12. Liquid Ventilation

Introduction

We use the term “liquid ventilation” here to describe multiple rapid infusions of the lungs with a breathable liquid capable of introducing oxygen and removing carbon dioxide. In cryonics applications, the liquid will be chilled for the purpose of rapidly cooling a patient.

Although boluses of cold perfluorocarbon liquid have been delivered to the lungs of at least one cryonics patient,[1] liquid ventilation by our definition has not been employed in a cryonics case at the time of writing. However, the procedure has been extensively tested in animal studies which initially achieved peak cooling rates of 0.5 degrees Celsius per minute[2] and later 1.0 to 1.3 degrees Celsius per minute (see Figures 12-1 and 12-2). These studies suggest that liquid ventilation has the capability to achieve cooling after cardiac arrest at several times the rate attainable by immersion in ice and water alone, and may cool the body more rapidly than any procedure other than extracorporeal bypass (ECB)[3] while being minimally invasive and appropriate for field deployment.

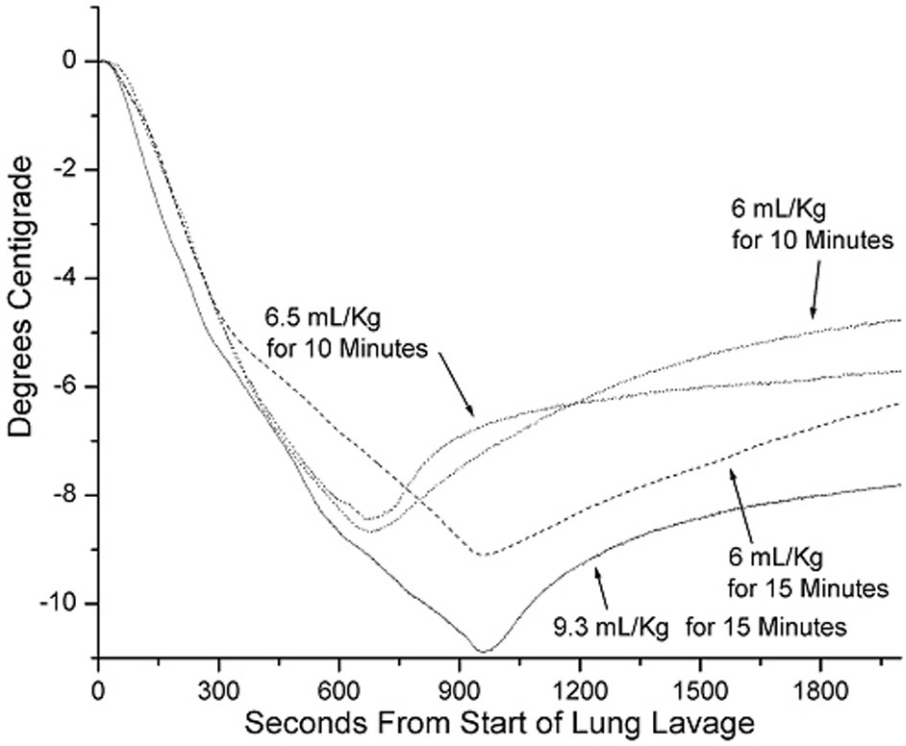

Figure 12-1. Cooling curves from experiments with liquid ventilation devices. These curves were submitted with an international patent application in 2008. A peak cooling rate of greater than 1 degree Celsius was achieved repeatedly, and even at the lower temperature range of 9 to 11 degrees below normal body temperature, the lowest of the curves shows that a rate of approximately 2 degrees in 5 minutes was recorded (0.4 degrees per minute). Temperatures were measured tympanically.[3]

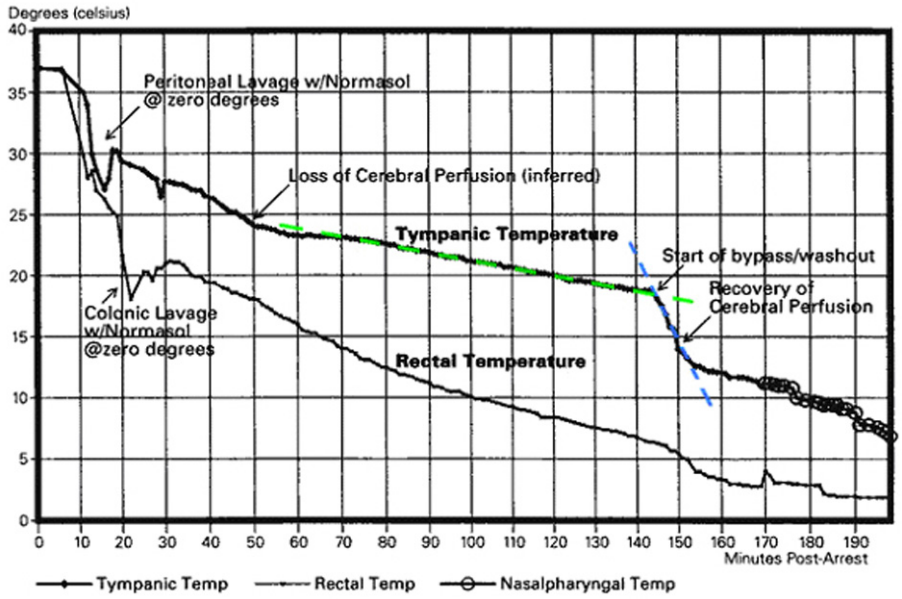

Figure 12-2. Cooling curves from a cryonics case show the approximate cooling rate when the patient received only surface cooling in an ice bath (green dashed line, about 0.06 degrees per minute) and was subsequently cooled via extracorporeal bypass (blue dashed line, about 1.3 degrees per minute).[3]

Because liquid ventilation requires no surgical procedures (only intubation), we may expect that it should be usable in many environments after pronouncement of legal death. By comparison, ECB usually entails removing the patient from the place where death was pronounced, loading the patient into a vehicle, and moving the patient to a location such as a mortuary where perfusion of the circulatory system with chilled organ preservation solution can be initiated. Relocating the patient, setting up and debubbling the perfusion circuit, and obtaining vascular access via femoral cutdown can impose a total delay of 2 to 3 hours, during which the patient typically receives nothing more than surface cooling in a portable ice bath while chest compressions continue.

Gravity-fed perfusion with stepped concentrations of cryoprotective solution has been introduced by Alcor for field neurovitrification, but this too requires relocating the patient to (usually) a mortuary where femoral cutdown

is performed. If it is preceded by liquid ventilation, cooling will be achieved more rapidly.

In both of these scenarious we believe that a portable liquid ventilation device can be located at the bedside for use within minutes after a patient has been pronounced.

A liquid-ventilation prototype with the theoretical capability of cooling a human patient was completed and animal-tested successfully during 2011, but required manual adjustaments and a skilled operator, and was never used outside of a laboratory. Several liquid ventilation prototypes were developed during 2011 through 2019 by Suspended Animation, Inc., but none has been tested with complete success. For more information, see the section titled Subsequent Developments, below.

Origins and History

Fluorocarbons can have very low viscosity and low surface tension, are capable of dissolving oxygen and carbon dioxide, but are generally nonreactive and nontoxic. Certain fluorocarbons do not mix with either water or fats, so they can come into contact with cells and tissues without interacting with them chemically. These properties make them suitable as a substitute for air in the lungs.[4]

A *fluorocarbon* is a chemical compound containing carbon and fluorine atoms. A *perfluorocarbon*, or perfluorinated compound, sometimes referred to as a PFC, is a fluorocarbon containing only carbon and fluorine atoms. The two chemical terms now tend to be used interchangeably, but in this text we prefer *perfluorocarbon*, as it is the more accurate term to describe liquids currently being used for infusion of the lungs.[5]

The first successful experiments to ventilate the lungs with a liquid were described in a paper by Leland C. Clark, Jr. and Frank Gollan published in 1966.[6] The authors reported experiments with mice and cats that breathed perfluorocarbon liquids for up to one hour and were revived afterward without significant signs of injury.

Prior to 1966, experiments in liquid breathing had been pursued at the State University of New York at Buffalo by Johannes Kylstra, who reported

his work in 1962.[7] He used a saline solution which he managed to load with oxygen under high pressure, but the saline could not remove carbon dioxide fast enough, and severe respiratory acidosis was the unfortunate result. Unlike perfluorocarbons, saline can also cause lung dysfunction by dissolving surfactant that is naturally present inside the lungs to prevent alveoli from collapsing.

