction in the work of breathing and stabilization of minute ventilation. CPAP increases mean airway pressure, and the associated increase in FRC should improve ventilation-perfusion relationships and potentially reduce oxygen requirements. Additionally, CPAP may expand or stint upper airway structures preventing collapse and upper airway obstruction. Indications for CPAP include respiratory distress syndrome, pulmonary edema, atelectasis, apnea of prematurity, recent extubation, tracheal malacia or other similar abnormality of the lower airways, and transient tachypnea of the newborn [3].

Mechanical ventilation, the other method commonly employed in the NICU, is at base the removal of carbon dioxide from the blood, and is a function of minute ventilation (respiratory rate x tidal volume). Such ventilation can improve arterial oxygenation when either the fraction of inspired oxygen concentration (FiO₂) and/or the mean airway pressure are increased [4]. Indications for mechanical ventilation are hypoxemia/cyanosis from lung disease, which are inadequately treated with supplemental oxygen alone or with CPAP; hypoventilation or frank apnea, increased work of breathing, severe systemic disease especially with circulatory failure requiring airway control [5].

The first step in managing a patient on a ventilator is to choose appropriate goals for ventilation and oxygenation which essentially depend on the patient's pathological state. Furthermore, the appropriateness of initial ventilator support needs to be rapidly confirmed by checking the blood-gas ration within 15-20 minutes if possible, and making adjustments accordingly. Initial settings on mechanical ventilators are usually chosen based on typical minute ventilation requirements. Today, the most common method physicians can employ to optimize ventilator settings involves the usage of X-rays to help determine positive end expiratory pressure (PEEP) and O₂ saturation levels. However, there are no current well-defined parameters used to guide physicians in making the proper ventilation settings after such initial settings are in place. Instead, physicians are left to their own utility of years of experience in the field.
Unfortunately, problems arise when too small a FRC can result in the inability to oxygenate blood and possibly death if blood entering the lung actually exits the lung without coming into contact with an exchangeable gas surface; this is called shunting. Thus, current trial and error methods used to adjust ventilator settings to prevent this sort of shunting without knowing the FRC, and can cause too much PEEP or CPAP which in turn can cause barotraumas, preventing the blood from going into the lung. Furthermore, in knowing the FRC physicians can not only optimize ventilator settings to achieve maximum oxygenation of the blood, but can assess the need for extracorporeal membrane oxygenation (ECMO).

ECMO is used when a ventilator does not provide sufficient oxygen or remove enough carbon dioxide. It is a form of long-term heart-lung bypass used in infants, children, and adults in cardiac and/or respiratory failure despite maximal medical treatment. Typical respiratory failures include Acute Respiratory Distress Syndrome (ARDS), Pneumonia, Sepsis, Congenital Diaphragmatic Hernia (CDH), Pulmonary Hypertension, and inborn errors of metabolism. The process of ECMO provides that all the blood is pumped out of the body and run through an artificial heart-lung machine to oxygenate and remove carbon dioxide from the blood before it returns to the body. In some cases (about 20% of the time), babies do not improve even with the use of ECMO, and in other cases a complex problem cannot be diagnosed until after ECMO has begun. Thus, due to the invasive nature of ECMO, babies are at a greater risk for death. Nevertheless, successful ECMO takes over the work for the lungs so they can rest and heal.

Thus, the Dr. William Walsh, M.D. and the Division of Neonatology at Vanderbilt Children’s Hospital have an interest in determining the functional
residual capacity (FRC) in neonates who are mechanically ventilated. Such information will allow doctors and researchers to optimize ventilator settings so as to prevent shunting or to prevent over oxygenation of neonates coming in at 100% oxygen with air in lungs. Additionally, knowing the FRC will allow physicians to utilize appropriate methods to facilitate breathing in neonates suffering from lung pathologies, and specifically allow physicians to assess the need for ECMO. Due to the critical nature of mechanically ventilated neonates, methods must be simple, non-invasive, and allow free, non-obstructive access to neonates. Furthermore, the method must provide portability as it will be employed in the Neonatal Intensive Care Unit (NICU) which includes 60 intensive and intermediate beds, a 3 bed ECMO unit, and 10 bed intensive care nursery.

**Methodology**

**Innovation Workbench**

The Innovation Workbench software package was used to help develop ideas of how to measure the FRC within the constraints of maintaining ventilator support and working in an open system. Two possible solutions suggested by the software was to find a way to maintain ventilator support with a closed system or to devise a way to measure the FRC without using a closed system. The entirety of the Innovation Workbench process is documented in Appendix C.

**Design**

An extensive literature review has provided us with a unique solution meeting all design criterions. In “A Method for Measuring Functional Residual Capacity in Neonates with Endotracheal Tubes.” by Schwartz, Fox, and Shaffer [8], it was show that a closed circuit helium dilution technique could be used with high effectiveness in the determination of functional residual capacity and in the estimation of endotracheal tube leakage. The helium dilution technique has been proven capable of measuring the FRC without suspending neonate ventilation.
In this technique, a closed system consisting of a helium sensor, an air pump, medical grade tubing and a respirating enclosure is separated initially from the neonate and the CPAP ventilator by a three-way valve. A diagram of the closed system is shown in Figure 3. The respirating enclosure consists of an anesthesia bag and a plexiglass box with three orifices. Two of these orifices connect either end of the anesthesia bag with medical tubing from the closed helium dilution system. The third orifice opens to tubing connecting to the ventilator and allows the ventilator to apply a pressure differential between the bag and the inside of the plexiglass enclosure, thus ventilating the baby. The neonate is only ventilated via the respirating enclosure during the 60-second period of the helium dilution procedure, which will be described later. Otherwise, the neonate is ventilated via direct ventilation. The method of ventilation is controlled by the three-way valve and the baby remains ventilated in some way regardless of this valve’s position.

