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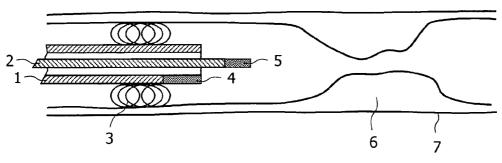
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(54) Title: CATHETER SYSTEM AND METHOD FOR FINE NAVIGATION IN A VASCULAR SYSTEM



(57) **Abstract:** The invention relates to a catheter system comprising a first, outer catheter (1) and a second catheter element contained in it, which can particularly be a guide wire (2). A respective active localizer (4, 5) is placed on the first and on the second catheter element (1, 2), for example sensors of a magnetic tracking system. The first catheter element (1) preferably has a fixing device (3), by means of which it can be fixed relative to the vascular system (7). If the guide wire (2) is, for example, to be navigated through a stenosis (6), the position of its localizer (5) relative to the localizer (4) is measured on the catheter element at rest (1), so that its position relative to the vessel (7) is known. Since interference factors such as organ movement balance each other during the measurement of the relative position of the localizers (4, 5), the navigation can be carried out with very high accuracy.



Catheter system and method for fine navigation in a vascular system

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The invention relates to a catheter system comprising a first and a second catheter element, which are coupled to each other, as well as a method for navigation using such a catheter system.

A typical application of catheter systems consists in the exploration and treatment of stenosis (vessel constriction). The success of the medical intervention depends in essence on whether the catheter system can be positioned and navigated with greater precision in relation to the stenosis. As a rule, pre-operative images of the vascular system are used as what are called "vessel maps" on which the current position of the catheter system is shown for the doctor in attendance. Methods have been developed for this purpose, by means of which the self-movements of the vascular system caused by heartbeat and breathing can be largely compensated and which make rough navigation of the catheter to the stenosis possible.

However, the subsequent fine navigation of the catheter at the location of the stenosis remains problematic. A guide wire must be led through the stenosis for this purpose, which guide wire can follow the actual treatment catheter. In this context a catheter system with a tubular outer catheter is known from US 2003/0139689 A1, through the inner channel of which catheter system a guide wire runs. The guide wire can be pushed in advance independently of the outer catheter and has X-ray proof markings at its tip, which markings can be located on an X-ray image. It should be possible to improve the steering of the catheter lead at vessel branching or stenoses by specially configuring the elasticity characteristics of the outer and inner catheter elements. A monitored navigation of the guide wire, however, requires X-ray fluoroscopic observation and possibly injecting contrast agents, involving a related burden on the patient.

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Against this background, it was an object of the present invention to provide means for simplified fine navigation for a catheter system in a vascular system.

This object is achieved by means of a catheter system having the features as mentioned in claim 1 as well as by a method having the features mentioned in claim 7.

Advantageous designs are given in the dependent claims.

The catheter system as invented comprises:

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- A first catheter element with at least a first active localizer placed on it, whose spatial position (i.e. position and/or orientation) can be determined by using suitable methods. An "active localizer" in this context is understood to mean a localizer that is not, or not only passively, represented on an image (such as an X-ray-proof marking), but that generates data or signals independently of the imaging method, which make it possible to determine a position. In particular, the active localizer itself can measure or emit signals. Active localizers that are not additionally subject to what are called "line-of-sight restrictions" are also designated as "non-line-of-sight" localizers.
 - A second catheter element with at least a second active localizer placed on it, whose spatial position can be determined.

The two catheter elements are coupled mechanically, where the coupling should be designed such that it makes a sliding movement of the catheter elements relative to each other possible. For example, the catheter elements could run next to each other as a string and be coupled to each other through eyebolts or guide bars in such a manner that they can be moved relative to each other only longitudinally. Each of the two catheter elements and in general even the two catheter elements together can be navigated and used together like a single catheter. It should be pointed out that the role of the first and the second catheter element is completely symmetrical, so the features required of a catheter element as given below can also be assumed mutatis mutandis for the other catheter element. Furthermore, it is obvious that the catheter system can analogously also contain more than two coupled catheter elements with active localizers.

