PCT WORLD INTELLECTUAL PROPERTY ORGANIZATION
International Bureau

INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 7 : A01N 1/02	A3	(11) International Publication Number: **WO 00/18226**
		(43) International Publication Date: 6 April 2000 (06.04.00)

(21) International Application Number: PCT/US99/22582

(22) International Filing Date: 29 September 1999 (29.09.99)

(30) Priority Data:
09/162,128 29 September 1998 (29.09.98) US

(71) Applicant: LIFE SCIENCE HOLDINGS, INC. [US/US]; 1510 West Montana Street, Chicago, IL 60614–2013 (US).

(72) Inventors: OWEN, Donald, R.; Vital Assist, Inc., Suite I, 5701 Crawford Street, Harahan, LA 70123 (US). KRAVITZ, David, C.; Life Science Holdings, Inc., Suite 500, 1510 West Montana Street, Chicago, IL 60614–2013 (US).

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

(81) Designated States: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, 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, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, ARIPO patent (GH, GM, KE, LS, MW, 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), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

Published
With international search report.
Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.

(88) Date of publication of the international search report:
25 May 2000 (25.05.00)

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

(57) Abstract

An organ perfusion apparatus and method for monitoring, sustaining and/or restoring the viability of the organ and for preserving the organ for storage and/or transport perfuse the organ at normothermic temperatures (normothermic perfusion mode), preferably prior to and followed by organ perfusion at hypothermic temperatures (hypothermic perfusion mode) for transport and/or storage of the organ. The restoring of organ viability is accomplished by restoring high energy nucleotide (e.g., ATP) levels in the organ, which were reduced by warm ischemia time, by perfusing the organ with a medical fluid, such as an oxygenated cross–linked hemoglobin–based bicarbonate medical fluid, at normothermic temperatures. In the normothermic perfusion mode, organ perfusion pressure is preferably controlled in response to a sensor disposed in an end of tubing placed in the organ, by a pneumatically pressurized medical fluid reservoir which may be used in combination with a stepping motor/cam valve which provides for perfusion pressure fine tuning, preventing overpressurization and providing emergency flow cut–off. In the hypothermic mode, the organ is perfused with a medical fluid, preferably a simple crystalloid solution augmented with antioxidants, intermittently or at a slow continuous flow rate. The medical fluid may be fed into the organ by gravity from an intermediary tank which has alow pressure head so overpressurization of the organ is avoided. In either mode, preventing overpressurization prevents and/or reduces damage to the vascular endothelial lining and to the organ tissue in general. Also, viability of the organ may be automatically monitored in either mode, preferably by monitoring fluid characteristics of the medical fluid that has been perfused through the organ, such fluid characteristics being indicative of organ viability. The perfusion process can be automatically controlled using a control program.

FOR THE PURPOSES OF INFORMATION ONLY

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AL	Albania	**ES**	Spain	**LS**	Lesotho	**SI**	Slovenia
AM	Armenia	**FI**	Finland	**LT**	Lithuania	**SK**	Slovakia
AT	Austria	**FR**	France	**LU**	Luxembourg	**SN**	Senegal
AU	Australia	**GA**	Gabon	**LV**	Latvia	**SZ**	Swaziland
AZ	Azerbaijan	**GB**	United Kingdom	**MC**	Monaco	**TD**	Chad
BA	Bosnia and Herzegovina	**GE**	Georgia	**MD**	Republic of Moldova	**TG**	Togo
BB	Barbados	**GH**	Ghana	**MG**	Madagascar	**TJ**	Tajikistan
BE	Belgium	**GN**	Guinea	**MK**	The former Yugoslav Republic of Macedonia	**TM**	Turkmenistan
BF	Burkina Faso	**GR**	Greece			**TR**	Turkey
BG	Bulgaria	**HU**	Hungary	**ML**	Mali	**TT**	Trinidad and Tobago
BJ	Benin	**IE**	Ireland	**MN**	Mongolia	**UA**	Ukraine
BR	Brazil	**IL**	Israel	**MR**	Mauritania	**UG**	Uganda
BY	Belarus	**IS**	Iceland	**MW**	Malawi	**US**	United States of America
CA	Canada	**IT**	Italy	**MX**	Mexico	**UZ**	Uzbekistan
CF	Central African Republic	**JP**	Japan	**NE**	Niger	**VN**	Viet Nam
CG	Congo	**KE**	Kenya	**NL**	Netherlands	**YU**	Yugoslavia
CH	Switzerland	**KG**	Kyrgyzstan	**NO**	Norway	**ZW**	Zimbabwe
CI	Côte d'Ivoire	**KP**	Democratic People's Republic of Korea	**NZ**	New Zealand		
CM	Cameroon			**PL**	Poland		
CN	China	**KR**	Republic of Korea	**PT**	Portugal		
CU	Cuba	**KZ**	Kazakstan	**RO**	Romania		
CZ	Czech Republic	**LC**	Saint Lucia	**RU**	Russian Federation		
DE	Germany	**LI**	Liechtenstein	**SD**	Sudan		
DK	Denmark	**LK**	Sri Lanka	**SE**	Sweden		
EE	Estonia	**LR**	Liberia	**SG**	Singapore		