Kylstra later became familiar with the work by Clark and Gollan, and adopted perfluorocarbons in new research that he began in May, 1969 at Duke University Medical Center, with funding from the U. S. Navy's Office of Naval Research. The Navy was interested in the possibility of using a breathable liquid to address the problem of decompression sickness among divers, commonly known as "the bends." Because a significant pressure differential can cause the lungs to collapse, deep-sea divers must breathe air that is pressurized. However, nitrogen, found naturally in the air, tends to dissolve in tissues under pressure. When the diver resurfaces, the nitrogen returns to a gaseous state, forming bubbles that can cause pain and, in extreme cases, death. Because liquids are effectively noncompressible, and need not contain any dissolved nitrogen, Kylstra hoped that filling the lungs with a breathable liquid could eliminate the problems associated with decompression.[8]

The research at Duke continued until 1975, after which it was summarized in a report titled "The Feasibility of Liquid Breathing in Man."[9][10] Kylstra stated that dogs and rats had recovered fully, with little or no detectable lung damage, after one hour of breathing an oxygenated perfluorocarbon known as FC-80. While he admitted that the solubility of carbon dioxide in pure perfluorocarbon remained less than ideal, he claimed that the solubility could be enhanced by adding sodium hydroxide, to the point where divers would be able to perform active work while breathing the mixture.

Despite his recommendation, liquid ventilation was never widely implemented and remained a curiosity. Many people today are aware of it because they have seen James Cameron's motion picture *The Abyss*, in which a live rat is supposedly shown immersed in perfluorocarbon liquid and the protagonist uses the same technique to survive at an extreme depth. Cameron

has stated that he picked up the idea when he was a 17-year-old high-school student. Supposedly, he attended a science lecture in which a deep-sea diver described his experience breathing saline solution aftter volunteering for one of Kylstra's experiments.[11][12]

Medical Applications

In addition to the possible use of liquid ventilation for deep-sea divers, Kylstra suggested that breathable liquids could be used in the treatment of respiratory problems. This idea attracted renewed interest in the late 1980s and early 1990s, at which time Alliance Pharmaceutical marketed perfluorooctyl bromide (a fluorochemical also known as perflubron) under the brand name *Liquivent*. This was used experimentally to treat premature infants who suffered acute respiratory distress syndrome (ARDS). Because perflubron was added to a flow of air or oxygen, and because the volume of liquid was usually no greater than residual lung capacity, the procedure was referred to as *partial* liquid ventilation (PLV), distinguishing it from Kylstra's earlier experiments which may be described as *total* liquid ventilation (TLV).[13][14] (Residual lung capacity is defined as the amount of air that remains in the lungs after expiration.)

ARDS cases had been traditionally treated with positive-pressure ventilation using oxygen, which can contribute to the development of lung disease. PLV promised to eliminate this risk, encouraging the FDA to allow "fast track" status, which permitted clinical trials. However, when additional trials suggested that the use of high-frequency oscillating ventilation with oxygen improved outcomes as much as using PLV with ordinary ventilators, the FDA chose not to approve perflubron, and Alliance discontinued it.[15]

In 1996, Mike Darwin and Steve Harris, MD started to develop an idea that had been proposed in 1984 by Thomas Shaffer, although he had never succeeded it making it work successfully.[16] If a perfluorocarbon is chilled before using it in liquid ventilation, it can lower the temperature of a human patient rapidly. A chilled liquid is far more effective for this purpose than a cold gas, because an equal volume of liquid is capable of removing many times more heat.

Infusing a chilled liquid would induce the lungs to function as an endogenous heat exchanger, taking advantage of their huge internal surface area, typically estimated to be about 160 square meters. Blood would be cooled as it flowed through the network of capillaries embracing the lungs, and would then circulate up to the brain, cooling it from within.[17] Such rapid cooling would be especially valuable for patients resuscitated after cardiac arrest, because mild hypothermia after resuscitation is known to reduce reperfusion injury.

Harris and Darwin also saw that if ventilation of the lungs with a chilled liquid continued for an extended period, it could induce deep hypothermia, making it ideal for cryonics patients, provided that some blood circulation could be maintained by chest compressions. The circulation would be required not only to continue oxygenation of the patient (if this was appropriate under the circumstances of the case) but also to convey warm blood from the brain the lungs, where it would be cooled before returning to the brain.

Cryonics Applications

The first design tested by Darwin and Harris involved pumping perfluorocarbon liquid through pre-chilled cartridges containing highly permeable filters, as shown in Figure 12-3. Darwin described this work initially in a cryonics magazine, and coauthored a patent under the name Michael Federowicz.[18][19]

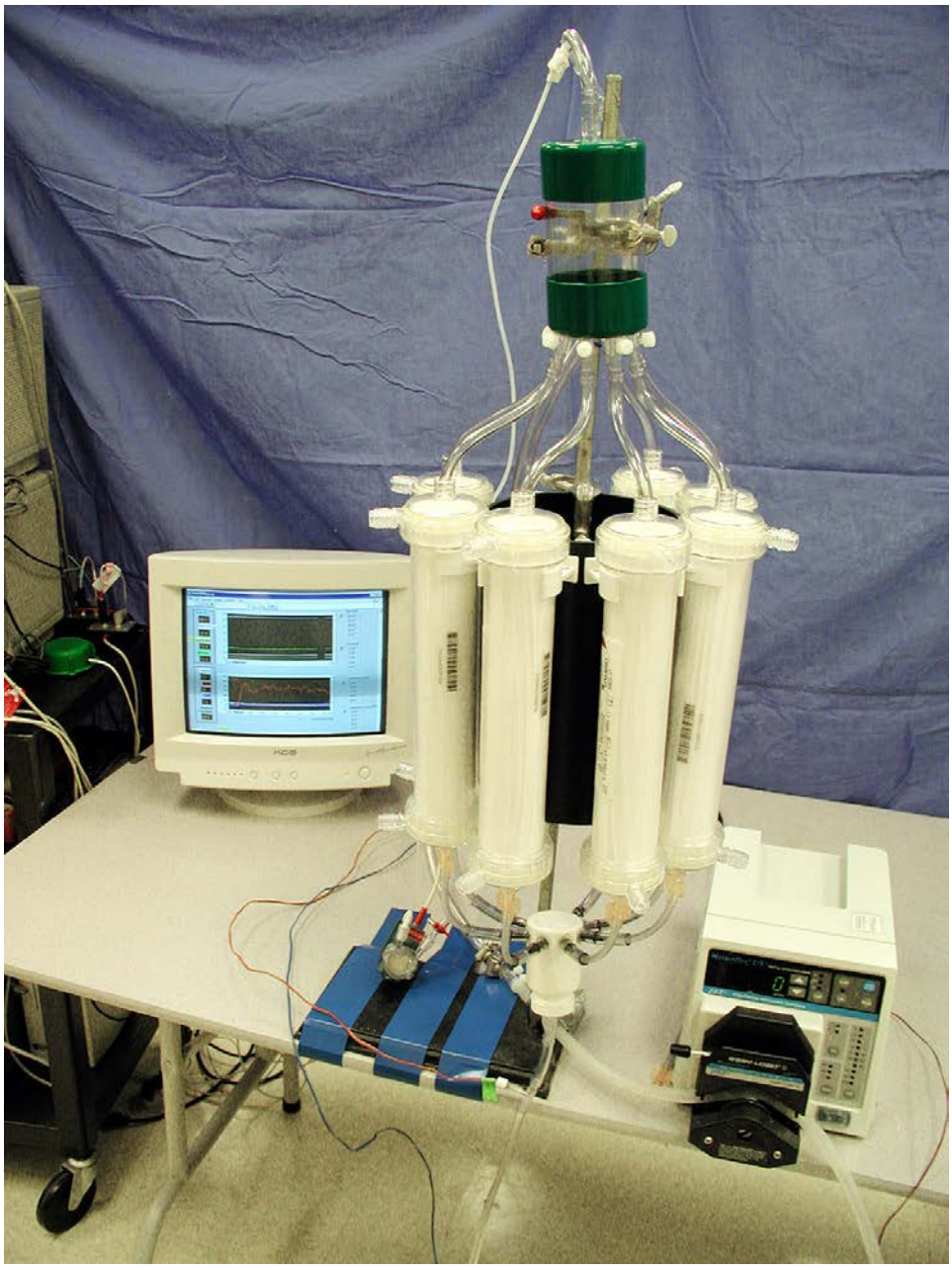

Figure 12-3. This cartridge system for cooling and oxygenating perfluorocarbon liquid was used experimentally for total liquid ventilation in 1996.

