

(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
22 September 2005 (22.09.2005)

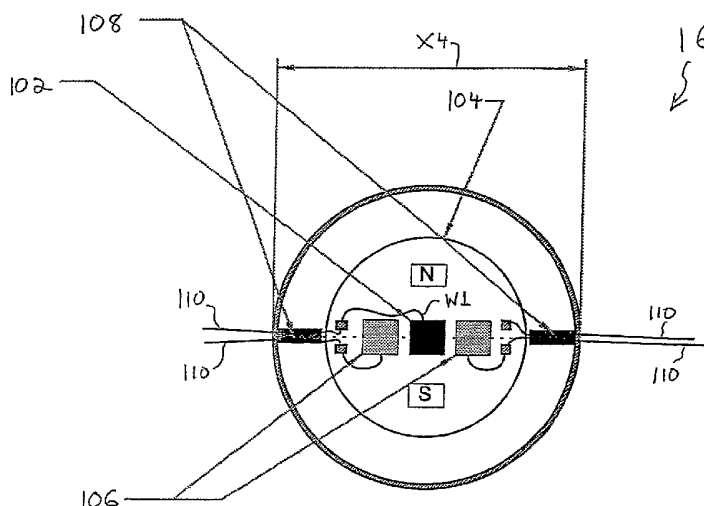
PCT

(10) International Publication Number
WO 2005/087084 A1

- (51) International Patent Classification⁷: **A61B 1/04**
- (74) Agent: **FARBER, George, S.**; Christensen O'Connor Johnson Kindness PLLC, Suite 2800, 1420 Fifth Avenue, Seattle, WA 98101 (US).
- (21) International Application Number: PCT/US2005/007083
- (81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, 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, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.
- (22) International Filing Date: 3 March 2005 (03.03.2005)
- (25) Filing Language: English
- (26) Publication Language: English
- (30) Priority Data: 10/793,483 4 March 2004 (04.03.2004) US
- (71) Applicant (for all designated States except US): **BOSTON SCIENTIFIC SCIMED, INC.** [US/US]; One Scimed Place, Maple Grove, MN 55311-1566 (US).
- (84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).
- (72) Inventors: **BARBATO, Louis, J.**; 8 Skyline Drive, Franklin, MA 02038 (US). **HAMM, Mark, A.**; 46 Forest Hill Avenue, Lynnfield, MA 01940 (US). **CHIN, Yem**; 35 University Avenue, Burlington, MA 01803 (US).

[Continued on next page]

(54) Title: VISION CATHETER SYSTEM



(57) Abstract: A disposable imaging catheter that produces high resolution, color images comparable to those obtained from an endoscope. The device may also be made to function as a guidewire. The device may also include a sheath which slides over the catheter body for stiffening and which may include a working channel for accepting interventional devices, as well as LEDs to illuminate the field of view. The vision catheter system includes a detector assembly, scanning mechanism, and distal objective lens. In one embodiment, a photodetector is mated to a lens/pinhole assembly that allow the detector to read light from a small discrete point. This assembly is then scanned in raster or spiral patterns via electric wire coils that actuate a magnetic scan plate to read the area of interest. By adding a fixed objective lens, such as an aspheric lens that is attached to the distal tip of the catheter body, the field of view or acceptance angle of the system is magnified, yielding a wide angle image similar to that commonly obtained from an endoscope.

WO 2005/087084 A1



Published:

— *with international search report*

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.

VISION CATHETER SYSTEM

FIELD OF THE INVENTION

The present invention relates to medical devices, and in particular, to a catheter with imaging capabilities.

5

BACKGROUND OF THE INVENTION

Many medical interventional procedures are dependent on endoscopes to deliver diagnostic and therapeutic catheters to GI, URO, and biliary locations throughout the body. In these types of procedures, the area for maneuvering the endoscope is limited by the working channel diameter. Further limitations regarding the areas that are accessible to the endoscope are due to the physical constraints caused the size and stiffness of the endoscope. Furthermore, with regard to the comfort of the patient, endoscopic procedures are often very painful and require sedation.

