

Design and Evolution of the Asporto Heart Preservation Device

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Abstract: The Asporto Heart Preservation Device is a system providing perfusion of cardioplegia to the donor heart using a computer-controlled peristaltic pump in a thermoelectrically cooled and insulated container. In 1998, a user interface was developed at the University of Minnesota consisting of a touch screen and battery-backed microcontroller. Power was supplied by a 120 VAC to 12 VDC converter. An upgrade to the insulated cooler and microcontroller occurred in 2002, which was followed by proof of concept experimental pre-clinical transplants and tests demon-

strating the efficacy of the device with isolated donor hearts. During the period between 2002 and 2006, a variety of donor organ containers were developed, modified, and tested to provide an optimal sterile environment and fluid path. Parallel development paths encompass formalized design specifications for final prototypes of the touch screen/microcontroller, organ container, and thermoelectric cooler. **Keywords:** cardioplegia, heart preservation, perfusion, hypothermia, mechanical perfusion, cardiac transplantation, donor heart. JECT. 2015;47:119–124

Donor heart preservation has largely stayed the same for over 50 years based on techniques developed by Drs. Shumway and Lower (1) which include a single flush of cardioplegic solution into the coronary arteries and static storage on ice in an insulated container. This simple procedure that provides a short, but manageable (3–4 hours) preservation time to permit transportation from the donor to recipient. However, it has long been known that coronary perfusion of organs during hypothermic storage improves the quality of the organ. Perfusion removes damaging metabolites (such as lactic acid) from the organ and allows for improved tissue viability (2–4). We describe a system to provide perfusion of the donor heart using a microcomputer-controlled peristaltic pump combined with a thermoelectric cooler and insulated container.

FIRST PROTOTYPE

The initial step to control the operation of single-channel peristaltic pump (Watson–Marlow Bredel, Wilmington, MA) encompassed software programming of a Motorola HC11 microcontroller (QED Board, Mosaic-Industries, Newark, CA). This software is interfaced to a DC motor

control board using a custom-designed printed circuit board interface (Figure 1).

The microcontroller, motor controller, and interface board are mounted to an aluminum assembly located in a nesting shell located below the standard 16 quart 12 VDC thermoelectric cooler (Coleman, Wichita, KS) (Figure 2A). The graphic user interface consists of a touch screen and 240 × 128 pixel CCFL-backlit LCD display (Q-Screen Controller, Mosaid Industries, Newark, CA) mounted to the front surface of the cooler (Figure 2B).

The pump is secured to Lexan clear polycarbonate box and placed inside the cooler with the heart container and 1 L bag of preservation solution. The preservation solution container is connected to the heart container with 1/4" and 1/16" Tygon tubing. The heart container consists of a single-use polyvinyl chloride plastic bag with a mesh lining, which is secured to both sides of the bag opening. This mesh suspends the heart off the bottom of the container with the intended purpose to prevent the waste fluid coming out of the coronary sinus from contacting the heart. The system is closed and the cardioplegic solution remains in the heart container until the solution is empty. The cardioplegic solution is essentially transferred from the source bag to the heart container.

Initial bench tests determined that using previously refrigerated the cooler was able to maintain the temperature of the bags of solution within an acceptable range of 4°C–6°C. A number of porcine hearts weighing between 280 and 374 g were used in the prototype device. There were problems with the first prototype due to its small internal volume, which limited the ability to use no

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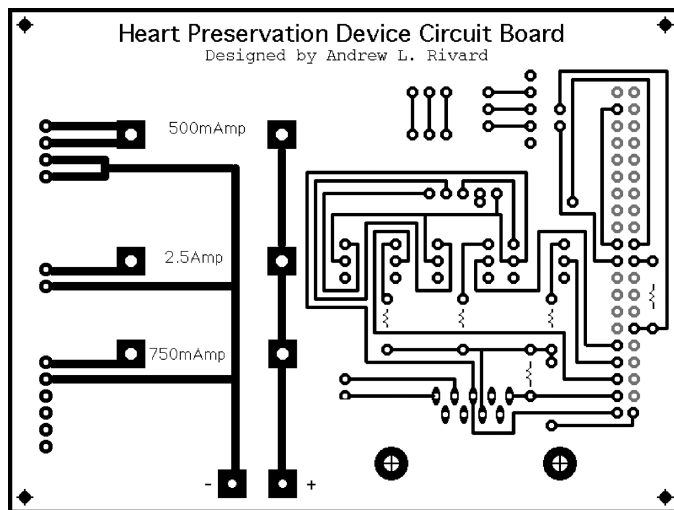


Figure 1. Heart preservation device circuit board. Surface mount view of the printed circuit interface board showing connections between the microcontroller to the motor controller for power, fuses, and opto-electronic relays.

more than 1 L of perfusate (5). More importantly, a few hearts developed air embolus from antegrade flow of air in the cardiac chambers (6). This was due to the suspension of the heart in the mesh bag allowing air to enter the left atrium (Figure 3).