However TLV (using fluid but no gas) entails problems. While perfluorocarbon liquid has a low viscosity, it is still about 80 times that of air, limiting the number of infusions per minute. Moreover, no way has been

found to improve the removal of carbon dioxide that Kylstra identified as a problem several decades ago. More significantly for cryonics applications, Harris and Darwin were unable to achieve cooling rates which basic physics suggested should be available. They speculated that "thermal equilibrium is not reached between blood and liquid in small airways at high TLV 'alveolar ventilation' rates. Thus, there appears to be a heat-diffusion limitation to TLV."[20]

To address these concerns, they developed a form of partial liquid ventilation which they described as *mixed mode*, adding gas in conjunction with perfluorocarbon liquid. They wrote: "We believe that the mixing of PFC and gas disrupts laminar liquid (PFC) flow in small airways by introducing turbulence to the fluid, thereby improving the small-scale (small airway) convection necessary for maximal heat transfer rates." In a patent that was issued in 2004 they claimed that mixed mode liquid ventilation had achieved a cooling rate of 12 degrees C in 30 minutes—a net drop of 10 degrees after equilibration, representing an average of about 0.3 degrees per minute. Graphs included in the patent suggested a peak rate of about 0.5 degrees per minute.[20]

An engineering company was retained to create a portable version of this system. When the results were considered unsatisfactory, a second engineering company was brought in. Meanwhile, the laboratory version of the apparatus evolved and became simpler as a result of in-house improvements, but was not portable, which made it unsuitable for cryonics field work or deployment with paramedics in conventional medicine.

Designs by Suspended Animation

In 2006, following unsatisfactory results from the second engineering company, Suspended Animation, Inc. in Boynton Beach, Florida developed a radically simplified, portable design. Charles Platt and Gary Battiato initially built a downsized replica (identified here as LV1) of the most recent laboratory version, as a proof-of-concept. This incorporated Battiato's creative suggestion to use a Pelican brand transportable container not only to transport the equipment but also as an icewater reservoir, with a perfluorocarbon tank

located in the center. The tank was entirely surrounded by ice and water, which not only helped to cool the tank but also insulated it actively from its surroundings—so long as ice remained in the water to absorb heat via latent heat of fusion. Heat incursions through the sides and bottom of the Pelican container were overcome simply by adding more ice, and thus this configuration eliminated bulky insulation. The nested-reservoir configuration also made the device simpler to deploy and more portable. See Figure 12-4.

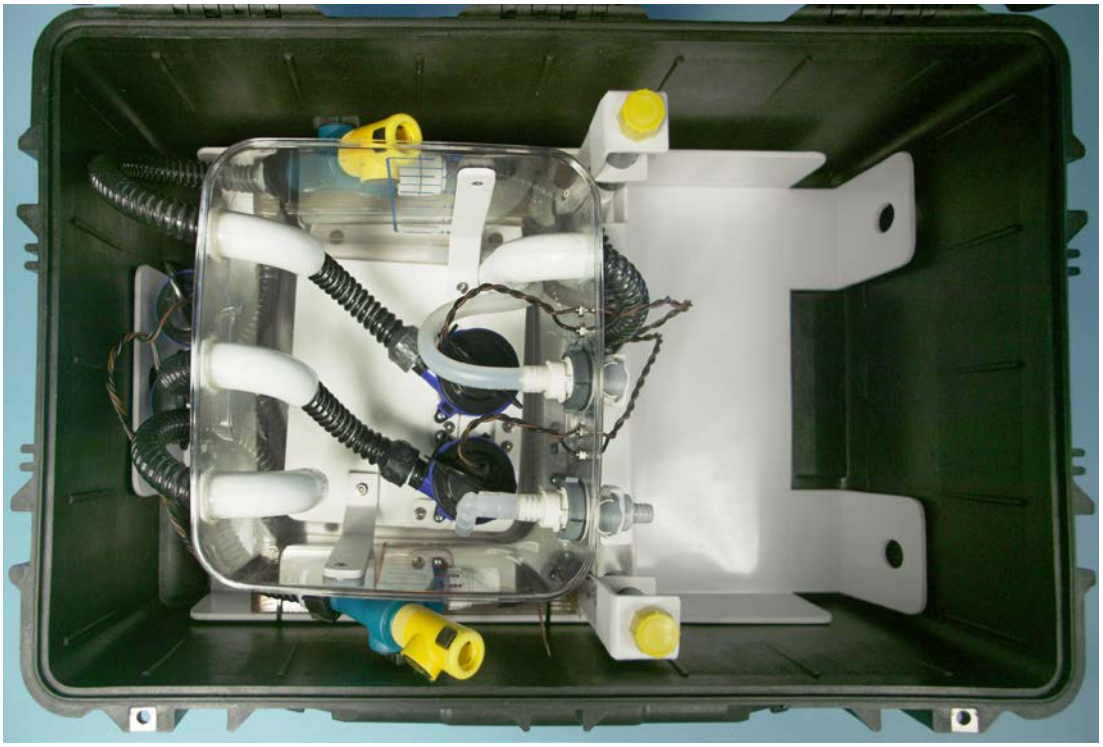

Figure 12-4. The first liquid ventilation device, LV1, developed at Suspended Animation. In this very simple design, small 12-volt submersible, centrifugal marine pumps were used to cool the perfluorocarbon through a heat exchanger, and to deliver perfluorocarbon via an infusion tube (not shown). A diaphragm pump created suction to return perfluorocarbon liquid to the central reservoir. Infusion and suction tubes were inserted in the yellow quick disconnects. The device could be controlled either manually or via a single 555 timer chip.

Shortly after the development of LV1, Darwin suggested that since liquid ventilation is likely to be used in conjunction with a portable ice bath, the heat exchanger in a liquid ventilation device could be cooled with water from the ice bath to avoid maintaining two separate reservoirs. While this suggestion seemed superficially attractive, it ignored several factors.

- The water in a portable ice bath may be contaminated with bodily excretions. Maintaining separation of the liquid ventilation system seems desirable for this reason alone.
- Provision would have to be made to avoid the risk of either overflows or a low level in the Pelican container, if water was pumped in or out.
- While the availability of a portable ice bath in conjunction with liquid ventilation is likely, it cannot be guaranteed. Various factors, such as damage to the bath or loss of the bath by airline baggage handling, may interfere. In some patient locations, moving a portable ice bath to the bedside may be impossible. The absence of an ice bath should not preclude the use of liquid ventilation.
- The design of LV1 used a pump to circulate water through a heat exchanger while simultaneously promoting circulation of water around the perfluorocarbon reservoir. Thus, one small pump served two purposes. Using water from a portable ice bath would require an additional pump to raise the water to the liquid ventilation system, and probably a second pump to return the warmed water to the ice bath, since a gravity feed might not be sufficiently rapid or reliable. Adding two pumps would increase the weight of the equipment and its power consumption, while also increasing the risk of equipment failure.
- Tubing to connect the liquid ventilation equipment with the portable ice bath would be vulnerable to kinks and accidental displacement during activity surrounding the ice bath. The tubing

would have to be insulated on the input side, which would add to its bulk and inconvenience. Even with insulation, the tubing would allow some heat incursion.

- Because of the large size of the portable ice bath, and the presence in it of a warm human body, “hot spots” would be likely in the bath. There would be no way to guarantee that water drawn from any particular location in the bath would be close to 0 degrees Celsius. Team members working under time pressure could easily make the mistake of drawing water from the ice bath in a location close to the patient’s body.
- The need for a portable ice bath would probably preclude the liquid ventilation equipment from being applied in conventional medicine.

Summing up, sharing water from a portable ice bath would add many problems while providing few benefits. By comparison, adding ice and water to the liquid ventilation reservoir provides several benefits and is a quick and simple operation.