A typical endoscope has an illumination channel and an imaging channel, both of which may be made of a bundle of optical fibers. The illumination channel is coupled to a light source to illuminate an internal body cavity of a patient, and the imaging channel transmits an image created by a lens at the distal end of the endoscope to a connected camera unit or display device. As an alternative to an imaging channel made of a bundle of optical fibers, a semiconductor-type camera can also be attached onto the distal tip. One drawback of this alternative is that such cameras are relatively large in size, in comparison to the dimensions needed for certain surgical procedures. Another issue with either the semiconductor-type camera or the bundle of fibers is that the ability to see a larger area requires moving the camera or the bundle of fibers. This type of movement is relatively complex to implement, and requires even more area. Furthermore, while endoscopes are a proven technology, they are relatively complex and expensive to manufacture.

Certain known systems have attempted to produce high-resolution images with a small diameter catheter, most involving optical fibers or fiber imaging bundles in some way. The cost and complexity of an imaging bundle-based vision catheter severely limits its application in the GI and URO fields. The size and number of individual light carrying fibers that comprise an imaging fiber bundle limit the image resolution. For these and other reasons, endoscopes have moved to imaging arrays at the distal tip of the

endoscope, which are cheaper, and produce higher resolution images, while increasing the life span of the scope. Due to the size of the arrays and the processing that must take place near the arrays, the endoscope diameters are generally quite large. In addition, they usually require a light source and working channel to allow the clinician to perform therapeutic procedures.

The present invention is directed to an apparatus that overcomes the foregoing and other disadvantages. More specifically, the present invention is directed to a much smaller profile catheter-based device that provides imaging capabilities that are comparable to those of endoscopes.

SUMMARY OF THE INVENTION

The present invention is directed to a vision catheter system. In accordance with one aspect of the invention, the device is in the form of a disposable imaging catheter that produces high-resolution color images that are comparable to those obtained from an endoscope. The device may also function as a guidewire to guide larger devices to areas of interest to facilitate diagnosis and treatment within various lumens of the human body, such as the vasculature, GI, urology (URO) and biliary tracts. The vision catheter system of the present invention is intended to reduce or eliminate the dependence on endoscopes while providing comparable imaging capabilities for many areas within the human body including certain areas that are inaccessible to endoscopes. The device is generally applicable in environments (even those outside the medical field) where low cost, remote imaging is needed.

In accordance with one aspect of the invention, the vision catheter system of the present invention is operable to provide usable images of anatomy that may be beyond the reach of a typical endoscope. In one application, the vision catheter system may be passed through the working channel of an endoscope, and may extend far beyond the distal tip of the endoscope.

In accordance with another aspect of the invention, the vision catheter system may be utilized without an endoscope, where the device acts as an imaging guidewire. In such applications, interventional surgical devices may be passed over the device and guided to the site of interest.

In accordance with another aspect of the invention, the vision catheter system may provide usable images with a large field of view, such as may be useful for navigating in

lumens, such as the vasculature, GI, URO, and biliary tracts. It can also provide images utilizing a small field of view, such as may be useful for guiding snares or forceps, monitoring tissue color, and being utilized with fluorescence capabilities for detecting margins of cancerous or dysplastic tissues.

5 In accordance with another aspect of the invention, the vision catheter system may include a stiffening sheath that slides over the catheter body. In another embodiment, a multi-lumen sheath may be provided that slides over the catheter body and which includes a working channel to accept interventional devices. In yet another embodiment, the stiffening sheath and multi-lumen sheath may be combined to form a multi-lumen
10 extrusion with a working channel. The sheath may also house LEDs or laser diodes to illuminate the field of view. In one particular implementation, three LEDs or laser diodes may be provided so as to provide three colors or wavelengths. These LEDs or laser diodes may be located on the sheath itself, or may be located on a proximal scanning plate.

15 In accordance with another aspect of the invention, the vision catheter system includes a detector assembly, scanning mechanism, and distal objective lens. In one embodiment, a photodetector is mated to a lens/pinhole assembly that allows the detector to read light from a small discrete point. This assembly is then scanned in raster or spiral
20 patterns via electric wire coils that actuate a magnetic scan plate to read the area of interest. By adding a fixed objective lens, such as an aspheric lens that is attached to the distal tip of the catheter body, the field of view or acceptance angle of the system is magnified, yielding a wide angle image similar to that commonly obtained from an endoscope.