The initial state of the baby before the procedure is standard, direct CPAP ventilation. Before the procedure begins the air pump within the closed system must be set and the helium sensor must be recording readings. The helium dilution procedure is initiated by charging the closed system with a known concentration of helium. The helium concentration is known simply from the indication of the helium sensor. Once the system has been charged, the solenoid valve is switched allowing helium and atmospheric air from the closed system to flow into the baby’s lungs. The solenoid valve should be switched when the neonate has completed his exhale and before he begins to inhale. After the solenoid has been switched, the baby is being ventilated via indirect ventilation and the respirating enclosure.
apparatus. Helium concentration values are now taken at 0, 45 and 60 seconds. After one minute, the solenoid valve is switched and the baby is returned to standard ventilation. At this point the entire procedure is over and the physician is ready for data analysis and the determination of the FRC.

The determination of FRC using this system is straightforward and follows the same general scheme as the standard helium dilution techniques described in the introduction. However, the problem now encountered is that of probable endotracheal tube leakage. The Cf actually measured is taken from a real world system where a leak may exist and the Cf needed in the standard dilution method to accurately determine FRC assumes a leakless system. The expected equilibrium value of Cf as if no leak had occurred must be calculated. This is done by taking two readings of helium concentration at 45 and 60 seconds, rather than a single reading, and applying the following equation.

\[
\hat{C}_f = \frac{C_{He}(t_2)}{\frac{C_{He}(t_1)}{C_{He}(t_2)}}^{(t_2-t_1)}
\]

Where \(\hat{C}_f\) is the helium concentration estimator, \(C_{He}(t_1)\) is the helium concentration at 45 seconds, \(C_{He}(t_2)\) is the helium concentration at 60 seconds, \(t_1\) is 45 seconds, and \(t_2\) is 60 seconds. This \(\hat{C}_f\) estimator is then plugged back into the standard helium dilution equation to account for the leakage and obtain an accurate estimate of the FRC.

Prototype

We constructed a prototype of our proposed device for testing. The prototype was constructed using a Collins Helium Analyzer (Collins Medical, Braintree, MA), Millipore peristaltic pump (Millipore, Billerica, MA), a simple three-way valve, a respirating chamber constructed from an 500 mL anesthesia bag and a custom plexiglass container, and a length of standard medical tubing and adapters. The Collins Helium Analyzer measures helium gas concentrations from 0-15% and displays to an analog display with half-percent demarcations or to a 0.25-inch output jack. The Millipore pump was chosen to provide a variable
flow rate to aid in gas mixing and maintain flow through the helium sensor. Additionally, we plan to use the helium sensor’s output jack to measure the helium concentration with a computer. The ventilator was omitted for early testing stages. The final volume of the system was 785 mL. A photo of the constructed prototype is shown in Figure 4.

Marketing Potential

The closed system helium dilution apparatus has a promising market potential. A production unit of the device tested would be a valuable tool for any neonatologist. Knowing the FRC of his patient would enable a physician to better evaluate the condition of his patient, more accurately diagnose his patient, and ultimately, more appropriately treat his patient. In addition, the device can assess the need for ECMO, and thus has the potential to save a hospital thousands of dollars. The ECMO procedure costs hospitals $5000 per day compared with $2000 a day with standard ventilation. Currently, no patents exist on this exact device, however, more costly alternatives to the device such as computerized tomography, CT, do exist. Currently, insurers and health care planners are expressing alarm over the extraordinary costs of modern imaging. Though the cost varies widely, a typical CT scan costs around $2000 (San Francisco Chronicle). Beyond the initial price of the unit, costs associated with the helium dilution procedure differ negligibly from those of standard ventilation. With the total cost of the device components at around $2500, it should prove invaluable to Neonatal Intensive Care Units worldwide [7].
Testing and Results

Prototype Testing

The constructed prototype was tested using mixtures of heliox gas (60% He₂, 40% O₂) with room air. The peristaltic pump was turned on to provide circulation of the air within the circuit to aid gas mixing. The flow rate was set to approximately 500mL/min. The test volume was a 60mL syringe. Tests of the system were conducted with the syringe volume at 20, 30, and 60mL. For each volume tests were performed with a static volume, and also with the volume varying to simulate breathing at near 30 breaths per minute with a tidal volume of about 10mL. For each test, the initial helium concentration of the sensing circuit was allowed to stabilize before the syringe was opened to the system. A computer was initially attached through the helium sensor’s output jack to record the sensor’s output. The computer would allow for more accurate readings of the sensor’s output than the half percent demarcations on the analog meter. However, attaching the computer into the output jack caused the device to stop outputting to the analog meter. We decided to forego the computer recording in order to visually inspect the status using the analog meter. After the syringe was opened to the system, the helium concentration was recorded at 45 and 60 seconds.