Afer successful testing of LV1, Platt developed a radically different tubing circuit that was built into LV2, the next prototype to be developed. LV2 was demonstrated at the Suspended Animation open house event in 2007, and was then moved to California where it was animal-tested extensively, achieving an impressive peak cooling rate of approximately 1 degree Celsius per minute. (See Figures 12-1, 12-5, and 12-6.)

Figure 12-5. The LV2 liquid ventilation assembly designed and fabricated at Suspended Animation and demonstrated in 2007. The control panel in the lower Pelican container could be lifted out so that ancillary items (such as the infusion pump and insulated delivery tube) could be stowed below it for transportation. Lids of the Pelican containers were removable, and the stainless-steel frame was disassembled for shipping in a separate box. The concept of a frame was discontinued in LV3 in favor of a simpler arrangement in which the two Pelican containers were stacked and a small wheeled subframe was added to the lower container. LV2 used a more powerful suction pump than LV1, but infusion was provided by the same small submersible pump as in LV1.

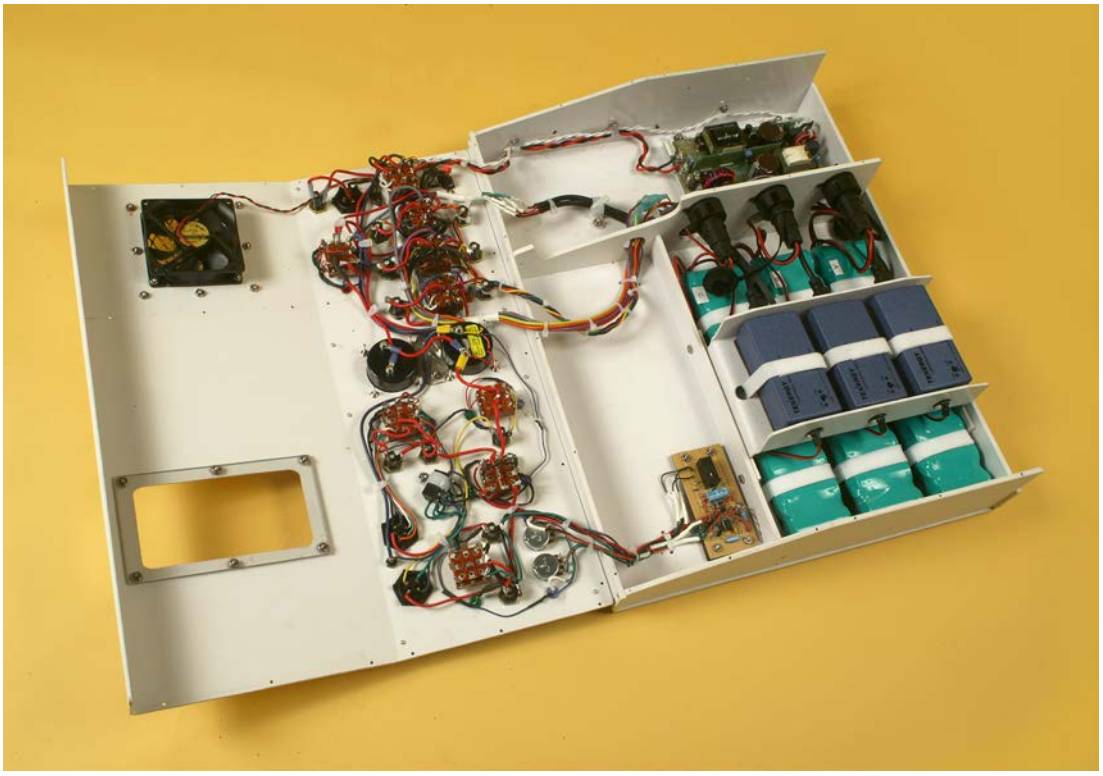

Figure 12-6. The control panel for LV2, opened to reveal three battery packs and chargers, an AC-DC converter in a separate compartment, and very simple control electronics on a 2x4 inch circuit board.

Platt relocated to California to work fulltime on design and fabrication of LV3. This new version incorporated suggestions and requests that had emerged during the testing of LV2. A larger suction pump addressed the issue of residual perfluorocarbon remaining in the lungs, and the primary Pelican case was redesigned to rest across the rails of a portable ice bath, above the patient's legs. This configuration was later abandoned as elevation of the suction pump above the patient greatly reduced its efficiency. The tubing circuit for LV3 is shown in Figure 12-7, while various views of the equipment are shown in Figures 12-8, 12-9, 12-10, and 12-11.

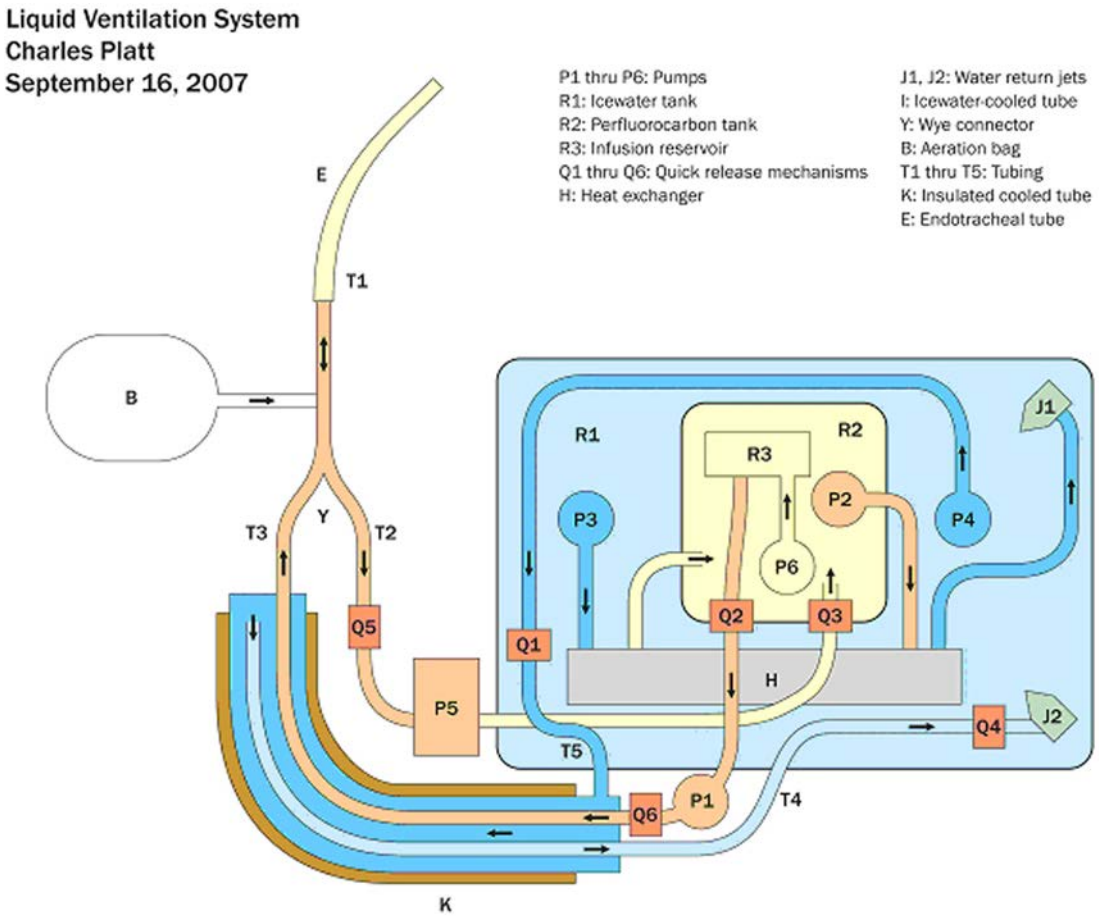

Figure 12-7. This diagram was created in preparation for a patent application filed in 2008. It shows the main components that were planned at that time for LV3, including the insulated delivery tube (K) with an icewater jacket, and external infusion and suction pumps (P1 and P5) to be mounted outside the Pelican container when the equipment was assembled.

Figure 12-8. In LV3, batteries and chargers were were mounted inside the lid of the primary Pelican container, alongside switches and control electronics. A more powerful infusion pump and a more powerful suction pump than in LV2 were mounted in a separate box, together with a small pump that cooled an icewater jacket on the delivery tube (the tube is not shown here).