The advantage of the described catheter system is that it allows a very precise fine navigation of the individual catheter elements. This is possible, because both catheter elements bear their own active localizers and can moreover be shifted relative to each other. One of the catheter elements can, therefore, be held fast, for example the first one, while only the other catheter element is pushed ahead. The position of the second localizer in relation to the first localizer can be determined with very high precision, as against the absolute spatial position of a localizer, which can typically be measured only with limited accuracy due to organ movements and/or disturbing ambient influences. The first localizer at rest can thus be used as a reference point for a fine navigation of the second localizer or the second catheter

element, respectively. Furthermore, the configuration of the markers as active localizers is advantageous, so that the navigation can be effected without the constant use of X-ray radiation.

The mechanical coupling of the catheter elements is preferably realized in that the first catheter element is hollow and has a channel running longitudinally, through which the second catheter element is guided. Typically, in this case, the first catheter element is the actual treatment catheter, which carries, for example, a balloon for widening a stenosis, while the second catheter element is a guide wire. The mechanical construction of such a catheter system can be similar to the one described in US 2003/0139689 A1.

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According to another design of the catheter system, this comprises at least one fixing device, with the help of which the first catheter element or the second catheter element can be fixed, in relation to a surrounding vessel. Fixing ensures that the catheter element concerned cannot move in relation to the vascular system, so that it serves as a reference for the observation of the movement of the other catheter element relative to the vascular system.

There are different options for the realization of the active localizers. According to a first alternative, at least one of the localizers can be a magnetic field sensor that can measure the strength and direction of an external (spatially and/or temporally inhomogeneous) magnetic field. The external magnetic field is generated here typically by a field generator near the examined patient and a conclusion about its spatial position can be drawn from the measurement data of the magnetic field sensor. In principle, the problem with such a "magnetic tracking" is that the magnetic field and thereby the accuracy of measurement suffers from interference from external factors such as metallic bodies etc. If, however, both active localizers of the catheter system are configured as magnetic field sensors, such interference affects both the sensors in equal measure, so they balance each other in the determination of the relative positions, up to interference of higher and therefore negligible orders.

According to another embodiment, at least one of the localizers contains a source for electromagnetic and/or acoustic radiation, where the position of this source can be located through external sensors. In particular a localizer can be an emitter for electromagnetic radiation from the near infrared (NIR) or an ultrasonic emitter. The position of such a radiation source can be determined, for example, by using stereoscopic methods, in which the intersection point of the lines of sight of the radiation source is determined from different spatial points.

The localizers on both catheter elements are preferably so placed that they lie at a distance of maximum 10 cm, particularly preferably 5 cm from each other in the typical usage of the catheter system. This way it is ensured that the distance between the localizers does not exceed the top limit, so that they are exposed to external influences to an almost equal extent. When measuring the relative positions of the two localizers, therefore, the corresponding influences balance each other, reducing them to an insignificant factor.

The invention further relates to a method for navigation of a catheter system in a vascular system, where the catheter system comprises a first and a second catheter element, which are coupled to each other so as to afford a sliding movement and each of them bears at least a first or second active localizer respectively. The catheter system can particularly be a catheter system of the kind mentioned above. The method comprises the following steps of:

a) determining the spatial position of the first localizer on the first catheter element relative to the vascular system.

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b) determining the spatial position of the second localizer on the second catheter element relative to the first localizer. In this step, the associated methods for position determination of the respective localizers can be used, where the relative position of the second localizer is obtained from the difference in the determined positions.

The advantage of the method is that it makes it possible to provide very precise fine navigation of the second catheter element in a vascular system (it being again pointed out here that, in principle, the role of the first and the second catheter element is symmetrical). The reason for this is that, during the navigation, the position of the second catheter element is determined relative to the first catheter element, which is possible with comparatively great accuracy. Effects from organ movements or external interference are experienced more or less equally by both localizers, so they are balanced in the relative position.

