(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
4 April 2002 (04.04.2002)

PCT

(10) International Publication Number
WO 02/026034 A3

(51) International Patent Classification[7]: A01N 1/02

(21) International Application Number: PCT/US01/26591

(22) International Filing Date: 27 August 2001 (27.08.2001)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
09/645,525 25 August 2000 (25.08.2000) US

(71) Applicant: **ORGAN RECOVERY SYSTEMS INC.** [US/US]; 2570 E. Devon Avenue, Des Plaines, IL 60018 (US).

(72) Inventors: **OWEN, Donald, R.**; Biosyn, Inc., 5700 Citrus Boulevard, Suite B, Harahan, LA 70123 (US). **KRAVITZ, David, C.**; Life Science Holdings, Inc., 2570 E. Devon Avenue, Des Plaines, IL 60018 (US). **BRASSIL, John**; 1137 Jeffrey Court West, Northbrook,IL 60062 (US). **BROCKBANK, Kelvin, G., M.**; 81 Rutledge Avenue, Charleston, SC 29401 (US). **BURROUGHS, Andrew**; 7404 7th Avenue, Kenosha, WI 53143 (US). **ISAACS, Dickon**; 1426 N. Greenview #2, Chicago, IL 60622 (US). **STEIBEL, Dennis, J.**; 1295 Thorndale Lane, Lake Zurick, IL 60047 (US). **FRASER, Richard**; 2083 Westridge Boulevard, Bortlett, IL 60103 (US). **HARRIS, Stanley**; Organ Recovery Systems, Inc., 701 E. Bay Street, Suite 433, MSC 1119, Charleston, SC 29403 (US). **SCHEIN, Douglas**; 2420 N. Seminary #1, Chicago, IL 60614 (US).

(74) Agents: **OLIFF, James, A.** et al.; Oliff & Berridge, PLC, P.O. Box 19928, Alexandria, VA 22320 (US).

(81) Designated States *(national)*: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW.

(84) Designated States *(regional)*: ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:
— *with international search report*

(88) Date of publication of the international search report:
20 March 2003

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: APPARATUS AND METHOD FOR MAINTAINING AND/OR RESTORING VIABILITY OF ORGANS

(57) Abstract: An organ perfusion apparatus and method monitor, sustain and/or restore vability of organs and preserver organs for storage and/or transport. Other apparatus include an organ transporter, an organ cassette and an organ diagnostic device. The method includes perfusing the organ at hypothermic and/or normothermic temperatures, preferably after hypothermic organ flushing for organ transport and/or storage. The method can be practiced with prior or subsequent static or perfusion hypothermic exposure of the organ. Organ viability is restored by restoring high energy nucleotide (e.g., ATP) levels by perfusing the organ with a medical fluid, such as an oxygeneted cross-linked hemoglobin-based bicarbonate medical fluid, at normothermic temperatures. In perfusion, organ perfusion pressure is preferably controlled in response to a sensor disposed in an end of tubuing placed in the organ, by a pneumatically pressurized medical fluid reservoir, providing perfusion pressure fine tuning, overpressurization preventing and emergency flow cut-off. In the hypothermic mode, the organ is perfused with a medical fluid, preferably a simple crystalloid solution containing antioxidants, intermittently or in slow continuous flow. The medical fluid may be fed into the organ from an intermediary tank having a low pressure head to avoid organ overpressurization. Preventing overpressurization prevents or reduces damage to vascular endothelial lining and to organ tissue in general. Viability of the organ may be automatically monitored, preferably by monitoring characteristics of th emedical fluid perfusate. The perfusion process can be automatically controlled using a control program.

WO 02/026034 A3

INTERNATIONAL SEARCH REPORT

International Application No
PCT/ 01/26591

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A01N1/02

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 A01N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
WPI Data, EPO-Internal

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 00 18226 A (LIFE SCIENCE HOLDINGS INC) 6 April 2000 (2000-04-06) the whole document ---	1-79, 239-241, 262-265
X	WO 96 29865 A (ORGAN INC; LIFE RESUSCITATION TECH (US); AMERICAN NAT RED CROSS (U) 3 October 1996 (1996-10-03) page 7, line 6-20 page 8, line 15-35 page 9, line 36 -page 10, line 14 page 11, line 8-37 page 18, line 35 -page 20, line 22 --- -/--	1-10, 15-47, 52-79, 239-241, 262-265