SOFTWARE

Perfusion of isolated organs such as the kidney is done using a pressure-controlled continuous flow rate. A continuous flow rate mimics the relative flow characteristics in the renal artery. The coronary arteries, however, have an

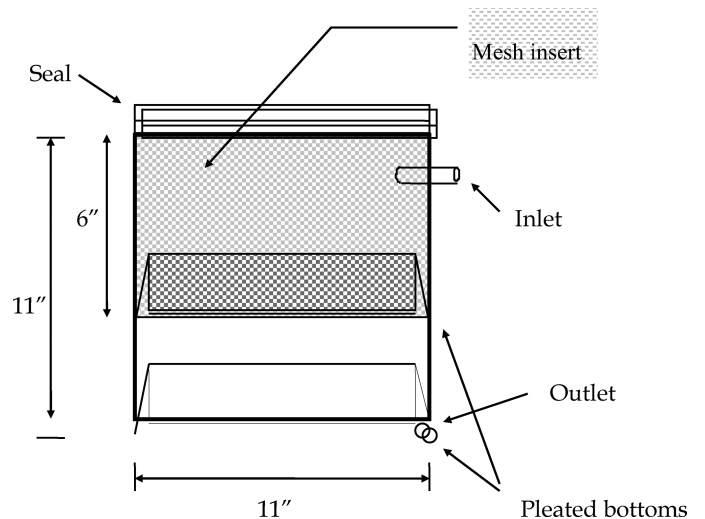
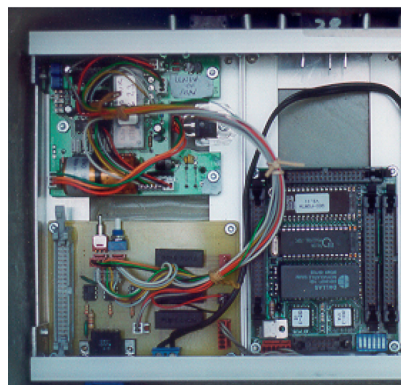


Figure 3. The mesh bottom heart container. This heart container design includes a mesh insert that suspends or cradles the heart from the bottom of the container. The perfusion solution enters near the top seal and drains from the bottom.

intermittent flow related to the filling and emptying of the heart associated with the opening and closing of the heart valves and intramyocardial pressure during myocardial contraction. Providing an intermittent flow allows the aortic valve to naturally close from a higher aortic root pressure that present in the ventricle. Maintaining this flow rate for a prolonged time is associated with myocardial edema and thus the software was designed to provide an intermittent flow rate—thus conserving overall volume and also mimicking the natural flow of the heart, since the natural flow through the heart and coronary vessels is also pulsatile (7).

Figure 2. The Asporto heart preservation device prototype #1. The inside (A) and front (B) views of the Hibernicor Asporto heart preservation device. A 12-V thermoelectric Peltier device top provides a hypothermic organ temperature between 4.5°C and 10°C. The inside view shows the placement of the electronics in the false bottom of the unit. The motor controller is placed in the top left position, the bottom left is the interface board, and placed to the right is the microcontroller.



A



B

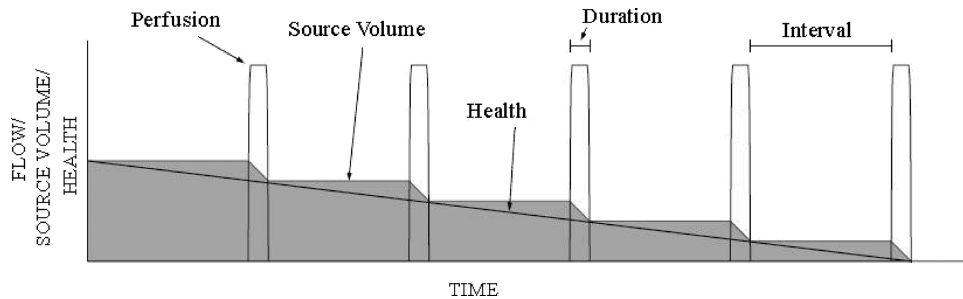


Figure 4. Graph of the intermittent perfusion vs. total perfusion source volume. As the perfusion program runs there is a drop in the total source volume. The initial size of the source volume determines the total amount of time allowable for transport of the organ. For example, a 3-L source volume with a perfusion rate of 150 mL/min for 1 minute duration infused at an interval of every 30 minutes would allow an overall preservation of 10 hours.