Figure 12-9. The pump boxfor LV3 was located on a platform that could slide out to allow access to the perfluorocarbon reservoir below. The whole assembly was designed to sit above the patient's legs on the rails of a portable ice bath, but its elevation greatly reduced the efficiency of suction from the lungs..

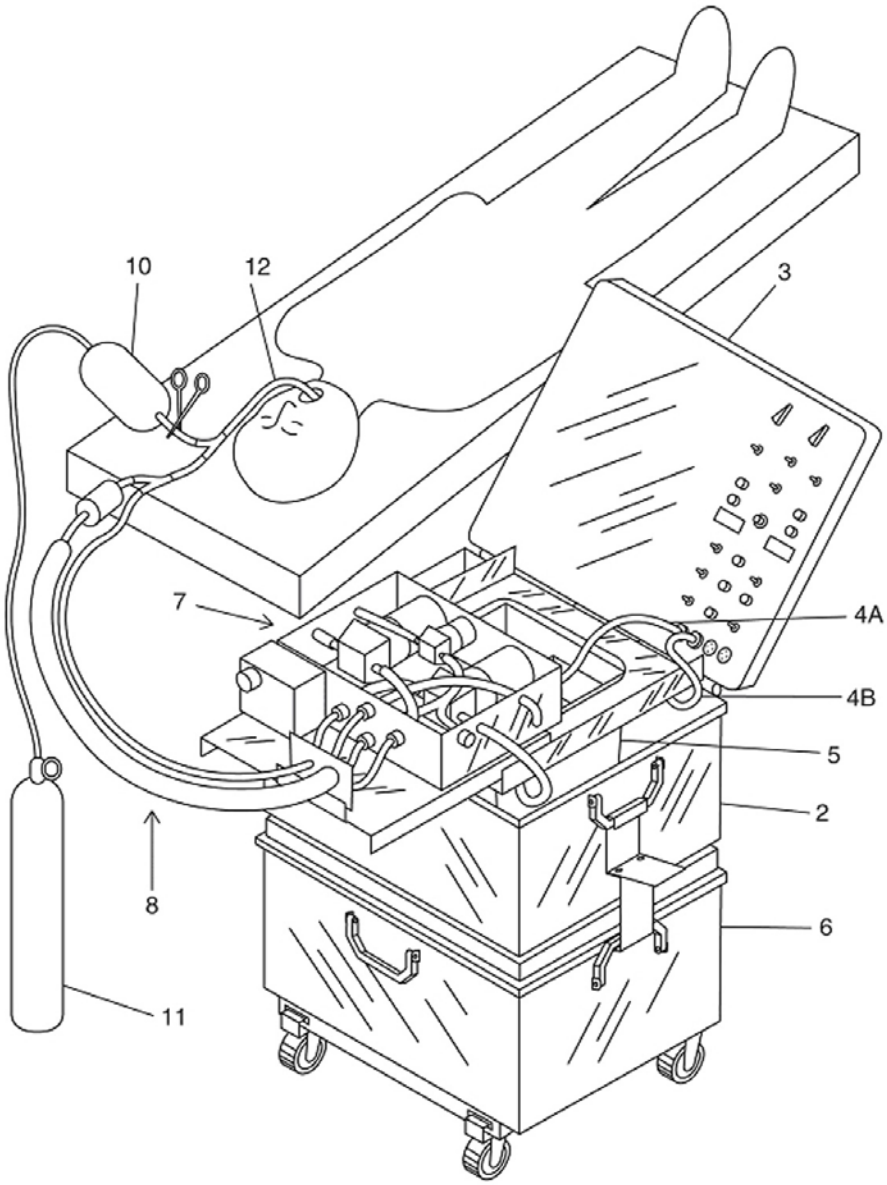

Figure 12-10. A diagram of LV3 that was included in the patent application in 2008, rendered in the style required by the U. S. Patent Office. Electronics in the lid of the primary Pelican container (3) control pumps on the upper tray (7) and in the perfluorocarbon reservoir below (5) via detachable cabling (4A, 4B). The jacketed delivery tube (8) can convey perfluorocarbon liquid to a hypothetical patient via an endotracheal tube (12), with oxygen delivered from a cylinder (11) via a conventional medical bag valve (10). Wheels beneath the secondary Pelican container (6) are on a removable subframe.

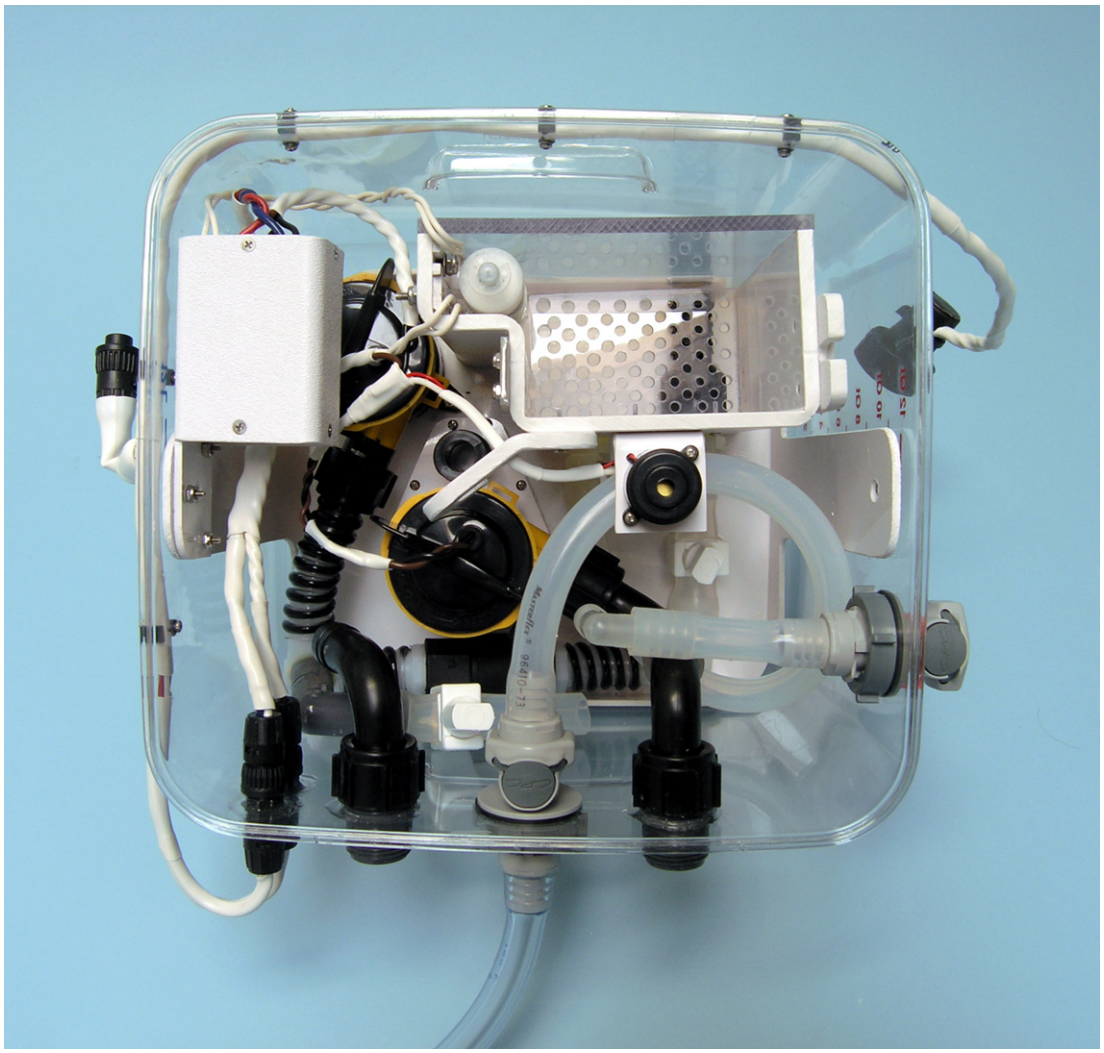

Figure 12-11. Overview of the perfluorocarbon reservoir in LV3. The sub-reservoir at top right was enlarged relative to the infusion reservoir in LV2, to provide sufficient capacity for cryonics cases, although the system was never used for this purpose.