Unfortunately, the results of this testing were very poor. In no case were we able to measure the volume of the syringe. In some cases the concentration of helium measured at 60 seconds was actually higher than the concentration measured after 45 seconds. We attribute the poor measurements to two causes. First, we believe the volume of our sensing circuit was too high. The increase of only 60mL would cause the helium concentration to drop only slightly. Combined with the poorly marked analog meter, this posed a serious problem. Secondly, we don’t believe we had adequate mixing of the gases in the sensing circuit. It was observed that during measurements the helium concentration would appear to stabilize, then change suddenly. This seems to indicate that the helium gas
was not well dispersed in the system. One solution to this problem would be to increase the flow rate of the pump to encourage more mixing of the gases. However, this is not possible since the Collins Helium Analyzer requires flow rates between 300 and 600mL/min. Additionally, the helium concentration measured would drop steadily throughout the measurement time. This indicates a leak was present in the system. This was not considered a major issue at the time because the estimator calculated should have compensated for any leak in the system.

Simulation

Additionally, we developed a simple two-compartment model (Fig. 5) of the system to simulate our system in MatLab (The MathWorks, Natick, MA). The model consists of the neonate’s lungs, the measuring system, and the environment it is placed in. The simulation tracks the concentrations of helium, oxygen, and carbon dioxide as well as the total gas volume over time for each compartment. Exchange between the two compartments is mediated by user definable ventilation parameters, tidal volume, duration of inhalation, duration of exhalation, as well as a definition of the gas mixture of the surrounding environment. Consumption of oxygen in the lungs as well as production of carbon dioxide is accounted for. Each step of the simulation requires four major groups of calculations. First, the time parameter of the system is updated. Second, gas exchange between the measuring circuit compartment and the lung compartment is calculated. Third, consumption of oxygen by metabolic processes and carbon dioxide production is accounted for in the lung compartment. Finally, any leak due to an uncuffed endotracheal tube is accounted for. The leak is modeled simply as a gas exchange between the
l lung compartment and the surrounding environment. Each gas exchange is calculated using the simple equation:

\[ C_{t+1} = \frac{C_t V_t + C_{t,\text{exchanged}} V_{\text{exchanged}}}{V_t + V_{\text{exchanged}}} \]

Where \( C_t \) indicates the concentration at time \( t \), \( V_t \) is the volume of the compartment at time \( t \), \( C_{t,\text{exchanged}} \) is the concentration of the gas in the mixture being exchanged, and \( V_{\text{exchanged}} \) is the volume being exchanged. The sign on \( V_{\text{exchanged}} \) is positive when gas is entering the compartment, and negative when gas is leaving the compartment. The full implementation of the simulation is provided in Appendix A.

Simulations were conducted to test both the accuracy of the proposed method and to assess the amount of oxygen and carbon dioxide in the lungs over the testing period. Two sets of simulations were run, one using system parameters described by Schwartz, et al. [8], and the second using the parameters of our prototype. Ventilation parameters were taken from Szymankiewicz, et al. [9], as examples of parameters for a normal ventilated neonate. The rate of oxygen usage was assumed to scale with body mass, and assumed a resting consumption rate of 300mL/min in a normal 70kg adult [10]. Using an average mass of 1.2kg, this corresponds to an oxygen consumption rate of 5.14mL/min. For all simulations, the starting concentrations of gas in the lungs were normal values for adults breathing room air. While this may not be an accurate starting point, it does offer a common starting point for all simulations. In each set of simulations, the leak rate was varied to assess the accuracy of our estimator. Estimates of the FRC were calculated from simulated data at 45 and 60 seconds, mimicking the prototype testing. A summary of simulation parameters is given in Table 1.
Simulations run using the system parameters from Schwartz, et al. [8], show that the equation suggested does indeed produce a good estimator of the equilibrium concentration and, thus, the FRC (Fig. 6). It is worth noting that the accuracy of the estimator improves as the leak rate gets smaller. This makes sense in terms of the equation. Figure 6 also shows that the oxygen content of the lungs stays at a safe level over the testing window. The initial rise in oxygen levels is due to our choice of starting states. Room air has a much lower oxygen content than the gas used in our simulated system, so the lungs’ levels rise dramatically in the first few moments of the simulation. Additionally, the carbon dioxide content of the lungs falls rapidly over the first few seconds and then rises steadily over the testing period. While the rise in carbon dioxide over the duration of the testing is not dangerous, it is something that should be monitored closely if testing lasts longer than a few minutes. The initial fall in carbon dioxide is due to the choice of normal lung gas concentrations as the starting point for the simulation. These concentrations are not truly valid for the ventilation parameters used in the simulation so the concentrations fall quickly to match the ventilation parameters. It is worth noting that, unlike the measured helium

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Referenced Value</th>
<th>Prototype Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>System Volume</td>
<td>185 mL [1]</td>
<td>785 mL</td>
</tr>
<tr>
<td>Patient FRC</td>
<td>26.5 mL [1]</td>
<td>30 mL</td>
</tr>
<tr>
<td>Tidal Volume</td>
<td>7.14 mL [2]</td>
<td>10 mL</td>
</tr>
<tr>
<td>Breathing Rate</td>
<td>48 breaths/min [2]</td>
<td>30 breaths/min</td>
</tr>
<tr>
<td>O₂ Consumption</td>
<td>5.14 mL/min [3]</td>
<td>N/A</td>
</tr>
<tr>
<td>Respiratory Quotient</td>
<td>0.8 [3]</td>
<td>N/A</td>
</tr>
<tr>
<td>Leak Rate</td>
<td>Varied, 0-0.2 mL/sec</td>
<td></td>
</tr>
<tr>
<td>Starting Gas %, Circuit</td>
<td>36.8% O₂, 8.1% He₂, 0% CO₂</td>
<td></td>
</tr>
<tr>
<td>Starting Gas %, Patient</td>
<td>13.15% O₂, 0% He₂, 5.26% CO₂</td>
<td>22% O₂, 0% He₂, 1% CO₂</td>
</tr>
</tbody>
</table>

**Table 1:** Simulation Parameters
concentration, leaks have little effect on the oxygen and carbon dioxide curves, and are actually beneficial in the case of carbon dioxide.

