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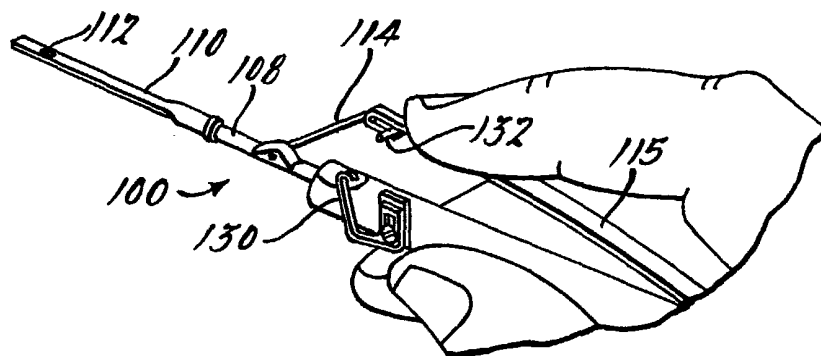
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- For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.*

(54) Title: RETINAL TISSUE IMPLANTATION INSTRUMENT



(57) Abstract: The disclosure relates to an instrument (100) for implanting retinal tissue (120) into the subretinal space (80) of the eye (50). A tubular nozzle (110) having an open end (118) and an aperture (112) in a sidewall thereof for the acceptance of retinal tissue (120), is telescoped over a mandrel (106). Retraction of the nozzle (110) relative to the mandrel (106) biases the retinal tissue (120) out of the open end of the nozzle (110) to effect deposition of the retinal tissue (120) in a target area of the eye (50).

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**RETINAL TISSUE IMPLANTATION INSTRUMENT**BACKGROUND OF THE INVENTION

The present invention relates to an instrument for implanting delicate tissue and/or materials in the human body, more particularly to an instrument for surgically restoring eyesight by implanting fetal retinal tissue into the subretinal space in the back of the eye.

Most common eye problems, for example, myopia (nearsightedness), hyperopia (farsightedness), astigmatism (asymmetrical cornea, and presbyopia (the inability to focus on an object at close range) are due to errors in the refraction of light by the lens and cornea in the anterior part of the eye. Generally, these problems can be corrected by glasses, contact lenses, or corrective surgery.

However, blindness is most commonly due to damage of the retina in the back of the eye and, more specifically, is caused by abnormalities in the subretinal space under the retina.

The transparent, layered retina processes light images projected by the cornea and lens. The photoreceptor layer in the back of the retina transforms the light into electrical impulses. Other retinal layers transfer these impulses through the optic nerve to the brain which interprets the impulses into what we perceive as sight.

The subretinal space is the area between the retinal pigment epithelium (RPE) and the photoreceptors of the retina.

Normally, the photoreceptors are in close contact with the RPE. The RPE has many functions. It provides nutrition for the photoreceptors, and also removes waste products from the photoreceptors. In a normal eye, there are no blood vessels in the subretinal space. However, in some retinal diseases, blood vessels and connective tissue can grow in this space and cause blindness. Under certain disease conditions, the photoreceptors can be detached very easily from the RPE. The photoreceptors will then degenerate, resulting in vision loss or blindness, while the other layers of the retina may remain

functional. By replacing the diseased RPE and/or photoreceptors that can hook up to the functional part of the retina, vision may be restored.

5 The most frequent cause of legal blindness is macular degeneration and retinitis pigmentosa. The macula is located in the back of the eye in the central portion of the retina and is responsible for central vision. In patients with macular degeneration, there is initially a dysfunction of the RPE in the macular region, which later leads to ingrowth of  
10 blood vessels and destruction of the light-sensitive photoreceptors in the overlying retina. This results in impairment of central vision. Age related macular degeneration is an example of an eye disease that can be delayed by using the herein disclosed method and instrument.

15 Retinitis pigmentosa is a term for genetically caused photoreceptor degeneration. In these patients, the photoreceptors must be replaced. Again, the method and instrument of the present invention can be utilized.

20 It is to be noted that surgical correction of diseases in the subretinal space between the retina and the RPE is rendered extremely difficult by the environment in which the surgery must take place. Moreover, the surgical procedure disclosed herein to implant fetal retinal tissue into the subretinal space of the eye is complicated by the fact that  
25 fetal retinal tissue is in the nature of a transparent gelatinous mass and therefore extremely fragile.

#### SUMMARY OF THE INVENTION

30 In accordance with the present invention, I have developed an improved implantation instrument capable of handling fetal retinal tissue and placing this tissue into the subretinal space between the retinal pigment epithelium and the retina of the human eye.

35 I have discovered that intact sheets of fetal retinal tissue can be transplanted into the subretinal space by flattening and protecting it by a gel that disintegrates and

is subsequently absorbed by the recipient eye so as to leave the transplant free. The transplant develops organized parallel layers resembling normal retina, with fully developed photoreceptors. The transplant can replace diseased photoreceptors and/or RPE. Moreover, the fetal retinal tissue is immunologically tolerated in the subretinal space and is not subject to rejection provided there is little surgical trauma.

The instrument of the instant invention comprises a handpiece for the support of a mandrel, a sleeve support telescoped over the mandrel, a tubular sleeve slidably journaled on the sleeve support, a nozzle having an aperture for the acceptance of retinal tissue mounted on the sleeve and extending over the mandrel, and a toggle mechanism that controls the position of the nozzle relative to the mandrel. The handpiece, mandrel, sleeve support, sleeve and toggle mechanism are preferably made of stainless steel to facilitate autoclaving. The nozzle is molded from elastic plastic. However, the instrument can be manufactured primarily from plastic if desired, so as to be disposable.