In order to improve the accuracy of the method, the first catheter element is preferably fixed in relation to the vascular system. During a movement of the second catheter element, its position can then be measured in relation to the first localizer, where the fixing ensures that the first localizer simultaneously represents a defined reference point in relation to the vascular system.

In step a) of the method, the position of the first localizer must be determined in relation to the vascular system. This is possible particularly by generating an image of the vascular system with the catheter system contained in it and subsequently determining the spatial position of the first localizer relative to the vascular system on this image. Said image

can, for example, be an X-ray image or a magnetic resonance image. It should be ensured here that the position of the first localizer can be determined (passively) with sufficient accuracy on the image, for example by providing the first localizer with an X-ray-proof material. Another possibility is to register the previously recorded vascular map by a suitable method i.e. determine the mutual correlation between the coordinate systems of the vascular map and of the active localizer or of the real vascular tree. Furthermore, it should be ensured during magnetic resonance imaging that the catheter elements are compatible with it and do not contain, for example, any components which could lead to dangerous heating during the recording.

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The invention is elucidated below with the help of exemplary figures. Figs 1 to 6 show schematically successive steps during the navigation of a catheter system as invented in the region of a stenosis.

Fig. 1 shows the tip of a catheter system as invented in a vessel 7, where the vessel has a stenosis 6 due to deposits on the inner vessel walls. The catheter system comprises a first catheter element 1 (called "catheter" below for short), which has a channel inside, running longitudinally, through which a second catheter element is guided in the form of a guide wire 2. The guide wire 2 may be moved as desired relative to the outer catheter 1 in longitudinal direction.

Furthermore, the outer catheter 1 as well as the guide wire 2 bear in each case an active localizer 4 or 5 respectively on their tips. This may be, for example, a magnetic field probe of a magnetic tracking system. The spatial position of the catheter elements in relation to an external coordinate system can be determined by means of the localizers 4, 5 with comparatively good accuracy. This current spatial position is shown, as a rule, on a preoperatively generated 3-dimentional vessel map for navigation of the catheter system. The methods so far known typically deliver an accuracy of 2-3 mm for compensation of organ movements, so a rough navigation of the catheter system up to the stenosis 6 is already possible. This, however, makes subsequent fine navigation of the catheter system through the stenosis 6 more problematic. Efforts are made here to find a way through the stenosis 6 using the guide wire 2, where one has to proceed very carefully due to the hazard of loosening of the deposits. In many cases, the navigation of the guide wire through the stenosis 6 is the most time-consuming part of an intervention, which can take up to 20 minutes. This problem should be solved by the proposed catheter system and the method possible with it.

As already elucidated, the outer catheter 1 as well as the guide wire 2 bear in each case their own active localizer 4 or 5 respectively. Furthermore, it can be seen in Fig. 1 that the outer catheter 1 has an (optional) fixing device 3, by means of which its position relative to the vessel 7 can be fixed. For example, the device 3 can contain a braided grid, which can be expanded radially to clamp the outer catheter 1 firmly in the vessel 7. In this way it is ensured that the catheter 1 does not make any movement relative to the vessel 7, but identically follows its movement.

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After fixing the outer catheter 1 in the vessel, an X-ray-fluoroscopic image of the vascular system can be generated where preferably a contrast agent is injected simultaneously for highlighting the path of the vessel. The position of the catheter 1 or of a linked X-ray-proof marker (e.g. of the localizer 4) can then be determined on this X-ray image, so that the fixed position of the localizer 4 relative to the catheter system 7 is known for the subsequent steps of the method. This information can also be gleaned by registering a previously recorded vascular map by a suitable method i.e. by establishing the mutual correlation between the coordinate systems of the vessel map and of the active localizer or of the real vascular tree.

