Preservation of Organs

Inventors: Gale H. Thorne, Bountiful; Orin Lew Wood, Salt Lake City; Kay L. Knudson, Murray, all of Utah


Filed: Dec. 19, 1972

Appl. No.: 316,612

Abstract

Apparatus and method of preserving life organs, the apparatus having an organ container in which the organ may be subjected to elevated pressure, a pump pulsatilely delivering perfusate into the organ and an oxygenator to oxygenate the perfusate effluent from the organ. A constant pressure bias maintains a minimum pressure on the perfusate between pulses. A fluid flow control system delivers driving fluid in a pulsed manner to the pump at a selected rate and at selected pulse duration. The method includes delivering pulsed oxygenated perfusate to the organ and uniformly conducting perfusate away from the organ and providing a constant pressure bias on the perfusate. Loss or gain of liquid volume caused by waste secretion by the organ is compensated for.

Primary Examiner—Richard L. Huff
Attorney, Agent, or Firm—Garrettson Ellis

United States Patents

References Cited

Cited United States Patents

3,607,646 9/1971 deRoissart

3,632,473 1/1972 Belzer et al.

Other Publications


6 Claims, 4 Drawing Figures
3,892,628

1

PRESENATION OF ORGANS

This application is a division of application Ser. No. 863,869, filed Oct. 6, 1969, now U.S. Pat. No. 3,738,914.

BACKGROUND

Field of the Invention
The present invention relates to treatment of organs and more particularly to the clinical and laboratory preservation and perfusion of life organs.

BRIEF SUMMARY OF THE INVENTION
The present invention is directed to an improved method of artificially perfusing a life organ and includes the delivery of perfusate to the organ with pulsatile pressure while imposing a minimum pressure bias on the delivered perfusate between pressure pulses. This increases perfusate circulation through the organ between pulses as well as during the pulses.

BRIEF DESCRIPTION OF THE FIGURES
FIG. 1 is a schematic representation of one presently preferred system according to the present invention; FIGS. 2 and 3 are schematic circuit diagrams, each illustrating a presently preferred control unit which may respectively comprise part of the system of FIG. 1; and FIG. 4 is a schematic circuit diagram of another presently preferred control unit which may also be used in the system of FIG. 1.

DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENTS

FIG. 1

Referring now to FIG. 1, the organ preservation system, generally designated 20, is powered by a pneumatic source 22 which is preferably compressed oxygen. If desired, conventional laboratory supplied pneumatic source capable of generating pressures on the order of about 20 to 25 p.s.i. could be used. The compressed oxygen is communicated through line 24 to a control unit generally designated 26. The control unit 26 has a plurality of dials 28, 34 and 36 and gauges 30 and 31 which accommodate selective adjustment and monitoring of the compressed oxygen communicated through the line 24. Also, the control unit 26 pulses the input oxygen and communicates the pulsed oxygen to the output 32 of the unit 26. Significantly, dials 34 and 36 may be used to control the pulse rate and period of systole, respectively, of the output of the control unit. An on-off switch 27 and gauge switches 134 and 138 are also provided. A more detailed discussion of the structure and operation of the control unit 26 will be subsequently more fully described in connection with FIG. 2.

The pulsed output pressure, termed systolic pressure, from the control unit 26 is communicated through line 38 to a pump 40. One suitable embodiment of the pump 40 includes a cylindrical flexible pump bladder (not shown) fitted with silicone rubber tricuspid type check valves (not shown) in both ends to insure flow only in the desired direction. The rigid pump housing 46 encloses the bladder and seals the bladder at both ends, the pulsating pneumatic pressures from the control unit 26 being communicated between the pump bladder and the interior of the pump housing 46.

Perfusate, such as whole blood, disposed within the bladder of the pump 40, is communicated through the conduit 42 to the simulated aorta 44 with each high pressure pulse through the line 38. The simulated aorta 44 is a perfusate or blood-receiving chamber and has a tubular silicone bladder (not shown) enclosed in a rigid cylindrical housing 48. The interior of the cylindrical housing 48 is in communication with a constant biasing pressure through line 50 which is, in turn, coupled with the control unit 26. The pressure in line 50 has a pre-selected magnitude which exerts a biasing force upon the blood in the aorta 44. The bias pressure is preferably selectively adjustable in a range of about 0 to 200 millimeters of mercury above ambient. Thus, the forward bias pressure on the blood will serve as a minimum or diastolic pressure.

