Respiratory failure has many causes and levels of severity. Although treatment of the underlying cause is essential for recovery, many patients would not survive without lung support from mechanical ventilation. While mechanical ventilation is the standard method for lung support in severe respiratory failure, recent advances in extracorporeal carbon dioxide removal (ECCO₂R) are proving to be a useful alternative in many situations of acute respiratory distress. The future is likely to bring a change in the standard of care for treating acute respiratory failure.

Invasive Mechanical Ventilation
Ventilators have fulfilled the same basic function since they were invented – push air into the lungs and then allow the patient to exhale. While they have evolved to include high frequency ventilation, bilevel ventilation and intelligent ventilation, invasive mechanical ventilation still manifests deleterious consequences. The use of a tracheal tube alone is problematic as it presents the possibility of damage to the tracheal wall and the vocal chords, not to mention the anesthesia necessary to suppress the patient’s gag reflex and tendency to fight the ventilator. More serious adverse events, which may significantly affect morbidity and mortality, include barotrauma to the lungs, ventilator-associated pneumonia, impaired delivery of aerosolized medications, nutritional deficiency, immobility, deconditioning of the diaphragm, and ventilator dependence.¹²³

The trend in mechanical ventilation is to ameliorate some of the adverse events by reducing breath volume. The historical norm was 12 cc per kilo of body weight, which has been reduced to a new standard of 6 cc per kilo of body weight. The latest studies are suggesting that 3 to 4 cc per kilo of body weight may be an appropriate amount in more severe cases. One drawback to this approach is that when breath volume and frequency are reduced, the level of carbon dioxide in the blood naturally increases. Thus while the reduction in breath volume and frequency has demonstrated improved protection of the lungs, fewer complications, and reduced mortality, it is difficult for caregivers to implement due to the deleterious effects carbon dioxide retention.

Artificial Lungs
Extracorporeal lung therapy can be an alternative or adjunct to invasive mechanical ventilation, and has until recently been geared towards how much oxygen a patient needs. The therapy provided by such devices is usually referred to as extracorporeal membrane oxygenation, or ECMO. ECMO devices are like artificial lungs. Real lungs are simulated with a module that contains membranes in the form of hollow fibers. As in the lungs, when deoxygenated blood flows over the fiber membranes, oxygen gas diffuses across the membrane into the blood and carbon dioxide diffuses from the blood into the gas that flows through the fibers. With an ECMO device, venous blood is drawn from the body through a catheter, and is returned to the circulation after passing through the membrane module, hence the term extracorporeal. Such devices are commonly used during cardiopulmonary bypass surgery to support patients while their hearts or lungs are being repaired. Such devices are very complex, requiring around-the-clock monitoring, dedicated institutions,
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and trained personnel with specialized skills. In contrast to ECMO therapy, ECCO_R with the Hemolung Respiratory Assist System (ALung Technologies, Inc., Pittsburgh, PA) is intended to supplement the carbon dioxide removal needs of a patient in situations where carbon dioxide buildup in the blood (hypercapnia) is more of a problem than oxygenation. The Hemolung provides simple, effective, and minimally invasive extracorporeal therapy. Because it uses techniques similar to renal dialysis, Hemolung therapy is also referred to as Respiratory Dialysis. The Hemolung is specifically designed to provide partial extracorporeal support in a less invasive way than other extracorporeal lung devices, permitting its use in a wider range of patients in respiratory failure. Initial studies are showing that it may be an effective adjunct or potential replacement to invasive mechanical ventilation.4,5

The Hemolung Respiratory Assist System (RAS)

ECMO systems require many components, including a blood pump, a membrane oxygenator, a heat exchanger, a blood flow probe, separate electronic controllers for each of these components, and typically two catheters. The Hemolung RAS utilizes only three elements: one catheter, a single integrated controller unit, and a patented cartridge which combines a centrifugal blood pump and carbon dioxide removal membranes into a single cartridge.

The Hemolung cartridge is the only device on the market which actively mixes the blood flow as it passes over the fibers to significantly increase the efficiency of carbon dioxide removal. The increased efficiency allows the Hemolung to operate at much lower blood flows compared to ECMO systems, and with less than half the membrane surface area. Both of these factors increase biocompatibility by reducing the degree of exposure of a patient’s blood to artificial materials. In addition, a much lower blood flow means that instead of two large-bore catheters, only a single, smaller bore catheter is needed.

The Hemolung catheter is 15.5 Fr and is designed to allow two-directional flow. It consists of two wire-reinforced tubes, one inside the other. Blood from the patient is drawn into the outer tube through the annular region surrounding the inner tube. After passing through the cartridge, the decarbonated blood is returned to the patient via the circular inner tube. The use of wire reinforcement allows for thinner walls and higher flow rates than standard hemodialysis catheters.