Furthermore, extensive literature from studies examining cardioplegic administration for optimal cardiopulmonary bypass during open heart surgery shows that intermittent administration of cardioplegic solution provides adequate protection of the myocardium. A recent study by Hu et al. demonstrated that the optimal perfusion amount to maintain a complete endothelial layer is 150 mL infused every 2 hours (3). Thus the software was designed to provide both continuous and intermittent perfusion between .07 and 960 mL/min depending on revolutions per minute and tube size.

The overall health of the organ (transport time) is determined by the frequency of infusion intervals, pump rate, and duration of the perfusion cycle. The duration or total length of transport time is based on the initial setting of perfusion volume and the available total volume in the source bag (Figure 4). For example, a 3-L source bag would provide a total duration of 6 hours and 36 minutes if 150 mL was administered intermittently every 20 minutes. After powering the device on, a splash screen is displayed with

basic information and instructions to proceed by pressing the touch screen to select the initial pump priming screen (Figure 5). Air bubbles in the tubing are flushed through by actuating the pump using the reverse/forward buttons. Following connecting the heart to the aortic cannula by a zip tie and confirming the heart is deaired, a default program is initiated.

Although the preservation program is running, the source volume of preservation solution and calculated time remaining is displayed. In addition, the time to the next perfusion cycle is displayed (Figure 6). The software is power loss tolerate and maintains the perfusion schedule using a real-time battery backed clock.

Five different events are audit trailed from the time the perfusion program is started until the program is stopped (Table 1).

Additional features of service menu are available to users with a security code allowing access to set the clock date and time, calibrating the pump, and entering specific perfusion programs. One default and 25 additional

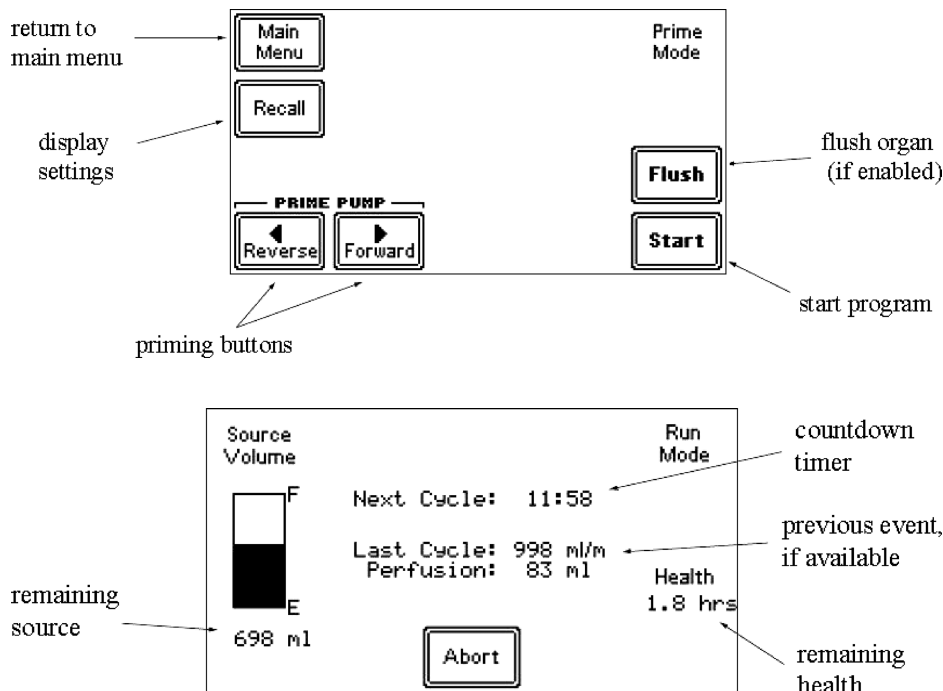


Figure 5. Graphical user interface of the main menu. The user interface is a touch screen with a graphics allowing the user to navigate through the system. A basic screen allows priming and starting a predetermined perfusion program.

