Veno-Venous Extracorporeal CO_2 Removal: Reduction in Dependence on Mechanical Ventilation via the Hemolung Artificial Lung System

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Clinical Need for Lung Support

For the Military:

- Increasing likelihood of acute lung injuries on the battlefield due to blunt trauma, massive resuscitation, smoke inhalation injury, and exposure to toxic chemical inhalants.
- Growing concern of terrorist attacks utilizing toxic industrial chemicals which cause lung injury

For Civilians:

- 150,000 Americans every year are dying from acute lung disease and injury.
- 400,000 Americans with chronic lung disease have life-threatening loss of lung function.

- Present-day therapies are inadequate, expensive, and can further traumatize the lung. Mortality for ARDS remains near 30-50%.
- *The Need*: a breathing support therapy which "rests" the lung, allowing it to heal.

The Hemolung Respiratory Support System

The Hemolung is an integrated extracorporeal CO_2 removal system developed by ALung Technologies. By ventilating the patient independently of the lungs, the need for mechanical ventilation is reduced, thereby reducing the risk of progressive lung damage. The system is expected to improve the treatment of patients with ALI, ARDS and COPD.

Key features include:

- Capable of supporting up to 50% of a patient's CO_2 removal requirements at blood flow rates similar to hemodialysis (500 – 750 mL/min) for up to 7 days.
- Completely integrated device – no need for separate pump and oxygenator.
- Vascular access with 15 or 18 Fr dual-lumen, veno-venous catheter placed in the jugular or femoral vein. This avoids arterial cannulation with its risk of limb ischemia.
- Integrated electronic controller allows for simple operation by incorporating alarms, blood flow meter, bubble detection, automatic gas handling, battery backup, and on-screen help.
- Proprietary fiber coatings (siloxane/heparin) allow for up to 7 days of continuous use with no plasma wetting or significant gas exchange degradation
- Requires minimal anticoagulation (ACT 150 – 180 sec or PTT 1.5 – 2.3X baseline)
- Small surface area and minimal priming volume. Seamless design reduces thrombus formation and increases safety.

Hemolung Controller

Hemolung CO_2 Removal Device

Animal Study Design

- 72 hour study in 7 mechanically ventilated sedated swine (54 kg)
- 15 Fr Hemolung catheter inserted in right jugular vein with tip residing in the right atrium
- Upon insertion of the device, minute ventilation was decreased and titrated to a normal arterial PCO_2 tension of 35-45 mm Hg with minimal ventilation support.
- Device performance continuously monitored, including:
  - CO_2 removal rate, blood flow rate, RPM, power
  - Vital signs, body temperature, ventilator settings, oxygen consumption and CO_2 production, plasma free hemoglobin, coagulation profile, blood gas analysis.

72 hour Animal Study Setup

Summary of Results

Use of the Hemolung system led to:

- No hemodynamic sequelae
- Significant persistent reduction in minute ventilation
- Maintenance of a steady CO_2 removal rate of 72 ± 1.2 ml/min at normocapnea (PCO_2 of 45 mmHg) over 72 hours
- Mean blood flow rates through the device were 447±4.8 ml/min
- Average Activated Clotting Time (ACT) 170 seconds ± 18 sec.

Necropsy and histopathology findings were unremarkable.

Results

Variables	Baseline	2 hours	24 hours	48 hours	72 hours
HR	100	86	77	89	84
SAP	130	130	117	114	116
MV	5.63	2.62 *	2.96 *	3.12 *	3.28 *
RR	9	5 *	5 *	5 *	5 *
TV	650	524 *	576 *	574 *	578 *
VO_2	313	320	260	278	262
VCO_2	262	135 *	141 *	152 *	147 *
PaO_2	96	78 *	103	109	112
$PaCO_2$	39	43	42	44 *	46 *
pH	7.46	7.41	7.47	7.45	7.44
PfHb	0.16	0.12	0.18	0.13	0.17
CO_2 rem	n/a	76	73	69	65 *
Blood flow	n/a	422	471	445	431
ACT	106	187	141	150	135

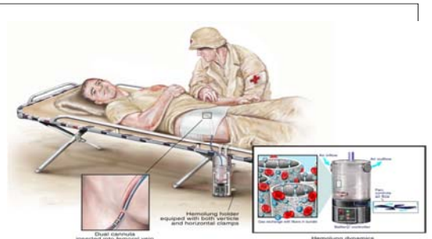
Heart rate (HR, beat per minute); systolic arterial pressure (SAP, mmHg); minute ventilation (MV, liters per minute); Respiratory rate (RR, breath per minute); tidal volume (TV, milliliters per minute); oxygen consumption (VO_2, milliliters per minute); Carbon dioxide production (VCO_2, milliliters per minute); partial pressure of oxygen in arterial blood (PaO_2, mmHg); partial pressure of carbon dioxide in arterial blood PCO_2, mmHg); hydrogen ion concentration in arterial blood (pH, relative units); plasma free hemoblobin (PfHB, milligrams per deciliter); Carbon dioxide removal by the Hemolung device (CO_2 rem, milliliters per minute); blood flow through the Hemolung device (Blood flow, milliliters per minute); activated clotting time (ACT, seconds). All data are means. Statistics by one-way ANOVA with repeated measures and adjustment to multiple comparisons. *Significant difference vs. baseline at $p<0.05$..

Conclusions

- The Hemolung Respiratory Support System can provide clinically significant levels of CO_2 exchange and allowed for a 50% reduction in minute ventilation
- Lung support was maintained over 72 hours with steady CO_2 removal rates and blood flows
- The custom Hemolung catheter was kink-resistant, non-irritating, and non-thrombogenic
- The Hemolung did not cause any unexpected changes in hemodynamics. No blood product transfusions were required.

Next Steps

- **FDA approval pending**
- **Injured animal model (ALI and ARDS) testing at ISR to test efficacy (ongoing)**
- **Clinical trial in COPD patients in FY 2010**



Depiction of potential future military application of a miniaturized Hemolung system on the battlefield.