

Pasta for all: Abiomed Breathe extracorporeal membrane oxygenation system



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More than 700,000 Americans died from heart-related causes in 1963. The high rate of 560 per 100,000 fortunately has dropped now by 68%. The concern for killer heart disease helped Michael DeBakey convince President Lyndon Baines Johnson to call for a National Artificial Heart Program. DeBakey treated LBJ, a chain smoker, who experienced his own first heart attack in 1955, and Johnson died in 1973 from heart failure at age 64 years. In the 66 years since, only recently have ventricular assist devices been used with expectations of reasonable survival and quality of life. The development of implantable hearts and single pumps has proven more difficult and costly than expected. Patients remain tethered to percutaneous drivelines, there is currently only a single commercially approved pump in the United States, and a total heart remains elusive. Similar development of an artificial lung has proven more difficult and followed progress of cardiopulmonary bypass developed to enable open heart surgery.

OXYGENATORS AND ARTIFICIAL PUMP-LUNGS

Efforts to mechanically oxygenate and ventilate the blood evolved from need for short-term cardiopulmonary support of emerging cardiac repairs. John Gibbon's success on May 19, 1954, is well known to cardiac surgeons today (Figure 1, A). As a graduate of Jefferson, the Gibbon story is particularly motivating to this author (B.P.G).¹ It is sobering that in the same year, 17 out of 18 patients supported by early screen and disc film oxygenators died. In 1931, during his residency, Gibbon had observed a patient die from a pulmonary embolism.² He later commented:

“During that long night, helplessly watching the patient struggle for life as her blood became darker and her veins more distended, the idea naturally occurred to me that if it were possible to remove continuously some of the blue blood from the patient's swollen veins, put oxygen into that blood

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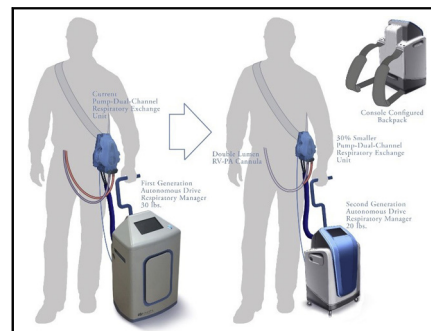
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The Breathe OXY-1 system included wearable pump-lung unit and a small, rolling gas-free console.

CENTRAL MESSAGE

An ECMO device free of compressed gases has been developed to provide patients an opportunity for its use at home and during ambulation.

See Commentary on page 114.

and allow carbon dioxide to escape from it and then to inject continuously the now-red blood back into the patient's arteries, we might have saved her life. We would have bypassed the obstructing embolus and performed part of the work of the patient's heart and lungs outside the body.”²

In 1965, during his training under Robert Gross, MD, at the Peter Brent Brigham, Bob Bartlett challenged himself to use prolonged postoperative cardiopulmonary bypass. He saw a need to rest the heart after surgery. He went to the lab to work on the problem of what his chief described as cardiopulmonary bypass being “lethal after an hour or 2 of use.”³ His effort on early membrane oxygenators paved the way for his lifelong development of extracorporeal membrane oxygenation (ECMO). Advances leading centrifugal blood pumps and hollow-fiber membrane oxygenators have made ECMO systems safer and less complicated. Most ECMO runs are 6 to 10 days or fewer, but longer uses are now common.

The benefit of ECMO in support of lung healing is growing believers. However, the reversibility of acute lung failure is poorly defined. Our group believed ECMO



FIGURE 1. Images of pioneers in the field of extracorporeal membrane oxygenation. A, Dr John Gibbon and his wife Mary “Maly” Gibbon with an early heart–lung machine in 1950s. B, Dr Willem Kolff attended a meeting wearing his wearable oxygenator. C, Dr Robert Bartlett holding an oxygenator developed in his laboratory for pumpless application.