Simulations using the system parameters taken from our prototype shed some light onto why we were unable to test the system reliably (Fig. 7). The error from the true FRC even with a leak rate of 0mL/min shows that 45 seconds was too short a time to allow thorough equilibration. It is also worth noting that the increase in the leak rate has a much greater effect on the FRC estimate with these parameters compared to the first parameter set. Finally, even with the largest leak rate simulated, the total change in helium concentration was only 0.5% over nearly two minutes. This corresponds with only one demarcation on the analog display of the Collins helium sensor. The difference in helium

Figure 6: Simulation results from reported parameters. Top Left: Estimates of FRC are calculated from data at 45 and 60 seconds. Bottom Left: Oxygen consumption over the measuring time. Bottom Right: Carbon dioxide production and build up over the measurement period
concentration at our measurement points of 45 and 60 seconds is less than 0.1%. This would have been very hard to differentiate. Oxygen and carbon dioxide curves for this simulation set are omitted since they provide little useful information in the absence of an oxygen consumer and carbon dioxide source.

While these simulations are no substitute for real world testing, they clearly demonstrate the feasibility of this method as well as some potential pitfalls. The simulations performed using the parameters from previous reports [8,9,10] show the method can provide a good estimator of the FRC even with relatively large leak rates. The simulations using the parameters of our prototype show that the volume of the measuring circuit must be kept low in order to speed equilibration and increase the change in helium concentration. However, the volume of the measuring is also constrained by the neonates need for adequately oxygenated air and low carbon dioxide levels. It is also important to note that these simulations assume perfect mixing within each compartment, so these simulations make no predictions about the error associated with incomplete mixing of the gases.

Safety Issues

Potential safety issues with our device were analyzed using the DesignSafe software. The bulk of the safety issues were issues all electrical devices must deal with. We intend to account for these hazards with standard electrical safety measures and trained service personnel. Another major concern

Figure 7: Helium concentrations simulated from the prototype parameter set for various leak rates
is the involvement of oxygen gas, which is highly flammable. However, the device is meant to be used in a hospital environment which already has strict protocols, such as no smoking, to reduce the danger in a building where oxygen gas is ubiquitous. Another concern is to maintain good oxygen content in the gas being inhaled by the patient. Proposed safety devices include sensors within the circuit to measure the oxygen and carbon dioxide content and methods to add oxygen and remove carbon dioxide if necessary. This has not been implemented yet. Additionally, only trained respiratory technicians, nurses, and doctors will use this device. They will be trained to monitor the patient throughout measurement and their previous training will dictate how to deal with any situation that may arise such as hypoxia or hypercapnia. A final concern involves patients with latex allergies. Our current prototype includes a latex anesthesia bag which could cause allergic reactions in sensitive patients. In the future we will use an anesthesia bag made from a hypoallergenic material such as nitrile rubbers. Additional precautions will include labels and user manuals indicating all potential hazards. The complete DesignSafe report can be found in Appendix B.

Conclusions

From the data collected, we conclude that the modified helium dilution methods proposed by Schwartz, et al., can be effective in measuring the FRC of ventilated neonates. However, care must be taken to ensure proper mixing of the gases and to minimize the volume of the measuring circuit within the constraints of providing adequate oxygen to the neonate and maintaining appropriate carbon dioxide levels. Sensing circuit volumes that are large with respect to the volume to be measured increase the error in the estimated volume due to leaks. Additionally, relatively large sensing circuit volumes make measuring the change in helium concentration more difficult.

This device has the potential for profound social impact. Determination of the FRC via helium dilution has the potential to save many lives by eliminating
the need for more dangerous or complicated procedures. The resulting impact on the friends and family of critically ill neonates will be most certainly be great.

Recommendations

Devices like this are not currently in widespread use, yet, they offer great potential as a tool to aid physicians in treatment of critically ill neonates. We recommend that work on this project continue with the following goals:

1. Rebuild the prototype with a smaller sensing circuit volume and a modern digital helium sensor and retest the device.
2. Incorporate oxygen and carbon dioxide sensors into the sensing circuit to monitor gas levels and provide feedback to physicians as potential trouble arises.
3. Incorporate methods to add oxygen to the system and remove carbon dioxide. In addition to the sensors mentioned above, this will increase the safety of the device for extended use if necessary.