INTERNATIONAL SEARCH REPORT

Inte ional Application No
PCT/US 99/22582

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)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 97 43899 A (BREONICS INC) 27 November 1997 (1997-11-27) see: page 14, line 5 - 28; page 18, line 16 - 36; example 8. ---	1-39
X	WO 97 45527 A (TRANS D A T A SERVICE INC ;HEACOX JOHN K (US); GARDETTO WILLIAM W) 4 December 1997 (1997-12-04) see: page 2, line 1 - 7; page 2, line 24 - page 3, line 4; page 8, line 22 - 26. - --- -/--	1-39, 65-71

[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
21 March 2000	31.03.00
Name and mailing address of the ISA 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	Authorized officer Klaver, J

2

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

INTERNATIONAL SEARCH REPORT

Int tional Application No
PCT/US 99/22582

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 29865 A (ORGAN INC ;LIFE RESUSCITATION TECH (US); AMERICAN NAT RED CROSS (U) 3 October 1996 (1996-10-03) see: page 5, line 25 - 37; page 8, line 15 - 24; page 11, line 33 - 35; page 27, line 4 - 14.	1-39, 65-71
X	page 7, line 20-26; page 25, line 1 - 17.	40-44, 54-61

X	WO 94 06292 A (PERFUSION MEDICAL LAB INC) 31 March 1994 (1994-03-31) see: page 8, line 20 - 30; page 9, line 26 - 36; page 13, line 17 - page 14, line 9; page 16, line 5 - 21; page 17, line 4 - 17.	1-39, 65-71
X	page 10, line 28 -page 11, line 29	40-44, 54-61

X	WO 91 09520 A (UNIV CALIFORNIA) 11 July 1991 (1991-07-11) cited in the application see: page 8, line 34/35; page 17, line 6 - 13; example 2.	1-39

X	EP 0 376 763 A (MCKELVEY KAREN ;MACKEY JOHN (US); OLSON MYRON (US); HOLLOWAY RAY H) 4 July 1990 (1990-07-04) see: col. 3, par. 1; col. 3, line 47 - col. 4, line 3; col. 4, line 9 - 19; col. 4, line 31 - 39; col. 6, line 23 - 58.	65-71
X	column 10, line 4-19	40-44, 54-61

X	WO 88 05261 A (TOPS SYSTEMS INC) 28 July 1988 (1988-07-28) see: page 3, line 29 - 36; page 4, line 14 - 28; page 9, line 28 - 36; page 12, 1st par.; page 13, line 34 - page 14, line 9; page 18, line 5 - 19; page 23, line 33 - page 24, line 2; Example 3.	1-39, 65-71
X	see page 14, par. 1; page 15, par. 5.	40-44, 54-61

X	US 3 881 990 A (BURTON THOMAS A ET AL) 6 May 1975 (1975-05-06) the whole document	65-71

X	US 5 051 352 A (MARTINDALE JAMES G ET AL) 24 September 1991 (1991-09-24) see: col. 5, line 15-col. 6, line 35; col. 7, line 1 - 32.	40-44, 62-64, 84-122

	-/--	

2

INTERNATIONAL SEARCH REPORT

Int tional Application No
PCT/US 99/22582

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication,where appropriate, of the relevant passages	Relevant to claim No.
X	US 5 326 706 A (YLAND MARC J ET AL) 5 July 1994 (1994-07-05) see: col. 1, line 60-65; col. 2, line 50 - 58; col. 3, line 18 - 32; col. 17, line 16 -. 33; figures; table in col. 9/10.	40-44, 54-61, 84-122
X	WO 91 14364 A (WATERS INSTR INC) 3 October 1991 (1991-10-03) see: page 13, 3rd full par.;page 16, line 9 - 26; page 21, 3rd par.	40-44, 53-61
X	US 5 141 847 A (SUGIMACHI KEIZO ET AL) 25 August 1992 (1992-08-25) cited in the application column 4, line 3-19	40,44, 54,60
X	FR 2 592 306 A (COUEGNAS JACQUES) 3 July 1987 (1987-07-03) the whole document	54-57
P,X	WO 99 15011 A (HASSANEIN WALEED H) 1 April 1999 (1999-04-01) see: page 12, line 1 - page 13, line 8; page 14, line 11 - 27; page 20, line 23 - page 21, line 29; page 22, line 5 - 26; page 49, line 8 - 15.	40,54, 60-64, 72-83
X	US 5 699 793 A (BRASILE LAUREN) 23 December 1997 (1997-12-23) the whole document	40, 84-109
X	WO 97 46091 A (MEDTRONIC INC) 11 December 1997 (1997-12-11) see: page 2, line 20/21; page 4, line 14 - 21;page 6, line 29 - page 7, line 14.	40,45, 54, 62-64, 84-109
X	US 4 473 637 A (GUIBERT RAUL) 25 September 1984 (1984-09-25) column 3, line 19-62; figure 1	45-53, 62-64
X	WO 86 00812 A (PHARMACIA AB) 13 February 1986 (1986-02-13) see: page 6, line 10 - 12; page 8, line 12 - 22; page 10, line 15 - 17.	72-83
X	US 4 231 354 A (KURTZ ROBERT J ET AL) 4 November 1980 (1980-11-04) see: col. 2, line 18 - 35; col. 3, line 1 -19;col. 3, line 49 - col. 4, line 15.	84-122