might prove a safe platform for recovery, bridge to transplantation, and even permanent support of irreversible lung disease. Our research group has had 22 years of generous support from the National Heart, Lung, and Blood Institute (NHLBI) that more recently included a commercial subcontractor to translate our lab’s prototypes into a portable console and a wearable pump–lung unit.⁴ Our hope is that we can engineer a system that would permit ECMO systems to leave the bedside, encourage exercise, and be suitable for use out of the hospital. Like others, we were aware of the challenges, but we were convinced of the potential value of easing the burden of long-term breathlessness with a mechanical solution. Since 1985, we have been participants in the ongoing bench and clinical development of mechanical heart support. Early in our NHLBI support, the vision was given a confirmatory nod from Willem “Pim” Kolff, MD, who paraded through the American Society for Artificial Internal Organs meeting in 2000 with a faux pump oxygenator strapped to his chest (Figure 1, B). The innovator of dialysis and a total artificial heart convinced us the lung was the next frontier. For years, Bob Bartlett held encouraging breakout sessions at American Society for Artificial Internal Organs annual meetings for the exchange of ideas about artificial lungs. He focused on a novel pumpless compliant system (Figure 1, C) while our group with deep roots in blood pumps planned for a pump–lung for all candidates.

During late 2008, we learned from C. W. Hoopes (personal communication) that patients could ambulate while supported on ECMO, and we adopted his lead in 2010.⁵ Growing numbers of cases have been reported with durations of support well beyond 3 weeks. The longest reported is of a 7-year-old with a 30% burn and smoke inhalation

who recovered near normal pulmonary function after 20 months of ECMO.⁶ The patient required several modes of ECMO: venoarterial (VA) for 2 weeks, venovenous (VV) for 2 months, right atrium-to-pulmonary artery for 15 months, and extracorporeal carbon dioxide removal for 2 months. It appears that lungs can recover from severe injuries in the case that scarring fibrosis can be mitigated. Consolidated stiff lungs are filled with inflammatory cells. They cannot be forced open by deleterious positive ventilatory pressures until these inflammatory cells are gone. Kenneth Palmer, MD, of the Karolinska Institute has documented normalization of a lung over months of poor elasticity without use of high positive end-expiratory pressure and peak pressures.⁷ Absent adjuvant antifibrotic medicines, our team believes in the need for lung rest and for safe, long-term support. Following the Extracorporeal Life Support Organization meeting in 2017, Palmer spoke to our group of his landmark experience with an out-of-hospital ECMO experience.⁷ His team had been supporting a 59-year-old woman with idiopathic pulmonary fibrosis for 160 days on VV ECMO as a bridge to transplant. She was emotionally depleted from her long wait and asked to go home for a meal. He engineered a 440-km day trip from the intensive care unit (ICU). He believed the so-called pasta reprieve gave her the emotional boost to survive an additional wait of 69 days in the ICU before a donor was located and successful transplantation could be performed. We asked: Why is an ICU required if a trip home is possible?

In 2014, Breethe Inc was formed to license our technology as a spinout from the University of Maryland, Baltimore. In 2020, just before its application to the Food and Drug Administration for 510K approval, the company was

sold to Abiomed Inc (Danvers, Mass). We are all anxious to watch its use grow in ICUs and anticipate that its performance will justify approval for long-term use, ambulation, and even a safety study for use at home.

BREETHE OXY-1 SYSTEM

The Breethe OXY-1 system is fundamentally different from all other commercial ECMO systems. Although suitable for VV and VA modes of application providing full physiologic needs, it is built to permit an out of ICU consideration and perhaps home use. It is simple to use and unclutters usually congested ICUs. It forgoes an integrated heater-cooler, and alarms are reduced to flow and outlet saturation. It has a lightweight console and is on wheels that beg for the patient to be transported or ambulate in the hospital (Figure 2). This small roller unit appears to be shaped to mimic the *Star Wars* R2-D2 robot. It houses control units for the blood pump's speed and sweep gas flows. It has a rechargeable 3.5-hour battery, and a 3-L continuous flow oxygen concentrator plus a ventilator fan. The console may be plugged into wall A/C outlet and oxygen outlets. When disconnected from them, its battery engages to run the blood pump and an oxygen concentrator.



FIGURE 2. Patient transport and ambulation are easier using the smaller roller console alone. Patient shown in computed tomography scanner with pump-lung unit hung-on console.