The blood forced through the aorta 44 by the pump 40 is communicated through line 52 to a temperature bath 54. Although any suitable temperature bath could be used, one suitable type includes a coil of line 52 disposed within a constant temperature water bath.

Blood emitted from the temperature bath 54 is then communicated through a port 56 to the interior of an organ container 58. Organ container 58 is preferably formed of transparent material such as, for example, acrylic plastic so that the organ (not shown) therein may be readily visually observed without disrupting the environment. The container 58 is constructed so as to accommodate elevated internal pressures such as on the order of about three atmospheres (45 p.s.i.g.). Also, the interior of the container 58 is preferably regulated in temperature with conventional heat exchange apparatus 238 (FIG. 4). Thus, the container 58 secures an organ (not shown) in a selected temperature and pressure environment.

Preferably, a tube 60 is connected to the organ (not shown) so as to receive excreted waste or by-products of the organ perfusion, such as urine or bile (when the organ is respectively kidney or liver). The secretions are conducted to an accumulator 62 where they are made available for examination and/or laboratory testing. The secretions may or may not be returned to the system as perfusate depending upon the preservation requirements of the particular organ.

After the pulsed blood has been circulated through the organ, the blood is then carried away from the organ through line 64 to an oxygenator 66. The oxygenator 66 may be of any suitable conventional type, for example, a membrane oxygenator. Fresh oxygen is communicated to the oxygenator 66 through line 68 from the control unit 26. In the oxygenator 66, carbon dioxide in the blood is exchanged for oxygen, carbon dioxide rich fluid being communicated away from the oxygenator 66 through line 70 to the control unit 26.

The oxygenated blood effluent from the oxygenator 66 is conducted by line 72 to simulated atrium 74. Significantly, an additional supply of blood or other perfusate is also in communication with the atrium 74 through line 76. The supply is maintained in a reservoir 78 to compensate for any reduction in blood volume in the system resulting from secretion of fluids through the line 60 to the accumulator 62. Also, it should be appreciated that the container 58 is disposed at a greater vertical height than the oxygenator 66 and the oxygenator 66 is, in turn, disposed at a greater height than the atrium 74. Thus, the flow of blood from the organ in
the container 58 through the oxygenator 66 and to the atrium 74 is gravity flow.

Atrium 74 is a flexible silicone rubber receiver or chamber for receiving the blood or other perfusate from the oxygenator 66 and the reservoir 78. Atrium 74 carries a substantial supply of blood and, therefore, ensures a non-interrupted venous inflow of blood to the pump 40 and also provides a relatively uniform pressure head for passive filling of the pump 40. Thus, the atrium 74 cooperates with the pump 40 to closely simulate natural physiologic conditions.

Briefly summarizing the method of preserving an organ in the container 58, the system is primed with perfusate such as whole blood and purged of all air or gas in the blood circulatory system. Pneumatic pressure, such as compressed oxygen, is pulsed by the control unit 26 which, in turn, actuates the pump 40 forcing blood into the aorta 44 and, thereafter, through the temperature control bath 54 into the organ (not shown). A bias pressure on the aorta 44 regulated through the control unit 26 ensures a minimum diastolic pressure in the system.

Any liquid waste or like product created by the organ in the container 58 during perfusion and preservation is delivered by the organ secretion ducts to the tube 60 which conducts the secretion to the accumulator 62. The secretion is then readily available for examination and/or laboratory testing or it may be returned to the system as perfusate. A perfusate reservoir 78 regulates and maintains a fixed volume of blood within the system and thus compensates any fluid removed through the tube 60 as a secretion.

A pressure head is developed at the oxygenator 66 and the atrium 74 by locating the organ container 58 at a greater vertical height than the oxygenator 66, oxygenator 66 being in turn at a greater vertical height than atrium 74. The developed pressure head is sufficient to drive the blood through the oxygenator 66. Also, the control system 26 is manually set to regulate and control the rate of oxygenation as required by the organ.