Figure 6. Graphical display of active perfusion. This display allows the user to see in real time, the time remaining for transporting the organ to the destination and also if the pump is actively infusing preservation solution.

Table 1. Audit trail of the perfusion program.

Event	History
Flush	Flushed amount, flushed flow rate
Start	Remaining source volume
Stop	Perfused amount, perfused flow rate
Power	none—this is when the power is restored
BEGIN	Date and time of “Start”
END	Date and time of “Stop”

perfusion programs are possible with inputs of flow, duration, and amount. The health or duration of total perfusion time is automatically calculated for the user (Figure 7).

The pump’s flow rate is monitored through the use of an optical encoder. Since the pump’s rotational speed is expected to maintain linear relationship to the flow rate, a flow rate can be calibrated to a power supplied to the pump. The calibration procedure involves priming the tubing, selecting a power, and then pumping water into a graduated cylinder for a period of time. The user inputs the observed amount, the graduated cylinder was filled and the flow is calculated for that amount.

Basic flow calibration tests demonstrated that the power vs. flow/speed relationship is not entirely linear due to pump slippage; and these values are only accurate near the reference power setting. Thus, the calibration display can only be used for rough estimates of power vs. flow. During pump operation, the feedback provided by the optical encoder is used to maintain the correct power, as the speed (optical encoder counts) vs. flow relationship is linear if the pump is calibrated near the actual flow rate used. A major weakness of the control program is that it is currently unable to detect if the source bag is empty. It has been observed that the pump speed will increase slightly when the source runs out due to suction in the tubing. Unfortunately, this speed increase may not be sufficient to accurately detect an empty bag. Currently, the only way the preservation program terminates

is when the source volume is estimated to be below 10 mL or the “Stop” button is pushed.

SECOND PROTOTYPE

As mentioned above, the small internal volume of the 16 quart Coleman cooler was not sufficient to hold more than a 1-L bag, the pump, and organ container. This limited the overall duration (length of time) of which the heart could be adequately preserved using either intermittent or continuous perfusion. A decision had to be made whether or not the cardioplegic solution would be re-circulated through the heart or to choose a larger cooler to accommodate a larger source volume of cardioplegia for a closed system. Because of potential damage to the heart tissue from re-circulating metabolites, a larger off-the-shelf 26 quart thermoelectric cooler was chosen (Koolatron, Brantford, ON) to maintain a closed one-pass fluid path similar to the first prototype (Table 2). Furthermore, the increase of metabolites cannot be counterbalanced by more cooling.

A strategic step in the preservation device evolution was updating the design included mounting the pump in a stainless steel holder within the cooler, developing an integrated motor controller and interface board, and finally mounting the electronics into aluminum case (Figure 8). The combination of the motor controller and interface board was intended to simplify the connections between the power supply and microcontroller. The software was revised to end the perfusion cycle program when the calculated volume of the source bag is empty.

Instead of on the bottom, the electronics case was secured to the front of the thermoelectric cooler that protected the electronics and allowed the user to easily access the graphical user interface. The thermoelectric cooler was tested using a large temperature-controlled oven and maintained inside temperatures below 8°C at an outside ambient temperature slowly rising to 60°C over a 6-hour duration. The electronics passed initial electronic safety tests including dielectric strength, insulation resistance, ground bond, patient connected isolation, and leakage current. This second prototype was then brought forth for non-GLP pre-clinical testing at the Experimental Surgical Services located in the University of Minnesota. In summary, the pre-clinical experiments showed that the myocardial pH of isolated porcine hearts are improved by

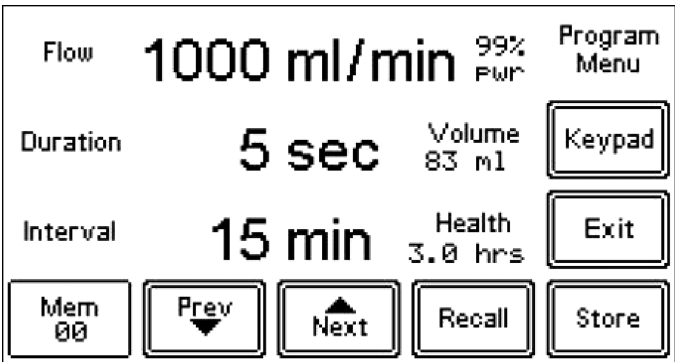


Figure 7. Graphical user interface of the advanced user functions. This display allows the advanced user or researcher to set intermittent or continuous perfusion parameters for a default as well as 25 additional user defined perfusion programs.

