



INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

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(21) International Application Number: PCT/US98/16469 (22) International Filing Date: 7 August 1998 (07.08.98) (30) Priority Data: 60/055,127 8 August 1997 (08.08.97) US (71) Applicant: DUKE UNIVERSITY [US/US]; Erwin Road, Durham, NC 27708 (US). (72) Inventor: DUHAYLONGSOD, Francis, G.; 4218 Trotter Ridge Road, Durham, NC 27707 (US). (74) Agents: MACEY, Harry, J. et al.; Morrison & Foerster LLP, 755 Page Mill Road, Palo Alto, CA 94304-1018 (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, GE, GH, GM, HR, HU, ID, IL, 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, SZ, 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 <i>With international search report.</i> <i>Before the expiration of the time limit for amending the claims</i> <i>and to be republished in the event of the receipt of amendments.</i> (88) Date of publication of the international search report: 29 April 1999 (29.04.99)
(54) Title: COMPOSITIONS, APPARATUS AND METHODS FOR FACILITATING SURGICAL PROCEDURES (57) Abstract Methods are provided for conducting surgical procedures in a patient wherein, during the surgical procedure, autonomous ventricular electrical conductivity and escape beats are reversibly and transiently suppressed to facilitate the surgical procedure. Also provided are compositions which are capable of inducing ventricular asystole in a patient. The compositions may include an AV node blocker. In one embodiment, compositions including an atrioventricular (AV) node blocker and a β-blocker are provided, wherein the β-blocker is present in an amount sufficient to substantially reduce the amount of AV node blocker required to induce ventricular asystole in the patient. The compositions and methods may be used for inducing temporary ventricular asystole in a beating heart, and to facilitate the performance of a variety of surgical techniques, including minimally invasive microsurgical techniques. Methods for performing a surgical procedure on a human patient are provided wherein a composition capable of inducing transient reversible ventricular asystole is administered to the heart, for example by intracoronary injection. The heart then is electrically paced using an electrical pacing system, thereby to maintain the patient's blood circulation. The electrical pacing is then selectively intermittently stopped to allow ventricular asystole to occur, and the steps of the surgical or therapeutic procedure, such as suturing, are conducted during the time that the electrical pacing is intermittently stopped. The methods and compositions advantageously may be used in a range of different surgical procedures including cardiac, vascular and neurosurgical procedures.		

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INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 98/16469

A. CLASSIFICATION OF SUBJECT MATTER

IPC 6 A61K31/27 A61K31/135 A61N1/37 //(A61K31/27,31:135)

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 6 A61K A61N

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	OTORII, TAKESHI: "Effects of .beta.-adrenoreceptor blocking agents on deslanoside-induced arrhythmia and cardiac arrest in guinea pigs" JAP. CIRC. J. (1971), 35(12), 1535-40 CODEN: JCIRA2, XP002086314 see page 1537, right-hand column, paragraph 3 ---	1, 13, 14, 81
X	EP 0 525 475 A (ALCON LAB INC) 3 February 1993 see claims 1-14 ---	81-96
X	WO 95 08364 A (STANFORD SURGICAL TECHNOLOGIES) 30 March 1995 see claims 33-41 ---	69-78
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☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

° Special categories of cited documents :

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"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

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"&" document member of the same patent family

Date of the actual completion of the international search

4 March 1999

Date of mailing of the international search report

12/03/1999

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INTERNATIONAL SEARCH REPORT

International Application No

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P, X	US 5 735 290 A (CURTIS PATRICIA E ET AL) 7 April 1998 see column 11, line 9-17 ---	69-78
X	WO 96 21489 A (HEARTPORT INC) 18 July 1996 see claims 32-44 ---	69-78
X	EP 0 783 902 A (BIOTRONIK MESS & THERAPIEG) 16 July 1997 see the whole document ---	108-114
X	US 4 827 906 A (ROBICSEK FRANCIS ET AL) 9 May 1989 see abstract ---	108-114
P, X	WO 98 16164 A (MAYER PAUL W) 23 April 1998 see abstract -----	108-114

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 98/16469

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.:

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- ☐ 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: 1-68,79-107

A method of inducing reversible ventricular asystole comprising administering a compound such as a atrioventricular node blocker or cholinergic receptor agonist optionally together with a beta-blocker to the heart and compositions comprising the active ingredients.

2. Claims: 69-78

A method of preparing a patient for coronary artery bypass comprising placing a delivery device in a coronary vessel and delivering a cardioplegic agent to the patient with the device

3. Claims: 108-114

A pacing system comprising a pacer, a switch and an actuator.

INTERNATIONAL SEARCH REPORT

Information on patent family members

i. national Application No

PCT/US 98/16469

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Information on patent family members

national Application No

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