The oxygenated blood entering the atrium 74 is made available to the pump 40 in a continuous uninterrupted manner so that the pump 40 may be efficiently filled with blood when the pneumatic line 38 is vented to ambient pressure, as between successive systolic pressure pulses. When the pneumatic line 38 is vented to ambient pressure, the pressure head in the atrium 74 opens the upper pump valve (not shown) and allows the pump to be refilled preparatory to initiation of another cycle of pumping.

The Control Unit Embodiment of FIG. 2

Referring to FIG. 2, the control unit 26 comprises a pressure source 22 which, as above described, may be compressed oxygen. It is presently preferred that the pressure from source 22 enter the control unit 26 at about 20 p.s.i.g. (pounds per square inch gauge). The pressure from the source 22 is communicated through line 90 to an oscillator circuit 92. Oscillator circuit 92 has an or/nor gate 94 one side of which is in communication with lines 90. The other side of the or/nor gate 94 is in communication through line 96 with a pneumatic capacitor 98. A needle valve 100 controls the flow of fluid from the capacitor 98 to a fixed resistor 102 and also to or/nor gate 104.

The regulated pressure supplied to the gate 94 passes freely through the gate until sufficient control pressure builds up in the capacitor 98 to switch the gate 94 off. When the gate 94 is off, the capacitor 98 discharges through the needle valve 100 and vents through the restrictor 102. When the pressure in pneumatic capacitor 98 reaches a predetermined minimum level, the gate 94 switches on again to conduct the 20 p.s.i.g. pressure through line 96 to again allow the pressure to build up in the capacitor 98. During the period when the gate is off the 20 p.s.i.g. pressure is conducted through line 106 to the gate 104. Thus, 20 p.s.i.g. pressure is alternately conducted to the gate 104 and vented through the restrictor 102. The rate of alternation is termed the "pulse rate" and the pulse rate is determined by the setting on the needle valve 100, needle valve 100 controlling the rate of charge and discharge of the capacitor 98. The needle valve 100 may be manually set by turning knob 34 (FIG. 1).

A pressure regulator 108 reduces the 20 p.s.i.g. input pressure to 10 p.s.i.g. and thereafter conducts the reduced pressure through line 110 to the gate 104. A high pressure pulse in the line 106 switches the gate 104 to the on position so that the 10 p.s.i.g. pressure through line 110 is conducted through line 112 as a pulse to the switching valve or fluid valve 116.

Fluid valve 116 responds to the pressure pulse from gate 104 by opening communication between line 118 and the output 32 of the control unit 26 (see also FIG. 1). Line 118 communicates pressure from the source 22, a regulator 120 being interposed into the line to accommodate selective regulation of the pressure to the pump 40 (FIG. 1). When gate 104 is switched off, i.e., when the oscillator 92 vents through the fixed resistor 102, the fluid valve 116 will be operated to vent the increased pressure developed in the pump 40. Fluid valve 116 is biased toward the vent position by fluid pressure existing in line 122. A pressure regulator 124 is disposed in the line 122 and controls the amount of pressure delivered to the right side of the fluid valve 116. Thus, the setting on regulator 120 determines the pressure which is necessary to move the valve 116 from the extreme left position to the extreme right position to accommodate driving fluid pressure to the output 32. The time period during which driving fluid is communicated through the output 32 is increased by increasing the pressure setting on the regulator 124. Hence, regulator 124 determines the period or duration of the systolic pressure.

A pneumatic capacitor 126 is interposed between the regulator 124 and the pressure source 22 to dampen minor fluctuations in the pressure line caused by the oscillator circuit 92.

Fluid pressure from the source 22 is communicated through line 128 to the aorta 44 (FIG. 1) as above described. A regulator 130 controlled by knob 28 (FIG. 1) is disposed in the line 128 and is adjustable to set the bias fluid pressure in line 128 to a predetermined minimum diastolic pressure.