 It will be appreciated that the vision catheter system of the present invention
25 includes components that are widely available and that can easily be assembled. The simple design thus allows for the production of catheters that are relatively inexpensive and disposable and which have imaging capabilities while still remaining relatively small in diameter.

BRIEF DESCRIPTION OF THE DRAWINGS

30 The foregoing aspects and many of the attendant advantages of this invention will become more readily appreciated as the same become better understood by reference to

the following detailed description, when taken in conjunction with the accompanying drawings, wherein:

FIGURE 1 shows a vision catheter system formed in accordance with the present invention;

5 FIGURE 2 shows a stiffening sheath that slides over the catheter body of FIGURE 1;

FIGURE 3 shows a multi-lumen sheath that slides over the catheter body of FIGURE 1 and which includes a working channel to accept interventional devices;

10 FIGURE 4 is a cross-sectional view of a sheath that slides over the catheter body of FIGURE 1 and which includes three laser diodes for illuminating a field of view; and

FIGURE 5 is a cross-sectional view of a scanning mechanism and detector assembly within the vision catheter system of FIGURE 1.

DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENT

15 FIGURE 1 is a diagram of a vision catheter system 10 formed in accordance with the present invention. The vision catheter system 10 includes a flexible catheter body 12 having a distal end 14. The vision catheter system 10 also includes a scanning mechanism and detector assembly 16, which will be described in more detail below with reference to FIGURE 4.

20 In one embodiment, the scanning mechanism and detector assembly 16 causes a scan to occur of an image at the distal end 14 of the catheter body 12. The scanning effect causes the field of view that is sensed by the distal end 14 to effectively increase. The sensed image may be transferred to a computer or processor, and may further be recorded and/or displayed on a monitor. The vision catheter system 10 also includes a distal objective lens 30 that is placed in front of the scanning mechanism and detector assembly 16. The distal objective lens 30 is equipped with a flush port to clean the lens. In one embodiment, the distal objective lens 30 (FIGURE 1) may be an aspheric lens that is attached to the distal tip of the catheter body, through which the field of view or acceptance angle of the system is magnified, yielding a wide angle image such as that commonly obtained from an endoscope.

30 In one embodiment, the vision catheter system 10 can be equipped with two objective lenses, such as gradient index (GRIN) rod lenses that also yield stereo vision, which can be made to provide a three-dimensional image with perspective. This

embodiment can include two detector/lens assemblies, which may be located on the same scanning mechanism. The two images can then be combined to create a three-dimensional image with perspective. Because of the small diameter, cylindrical objective lenses can be spaced slightly apart or near the outer diameter of the sheath. In addition, a
5 central guidewire lumen can be provided to allow access to more remote areas within the body.

The catheter body 12 also includes a proximal end 18 that has an electrical connector 20. The electrical connector 20 has a dimension X1 which is designed to be small enough to allow backloading of larger sheaths, as will be described in more detail
10 below with reference to FIGURES 2 and 3. The electrical connector 20 provides electrical connections for the catheter body 12, such that the image signals from the imaging fibers can be received and processed. In one embodiment, the vision catheter system 10 may serve as a guidewire with a single pixel scanning camera that operates on a principle similar to the way a television works, which can be used by itself or in
15 conjunction with other components to increase its capabilities. In one embodiment, the vision catheter system 10 may be formed as a 2-3 mm profile catheter that provides high resolution images.

FIGURE 2 is a diagram of a stiffening sheath 40 that slides over the catheter body 12. The stiffening sheath 40 includes stiffening walls 42, and has a lens 46 located
20 on the distal tip. The stiffening sheath 40 has an internal diameter X2, which is intended to be larger than the external diameter X1 of the electrical connector 20 of the vision catheter system 10, such that the stiffening sheath 40 can be backloaded over the catheter body 12.