All electronics were built into the lid of the primary Pelican case of LV3, while infusion and suction pumps were placed in their own module, consisting of box on a sliding tray that allowed access to the perfluorocarbon reservoir. These features were described and illustrated in an international patent application filed in 2008.[19]

In response to requests for a more automated version that would be appropriate for standby-stabilization personnel in cryonics cases, Platt started work on LV4 in 2009, but encountered problems relating to his extensive use of microcontrollers for functions including the display of prompts and error messages, the monitoring of all processes and temperatures, the saving of data at half-second intervals on flash memory, and the update of a realtime display of all experimental parameters. In 2010 Platt suggested passing the project back to Suspended Animation in Florida, and the prototype that he had developing was shipped to Florida later in the year (see Figure 12-12).

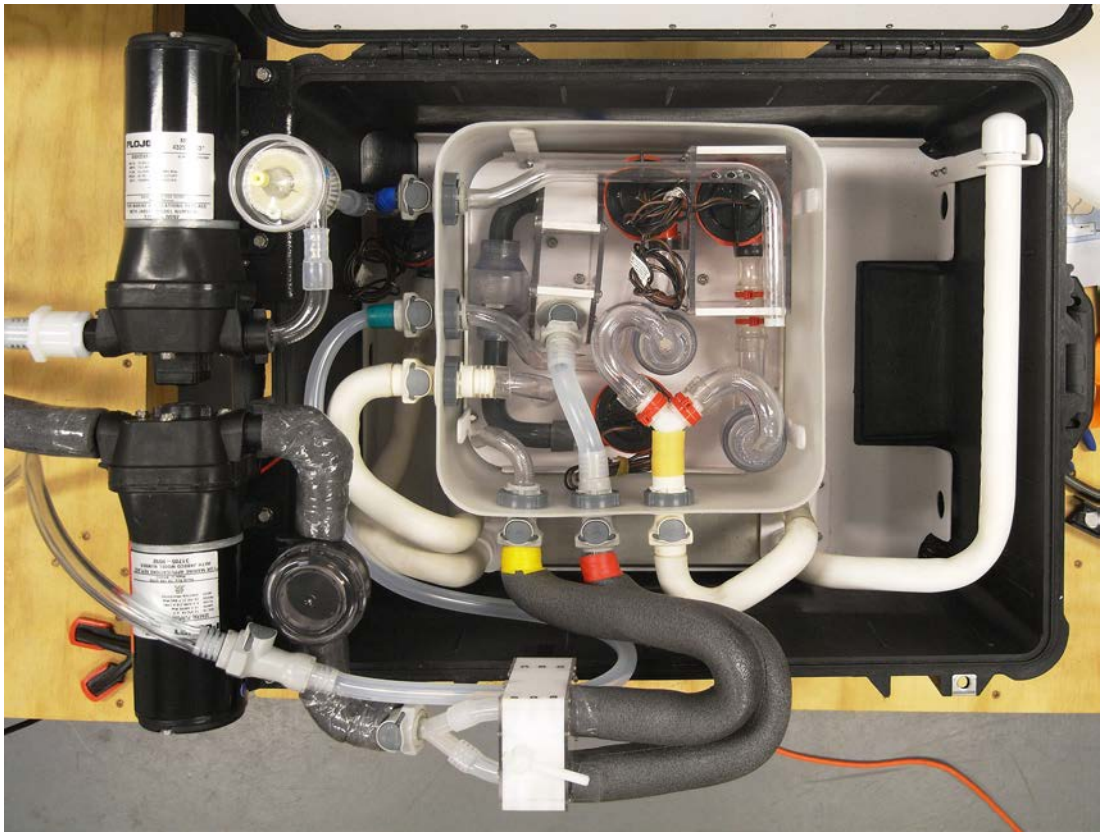

Figure 12-12. For LV4, a larger perfluorocarbon reservoir accommodated two sub-reservoirs, one to measure infusion volume and a second to measure the returned volume in each cycle, so that a running average could be calculated, indicating whether liquid was accumulating in the lungs. The additional sub-reservoir entailed complications such as a need for check valves and other associated plumbing. To

allow maximum flow rates, custom-curved polyethylene and polyvinyl tubing were used instead of elbows and tees throughout. The two black, detachable pumps at left are the suction pump (top) and infusion pump (bottom), with a filter and a strainer alongside them. The empty space at right was to accommodate ice and water. Control electronics had not been installed when this picture was taken.

Suspended Animation announced its intention to finish and test LV4 with new, LabView-based control electronics by May, 2011. This ambition was only partially fulfilled when an initial test was reported to have failed as a result of a valve malfunction. Later in the year, Suspended Animation reported informally that a subsequent test had been successful using a pig cadaver, with a claimed peak cooling rate of around 1 degree C per minute. No additional information was provided.

Design Features

Some features remained constant throughout versions LV2 through LV4. In particular:

- All equipment was transportable in two model-1620 Pelican-brand cases. The primary case housed reservoirs and cooling pumps. The secondary case stored loose parts and tubing that had to be removed and assembled on-site in conjunction with the primary case, which was stacked above the secondary case during use.
- Ice was used as the cooling agent, because its high latent heat of fusion allows a relatively small weight to absorb large amounts of heat. Ice is readily available in any part of the country and is already required in stabilization procedures. Melting ice is incapable of reducing perfluorocarbon temperature below 0 degrees Celsius, which is considered an advantage, as lower temperatures would be potentially harmful to human tissue.

- Since the lungs are nonsterile, medical-grade peristaltic pumps were considered unnecessary. Peristaltic pumps are heavy, consume a lot of power, and are unavailable in 12-volt versions. A fundamental design goal was to have an all-12-volt system so that it would be fully portable and could be run, if necessary, from internal nickel-metal hydride batteries or an external car battery.
- Low-cost, small, high-volume centrifugal marine pumps were used to circulate perfluorocarbon and icewater through a heat exchanger. Larger diaphragm pumps were used for infusion and for suction in LV3 and LV4, since they are very robust and are able to run dry or pump a mixture of gas and liquid without damage. The diaphragm pumps are much heavier than the centrifugal pumps, but this was considered a necessary tradeoff.
- Three sets of nickel-metal hydride batteries were included, each rated to deliver up to 10 amp-hours, for a theoretical total of 30 amp-hours. The batteries proved capable of powering the system during operation for up to half an hour without a significant voltage drop. A medical-grade AC-DC converter was also included, capable of supplying almost 30 amps.
- In the interests of simplicity, the infusion volume was set by inserting plastic tabs into a small reservoir, to displace some of the liquid volume. This system proved more reliable than other volume-measurement strategies such as using flow sensors, weighing the reservoir, or using pressure-driven or ultrasonic level sensors.
- The equipment was designed for rapid assembly and for easy disassembly to allow cleaning.

Some of these features were upgraded in yet another version of the equipment, LV5, which was built by Charles Platt in response to a request for a system with simpler electronics that would be specifically suited for continuation of lab testing. This version is shown in Figure 12-13. It was

begun in February, 2011 and was completed and delivered in May, 2011. It featured an enlarged perfluorocarbon reservoir and a greatly simplified system for setting infusion volume, using a float-based level sensor mounted on a screw thread. A separate return reservoir was added for assessing volume suctioned from the lungs, and a drain valve allowed easier removal of water accumulating from melted ice. A manually operated pinch valve was included to switch between infusion and suction modes, and several fail-safes were added to simplify setup and reduce any risk of operator error. The control electronics in LV5 consist of a single 40-pin PIC microcontroller which could be reprogrammed via an external port. The system had sufficient capacity for human lungs, but was never used in cryonics cases.