No concentrated gas is contained. To sweep carbon dioxide, a fan forces ambient air at 1 to 10 L/minute into the outer portion (20%) of the oxygenator membranes. The ambient air does not mix with the near pure oxygen flow from the concentrator. Fan-driven air enters a manifold separated from the oxygen source that supplies the inner portion of the membranes (Figure 3). Table 1 summarizes the similarities and differences between the Breethe OXY-1 system and other ECMO systems.

Pump-Lung Unit

The pump-lung unit (PLU) was based on a circumferential-radial flow oxygenator and a centrifugal pump. It was designed using computer-aided design for 3-dimensional geometry modeling and computational fluid dynamics analysis for blood flow and gas exchange.⁸ It was prototyped virtually and then using printed parts. Molds were produced when bench tests indicated that functional goals were met. The PLU was designed to be disposable because the team at Breethe knew replacement would be inevitable during longer-term support due to the membrane material limitations (eg, biofouling and thrombosis). However, animal studies are promising at 30 days. The PLU is transparent on the vein and artery side of the opaque fiber bundles. This permits visual inspection for thrombosis and alterations in pattern of blood flow. The PLU is enclosed in a nondisposable clam shell (Figure 4). It snaps closed and contains the electromagnetic motor for the pump and oxygen plus bubble sensors placed on the outflow. A disposable condensation tray is located at the base of the shell. It is designed to capture water that condenses on exit from the gas port of the oxygenator. The PLU may be worn from a

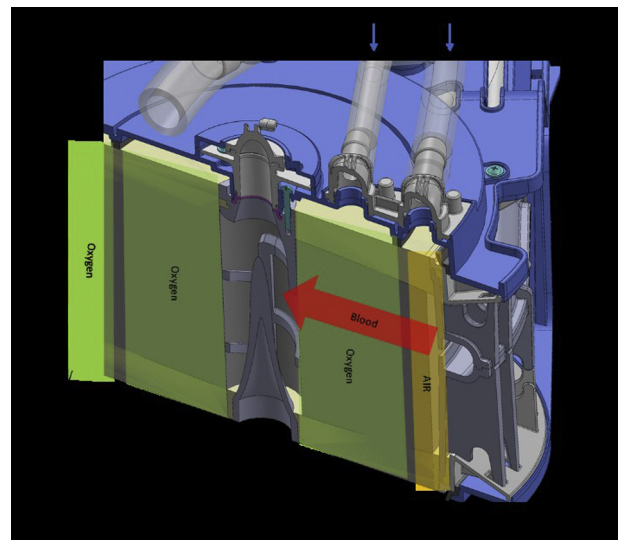


FIGURE 3. The unique separation of the gas manifolds permits atmospheric air to serve carbon dioxide sweep and oxygen to be sourced from a reduced-size 3 L/minute concentrator.

TABLE 1. Similarities and differences between the Breathe OXY-1 system (Abiomed, Danvers, Mass) and other extracorporeal membrane oxygenation (ECMO) system

Type	Major components	Sweep gas source	Cannulation and support mode	Ambulation/mobility
Standard ECMO systems	Oxygenator, pump, heat exchanger, external tubing, and implanted cannulas	Wall oxygen or compressed oxygen tank	Central or peripheral VA ECMO Peripheral or central VV ECMO	Bulky, difficult
ECCO2R	Oxygenator, external tubing, implanted cannulas	Wall oxygen or compressed oxygen tank	Peripheral VV or AV ECCO2R	Balky, difficult
Breathe OXY-1	Oxygenator with integrated pump, external tubing, implanted cannulas	Wall oxygen or self-generated oxygen and/or air	Central or peripheral VA ECMO Central or peripheral or VV ECMO	Compact, simple, easy

VA, Venoarterial; VV, venovenous; ECCO2R, extracorporeal carbon dioxide removal.

shoulder strap or, more commonly in the hospital, hung from the console’s extendable handle.