In one embodiment, an objective lens is housed at the distal tip of the stiffening
25 sheath 40. This allows the user to change the distance between the detector/lens assembly and the objective lens, thus providing a zoom capability. While this tends to increase the profile of the system, it also may be designed to allow room for a working channel, which provides for additional interventional capabilities in a device that is still relatively small in diameter.

FIGURE 3 is a diagram of a multi-lumen sheath 50. The multi-lumen sheath 50
30 has walls 52 and includes a working channel 54 that can accept the usual interventional devices currently used in the medical field, and also has a lens 56 located on the distal tip. The multi-lumen sheath 50 has an internal diameter X3, which is intended to be larger

than the external diameter X1 of the electrical connector 20, such that the multi-lumen sheath 50 can be backloaded over the catheter body 12. In one embodiment, the stiffening sheath 40 of FIGURE 2 and multi-lumen sheath 50 of FIGURE 3 may be combined and may be formed of a multi-lumen extrusion with a working channel. As
5 illustrated in FIGURE 4, in one embodiment, the sheath 60 may also house three LEDs or laser diodes 67, 68, and 69 to illuminate the field of view. The sheath 60 has an internal diameter X4, which is intended to be larger than the external diameter X1 of the electrical connector 20 of the vision catheter system 10, such that the sheath 60 can be backloaded over the catheter body 12. In one particular implementation, the LEDs or laser diodes
10 may be made to provide three colors or wavelengths. These LEDs or laser diodes may be located on the sheath or they may be located on the proximal scanning plate, as will be described in more detail below with respect to FIGURE 5.

FIGURE 5 is a cross-sectional view of one embodiment of the scanning mechanism and detector assembly 16 of the vision catheter system 10. As shown in
15 FIGURE 5, the scanning mechanism and detector assembly 16 includes a detector 102, a scanning plate 104, emitters 106, torsion springs 108, and electrical conductors 110. The detector 102 is coupled to the external electronics by a wire W1.

In one embodiment, the detector 102 is a photodetector that is mated to a lens/pinhole assembly that allows the detector 102 to read light from a small discrete
20 point, while rejecting all light from the remainder of the field of view. This assembly is then scanned in raster or spiral patterns via electric wire coils that actuate the magnetic scan plate 104 to read the object or area of interest. In other embodiments, other scanning schemes may also be utilized. In one embodiment, the wire W1 which connects to the detector 102 may be designed to be a small solid conductor wire, which is flexed by the
25 scanning plate 104 motion, and may be intended to break due to fatigue after several hours of operation. This feature can be intended to ensure that a version of the vision catheter system 10, which is made to be disposable for sanitary and other reasons, will not be reused. In one embodiment, the torsion type springs 108 are generally intended to have a resonant frequency at or near the desired frequency of operation. The electrical
30 conductors 110 traverse the torsion springs 108, thus minimizing breakage during the scan.

After the scan, the imaging signal information is then assembled by a computer via the electrical connector 20 (see FIGURE 1) to form an image. In one embodiment,

false color mapping (which is used in both CCD or CMOS imaging arrays) may then be utilized to calculate color.

In one embodiment, the scanning plate 104 may be designed and built as a photo etched component and a printed circuit designed to accept the photo-detectors and LEDs to provide a smaller scanning plate and more robust assembly. The manufacturing process may utilize existing technology, such as EDM, laser machining, or chemical etching. Electrical circuits can also be deposited onto the scanning plate using known industrial processes. In one embodiment, the scanning plate 104 may be designed and built using MEMS technology. In one implementation utilizing MEMS technology, the device can be fabricated in a 1 mm package.

In another embodiment, as nanotechnology processing improves, the vision catheter system 10 can be fabricated in an even smaller package. In addition, by using selected illumination wavelengths (e.g., 1500 nanometers) imaging through blood may be made possible by utilizing certain polarization techniques. The small size of the camera due to nanotechnology, and the ability to image through blood, can enable the vision catheter system to be utilized in certain coronary or other applications.