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
17 June 2002	03. 09. 02

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Klaver, J

Form PCT/ISA/210 (second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

International Application No
PC[redacted]S 01/26591

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 96 30111 A (ORGAN INC; LIFE RESUSCITATION TECH (US)) 3 October 1996 (1996-10-03) cited in the application page 6, line 23 -page 7, line 1 page 8, line 18 -page 9, line 13 page 12, line 18-34 page 15, line 30 -page 16, line 14 page 27, line 34 -page 28, line 37 -----	1-10, 15-47, 52-79, 239-241, 262-265

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 01/26591

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

1-79, 239-241, 262-265

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest.

☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claims: 1-79, 239-241, 262-265

a). Apparatus for holding an organ comprising a portable housing and an organ supporting surface, wherein the portable housing is configured to be received by at least one of a perfusion device, an organ transporter and an organ diagnostic device and includes openings to allow tubing to pass therethrough and be connected to the organ and wherein a bottom portion of the housing is liquid tight.
(Claims 1 - 36, 44 - 79 and 262 - 265)
b). Saleable kit comprising
- a portable housing
- an organ supporting surface, wherein the portable housing is as defined under a) above
- tubing connectable to the organ and
- at least one connection device to allow connection of the tubing to one of the devices.
(Claims 37 - 43)
c). Apparatus for holding an organ comprising a portable housing, a pump and an organ supporting surface wherein the pump is connected to at least two different areas of an organ with at least two different tubes.
(Claims 239 - 241)

2. Claims: 80 - 105, 167 - 169, 192, 193

a). Method of controlling perfusion of an organ with a medical fluid comprising one or more of
- inputting organ data
- selecting a perfusion mode
- selecting a type of flow control for each selected mode
- controlling the fluid flow based on the selected perfusion mode and flow control
- detecting operating conditions experienced by the fluid and organ during perfusion
- comparing detected conditions with prestored ones and generating a signal indicative of organ viability based on the comparison and
- generating a message relating to organ viability based on the generated signal and/or making automatic adjustments to regulate viability.
(Claims 80 - 92, 192)
b). Recording medium that stores a control program including instructions for the various steps as defined in the method under a).
(Claims 93 - 105)
c) Method of perfusing an organ comprising perfusing an organ with a medical fluid, collecting the fluid that has passed the organ, passing the collected fluid through a sensor and determine the organ viability
(Claims 167 - 169)

d) Control system for controlling perfusion comprising at least one of the devices necessary for each of the steps mentioned under a) above.
(Claim 193)

3. Claims: 106 - 156

Method of maintaining and/or restoring viability of an organ subjected to a period of ischemia or hypoxia comprising at least one of perfusing and flushing said organ with a first medical fluid at a first hypothermic temperature to reduce or stop catabolic changes.
Flushing may be performed prior or subsequent to the perfusion step.
Method may further comprise a second perfusion step with a second (preferably oxygenated) fluid at a different temperature.

4. Claims: 157 - 161

Method of maintaining and/or restoring viability of an organ subjected to a period of ischemia or hypoxia comprising perfusing said organ with a first medical fluid at a first temperature to reduce or stop catabolic changes and perfusing the organ with a second (preferably oxygenated) fluid at a second temperature to store and/or transport the organ.

5. Claims: 162-166

Method of perfusing an organ comprising perfusing the organ utilizing a medical fluid reservoir in communication with a pressure source and a fluid pathway, wherein reservoir and pathway are configured to perfuse the organ at a pressure that is controlled either by a pressure source that is a cuff disposed around the container or by a variable valve or a pressure head disposed on the pathway.

6. Claims: 170 - 178

Method of transporting or storing an organ comprising
a) perfusing the organ at a mild hypothermic temperature to repair damage from warm ischemia, preferably with an oxygenated fluid;
b) perfusing the organ at a hypothermic temperature, such as one that is less than the temperature in step a), preferably with a non-oxygenated fluid;
c) transporting and/or storing the organ at a mild hypothermic temperature such as a temperature that is greater than in step b); and
d) perfusing said organ at a mild hypothermic temperature to

repair damage from hypothermic transport or storage of step c).