Table 2. Thermoelectric cooler technical specifications.

Height	394 mm (17.25")
Width	406 mm (16")
Depth	292 mm (11.5")
Weight	4.9 kg (11 lbs)
Capacity	24 L (26 qts)
Power usage	4 A, 48 W, 12 VDC

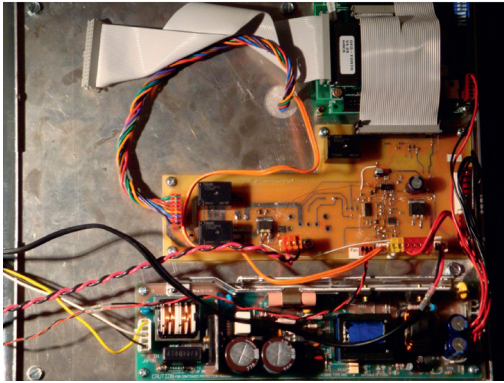


Figure 8. The Asporto heart preservation device prototype #2. The inside view shows the electronics mounted in an aluminum box for protection. The motor control board and interface board have been combined into a single board located in the center. A 120 VAC/12 VDC transformer is below, and the micro-controller is above the interface board.

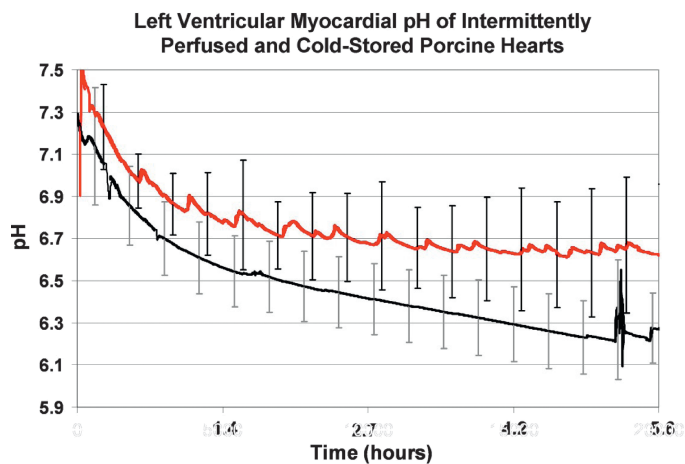


Figure 9. Left ventricular myocardial pH of intermittently perfused and cold-stored porcine hearts (image used with permission). Myocardial pH of the non-perfused hearts declined exponentially immediately following a flush of one liter of cardioplegic solution. Intermittent perfusion the isolated heart maintained a higher pH level than hearts not perfused. The effect of perfusion was immediate and appears to be more important in the first 30 minutes of storage when the large drop in pH occurs. The top line represents an average of perfused heart pH and the bottom line represents non-perfused hearts.

intermittent antegrade perfusion (8) (Figure 9). The successful results were an important step demonstrating a potential clinical benefit of the device. Fortunately, the results of the animal study are consistent with other experiments done since the 1960s (9–11). In the donor heart, there is a decrease in pH due to acid production from anaerobic glycolysis that directly causes myocyte death. When the acidosis is reversed by perfusion by the device, the heart cells are better able to resist necrosis from cell membrane disruption.

ORGAN CONTAINER EVOLUTION

Initial experiences with donor heart imaging included the observations of air embolism identified by gross pathology and confirmed by perfusion magnetic resonance imag-

ing (6). Since then, we have successfully addressed the problem of air bubbles and embolus formation using a rigorous de-airing protocol based on the American Society of Extracorporeal Technology Standards for perfusion practice (12). The first step is to submerge the heart in saline to provide a completely airless environment. An important and critical step in creating a completely air-free fluid path is thorough ballotement (manual cardiopulmonary resuscitation) of the heart although submerged in 1 L of saline solution before connecting the aortic cannula to the bag port. Manual cardiac ballotement creates a natural forward flow of saline through the atrioventricular and semilunar valves thus moving air out of the heart into the aortic root. The root air is removed by manual syringe aspiration from T-connector with a luer port located between the heart container and arterial filter. Aspiration at this point creates an antegrade flow in the root to dislodge any bubbles located in the aortic root, the hinge points of the aortic valve, along the orifices of the coronary arteries, or in the left ventricular outflow tract. Next, at the start of the fluid path, a spike allows penetration of the source bag seal. In the fluid path, there is a pediatric arterial air filter to catch small air bubbles from entering the heart. Any residual air in the source bag of cardioplegia is trapped in the afferent bowl of the arterial filter and evacuated manually by syringe aspiration. Then silicone tubing is secured to the peristaltic pump by a tubing holder allowing compression of the tubing between a roller pump head and spring tension occlusion plate.