In the next step (Fig. 2), the inner guide wire 2 is pushed ahead through the stenosis 6, where the spatial positions of the magnetic localizers 4 and 5 are (actively) measured continuously. The difference between these two positions provides the position of the localizer 5 on the guide wire 2 relative to the vascular system, because the localizer 4 on catheter 1 is fixed relative to the vascular system. This measurement of the relative position has great accuracy, because both localizers 4, 5 are affected almost equally by the movements of the vascular system due to their close proximity, the differences in the localizers thus balancing each other. The same is applicable for interference due to metals in the vicinity (e.g. the C-arc of X-ray equipment) or the like. The movement of the guide wire 2 can therefore be followed with great precision, for example, on a static vessel map. This makes it possible to navigate the guide wire 2 very much faster through the stenosis 6 than by the conventional method, until it reaches the end position on the other side of the stenosis 6 as shown in Fig. 2.

After passing the stenosis 6, the fixing of the outer catheter 1 is released and it is then pushed through the stenosis 6 following the guide wire 2 (Figs. 3, 4).

Subsequently, the guide wire 2 can be retracted in the outer catheter 1 up to a position shortly before the stenosis 6 (Figs. 5, 6).

WO 2005/082441 PCT/IB2005/050523

The catheter system as invented and the navigation method associated to it thus make a very precise fine navigation possible, which is particularly helpful in the area of stenoses. The core concept here is to provide two catheter elements movable relative to each other, each with its own active localizer, through which the relative movement of the catheter elements can be measured with high accuracy, because the interference factors (movement, fields etc) are balanced. Furthermore, one of the catheter elements can be fixed to the surroundings, so that the movement of the other catheter element relative to these surroundings can be observed. In this manner, iterative navigation with high precision is possible. Other advantages of the method consist in the fact that catheter navigation is possible with comparatively low X-ray burden. Moreover, the method supports techniques based on (especially two) localizers, for example the selection of a region of interest with the help of the localizers and method for movement compensation, which are based on the local reference sensors and movement models.

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Even though the medical application of the catheter system for navigation through a stenosis is shown in the figures, the present invention is in no way restricted to such applications, but can be used in all cases with comparable problems.

PCT/IB2005/050523 WO 2005/082441 8

CLAIMS

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- 1. A catheter system, comprising:
- a first catheter element (1) with at least a first active localizer (4) placed on it, whose spatial position can be determined;
- a second catheter element (2) with at least a second active localizer (5) placed on it, whose spatial position can be determined; 5 wherein the first and the second catheter element are coupled in such a manner that a sliding movement relative to each other is possible.
- 2. A catheter system as claimed in claim 1, characterized in that the first catheter 10 element (1) has a channel running in longitudinal direction, through which the second catheter element (2) is guided.
- 3. A catheter system as claimed in claim 1, characterized in that it comprises a fixing device (3), by means of which at least one of the catheter elements (1) can be fixed in a 15 surrounding vessel (7).
 - A catheter system as claimed in claim 1, characterized in that at least one of 4. the localizers (4, 5) is a magnetic field sensor in an external magnetic field for determining the position.

5. A catheter system as claimed in claim 1, characterized in that at least one of the localizers contains a source for electromagnetic and/or acoustic radiation.

- 6. A catheter system as claimed in claim 1, characterized in that the localizers (4, 5) are arranged such that they are at a distance of less than 10 cm, preferably less than 5 cm 25 from each other during the use of the catheter system.
 - 7. A method for navigation of a catheter system in a vascular system (7), wherein the catheter system contains a first and a second catheter element (1, 2), which are coupled to

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PCT/IB2005/050523

each other such that they can slide with respect to each other and carry at least a first or second active localizer (4, 5) respectively, the method comprising the following steps of:

- a) determining the spatial position of the first localizer (4) relative to the vascular system (7);
- 5 b) determining the spatial position of the second localizer (5) relative to the first localizer (4).
 - 8. A method as claimed in claim 7, characterized in that the first catheter element (1) is fixed relative to the vascular system (7), while the second catheter element (2) is moved.
 - 9. A method as claimed in claim 7, characterized in that an image is generated of the vascular system (7) with the catheter system contained in it and in that the spatial position of the first localizer (4) relative to the vascular system (7) is determined on this image.
 - 10. A method as claimed in claim 7, characterized in that the catheter system is designed at least as claimed in one of the claims 1 to 6.

