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Declaration under Rule 4.17:

— of inventorship (Rule 4.17(iv)) for US only

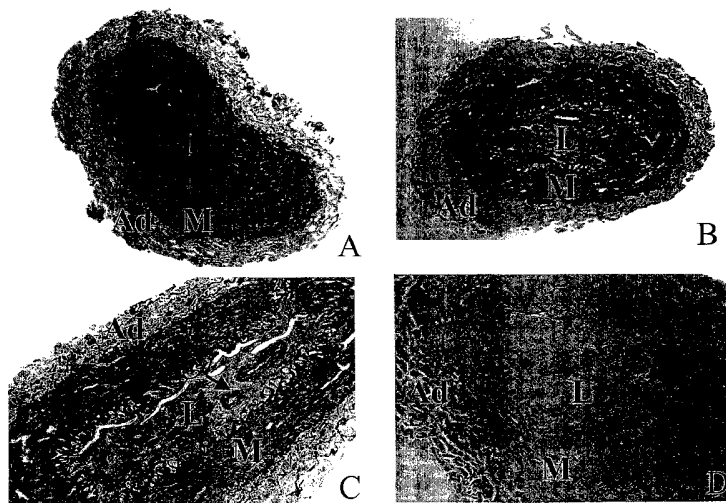
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(54) Title: AN IN VIVO ANIMAL MODEL OF CHRONIC ARTERIAL OCCLUSION AND USE OF COLLAGENASE TO FACILITATE GUIDE WIRE CROSSING IN CHRONIC ARTERIAL OCCLUSIONS



(57) Abstract: The field of the invention relates to percutaneous interventions of occluded arteries using local infusion of collagenase or a combination of enzymes that include collagenase. A method of is provided for treating chronically occluded animal tubes and cavities by administering a therapeutic effective amount of a proteolytic enzyme-containing formulation adjacent to an occluding atherosclerotic plaque, waiting for a pre-angioplasty waiting period, followed by crossing the plaque with an angioplasty guide wire. An in-vivo animal model of developing a chronic arterial occlusions is provided having the steps of isolating a segment of an animal artery, stopping blood flow with occlusive ligatures in the isolated arterial segment of the animal artery, injecting topical thrombin into the isolated arterial segment to form an acute thrombotic occlusion, and waiting while the acute thrombotic occlusion is converted into a chronic fibrotic occlusion.



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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.

INTERNATIONAL SEARCH REPORT

International Application No
PCT/CA 02/01476

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61K38/48 A61P7/02

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 A61K A61P

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.
Y	US 5 024 829 A (BERGER HARVEY J ET AL) 18 June 1991 (1991-06-18) column 6, line 45 - line 55 ---	1-8,32
Y	US 5 163 421 A (ROSENSCHEIN URI ET AL) 17 November 1992 (1992-11-17) column 10, line 15 - line 30 ---	1-8,32
Y	US 5 503 850 A (O'REAR III EDGAR A ET AL) 2 April 1996 (1996-04-02) column 9, line 61 -column 10, line 5 --- -/--	1-8,32

Further documents are listed in the continuation of box C.

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

14 January 2003

Date of mailing of the international search report

20.06.03

Name and mailing address of the ISA

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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.
Y	YOON H C ET AL: "A porcine model of chronic peripheral arterial occlusion." JOURNAL OF VASCULAR AND INTERVENTIONAL RADIOLOGY: JVIR. UNITED STATES 1996 JAN-FEB, vol. 7, no. 1, January 1996 (1996-01), pages 65-74, XP009003811 ISSN: 1051-0443 "Surgical and Angiographic Protocol" -----	1-8,32

INTERNATIONAL SEARCH REPORT

International application No.
PCT/CA 02/01476

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:

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.:

1-8, 32
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

1. Claims: 1-8,32

A method of developing a chronic arterial occlusion in-vivo animal model and an animal model formed by this method.

2. Claims: 9-31

A method of treating chronically occluded animal tubes and cavities.

INTERNATIONAL SEARCH REPORT
Information on patent family members

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