It will be appreciated that the present invention provides a vision catheter system that is relatively easy to build and which can be made from widely available components. Due to the modular design, simple, low cost components and extrusions can be utilized. The vision catheter system can be formed as a disposable imaging catheter that produces high resolution, color images comparable to those obtained from an endoscope. The device may also function as a guidewire to locate and guide larger devices to the areas of interest to facilitate diagnosis and treatment. The system reduces or eliminates the dependence on endoscopes while providing comparable images of many areas within the human body including even certain areas that are inaccessible to endoscopes. The device is also applicable outside the medical field where low cost, remote imaging is desired.

While the preferred embodiment of the invention has been illustrated and described, it will be appreciated that various changes can be made therein without departing from the spirit and scope of the invention.

The embodiments of the invention in which an exclusive property or privilege is claimed are defined as follows:

1. A vision catheter system, comprising:
 - a catheter body;
 - a detector; and
 - a scanning component for moving the detector to scan an area of interest.
2. The vision catheter system of Claim 1, wherein the outer diameter of the catheter body is less than or equal to 3 mm.
3. The vision catheter system of Claim 1, wherein the detector comprises a single pixel scanning camera.
4. The vision catheter system of Claim 1, wherein the detector comprises a photodetector which is mated to a lens assembly that allows the detector to read light from a small discrete point, while generally rejecting light from the remainder of the field of view.
5. The vision catheter system of Claim 1, wherein the scanning component comprises a scan plate.
6. The vision catheter system of Claim 5, further comprising one or more springs that are coupled to the scan plate.
7. The vision catheter system of Claim 5, further comprising electric wire coils which actuate the scan plate.
8. The vision catheter system of Claim 1, wherein the scan is performed in a spiral pattern.
9. The vision catheter system of Claim 1, wherein the scan is performed in a raster pattern.
10. The vision catheter system of Claim 1, further comprising an objective lens.

11. The vision catheter system of Claim 1, wherein the objective lens is attached to the distal end of the catheter body and provides a wide angle image such as that commonly obtained from an endoscope.

12. The vision catheter system of Claim 1, further comprising a stiffening sheath that slides over the catheter body.

13. The vision catheter system of Claim 1, further comprising a sheath that slides over the catheter body and which includes a working channel to accept interventional devices.

14. The vision catheter system of Claim 1, wherein a field of view is provided by the vision catheter without requiring the use of an endoscope.

15. The vision catheter system of Claim 1, further comprising an endoscope, wherein the catheter body may be passed through the working channel of the endoscope and can extend beyond the distal tip of the endoscope.

16. The vision catheter system of Claim 1, wherein the vision catheter may be utilized as an imaging guidewire, wherein interventional surgical devices may be passed over the catheter body and guided to the site of interest.

17. A vision catheter comprising:
a flexible catheter body that can be maneuvered to an area of interest during a surgical procedure;
a detector assembly;
a scanning mechanism for moving the detector assembly to scan the area of interest for obtaining image signals corresponding to the area of interest such that an endoscope is not required for obtaining image signals corresponding to the area of interest.

18. The vision catheter of Claim 17, wherein the scanning mechanism comprises an electromagnetic scan plate.

19. A method for obtaining images of an area of interest during a surgical procedure without requiring the use of an endoscope, the method comprising:

providing a vision catheter with a scanning mechanism; and
utilizing the vision catheter to scan an area of interest to obtain the desired
images.