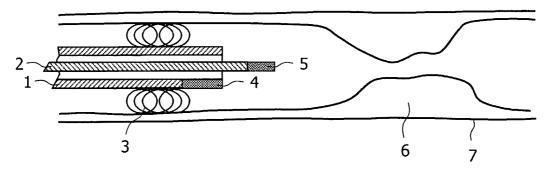


FIG.1

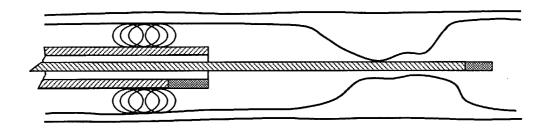


FIG.2

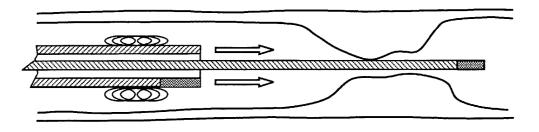


FIG.3

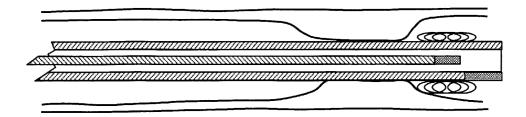


FIG.4

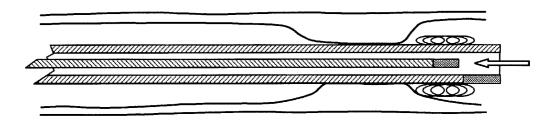


FIG.5

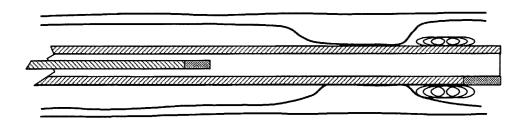


FIG.6

Inter nal Application No
PCT/IB2005/050523

A. CLASSIFICATION OF SUBJECT MATTER IPC 7 A61M25/00 A61M25/01

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 A61M

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)

EPO-Internal

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	WO 94/11038 A (CARDIOVASCULAR IMAGING SYSTEMS, INC) 26 May 1994 (1994-05-26) page 9, line 20 - page 16, line 17; figures	1-6
Y	WO 97/00043 A (MARTINELLI, MICHAEL, A) 3 January 1997 (1997-01-03) page 3, last line - page 5, line 22; claims; figures	1-6
Υ	US 5 269 793 A (SIMPSON ET AL) 14 December 1993 (1993-12-14) column 5, line 56 - column 7, line 39; figures	1-6
Y	US 2003/060700 A1 (SOLF TORSTEN ET AL) 27 March 2003 (2003-03-27) paragraphs '0029! - '0041!; figures	1-6

	-/				
Further documents are listed in the continuation of box C.	Patent family members are listed in annex.				
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14 April 2005	26/04/2005				
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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	Vänttinen, H				

Inter_i al Application No PCT/IB2005/050523

	ation) DOCUMENTS CONSIDERED TO BE RELEVANT	To-to
Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Υ	US 5 203 338 A (JANG ET AL) 20 April 1993 (1993-04-20) column 4, line 11 - column 8, line 33; figures	1-6
Y	EP 1 199 031 A (PHILIPS INTELLECTUAL PROPERTY & STANDARDS GMBH; KONINKLIJKE PHILIPS EL) 24 April 2002 (2002-04-24) paragraphs '0016! - '0027!; figure 1	1-6
Α	US 2003/163037 A1 (BLADEN JOHN STUART ET AL) 28 August 2003 (2003-08-28) paragraphs '0038! - '0112!; figures	1-5
Α	US 6 632 196 B1 (HOUSER RUSSELL A) 14 October 2003 (2003-10-14) column 4, line 29 - column 9, line 34; figures	1-3,5
Α	WO 95/18646 A (CORTRAK MEDICAL, INC) 13 July 1995 (1995-07-13) page 8, line 15 - page 18, line 22; figures	1-3,5
Α	US 2003/139689 A1 (SHTURMAN LEONID ET AL) 24 July 2003 (2003-07-24) cited in the application abstract; figures	1