The Hemolung controller is a fully integrated user interface which operates and monitors all aspects of the system, including alarms. The cartridge is magnetically mounted on the controller, which drives the spinning of a hollow cylinder in the core of the cartridge. Spinning of this cylinder acts to centrifugally pump the blood and to create mixing of the blood near the fibers, which is how the efficiency of carbon dioxide removal is increased. Using integrated sensors for the rate of gas flow, the rate of blood flow, the presence of bubbles in the blood, and the concentration of carbon dioxide in the gas flow, the controller provides continuous safety monitoring and alarming. Two unique aspects of the Hemolung controller are the real-time measurement and display of carbon dioxide removal as well as the digitally controlled, vacuum-driven sweep gas. The controller can also switch between the use of either 100% oxygen or room air as the sweep gas.

Utility

Chronic obstructive pulmonary disease (COPD) is estimated to affect 11.8% of men and 8.5% of women6 and is the fourth leading cause of death worldwide.7 Patients with acute exacerbation of COPD, or with any
form of acute hypercapnic respiratory failure, have high levels of CO\(_2\) in the bloodstream that cannot be eliminated with their native lungs. Respiratory dialysis with the Hemolung RAS provides an important alternative to mechanical ventilation in this situation.

In patients supported with noninvasive ventilation through a nasal tube or mask who have yet to be put on a ventilator, ECCO\(_2\)R therapy with the Hemolung may avoid intubation and mechanical ventilation by reducing the work of breathing, correcting acidosis and giving the patient time to recover from acute decompensation. In patients already on a ventilator, ECCO\(_2\)R therapy with the Hemolung permits de-escalation of the ventilator settings while simultaneously correcting acidosis. This enables lung protective ventilation. A pilot study of the ECCO\(_2\)R device in 20 hypercapnic patients with COPD confirms this potentially valuable additional modality for treatment of hypercapnic respiratory failure.

The trends in respiratory failure are moving in the direction of extracorporeal lung assist, with growing importance on earlier intervention of lung syndromes to slow disease progression. However, benefit has to outweigh the potential risks. Extracorporeal respiratory assist devices are generally divided into three categories. High blood flow devices, with ECMO on the extreme end, move blood from the body at a rate of 2.5 – 7 liters per minute and are typically used for high acuity patients with extreme oxygen needs. The middle category treats the mild to moderate acute respiratory distress syndrome (ARDS) patient, and includes devices that can be modifications of ECMO devices that typically move blood at a rate of 1.0 – 2.5 liters per minute. Their utility with the COPD population is debatable. The third category covers low flow devices that have a blood flow range from 350 – 550 mL per minute. This last category covers kidney dialysis devices that have been modified to use an existing oxygenator, as well as the Hemolung RAS device, the only device developed from the ground up to be a true, low-flow, CO\(_2\) removal device.

The end goal with artificial lung support is to make it simple, easy, safe, and effective, and ultimately, for it to be portable. To achieve these goals, the device must mimic the efficiency of native lungs and connect to the venous system of the body via very small vascular access points. The Hemolung RAS device removes CO\(_2\) at a rate of 50 to 100 mL/min, using a blood flow rate of 350 to 500 mL/min via a 15.5 Fr catheter. The active mixing technology enhances gas exchange 150% over passive diffusion devices. The entire system can operate on a rechargeable battery, allowing the patient to ambulate.

**Health and Economics**

The Hemolung RAS may have a significant economic impact by reducing the length of hospital stay for patients with hypercapnic respiratory failure. A study\(^9\) of 51,009 patients across the United States showed that ICU patients that required mechanical ventilation had an average cost and length of stay of $31,574 + $42,570 and 14.4 days + 15.8 days. In contrast, ICU patients that did not require mechanical ventilation had an average stay of 8.5 days + 10.5, with a cost of $12,931 + $20,569. The study concluded that interventions that result in reduced intensive care unit length of stay and/or duration of mechanical ventilation could lead to substantial reductions in total inpatient cost.

Hospital reimbursement is based on diagnosis, rather than length of stay or total services rendered. This information increases the importance of finding devices that can prevent high-risk patients from receiving invasive ventilation as well as help wean patients already receiving invasive ventilation.

**The Paradigm of Care**

Greater focus is needed worldwide to change
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the paradigm of healthcare for patients with acute hypercapnic respiratory failure. Failure rates with noninvasive ventilation can be high\(^1\), and there is a large portion of the COPD population that would benefit from earlier treatment with a minimally invasive device. Making such a device simple enough that it does not require specialty personnel for operation could potentially change the standard of care for this significant patient population.

As originally published in MassDevice on Jan 22, 2014.

About the Hemolung RAS

The Hemolung RAS from ALung Technologies provides Respiratory Dialysis\(^\circ\), a simple, minimally-invasive form of extracorporeal carbon dioxide removal (ECCO\(_2\)R). The system utilizes patented technology to provide highly efficient CO\(_2\) removal at dialysis-like blood flow rates which are achieved through a single 15.5 Fr venous catheter. For more information, please visit http://www.alung.com.

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