2

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 99/22582

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.:

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 - 39, 65 - 71

Method of maintaining or restoring viability of an organ comprising: a) perfusing the organ with an oxygenated medical fluid, preferably at a temperature of > 15° C, optionally and preferably followed by a perfusion at a lower temperature with a second medical fluid.
b) storing and transporting the organ in an organ cassette including a portale housing, supporting surface and tubing.

Apparatus for use in the method of claims 1 - 39

2. Claims: 40 - 44, 54 - 61

Method for perfusing an organ utilizing at least one medical fluid reservoir and a perfusion pressure controller.
Appratus for use in this method.

3. Claims: 45 - 53

Method for transporting an dstoring an organ comprising
a. perfusing at normothermic temperature, preferably with oxygenated fluid
b. perfusing at hypothermic temperature, preferably with non-oxygenated fluid
c. transporting and storeing organ at hypothermnic temperature
d. perfusing at normothermic temperature to repair damage of step c.

4. Claims: 62 -64

Apparatus for perfusing an organ comprsing reservoir, pathway, one or more heat exchangers and control device for regulating heat exchanger(s), preferably a microprocessor.

5. Claims: 72 - 83

Perfusion solution kit comprising a sealable package containing a first container holding a first (preferably oxygenated) perfusion solution and a second container holding a different perfusion solution.

6. Claims: 84 - 109

Control system for controlling perfusion of an organ comprising: input, perfusion mode selector, flow control

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

selector and -controller, detector, comparator and indicator. Method of controlling perfusion of an organ by using this system.

7. Claims: 110 - 122

Recording medium for storing control program for use in perfusion system.

INTERNATIONAL SEARCH REPORT

Information on patent family members

Int[illegible]ional Application No
PCT/US 99/22582

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9743899 A	27-11-1997	US 5843024 A	01-12-1998
		AU 3067197 A	09-12-1997
		CA 2255657 A	27-11-1997
		CN 1226132 A	18-08-1999
WO 9745527 A	04-12-1997	US 5965433 A	12-10-1999
		CA 2228422 A	04-12-1997
		EP 0842261 A	20-05-1998
WO 9629865 A	03-10-1996	AU 5375496 A	16-10-1996
WO 9406292 A	31-03-1994	US 5338662 A	16-08-1994
		AU 5131093 A	12-04-1994
		CA 2144952 A	31-03-1994
		EP 0665713 A	09-08-1995
		US 5494822 A	27-02-1996
WO 9109520 A	11-07-1991	US 5066578 A	19-11-1991
		US 5075210 A	24-12-1991
		AU 7175591 A	24-07-1991
EP 0376763 A	04-07-1990	AU 633280 B	28-01-1993
		AU 4382789 A	03-05-1990
		CA 2001553 A	26-04-1990
		JP 4099701 A	31-03-1992
WO 8805261 A	28-07-1988	NONE	
US 3881990 A	06-05-1975	US 3777507 A	11-12-1973
US 5051352 A	24-09-1991	NONE	
US 5326706 A	05-07-1994	NONE	
WO 9114364 A	03-10-1991	NONE	
US 5141847 A	25-08-1992	JP 1930030 C	12-05-1995
		JP 3075063 A	29-03-1991
		JP 6053160 B	20-07-1994
FR 2592306 A	03-07-1987	NONE	
WO 9915011 A	01-04-1999	AU 9504298 A	12-04-1999
US 5699793 A	23-12-1997	US 6024698 A	15-02-2000
		AU 2517395 A	18-12-1995
		AU 2595195 A	18-12-1995
		EP 0759692 A	05-03-1997
		WO 9531944 A	30-11-1995
		WO 9531897 A	30-11-1995
WO 9746091 A	11-12-1997	US 5716378 A	10-02-1998
		AU 3142897 A	05-01-1998
US 4473637 A	25-09-1984	NONE	
WO 8600812 A	13-02-1986	AU 4671385 A	25-02-1986
		CA 1246449 A	13-12-1988

INTERNATIONAL SEARCH REPORT

Information on patent family members

Int. ional Application No
PCT/US 99/22582

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 8600812 A		EP 0188595 A	30-07-1986
		JP 61502821 T	04-12-1986
US 4231354 A	04-11-1980	AU 522816 B	24-06-1982
		AU 4889179 A	17-01-1980
		DE 2928223 A	24-01-1980
		FR 2430771 A	08-02-1980
		GB 2025662 A,B	23-01-1980
		IT 1117406 B	17-02-1986
		JP 55014096 A	31-01-1980