7. Claim : 179

Apparatus for perfusing an organ comprising:
a medical fluid reservoir;
a fluid pathway connected to the reservoir and connectable to the organ;
a first heat exchanger in communication with the fluid reservoir;
and a controller for controlling the heat exchanger to allow perfusion at various hypothermic temperatures.

8. Claims: 180 - 191

A perfusion solution kit comprising a saleable package containing a first container holding a first perfusion solution for hypothermic perfusion at a first T and a second container holding a second, different solution for hypothermic perfusion at a second T, which is lower than the first T.

9. Claims: 194 - 228, 284 - 294

Portable transporter for holding a portable housing comprising:
a base portion to facilitate an upright position of the transporter;
a top portion;
a pump;
a power supply;
a compartment for holding a portable housing configured to hold at least one organ, optionally comprising further constructional or controlling elements such as tube sets, latches, wheels or a control panel or an additional compartment for holding a coolant .

10. Claims: 229 - 234

Method of controlling operation of a transporter comprising:
using a set of controls provided on the transporter to select an operation; and
displaying the operation selected, which operation is at least one of priming, washing, error handling, perfusing and idle.

11. Claims: 235 - 238

Apparatus for holding an organ comprising:

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

a portable housing;
a pump;
a pulse controller; and
an organ supporting surface wherein pump and pulse controller receive at least one of flow data, tachometer data and pressure data from a pressure sensor and converts the data into an output to drive the pump.

12. Claims: 242 - 248, 261

a). Organ assessment system comprising an organ support and at least one organ parameter sensor; an organ perfusion apparatus, wherein the system is adapted to assess the organ parameters while maintaining the status of the organ during the assessment (claim 242).
b). Organ assessment system comprising a computer, an analyzer, an organ evaluation instrument in (wired or wireless) communication with computer and analyzer, a perfusate chamber and an organ chamber configured to receive an organ (claims 244 - 247).
c). Method of assessing an organ comprising holding an organ, sensing an organ parameter and diagnosing the organ during a time the organ is held (claim 243).
d). Method of analyzing the viability of an organ comprising detecting organ parameters, compiling the organ parameters and producing an index of viability of the organ based on the compiled parameters (claim 248).
e). Method of determining the viability of an organ comprising flushing the organ, string the organ in a transporter at cold T, assessing the viablity and transporting viable organs to implant sites (claim 261).

13. Claims: 249 - 260

Method of improving an organ or a tissue comprising removing the organ/tissue from a body, enhancing the organ/tissue, e.g. by radiation or chemotherapy, and implanting the enhanced organ/tissue into a body.

14. Claims: 266 - 275, 283

a) A method of remotely monitoring an organ comprising remotely monitoring information during transportation and storage, e.g. monitoring location or viability parameters of the organ (claims 266 - 270).
b). Transporter for carrying an organ comprising an information transmission device such as GPS (claims 271 - 275, 283).

15. Claim : 276

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Organ transportation device comprising a transporter and a portable housing fit securely together to provide high efficiency heat transfer.

16. Claims: 277 - 280

Kit comprising a saleable package containing a set of tubes configured to connect an organ to a perfusion apparatus.

17. Claims: 281, 282

Apparatus for holding an organ comprising a portable housing and a removable organ supporting surface.

18. Claims: 295, 296

Apparatus for holding an organ comprising a sensor to detect the presence of a portable housing for an organ in the apparatus.

19. Claim : 297

Method of analyzing factors involved in organ transplantation or implantation comprising comparing outcomes of organ transplants in recipients and comparing organ history during transport and/or storage.

INTERNATIONAL SEARCH REPORT

nation on patent family members

International Application No
PC[redacted]S 01/26591

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 0018226 A	06-04-2000	AU 6274899 A	17-04-2000
		CN 1320014 T	31-10-2001
		EP 1117293 A2	25-07-2001
		TW 442306 B	23-06-2001
		WO 0018226 A2	06-04-2000
WO 9629865 A	03-10-1996	AU 5375496 A	16-10-1996
		WO 9629865 A1	03-10-1996
WO 9630111 A	03-10-1996	US 5586438 A	24-12-1996
		AU 5376496 A	16-10-1996
		EP 0817670 A1	14-01-1998
		WO 9630111 A1	03-10-1996