References

7. “Curbing the Costs of Medical Scans, Insurers seek to rein in on fast-growing use of pricey, high-tech MRI’s and CT’s”; Victoria Colliver; Sunday April 24, 2005. <http://sfgate.com/cgi-bin/article.cgi?file=/c/a/2005/04/24/BUGD3CDRAP1.DTL>
Appendices

Appendix A
Implementation of simulation

function state =
define_state(time, pat_O2, pat_CO2, pat_He, pat_vol, sys_O2, sys_CO2, sys_He, sys_vol);
% state =
define_state(time, pat_O2, pat_CO2, pat_He, pat_vol, sys_O2, sys_CO2, sys_He, sys_vol);
%
% Defines a structure with the passed parameters
%
% time = time, in sec
% pat_O2 = oxygen content of lung gas, as a decimal percentage
% pat_CO2 = carbon dioxide content of lung gas, as a decimal percentage
% pat_He = helium content of lung gas, as a decimal percentage
% pat_vol = volume of lung compartment, in mL should equal FRC at time = 0 sec
% sys_O2 = oxygen content of measuring circuit gas, as a decimal percentage
% sys_CO2 = carbon dioxide content of measuring circuit gas, as a decimal percentage
% sys_He = helium content of measuring circuit gas, as a decimal percentage
% sys_vol = volume of gas in the measuring circuit compartment, in mL
%
% Doug Anderson, April 2005

state.time = time;

state.pat_O2 = pat_O2;
state.pat_CO2 = pat_CO2;
state.pat_He = pat_He;
state.pat_vol = pat_vol;

state.sys_O2 = sys_O2;
state.sys_CO2 = sys_CO2;
state.sys_He = sys_He;
state.sys_vol = sys_vol;
function state = sim_dilution(breaths, start_state, tidal, insp_dur, exp_dur, O2_use, rq, leak_rate);
% sim_dilution(breaths, start_state, tidal, insp_dur, exp_dur, O2_use, rq, leak_rate);
% % Simulates Helium dilution method
% % breaths = number of breaths to simulate, must have positive integer value
% % start_state = structure holding the starting values for the simulation,
% %    first element in returned array of structures equals start_state,
% %    pat_vol in start_state should equal the FRC
% % tidal = tidal volume, in mL
% % insp_dur = duration of inspiration, in sec
% % exp_dur = duration of expiration, in sec
% % O2_use = rate of oxygen consumption, in mL/sec
% % rq = respirator quotient
% % leak_rate = rate of gas leak/exchange with environment (assumes room air), in mL/sec
% % Doug Anderson, April 2005
state(1) = start_state;
index = 2;
for i=2:breaths
    state(index) =
        inhale(state(index1),tidal,insp_dur,O2_use,rq,leak_rate);
    index=index+1;
    state(index) =
        exhale(state(index-1),tidal,insp_dur,O2_use,rq,leak_rate);
    index=index+1;
end
function new_state =
inhale(curr_state,tidal,duration,O2_use,rq,leak_rate);

% new_state = inhalе(curr_state,tidal,duration,O2_use,rq,leak_rate);
% %
% % Simulates the inhalation step of heliпum dilution
% %
% curr_state = the current state of the model
% tidal = tidal volume, in mL
% duration = duration of inhalation, in sec
% O2_use = rate of consumption of oxygen, in mL/sec
% rq = respiratory quotient
% leak_rate = leak rate, in mL/sec
% %
% Doug Anderson, April 2005
%
%Advance Time
new_time = curr_state.time + duration;

%Exchange Gases
sys_vol = curr_state.sys_vol - tidal;
sys_O2 = ((curr_state.sys_O2*curr_state.sys_vol)-
     (curr_state.sys_O2*tidal))/sys_vol;
sys_He = ((curr_state.sys_He*curr_state.sys_vol)-
     (curr_state.sys_He*tidal))/sys_vol;
sys_CO2 = ((curr_state.sys_CO2*curr_state.sys_vol)-
     (curr_state.sys_CO2*tidal))/sys_vol;
pat_vol = curr_state.pat_vol + tidal;
pat_O2 = ((curr_state.pat_O2*curr_state.pat_vol)+(curr_state.sys_O2*tidal))/pat_ vol;
pat_He = ((curr_state.pat_He*curr_state.pat_vol)+(curr_state.sys_He*tidal))/pat_ vol;
pat_CO2 = ((curr_state.pat_CO2*curr_state.pat_vol)+(curr_state.sys_CO2*tidal))/pa t_vol;

%Account for consumption of O2 and creation of CO2
used_O2 = O2_use*duration;
made_CO2 = O2_use*duration*rq;
pat_O2 = ((pat_O2*pat_vol)-used_O2)/pat_vol;
pat_CO2 = ((pat_CO2*pat_vol)+made_CO2)/pat_vol;