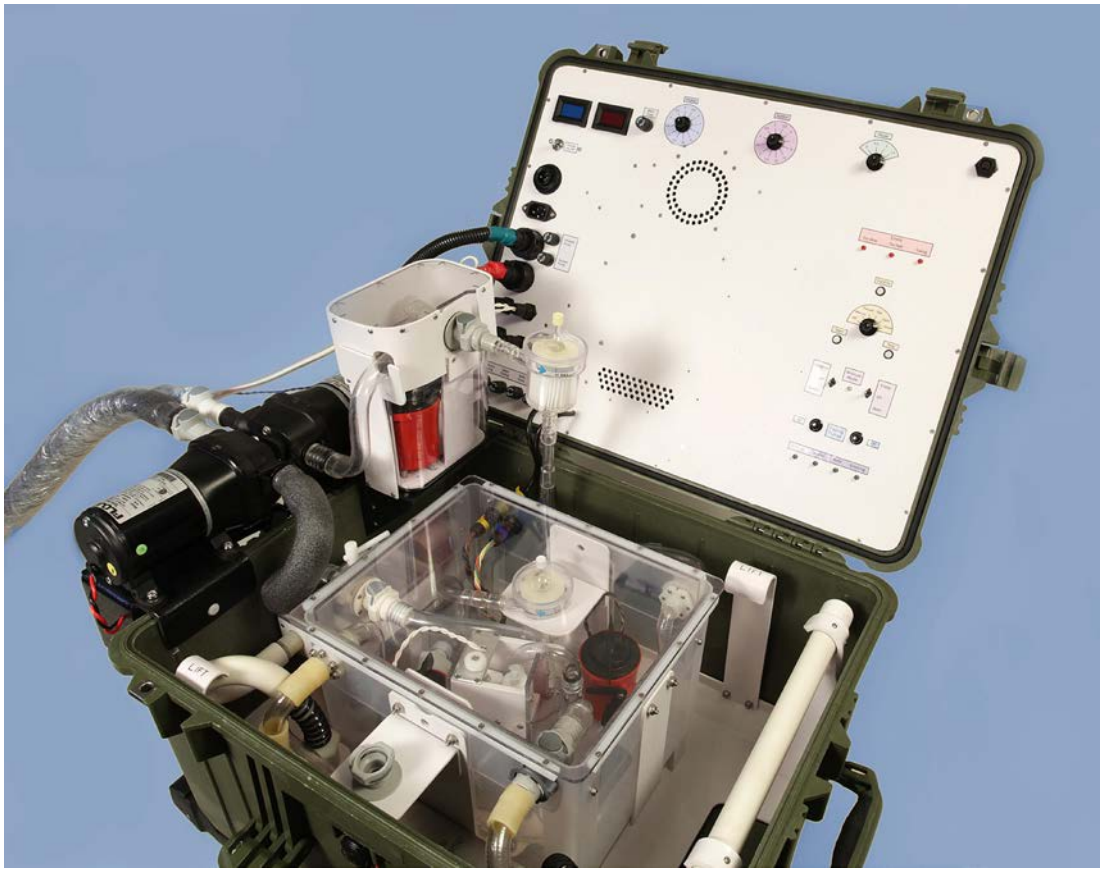

Figure 12-13. LV5 was developed by Charles Platt in 2011 primarily for laboratory work. It uses a similar tubing configuration to that in LV4, with the addition of an elevated return reservoir (visible here with a red pump inside it), allowing simple visual assessment of liquid volume during suction cycles. The main perfluorocarbon reservoir was increased to the maximum size permitted by available space, and an icewater drain port was added (visible near the front of the Pelican container). Greatly simplified controls are visible at the right-hand side of the lid. Various connectors are visible on the left, allowing disconnection of all components for easy cleaning. A socket at top-right enabled the internal PIC microcontroller to be reprogrammed at any time. As this design was intended for laboratory use, there is no provision for battery power, although a socket at the left side of the lid allows connection of an external 12VDC source if one is available.

Subsequent Developments

In 2018, a comparison test was performed between LV5 and the most recent prototype developed independently at Suspended Animation, Inc. The comparison was informal, using different animal models at different laboratories, but was useful insofar as some problems became apparent with the SA version.

In 2019, because LV5 was now eight years old, and because there was renewed interest in using liquid ventilation in cryonics cases, Alcor contracted for new equipment, tentatively named LV5.1, to be developed jointly by Steve Graber in Scottsdale and Charles Platt at his own workshop in Northern Arizona. Graber was to build the hardware, while Platt would write the control software.

Later in 2019 it was decided that Graber would commission his own software for LV5.1 while Platt would develop hardware and software for a prototype referred to as LV5a. While LV5.1 was expected to be more innovative, LV5a would be as similar as possible to LV5, to minimize the risk of unexpected problems in development. At the time of writing, neither LV5.1 nor LV5a has been completed. Meanwhile, equipment at SA is undergoing more development.

While the concept of liquid ventilation is extremely easy to understand, building functional prototypes has been surprisingly elusive.

During eight years of testing LV5, the peak cooling rate of slightly more than 1 degree Celsius per minute has been consistent, although this rate inevitably levels off asymptotically as body temperature drops closer to the temperature of the perfluorocarbon. In experiments where animals were not sacrificed, almost all were subsequently revived and showed no signs of long-term injury. All experiments were performed under Department of Agriculture regulations which control procedures in animal laboratories, and general anesthesia was used in all cases.

Operation

Operation of LV3 and LV5 has entailed the following steps. A similar setup procedure is likely in future versions, although several steps will be automated. Additional details are not known at this time.

- Setup. Unpack the secondary Pelican case. Attach removable wheels to the secondary case. Stack the primary case on top of the secondary case and use the provided clamps to hold the cases together. Attach the infusion pump, suction pump, and delivery tubing to the tubing assembly in the primary Pelican case. Select infusion time and suction time, for each cycle. In LV3: Insert volume displacement tabs in the infusion reservoir as needed to allow delivery of a selected volume in each cycle. In LV5: Turn a screw that moves a level sensor, to establish the preferred infusion volume.
- Power. Make sure that all power switches are off. Select a power source: Batteries, AC, or external 12VDC. Check that batteries are fully charged, if they are to be used.
- Liquids. Pour perfluorocarbon liquid into the perfluorocarbon reservoir. Load the icewater reservoir with water and ice. Distilled water is preferred, as it leaves no residues. Cube ice is preferred, as it is less liable to clog the plenum under the perfluorocarbon reservoir.
- Cooling. Make sure all pump switches are off before turning the power on. Start the cooling pumps that circulate water and perfluorocarbon through the heat exchanger.
- Volume check. After about 10 minutes, the perfluorocarbon liquid should be close to 0 degrees Celsius. Place a graduated cylinder under the ET tube, put the system in manual cycling mode, and run some test cycles to verify that the infusion pump delivers the selected volume within the selected time. Adjust the speed of the

infusion pump if necessary. (This step will almost certainly be eliminated in cryonics cases, where the control of infusion speed should be of less concern, as minor lung injury may be considered of secondary importance to the cooling rate.)

- Standby mode. Top off the perfluorocarbon reservoir if necessary, to compensate for accumulation of liquid in tubing. Run cooling pumps as needed. Add ice if needed. Remove accumulation of water from melted ice, if needed (a secondary pump is used for this, but a simpler method is likely in deployable equipment).
- Cycling. When signalled by the operator, begin infusion-suction cycling, either using automatic control or using manual control, as desired.
- Finishing. When the operator wishes to end the procedure, run the suction pump continuously to clear any residual perfluorocarbon liquid from the lungs.
- Cleanup. Turn power off, disconnect tubing, empty the reservoirs, and recover perfluorocarbon liquid if possible, for subsequent filtration and reuse.

Future Development

During laboratory tests, the infusion volume has been established with reference to the body weight of the animal, because the body weight of lab animals used in the tests is roughly proportional with lung volume. Human patients will require a different methodology.

Kylstra's research in the early 1970s established some basic parameters for moving liquid into and out of the human lungs. He used a recognized medical procedure to infuse saline into one lung of a "healthy volunteer" while the other lung continued to breathe normally. The volunteer remained conscious during the procedure, receiving only a local anesthetic to numb his larynx and trachea, and in Kylstra's sardonic phrase, "did not experience intolerable sensations arising from the flow of saline."

Having determined that 500ml saline could be drained from the lung in a minimum time of 9.4 seconds, while infusion of the liquid under pressure could be faster, Kylstra concluded that the human lungs could be ventilated with liquid at a rate of 3 liters per minute. Liquid ventilation using diaphragm pumps for infusion and suction may achieve a rate slightly higher, but this remains a matter of conjecture until the procedure is used in human cryonics cases.

Several factors limit the infusion rate. A human trachea is of similar diameter to a canine trachea, even though the human lungs have a greater volume. An endotracheal tube must fit inside the trachea, and if liquid spurts from the tip of the tube with excessive force, it may cause mechanical injury to the lungs. The LV systems described in this chapter typically deliver 100 ml of liquid within about 2 seconds. We expect this rate to remain with little change in future versions.