ational application No. PCT/IB2005/050523

Box II Observations where certain claims were found unsearchable (Continuation of item 2 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. X Claims Nos.: 7-10 because they relate to subject matter not required to be searched by this Authority, namely:
Rule 39.1(iv) PCT - Method for treatment of the human or animal body by therapy and surgery
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 III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)
This International Searching Authority found multiple inventions in this international application, as follows:
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.

Inter 1al Application No PC1/1B2005/050523

					1005/050525
Patent document cited in search report		Publication date		Patent family member(s)	Publication date
WO 9411038	A	26-05-1994	US AT CA DE DE EP ES JP WO US	5314408 A 257717 T 2147360 A1 69333384 D1 69333384 T2 0746346 A1 2217263 T3 8503629 T 9411038 A1 5458584 A	24-05-1994 15-01-2004 26-05-1994 19-02-2004 04-11-2004 11-12-1996 01-11-2004 23-04-1996 26-05-1994 17-10-1995
WO 9700043	<u></u> А	03-01-1997	US EP JP WO	5592939 A 0836413 A1 11510406 T 9700043 A1	14-01-1997 22-04-1998 14-09-1999 03-01-1997
US 5269793	Α	14-12-1993	EP JP JP WO	0483270 A1 3045306 B2 4506912 T 9101156 A1	06-05-1992 29-05-2000 03-12-1992 07-02-1991
US 2003060700	A1	27-03-2003	DE EP JP	10115341 A1 1245191 A2 2002306473 A	02-10-2002 02-10-2002 22-10-2002
US 5203338	A	20-04-1993	US US US AT CA DE DE EP JP WO	5976093 A 6234971 B1 2003036729 A1 5997523 A 157269 T 2098570 A1 69127462 D1 69127462 T2 0563179 A1 6503246 T 3367666 B2 9211055 A1	02-11-1999 22-05-2001 20-02-2003 07-12-1999 15-09-1997 18-06-1992 02-10-1997 02-04-1998 06-10-1993 14-04-1994 14-01-2003 09-07-1992
EP 1199031	Α	24-04-2002	DE EP JP US	10051244 A1 1199031 A2 2002200058 A 2002077546 A1	16-05-2002 24-04-2002 16-07-2002 20-06-2002
US 2003163037	A1	28-08-2003	US US AU CA CA DE DE EP ES WO JP US	6522907 B1 6757557 B1 675077 B2 4726693 A 2142338 A1 2288411 A1 2358682 A1 69318304 D1 69318304 T2 0655138 A1 2115776 T3 9404938 A1 3432825 B2 8500441 T 5913820 A	18-02-2003 29-06-2004 23-01-1997 15-03-1994 03-03-1994 03-03-1994 04-06-1998 20-08-1998 31-05-1995 01-07-1998 03-03-1994 04-08-2003 16-01-1996 22-06-1999

Int: al Application No PC1/1B2005/050523

Patent document cited in search report		Publication date		Patent family member(s)		Publication date
US 2003163037	A1		US US	6374134 6516212	-	16-04-2002 04-02-2003
US 6632196	B1	14-10-2003	US AU WO	5865801 / 5669796 / 9703604 /	Α	02-02-1999 18-02-1997 06-02-1997
WO 9518646	A	 13-07-1995	US AU EP JP WO	5419763 1448595 0738167 9507151 9518646	A A1 T	30-05-1995 01-08-1995 23-10-1996 22-07-1997 13-07-1995
US 2003139689	A1	24-07-2003	WO	03043685	A2	30-05-2003