Blood Flow

The blood pump is centrifugal and based on a hybrid magnetic and hydrodynamic bearing. It rotates from a magnetic drive. It is supported on a single-point mechanical bearing and is coupled with a magnetic bearing. The mechanical bearing is a sapphire ball against an ultrahigh molecular weight polyethylene cup. The bearing system has been iterated to optimize washing through secondary flow paths. The impeller is a starfish design and shrouded. The pump’s hydrodynamic performance (pressure-flow curves) resembles that of the Rotoflow (Allentown, Pa), and the biocompatibility profile tracks the Centrimag (Abbott, Abbott Park, Ill). Venous blood is delivered into the housing through a wraparound, snakelike slit fashioned to ensure uniform delivery of pressure and flow through the membranes. The flow between the housing and the membrane

bundle is mostly circumferential. The outflow from the oxygenator may be directed back into a patient’s venous system (VV mode) or into an artery (VA mode).

The membrane bundle uses skinned microporous hollow fibers for its gas exchange. These membranes are standard in ECMO systems and reasonably durable and thromboresistive. The PLU is not coated with an antithrombotic agent. Although there are considerable market forces to do so, to date our internal data fail to demonstrate benefit. The venous blood flows through the cylindrical membrane bundle in an outside-to-inside direction. The reducing radius across the path serves to accelerate the rate of flow (Figure 5). This reduces low-flow-induced stasis but is less efficient in oxygen transfer by nature of its rapid rate in the inner smaller radii portions of the cylinder.⁸ The membrane bundle is 2.4 m². Its size reflects a balance to meet the current market demands of outlet Po₂ >300 mm Hg at a rate of flow of 5 L/minute, while meeting the biocompatibility design goal.

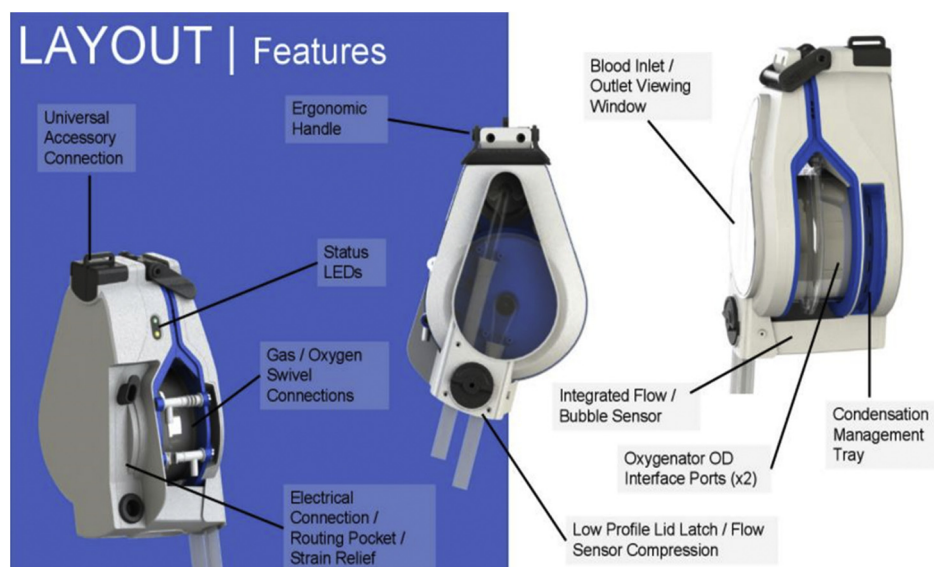


FIGURE 4. The disposable head of the pump-lung unit is clamped in the reusable shell that contains the pump motor and sensors. LED, Light-emitting diode; OD, outer diameter.

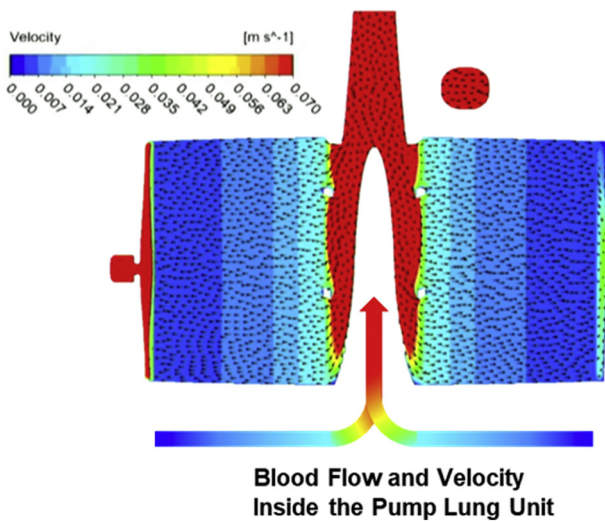


FIGURE 5. The uniform pressure outside in flow through the cylindrically wrapped bundle of hollow membranes induces a uniform increase in velocity of blood flow.