Unresolved Issues

A very significant issue in cryonics cases will be the challenge of applying chest compressions concurrently with liquid ventilation. During the majority of the experiments, cardiac arrest was not induced, and thus the issue of cardiopulmonary support was irrelevant. In the minority of experiments that did involve cardiac arrest, application of CPS was judged to be difficult and inappropriate, because the shape of the canine rib cage was incompatible with mechanical chest compressions.

However, Suspended Animation has reported that its first successful test of LV4, in conjunction with a pig cadaver, was performed in conjunction with chest compressions administered via an Autopulse system. Apparently, there was no conflict between the compressions and the infusions of chilled liquid. It is possible that liquid in the lungs may actually enhance the effectiveness of CPS by transmitting the compressive force more effectively. If necessary, liquid ventilation cycles could be synchronized with mechanical chest compressions to optimize cooling. Much work in this area remains to be done.

The concurrent, simultaneous use of a portable ice bath in conjunction with liquid ventilation should increase the cooling rate compared with liquid

ventilation used alone, although not by merely summing the rates that can be achieved by each method. Cooling will always be more effective initially, when the temperature difference between the coolant and the body temperature is greatest. Beyond this, we are unable to generalize in the absence of experimental data.

Liquid ventilation in its current mode will increase the expenses associated with deployment by requiring transportation of additional equipment and consumables, and additional personnel during stabilization.

LV1, LV2, LV3, and LV5 require an operator to add gas to the liquid flow by using a bag valve during each infusion cycle; LV4 was intended to use an automated system for this purpose. The relative merits of the two approaches have not been evaluated, but if a person is required to handle a bag valve, this task will occupy his whole attention.

Someone will be required to add ice when necessary, drain excess water from the icewater reservoir, and monitor the patient temperature, while supervising the operation of two heat exchanger pumps, infusion pump, suction pump, and two additional pumps associated with the reservoirs. Possibly this role can be intermittent, allowing the same person to perform other stabilization duties such as monitoring cardiopulmonary support.

The need for battery power in a liquid ventilation system remains a matter of debate. In almost any imaginable indoor scenario, AC power will be available. If liquid ventilation is used in a rented vehicle, personnel may use jumper cables to tap the vehicle’s battery, although this will actually provide 14 volts or slightly more, and raises the risk of a loose connection resulting in a dramatic (possibly explosive) short circuit. Using batteries built into the liquid ventilation device would undoubtedly be safer, but they raise another problem: We have very little experience regarding the reactions of air transport security personnel when they view an x-ray of checked baggage containing multiple battery packs. Nickel-metal hydride batteries are not controlled by TSA regulations, but lithium-ion batteries are subject to limitations because of their greater potential fire hazard, and we have no way of knowing whether a typical baggage screener can tell the difference.

LV2 was flown successfully from Florida to California as checked baggage, with a large laminated card inside stating that the batteries were

nickel-metal hydride. LV4 was transported from Arizona to Florida via Federal Express. No other experience with long-distance transport of liquid ventilation equipment exists at this time.

The design for LV4 attempted to address the issue of battery transport by mounting the batteries in a separate, external box that could be shipped separately, while the AC-DC converter was mounted inside the lid of the primary Pelican case. Using this configuration, if the battery pack is embargoed, the rest of the equipment can still be used with an AC power source.

A final issue involves conflicting design requirements for laboratory/clinical use and for cryonics patients. The laboratory version of liquid ventilation equipment must be capable of short cycles and smaller volumes appropriate to animal testing, and must be elaborately instrumented for data capture. Researchers want to have manual control over many features, even though this adds to the complexity of the control panel. In the future, we may expect that a simplified cryonics-purposed liquid-ventilation device will be developed using presets with prompts and error messages. LV5.1 and LV5a are being designed with this in mind.

References

1. Three boluses of perfluorocarbon, totalling more than 2 liters, were infused into the lungs of Alcor patient A-1876 by Mike Darwin on March 3rd, 2002 as described in “Fear, Anger, and Hope: The Cryopreservation of Alcor Member A-1876” by Charles Platt. *Cryonics* magazine, Vol. 23:1, 1st Quarter 2002.

2. “Rapid (0.5 degrees C/min) minimally invasive induction of hypothermia using cold perfluorochemical lung lavage in dogs” by Steven B. Harris, Michael G. Darwin, Sandra R. Russell, Joan M. O’Farrell, Mike Fletcher, and Brian Wowk, *Resuscitation* 50, August 2001, pp. 189-204.

3. See cooling curves in Figure 12-1 and Figure 12-2. Figure 12-1 was taken from international patent application WO2009042220 filed on September 26, 2008 by Critical Care Research et al, viewable at

www.wipo.int/patentscope/search/en/detail.jsf?docId=WO2009042220 (accessed February 17, 2011). Figure 12-2 is from "The Cryopreservation of James Gallagher" by Mike Darwin, viewable at http://www.alcor.org/Library/html/casereportC2150.htm (accessed February 28, 2011), originally published in *CryoCare Report* number 6, January 1996. While a comparison between animal studies and a human case is of limited value, and while the curves in Figure 12-1 refer to a temperature range that is more limited than the curves in Figure 12-2, it seems safe to infer that (a) extracorporeal bypass can achieve a radically faster cooling rate than either liquid ventilation or surface cooling, and (b) liquid ventilation is almost certainly more powerful than surface cooling. The figures show that in the temperature range 9 to 11 degrees Celsius below normal body temperature, (probably representing actual temperatues from approximately 28 down to 26 degrees), using a canine model, the cooling rate was about six times as fast as the rate recorded for the human case between 23 to 20 degrees, all temperatures being measured tympanically

4. Fluorocarbon properties described in http://en.wikipedia.org/wiki/Fluorocarbon (accessed February 17, 2011).

5. Chemical definitions found at http://en.wikipedia.org/wiki/Perfluorinated_compound (accessed February 17, 2011).

6. "Survival of Mammals Breathing Organic Liquids Equilibrated with Oxygen at Atmospheric Pressure" by Leland C. Clark, Jr. and Frank Gollan. *Science* 24, June 1966: Vol. 152 no. 3730.

7. Kylstra delivered a paper titled "Of Mice as Fish" at a medical conference, as described in "Artificial blood—an emergency air-lift?" by Dr. Michael Rose, in *New Scientist* magazine, November 27, 1980.

8. Overview of liquid breathing at http://www.medic8.com/medicines/Perflubron.html (accessed February 17, 2011).

9. Scanned pages of the typewritten report are archived att http://www.dtic.mil/cgi-bin/GetTRDoc?AD=ADA037089&Location=U2&doc=GetTRDoc.pdf (accessed February 16, 2011).

10. Research summarized at http://archive.rubicon-foundation.org/4257 (accessed February 16, 2011).

11. Wikipedia entry on “The Abyss” at http://en.wikipedia.org/wiki/The_Abyss (accessed February 16, 2011).

12. Interview with James Cameron at http://www.ldsfilm.com/directors/Cameron.html (accessed February 16, 2011).

13. “Liquid Ventilation of Preterm Baby” by Jay S. Greenspan , Marla R. Wolfson , S. David Rubenstein , and Thomas H. Shaffer in *The Lancet*, Volume 334, Issue 8671, November 4th, 1989.

14. “Partial Liquid Ventilation with Perflubron in Premature Infants with Severe Resperatory Distress Syndrome” by Leach et. al., *New England Journal of Medicine*, Volume 335, Number 11, September 12th, 1996.

15. Wikipedia entry on liquid breathing at http://en.wikipedia.org/wiki/Liquid_breathing (accessed February 16, 2011).

16. This claim is made in U. S. Patent 6,694,977 filed by Federowicz et al., issued February 24th, 2004.

17. “Here, Breathe this Liquid!” by Charles Platt in *Discover* magazine, vol. 22, No. 10, first published 2001.

18. Darwin’s article was titled “A Bypass on the Way to Bypass” in *CryoCare Report*, number 7, April 1996.

19. U. S. Patent 5,927,273, issued in July, 1999.

20. This statement is made in U. S. Patent 6,694,977, issued in February, 2004.

21. The patent application for LV3 can be viewed at www.wipo.int/patentscope/search/en/detail.jsf?docId=WO2009042220 (accessed February 17, 2011).