Pressure gauge 30 is coupled to a switch 134 (see also FIG. 1) disposed in line 136. When switch 134 is in one position, the driving pressure to the pump 40 is registered on the gauge 30. When the switch is placed in the other position, the bias pressure to the aorta 44 is indicated on the gauge 30. The other gauge 31 is coupled to a switch 138 which is disposed in line 140. In one position the switch 138 causes the gauge 31 to reg-
ister the supply pressure from the pressure source 22 and, in the opposite position, causes gauge 31 to register the pressure on the right side of fluid valve 116.

The Embodiment of FIG. 3

The control unit embodiment generally designated 144 and best illustrated in FIG. 3 is, in many respects, substantially identical to the control unit 26, like parts having like numerals throughout. The control unit 144 has a fluid valve control subsystem generally designated 149 and including a fluid valve 146 which is biassed by spring 148 toward the vent position. Thus, in the absence of a high pressure systolic pulse at the left-hand side of the fluid valve 146, the pump 40 (FIG. 1) will be vented through the valve 146. The spring bias eliminates the requirement for a regulated fluid pressure source to switch the fluid valve to vent (i.e., to terminate the systolic output).

The period of systole output is controlled by the or/nor gates 150 and 152 and the needle valve 154 as will now be described. The pulse signals of the oscillator 92 switch the gate 150 to the on condition, causing fluid in line 156 to be conducted through the gate 150 and through restrictor 158 to the input 160 of gate 152. It should be observed that the fluid in line 156 is communicated from a pneumatic capacitor 162 which, in turn, connected to input line 164. Capacitor 162 provides a more constant pressure to the oscillator circuit 92. Input line 164 is in communication with the fluid supply 22 when switch 166 is in the illustrated position. Switch 166 permits regulation of the supply pressure prior to placing the control unit 144 in the on condition. The pressure regulation is accommodated by regulator 168. Fluid from the pressure source is initially filtered through filter 170 and, when switch 166 is in the illustrated closed position, the regulated fluid pressure is conducted through line 164 to the capacitor 162 and made available to the gate 150.

When gate 150 is in the on condition, as above described, a pressure pulse will appear at gate 152 switching gate 152 to the on condition. Thus, the gate 150 isolates the systolic control subsystem 149 from the oscillator circuit 92.

When gate 152 is in the on condition, the fluid in line 156 is communicated through line 172 to the left-hand side of fluid valve 146 causing the valve to communicate the fluid pressure in line 118 to the pump at output 32 (see FIG. 1). Significantly, the amount of pressure required to place gate 152 in the on condition is governed by the needle valve 154. Thus, the needle valve 154 is adjusted to regulate the period of systolic output of the fluid valve 146. When gate 152 is again switched to the off condition, the spring 148 will return the fluid valve 146 to the vent position, fluid in the left-hand side of the valve 146 being vented through restrictor 174.

It should be appreciated in the control unit 144 that the gauge 31 and the switch 138 are connected so that in one position gauge 31 monitors the pressure as regulated prior to placing the switch 166 in the on condition and, in the opposite position, monitors the pressure as supplied to the oscillator circuit. The control unit 144 has the advantage of more positive control of the switching action of the fluid valve 146.

The Control Unit Embodiment of FIG. 4

The control unit illustrated in FIG. 4 and generally designated 180 is similar to the control units 26 and 144 above described, like parts having like numerals throughout. The control unit 180 differs in that it provides a parallel circuit operating and controlling two fluidic pumps simultaneously. Also, the unit 180 is constructed for operation under hyperbaric conditions.

Most of the components of the control unit 180 are carried within a hyperbaric chamber 182 which may be formed of acrylic plastic and which is constructed so as to maintain a hyperbaric environment. The chamber 182 also contains the organ container 56 (not shown in FIG. 4).

The unit 180 comprises an oscillator circuit 184 which is substantially similar to the oscillator circuit 92 above described, circuit 184 comprising a gate 94, a fluidic capacitor 98 and a needle valve 100. The control unit 180 differs from control unit 92 in that a restrictor 186 is disposed between the line 106 and restrictor 102. Restrictor 186 minimizes the volume of pneumatic fluid required by the unit 180 and allows the size of the capacitor 98 to be minimized. The operation of oscillator 184 is essentially identical to the operation of oscillator 92 above described.