20. The method of Claim 19, wherein the scanning mechanism comprises an
electromagnetic scan plate.

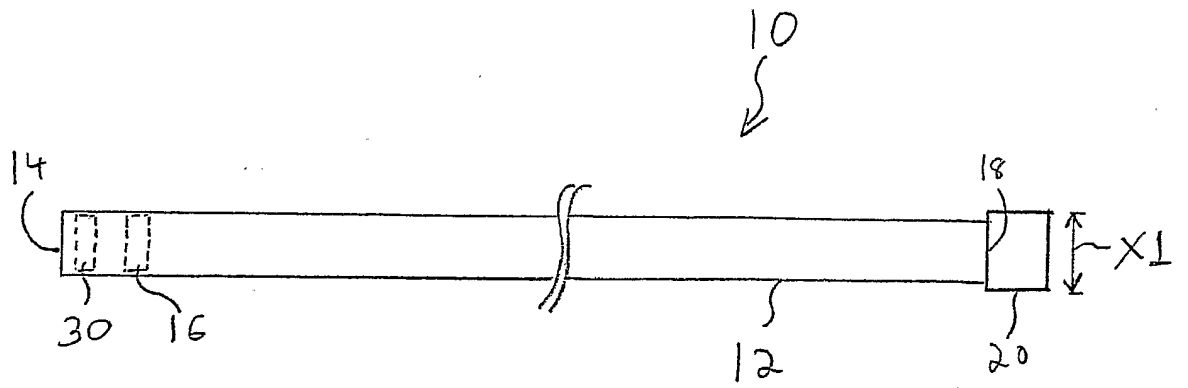


FIG. 1

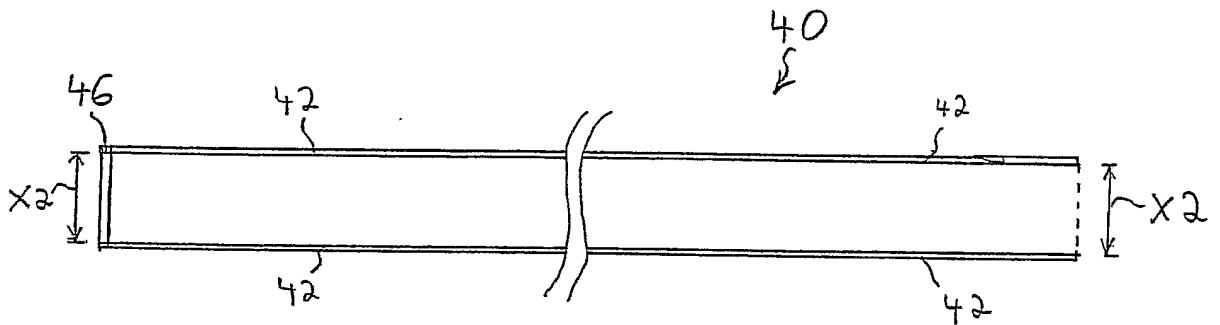


FIG. 2

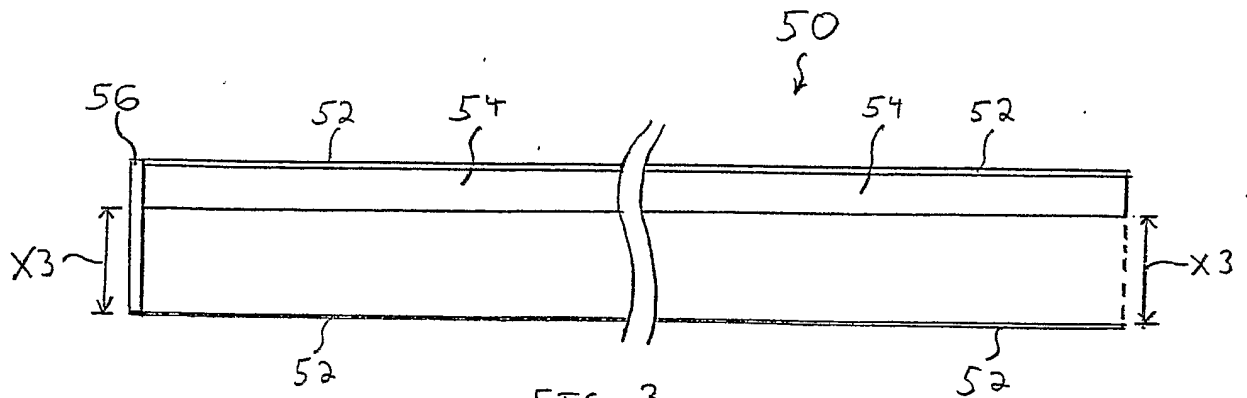


FIG. 3

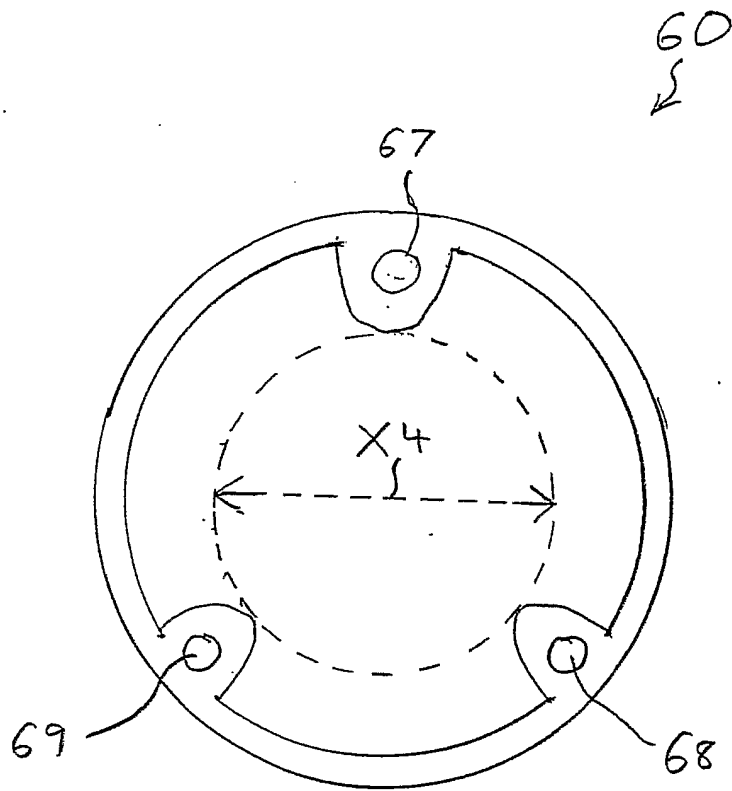


FIG. 4

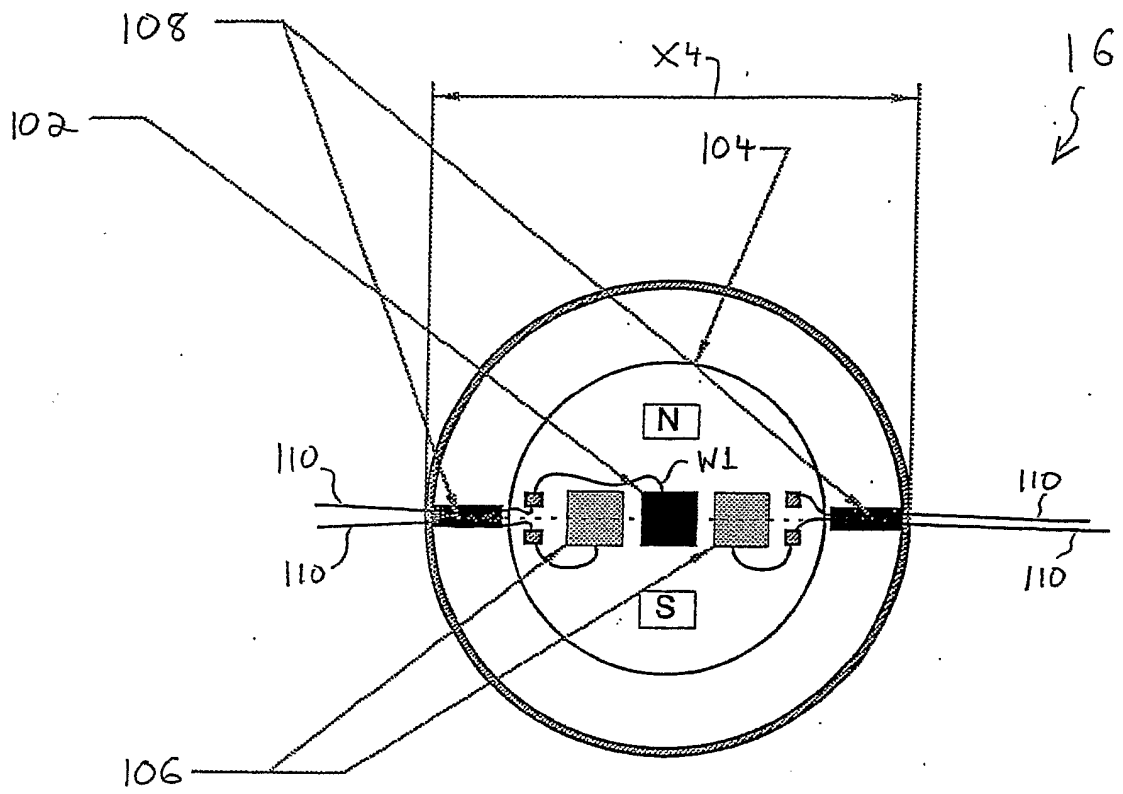


FIG. 5

INTERNATIONAL SEARCH REPORT

International Application No PCT/US2005/007083
--

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61B1/04

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 A61B

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, WPI Data, PAJ

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 2003/130562 A1 (BARBATO LOUIS J ET AL) 10 July 2003 (2003-07-10) paragraph '0006! - paragraph '0016! paragraph '0033! - paragraph '0040! figures 1,2	1-18
X	US 2002/139920 A1 (SEIBEL ERIC J ET AL) 3 October 2002 (2002-10-03) paragraph '0014! - paragraph '0020! paragraph '0048! - paragraph '0054!; figures 1-4	1-18
X	US 6 485 413 B1 (BOPPART STEPHEN A ET AL) 26 November 2002 (2002-11-26) column 2, line 30 - column 3, line 27 figures 4,6-8	1,17
	----- -/--	

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