%Account for leakage
pat_O2 = ((pat_O2*pat_vol)-(pat_02*leak_rate*duration)+(0.22*leak_rate*duration))/pat_vol;
\[
\begin{align*}
\text{pat}_\text{CO2} &= \frac{((\text{pat}_\text{CO2} \times \text{pat}_\text{vol}) - (\text{pat}_\text{CO2} \times \text{leak}_\text{rate} \times \text{duration}) + (0 \times \text{leak}_\text{rate} \times \text{duration}))}{\text{pat}_\text{vol}}; \\
\text{pat}_\text{He} &= \frac{((\text{pat}_\text{He} \times \text{pat}_\text{vol}) - (\text{pat}_\text{He} \times \text{leak}_\text{rate} \times \text{duration}) + (0 \times \text{leak}_\text{rate} \times \text{duration}))}{\text{pat}_\text{vol}}; \\
\text{new}_\text{state} &= \text{define}_\text{state}(\text{new}_\text{time}, \text{pat}_\text{O2}, \text{pat}_\text{CO2}, \text{pat}_\text{He}, \text{pat}_\text{vol}, \text{sys}_\text{O2}, \text{sys}_\text{CO2}, \text{sys}_\text{He}, \text{sys}_\text{vol}); \\
\text{function new}_\text{state} &= \text{exhale}(\text{curr}_\text{state}, \text{tidal}, \text{duration}, \text{O2}_\text{use}, \text{rq}, \text{leak}_\text{rate}); \\
% new_state = exhale(curr_state,tidal,duration,O2_use,rq,leak_rate); \\
% Simulates the exhalation step of helium dilution \\
% curr_state = the current state of the model \\
% tidal = tidal volume, in mL \\
% duration = duration of inhalation, in sec \\
% O2_use = rate of consumption of oxygen, in mL/sec \\
% rq = respiratory quotient \\
% leak_rate = leak rate, in mL/sec \\
% Doug Anderson, April 2005 \\
% Advance Time \\
\text{new}_\text{time} &= \text{curr}_\text{state}_\text{.time} + \text{duration}; \\
% Exchange Gases \\
\text{sys}_\text{vol} &= \text{curr}_\text{state}_\text{.sys}_\text{vol} + \text{tidal}; \\
\text{sys}_\text{O2} &= \frac{((\text{curr}_\text{state}_\text{.sys}_\text{O2} \times \text{curr}_\text{state}_\text{.sys}_\text{vol}) + (\text{curr}_\text{state}_\text{.pat}_\text{O2} \times \text{tidal})))}{\text{sys}_\text{vol}}; \\
\text{sys}_\text{He} &= \frac{((\text{curr}_\text{state}_\text{.sys}_\text{He} \times \text{curr}_\text{state}_\text{.sys}_\text{vol}) + (\text{curr}_\text{state}_\text{.pat}_\text{He} \times \text{tidal})))}{\text{sys}_\text{vol}}; \\
\text{sys}_\text{CO2} &= \frac{((\text{curr}_\text{state}_\text{.sys}_\text{CO2} \times \text{curr}_\text{state}_\text{.sys}_\text{vol}) + (\text{curr}_\text{state}_\text{.pat}_\text{CO2} \times \text{tidal})))}{\text{sys}_\text{vol}}; \\
\text{pat}_\text{vol} &= \text{curr}_\text{state}_\text{.pat}_\text{vol} - \text{tidal}; \\
\text{pat}_\text{O2} &= \frac{((\text{curr}_\text{state}_\text{.pat}_\text{O2} \times \text{curr}_\text{state}_\text{.pat}_\text{vol}) - (\text{curr}_\text{state}_\text{.pat}_\text{O2} \times \text{tidal})))}{\text{pat}_\text{vol}}; \\
\text{pat}_\text{He} &= \frac{((\text{curr}_\text{state}_\text{.pat}_\text{He} \times \text{curr}_\text{state}_\text{.pat}_\text{vol}) - (\text{curr}_\text{state}_\text{.pat}_\text{He} \times \text{tidal})))}{\text{pat}_\text{vol}}; \\
\text{pat}_\text{CO2} &= \frac{((\text{curr}_\text{state}_\text{.pat}_\text{CO2} \times \text{curr}_\text{state}_\text{.pat}_\text{vol}) - (\text{curr}_\text{state}_\text{.pat}_\text{CO2} \times \text{tidal})))}{\text{pat}_\text{vol}}; \\
% Account for consumption of O2 and creation of CO2
used_O2 = O2_use*duration;
made_CO2 = O2_use*duration*rq;

pat_O2 = ((pat_O2*pat_vol)-used_O2)/pat_vol;
pat_CO2 = ((pat_CO2*pat_vol)+made_CO2)/pat_vol;

%Account for leakage
pat_O2 = ((pat_O2*pat_vol)-
(pat_O2*leak_rate*duration)+(0.22*leak_rate*duration))/pat_vol;
pat_CO2 = ((pat_CO2*pat_vol)-
(pat_CO2*leak_rate*duration)+(0*leak_rate*duration))/pat_vol;
pat_He = ((pat_He*pat_vol)-
(pat_He*leak_rate*duration)+(0*leak_rate*duration))/pat_vol;