Unfortunately, an organ container with solid (rigid) walls with limited internal volume, which constrains the amount of fluid that can be added to the container. A solid organ container is used in the Sherpa Perfusion Cardiac Transport System (Paragonix Technologies Inc., Braintree, MA) (13). Once the volume exceeds the internal volume, no further fluid can be added without removing fluid or using a fluid circuit to reuse the cardioplegic solution. As the rigid wall container is being filled there is air inside the container, some of which could with agitation get into solution and into pulmonary veins, left atrium, left ventricle,

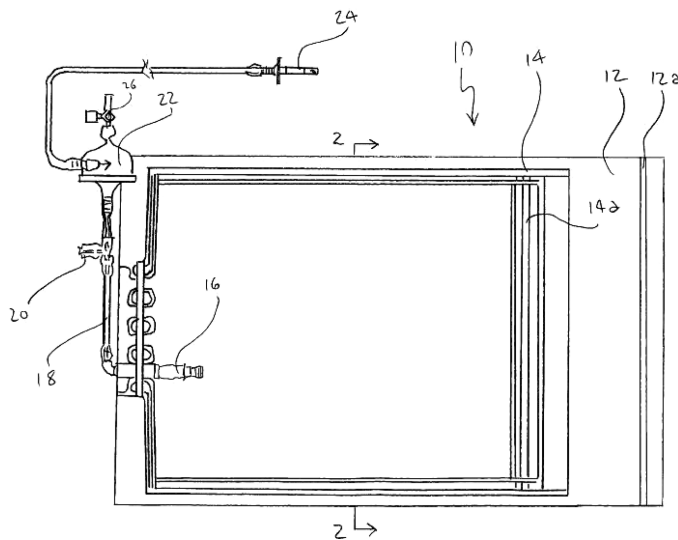


Figure 10. The closed fluid path and flexible heart container. A source of cardioplegic fluid is connected to a spike (24) and the fluid path is filled and deaired. The heart is placed inside the bag and the aorta is connected to a cannula (16). Air is removed via a syringe and needleless port (20 and 26). The inner and outer closures (12a and 14a) are sealed and the tubing (18) is connected to the pump.

and aortic root. Newer designs include for organ preservation use an air-free closed loop system, such as traditionally used in warm Langendorff perfusion systems (Organ Care System, Andover, MA) or in recirculating preservation fluid (LifeCradle, Frisco, TX) (14,15).

This problem of air embolus is addressed by a flexible container with port, similar to a blood bag. As long as the fluid path is bubble free, the flexible container can be filled and emptied in a completely airless manner. Similar to a rigid-walled container, a flexible container can be made in different sizes to accommodate a variety of volumes (Figure 10). In addition, with a flexible container, a re-sealable closure can provide a large enough opening for the heart.

Traditionally, a rigid-walled organ container can be made with simple mechanism for opening and closing with a watertight seal. Typically, this can be done with a screw-type top or press fit. Both of which are used in organ transportation. For example, a 500-mL Nalgene-type jar with a screw top is often used as a heart container. Alternatively, a Rubbermaid box with a large sealing top is often used as a lung container. The closure mechanism of both containers allows the organ to contained and removed at will. Alternatively, with a flexible container, a re-sealable closure can provide a large enough opening for the heart that may be the future evolution of donor organ containment.

CONCLUSION

The design of the Aspoto // Heart Preservation Device has developed over a 12-year period of challenges and

difficulties in addressing a number of basic issues facing mechanical heart preservation. An essential component of the device is the software used to provide a graphical user interface. This software interface allows the user to control the pump for priming and an important step, deairing. Deairing of the fluid path and donor heart is an important step to prevent air emboli into the coronary arteries, which can obstruct perfusion at the capillary level. Creative solutions to the simple containers used to hold a donor heart are central to address the practical problems of fluid transfer for perfusion while maintaining a protective and ultimately sterile environment for the donor heart. The heart preservation device's current design is specific to the heart, however, with modifications to the organ container and software program, could be potentially used with other organs.

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