Currently, the Breethe OXY-1 system connects to the patient via commercially available cannulas. There is a need for innovation to meet the cannulation needs of long-term ambulatory ECMO. There are several proposed variations on the dual-lumen percutaneous approach that would provide a reasonable ergonomic solution to the current loop affixed to the head band suitable in the ICU. Other considerations include unique central cannula that would be positioned and removed minimally invasively and exit from or below the ribs. Based on excellent outcomes with percutaneous large bore cannulas of the 1980 Pierce Donnachy pneumatic ventricular assist device, the planned smaller and perhaps dual-lumen single cannula should suffice for the paracorporeal pump-lung. In the initial clinical rollout of the Breethe OXY-1 system, the length of time the PLU was used in patients generally was longer than hours and varied from days to weeks. In 1 patient, a single PLU continued to be functional for up to 74 days. We think that the surface modification of the membrane oxygenator

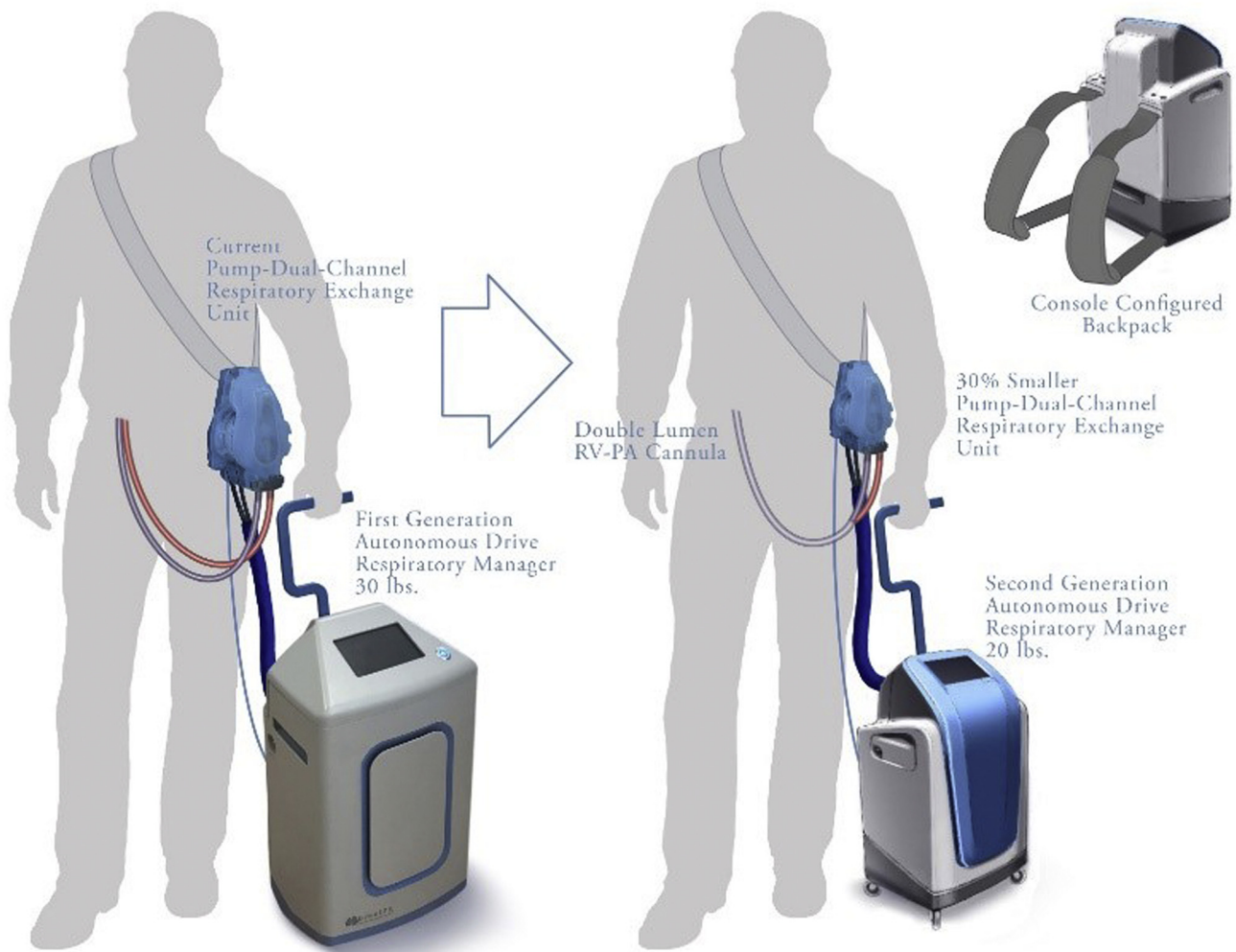


FIGURE 6. The Breethe OXY-1 system (Abiomed, Danvers, Mass) included wearable pump-lung unit and a roller small gas free console. A lighter pump-lung unit with a smaller console, possibly placed in a backpack, is under development. *RV-PA*, Right ventricle to pulmonary artery.

may have the potential to extend the duration of support of a single PLU. Additionally, the development of a quick connection may enable the easy replacement of the disposable PLU head so that patients can be supported for months.

CONCLUSIONS

The Breethe OXY-1 system evolved from early NHLBI funding approved by a diverse study section review and a lung division that, unlike the heart division, was relatively new to artificial lung support. In time it was obvious that a commercial partner was required and even suggested by the latest grant review. The pre-510K acquisition by Abiomed strengthened the team and permitted expansion. The roll out of the current OXY-1 system is approved for 4 hours has been purposely controlled to ensure quality production, timely distribution and support, and evaluation of case-by-case performance. The system is designed to be safe and simple to operate. It keeps sensors and alarms to those necessarily required. Because VA support is a large portion of the market for ECMO, the pump was designed to function well against the additional systemic afterload. Although we do ambulate many