new_state =
define_state(new_time,pat_O2,pat_CO2,pat_He,pat_vol,sys_O2,sys_CO2,sys_He,sys_vol);
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<th>Hazard / Failing Mode</th>
<th>Initial Assessment</th>
<th>Final Assessment</th>
<th>Status / Reference</th>
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<td>User / Task</td>
<td>Hazard / Failure Mode</td>
<td>Initial Assessment</td>
<td>Final Assessment</td>
<td>Status / Reference</td>
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</tr>
<tr>
<td>Physician and/or Nurse</td>
<td>chemicals and gases / helium</td>
<td>Minimal frequent negligible</td>
<td>Low</td>
<td></td>
</tr>
<tr>
<td>Physician and/or Nurse</td>
<td>chemicals and gases / oxygen</td>
<td>Minimal frequent negligible</td>
<td>Low</td>
<td></td>
</tr>
<tr>
<td>Physician and/or Nurse</td>
<td>electrical / electronic / energized equipment / live parts</td>
<td>Severely Remote Unlikely</td>
<td>Moderate</td>
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</tr>
<tr>
<td>Physician and/or Nurse</td>
<td>electrical / electronic / shorts / arcing / sparking</td>
<td>Severely Remote Unlikely</td>
<td>Moderate</td>
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<tr>
<td>Physician and/or Nurse</td>
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<td>Severely Remote Unlikely</td>
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<tr>
<td>Physician and/or Nurse</td>
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<td>Severe Remote Unlikely</td>
<td>Low</td>
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<tr>
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<td>electrical / electronic / power supply disruption</td>
<td>Severe Remote Unlikely</td>
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<tr>
<td>Physician and/or Nurse</td>
<td>flammable gas / O2 used in systems highly flammable</td>
<td>Catastrophic frequent unlikely</td>
<td>High</td>
<td></td>
</tr>
<tr>
<td>Physician and/or Nurse</td>
<td>chemicals and gases / helium</td>
<td>Minimal frequent negligible</td>
<td>Low</td>
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<td>Minimal frequent negligible</td>
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<tr>
<td>Physician and Nurse basic troubleshooting</td>
<td>electrical / electronic; improper wiring</td>
<td>Serious Remote Unlikely</td>
<td>Moderate</td>
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<tr>
<td>Physician and Nurse basic troubleshooting</td>
<td>electrical / electronic; unexpected start up / motion</td>
<td>Slight Remote Unlikely</td>
<td>Low</td>
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<tr>
<td>Physician and Nurse basic troubleshooting</td>
<td>electrical / electronic; power supply interruption</td>
<td>Slight Remote Unlikely</td>
<td>Low</td>
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<tr>
<td>Physician and Nurse basic troubleshooting</td>
<td>fire and explosions; flammable gas; O2 used in system; highly flammable</td>
<td>Catastrophic Frequent Unlikely</td>
<td>High</td>
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<tr>
<td>Physician and Nurse basic troubleshooting</td>
<td>chemicals and gases; helium</td>
<td>Minimal Frequent Negligible</td>
<td>Low</td>
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<tr>
<td>Physician and Nurse basic troubleshooting</td>
<td>chemicals and gases; oxygen</td>
<td>Minimal Frequent Negligible</td>
<td>Low</td>
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<tr>
<td>Neonate All Tasks</td>
<td>ventilation; air contaminants; possibility of bacterial/virus entering the system</td>
<td>Serious Remote Unlikely</td>
<td>Moderate</td>
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</tr>
<tr>
<td>Neonate All Tasks</td>
<td>ventilation; recirculating air; possibility of CO2 build up in the system</td>
<td>Serious Remote Unlikely</td>
<td>Moderate</td>
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<td>Neonate All Tasks</td>
<td>ventilation; airflow/direction; improper connection of solenoid valve</td>
<td>Serious Remote Unlikely</td>
<td>Moderate</td>
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</table>
Appendix C
Innovation Workbench Questionnaire

Ideation Process

Innovation Situation Questionnaire

1. Brief description of the problem
Functional residua capacity is the volume remaining in the lungs at resting expiratory level. It is the sum of residual volume (volume remaining in the lungs after maximal expiration) and the expiratory reserve volume (maximum volume of additional air that can be expired from the end of a normal expiration). If functional residual capacity is too small, then blood that enters the lung will exit without efficient oxygen exchange. Therefore, a device or method is needed to measure the functional residual capacity of a ventilated neonate in order to set the ventilator parameters such that functional residual capacity is large enough to create gas exchange between the lungs and blood, reducing the possibility of insufficient oxygenation of the blood and subsequent hypoxia. Knowledge of this information could reduce the number of infants placed on ECMO, a dangerous and expensive last resort to oxygenation.

2. Information about the system

2.1 System name
Measuring Neonatal Functional Residual Capacity

2.2 System structure
An enclosed system with a way to measure Helium gas volume or concentration.

2.3 Functioning of the system
Measure the functional residual capacity of a neonate lung using helium dilution methods without suspending ventilation.

2.4 System environment
In neonatal intensive care units (NICU), ventilators are used to facilitate the respiratory mechanics of infants. The device will connect to existing ventilators in the NICU. In these units, environmental conditions are tightly regulated.

3. Information about the problem situation

3.1 Problem that should be resolved
An enclosed system is hard to maintain because the ventilator provides a continuous inflow of air and the infant cannot rebreathe from a constant volume for any extended length of time.

3.2 Mechanism causing the problem
The helium dilution method requires a closed system to make a true measurement while maintaining ventilator support mandates an open system.

3.3 Undesired consequences of unresolved problem
Either ventilator support must be interrupted or a closed system cannot be used, compromising the measurement.

3.4 History of the problem
Helium dilution is a common method for measuring lung volume in adults. Unfortunately, the lack of a closed system and inability of infants to cooperate with such tests has prevented its use previously.

3.5 Other systems in which a similar problem exists

3.6 Other problems to be solved
Size, ease of use, and safety.
4. Ideal vision of solution
A device which can maintain a closed system without suspending ventilator support.

5. Available resources
Ventilators and a Sensormedic adult pulmonary function unit are available for testing the device. Additionally, the helium sensor, a peristaltic pump, and a variety of tubing and connectors is available.