The output of oscillator 184 in line 106 is simultaneously communicated to each of two fluid valve control subsystems 149 which may be substantially identical to the fluid valve control subsystem 149 above described and illustrated in FIG. 3. The subsystems 149 are connected in parallel and relate one with another with line 192 which equalizes the fluid pressure between gates 150 and also with line 194 which communicates fluid in line 156 to gates 152 simultaneously. Each of the fluid valves 146 is connected to a separate pump 196 and 198.

With reference to FIG. 4, fluid from the source 22 is communicated through the filter 170 to the regulator 168 as above described (FIG. 3). The system is operated when the switch 166 is moved from the off position illustrated in FIG. 4 to the on position opposite the position illustrated in FIG. 4. In the on position the oscillator 184 is energized and a pulsatile signal is developed by the subcircuits 149 to drive the pumps 196 and 198. The input pressure through the regulator 168 is also communicated through line 200 to switch 202 so that gauge 204 measures the pressure communicated through line 206 to the oxygenator 66. A restrictor 208 dampens pressure fluctuation in the line servicing the pressure gauge 204 protecting it from shock damage.

The pressure from the supply 22 is also conducted to regulators 210 and 212 which control the pumping pressure to pumps 198 and 196 respectively. A switch 214 is provided to selectively turn the pump 198 on or off so that a single pump may be operated if desired. Also, switch 216, in one position, allows the pressure available to pump 196 to be registered on the gauge 218 and, in the opposite position, allows the pressure in pump 198 to be monitored on gauge 218.

Gauge 218 is connected to switch 220 which in the illustrated position monitors the pressure on the selected one of the pumps 198 or 196 and, in the opposite position, monitors the pressure to the aorta. A regulator 222 controls the pressure supplied to the oxygenator 66 and a flow meter 224 monitors and controls the rate of flow to the oxygenator. Diodes 226 and 228 prevent application of negative pressure on the gauge 218 to avoid damaging the gauge.
A regulator 230 sets and controls the pressure in the hyperbaric chamber 182 and relief valve 232 functions as a safety valve to avoid overpressurizing the chamber 182. The pressure in the chamber 182 is monitored by a gauge 234 which is protected from pressure fluctuation by a restrictor 236.

If desired, as illustrated in FIG. 4, the hyperbaric chamber 182 may be provided with a heat exchanger 238 to maintain a constant predetermined temperature within the chamber 182 and/or of the perfusate.

The operation of the control circuit 180 is substantially similar to the operation of the control circuit 144 (FIG. 3) above. However, the unit 180 simultaneously drives two pumps which may be connected to the same or different organs. The system accommodates preservation of an organ in a manner closely approaching actual physiological conditions and accommodates a wide variety of controls to achieve maximum preservation effect.

The invention may be embodied in other specific forms without departing from the spirit or essential characteristics thereof. The present embodiments are, therefore, to be considered in all respects as illustrative and not restrictive, the scope of the invention being indicated by the appended claims rather than by the foregoing description, and all changes which come within the meaning and range of equivalency of the claims are therefore to be embraced therein.

What is claimed and desired to be secured by United States Letters Patent is:

1. In a method of artificially perfusing a life organ which method includes delivery of perfusate to the organ the improvement of:
   developing a pulsatile pressure in the perfusate delivered to the organ and imposing a minimum pressure bias on the delivered perfusate circulated through the organ between pressure pulses.

2. A method of artificially preserving life organs, comprising the steps of:
   placing the organ into a container;
   pulsatilely pumping perfusate into the organ, while maintaining a minimum pressure bias on the perfusate between pulses and conducting the perfusate uniformly from the organ;
   oxygenating the perfusate drawn from the organ with an oxygenator; and
   controlling the temperature and the pulse rate of the perfusate conducted to the organ.

3. In a method as defined in claim 2, wherein said placing step comprises subjecting the organ to elevated pressures within the container.

4. In a method as defined in claim 2 wherein said oxygenating step comprises disposing the container at a greater elevation than the oxygenator and delivering the perfusate from the organ to the oxygenator by force of gravity.

5. In a method as defined in claim 2 further comprising organ secretions away from the organ out of the container.

6. In a method as defined in claim 5 further comprising compensating for the volume of secretions conducted away from the organ by increasing the volume of perfusate available to the organ.