of our VA-supported patients, we are in the minority and recognize the long-term patient uses will come from those with acute and chronic lung diseases. The problem of how to carry enough ventilatory gas when mobility was solved by not including any. This became possible when it was decided to separate the gas flows into 1 for oxygen exchange and another for removal of carbon dioxide. The oxygen needs likely will be lower than the 3 L provided by the small concentrator. However, the sweep gas may reach flows of up to 10 L/minute, well beyond that provided by a portable concentrator or easily carried in large, concentrated oxygen tanks. The simplicity of a fan to blow atmospheric air and of committing the outer portion of the membrane bundle to chiefly carbon dioxide removal made the project come together. We hope we have the biocompatible blood flow path that will enable oral anticoagulation to support long term VV ECMO. The system will need to earn approval for longer term use and ambulation based on a planned patient use registry. If all goes well, patients with lung-only disease may leave the ICU to recover on a monitored floor. Should the experience demonstrate feasibility, a safety study for home use can be considered (Figure 6). We

believe in the need and that the time is upon us to begin to move patients away from acute, care-only settings like those of our patients with ventricular assist devices in 1994. We hope the cardiothoracic specialists will embrace the challenge. Currently, acute respiratory distress syndrome is experienced by more than 200,000 patients yearly and the average survival is between 30% and 50%. In addition, 2% to ~3% of about 15.7 million patients with chronic obstructive pulmonary disease are in end-stage lung failure. Potentially, these patients may benefit from the Breethe OXY-1 technology because of its simplicity, compactness, and improved mobility.

Conflict of Interest Statement

Dr Griffith is a cofounder of Breethe Inc and currently a consultant for the company, Dr Wu is a cofounder of Breethe Inc, and Dr Zhang has intellectual property interest related to blood oxygenators.

The *Journal* policy requires editors and reviewers to disclose conflicts of interest and to decline handling or reviewing manuscripts for which they may have a conflict of interest. The editors and reviewers of this article have no conflicts of interest.

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Key Words: ECMO, portable, console without compressed gases