13 May 2005

Date of mailing of the international search report

25/05/2005

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

Abraham, V

INTERNATIONAL SEARCH REPORT

Intel	nal Application No
PCT/US2005/007083	

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 2001/055462 A1 (SEIBEL ERIC J) 27 December 2001 (2001-12-27) abstract <div style="text-align: center; margin-top: 10px;">-----</div>	1, 17

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2005/007083

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. Claims Nos.: 19, 20
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 surgery
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 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:

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.

INTERNATIONAL SEARCH REPORT

Information on patent family members

Intel

Patent Application No

PCT/US2005/007083

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 2003130562 A1	10-07-2003	AU 2002357230 A1	30-07-2003
		CA 2472012 A1	24-07-2003
		EP 1464165 A2	06-10-2004
		WO 03061275 A2	24-07-2003
US 2002139920 A1	03-10-2002	US 6294775 B1	25-09-2001
		CA 2457506 A1	06-03-2003
		EP 1430534 A1	23-06-2004
		JP 2005501279 T	13-01-2005
		WO 03019661 A1	06-03-2003
US 6485413 B1	26-11-2002	US 5784352 A	21-07-1998
		US 6134003 A	17-10-2000
		US 5748598 A	05-05-1998
		US 5459570 A	17-10-1995
		US 6111645 A	29-08-2000
		US 6160826 A	12-12-2000
		US 6564087 B1	13-05-2003
		US 6501551 B1	31-12-2002
		US 6282011 B1	28-08-2001
		US 5956355 A	21-09-1999
		US 2001036002 A1	01-11-2001
		AU 1977597 A	16-09-1997
		EP 0883793 A1	16-12-1998
		JP 3628026 B2	09-03-2005
		JP 2000503237 T	21-03-2000
		JP 2002214127 A	31-07-2002
		WO 9732182 A1	04-09-1997
		WO 9723870 A1	03-07-1997
		WO 9701167 A1	09-01-1997
		WO 9533970 A1	14-12-1995
		DE 69227902 D1	28-01-1999
		DE 69227902 T2	17-06-1999
		EP 0581871 A1	09-02-1994
		JP 3479069 B2	15-12-2003
		JP 6511312 T	15-12-1994
		JP 2004105708 A	08-04-2004
		WO 9219930 A1	12-11-1992
US 5465147 A	07-11-1995		
US 5321501 A	14-06-1994		
EP 0971626 A1	19-01-2000		
JP 2001515382 T	18-09-2001		
WO 9838907 A1	11-09-1998		
US 2001055462 A1	27-12-2001	US 2004122328 A1	24-06-2004
		US 2004254474 A1	16-12-2004
		US 2002064341 A1	30-05-2002
		AU 7493301 A	02-01-2002
		JP 2003535659 T	02-12-2003
WO 0197902 A2	27-12-2001		