6. Allowable changes to the system
The ventilator, pulmonary function device, pump, and helium sensor cannot be internally modified. Any changes must maintain the flow of air to the infant and meet all applicable standards on patient safety and materials for pulmonary equipment.

7. Criteria for selecting solution concepts

8. Company business environment
The company has no other products. We anticipate all NICUs will have interest in the product and little competition currently exists in this market.

9. Project data
Timeline: Nov. 2004 - Research, Project Definition
Dec. 2004 - Research, Project Definition
Feb. 2005 - Prototype Development
Mar. 2005 - Prototype Development, Testing and Analysis
Apr. 2005 - Testing and Analysis
May. 2005 - Presentation

Team Members
Douglas Anderson - BME Student; Team Leader: Knowledge of web design, simple programming, basic circuit design, Matlab, physiology.
David Lammlein - ME Student: Knowledge of mechanics, dynamics, materials
Janine McKinnon - BME Student: Knowledge of data analysis, Matlab, communication skills, organizational skills
Dr. Paul King - Professor of BME; Advisor
Dr. Bill Walsh - Professor of Pediatrics; Director of Nurseries, Vanderbilt Children's Hospital; Advisor

Contact email: douglas.j.anderson@vanderbilt.edu

Problem Formulation
1. Build the Diagram
2. Directions for Innovation

4/3/2005 6:00:37 PM Diagram1

1. Find an alternative way to obtain [the] (closed system) that offers the following: provides or enhances [the] (uses inert Helium gas) and (measures FRC), does not influence [the] (maintains ventilator support).

2. Try to resolve the following contradiction: The useful factor [the] (closed system) should be in place in order to provide or enhance [the] (uses inert Helium gas) and (measures FRC), and should not exist in order to avoid hindering [the] (maintains ventilator support).

3. Find an alternative way to obtain [the] (maintains ventilator support) that offers the following: provides or enhances [the] (improves oxygenation), eliminates, reduces, or prevents [the] (lowers oxygenation), is not influenced by [the] (closed system).

4. Find an alternative way to obtain [the] (uses inert Helium gas) that does not require [the] (closed system).

5. Consider transitioning to the next generation of the system that will provide [the] (uses inert Helium gas) in a more effective way and/or will be free of existing problems.

6. Find an alternative way to obtain [the] (improves oxygenation) that does not require [the] (measures FRC) and (maintains ventilator support).

7. Consider transitioning to the next generation of the system that will provide [the] (improves oxygenation) in a more effective way and/or will be free of existing problems.

8. Find an alternative way to obtain [the] (measures FRC) that offers the following: provides or enhances [the] (improves oxygenation), does not require [the] (closed system).

9. Find a way to eliminate, reduce, or prevent [the] (lowers oxygenation).
Prioritize Directions

1. Directions selected for further consideration
   1. Find an alternative way to obtain [the] (closed system) that offers the following:
      provides or enhances [the] (uses inert Helium gas) and (measures FRC), does not
      influence [the] (maintains ventilator support).

      1.1. Improve the useful factor (closed system).
      » 1.2. Obtain the useful result without the use of [the] (closed system).
      1.3. Increase effectiveness of the useful action of [the] (closed system).
      » 1.4. Synthesize the new system to provide [the] (closed system).
      1.5. Apply universal Operators to provide the useful factor (closed system).
      1.6. Consider resources to provide the useful factor (closed system).

   8. Find an alternative way to obtain [the] (measures FRC) that offers the following:
      provides or enhances [the] (improves oxygenation), does not require [the] (closed
      system).

      8.1. Improve the useful factor (measures FRC).
      8.2. Obtain the useful result without the use of [the] (measures FRC).
      8.3. Increase effectiveness of the useful action of [the] (measures FRC).
      » 8.4. Synthesize the new system to provide [the] (measures FRC).
      8.5. Apply universal Operators to provide the useful factor (measures FRC).
      8.6. Consider resources to provide the useful factor (measures FRC).

2. List and categorize all preliminary ideas
   We should either discover a new method to create the closed system while maintaining
   ventilator support or find a way to account for the open system in the FRC calculation.

Develop Concepts

1. Combine ideas into Concepts
   Perhaps we can do both, creating a mostly closed system without compromising
   ventilator support. Use the ventilator to apply pressure to the closed system?

2. Apply Lines of Evolution to further improve Concepts
   Use a mathematical model to account for the leaks from a mostly closed system.
   Provide a method for applying the pressure produced by the ventilator to the gas in the
   closed system without allowing mixing (diaphragm maybe?).

Evaluate Results

1. Meet criteria for evaluating Concepts
   The method mentioned above seems to meet all the criteria for solving this problem.

2. Reveal and prevent potential failures
   The mostly closed system may not contain enough oxygen for long measurement times,
   additionally, CO2 buildup is a concern. The helium may leak too quickly to calculated
   a reasonable estimate of the FRC. The diaphragm like portion could be too stiff and not
transfer the pressure well enough to maintain ventilator support.

3. Plan the implementation
A prototype of the new system will be constructed in heavily tested before it is ever tried on an infant. The system will be tested without ventilator support with a syringe or other known volume acting for the FRC. It will also be tested on adults who do not need ventilator support to test its ability to measure a dynamic volume. Finally, a known volume in a distensible container will be used to test the system when ventilator support is applied to make sure the system for transferring the pressures functions properly and measurements can still be made. Only then will testing on infants be attempted.