Advancement and retraction of the sleeve and nozzle relative to the handpiece and mandrel is controlled by the toggle mechanism on the handpiece, one element of which is a spring. When the spring element of the toggle mechanism is pressed toward the handpiece, the sleeve and the nozzle thereon move outwardly on the mandrel to a point where the aperture in the nozzle is disposed outwardly of the tip of the mandrel creating a space in the nozzle that accepts retinal tissue therein.

When the tissue is in place inside the nozzle, the nozzle is partially retracted to bias the retinal tissue to a position adjacent the tip of the nozzle whereupon a toggle lock engages a peg on the spring element so as to lock the spring element and, therefore, the sleeve relative to the mandrel. The surgeon inserts the instrument on the target and holds his hand absolutely still. With a slight pressure on the spring

element, without movement of the handpiece, the toggle lock is released, and the sleeve and nozzle retract over the mandrel under the bias of the toggle spring, placing the tissue at the desired location.

5       The position of the toggle lock can be regulated so as to determine the space between the mandrel tip and the nozzle tip thereby adapting the instrument to the size of the transplant.

10       Mandrels and nozzles can be customized in different sizes and shapes for implantation of different kinds of fragile tissue; gels containing different trophic factors or drugs; or electronic microchips into the subretinal space. Mandrels and nozzles can be produced in sterile packages for one-time use.

15       The details of the instrument of the invention are more fully described in the following specification and drawings.

#### BRIEF DESCRIPTION OF THE DRAWINGS

FIG. 1 is a frontal view of the human eye;

20       FIG. 2 is a cross-sectional view of the human eye showing the implantation instrument inserted through the pars plana into the subretinal space;

FIG. 3 is an enlarged view taken within the circle "3" of Fig. 2;

25       FIG. 4 is an enlarged view of the area within the circle "4" prior to insertion of the instrument nozzle into the subretinal space;

FIG. 5 is a view, similar to Fig. 4, with the instrument nozzle in the subretinal space;

30       FIG. 6 is a view, similar to Fig. 5, with the instrument nozzle retracted and the retinal tissue in the target area of the subretinal space;

FIG. 7 is an elevational view of the instrument of the invention in the loaded condition;

FIG. 8 is a cross sectional view of the instrument of Fig. 7 after implantation of retinal tissue;

35       FIG. 9 is a view of a tissue prior to transfer through the receiving aperture I the instrument nozzle;

FIG. 10 is a view of the retinal tissue after the first increment of movement toward the tip of the instrument nozzle;

FIG. 11 is view of the retinal tissue in position in the instrument nozzle for implantation; and

FIG. 12 in a view of the retinal tissue after discharge from the nozzle of the instrument.

#### DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENT(S)

The environment in which the present invention has particular utility is illustrated in Fig. 1 and 2 of the drawings. The front of the eye 50 is covered by a transparent tissue, the cornea 52, surrounded by white conjunctive tissue 54. The sclera 56 is hard fibrous tissue that covers the exterior of the eyeball. The pupil 58 is the opening through which light passes to the back of the eye. The iris 60 changes the size of the pupil 58 to adjust to the amount of light. The transparent lens 62 is located behind the iris 60 and is suspended by a net of fibers 64. The fibers 64 are attached to the ciliary body 66 that extends to where the retina 68 begins. The part of the ciliary body 66 adjacent to the retina 68 is called pars plana 70. The lens 62 focuses light rays onto the retina 68. The bulk of the eyeball 50 behind the lens 62 is formed by the vitreous chamber 72, which is filled with a colorless, gelatin like substance.

The retina 68 covers most of the wall of the vitreous chamber 72 and comprises transparent layers that extend forwardly to the pars plana 70 and which processes light images projected from the cornea 52 and the lens 62.

The rear of the retina 68 contains photoreceptors 74, which transform light into electrical impulses. The electrical impulses are carried by nerves in the retina 68 to the optic nerve 76, which, in turn leads to the brain. A monolayer of cells termed the retinal pigment epithelium (RPE) 77 resides behind the retina 68. The choroid 78 is a layer of blood

vessels behind the RPE 77, that supplies oxygen and nutrients essential to the function of the eye 50. The RPE 77 transports these nutrients to the retina 68 and maintains a barrier between choroid 78 and retina 68.

5 The region between the retina 68 and the RPE 77 is called the subretinal space 80 (Fig 4-6). Normally, there is no "space". However, the retina 68 detaches very easily from the RPE 77 and it is in this "space" that the surgeon transplants the new piece of retinal tissue to replace damaged  
10 photoreceptors 74 and/or RPE 77.

The fovea 82 is a small depression in the center of the retina 68 that is essential for sharp (focussed) vision as well as color vision. The small area surrounding the fovea 82 is known as the macula 84 and is responsible for central  
15 vision. The point at which the optic nerve 76 leaves the retina 68 on its way to the brain is called optic disc 86.

In accordance with the present invention, surgical correction of retinal diseases in the subretinal "space" 80 between the retina 68 and the RPE 77 is facilitated by a novel  
20 implantation instrument 100.

As seen in Fig. 7 through 11, the instrument 100 comprises a handpiece 102, a tubular sleeve support 104, a mandrel 106 disposed internally of the sleeve support 104, a sleeve 108 slidably journaled on the sleeve support 104, and a  
25 nozzle 110 mounted on the sleeve 108 having an aperture 112 therein for the acceptance of retinal tissue 120. A toggle mechanism comprising a rigid link 114 and a spring link 115 controls advancement and retraction of the sleeve 108 and nozzle 110 relative to the mandrel 106. The handpiece 102,  
30 sleeve support 104, mandrel 106, sleeve 108 and toggle links 114 and 115 can be made of stainless steel to facilitate autoclaving. The instrument can also be made disposable by using plastic with some metal parts.

The mandrel 106 comprises an elongated flat and narrow  
35 strip of steel that is fixed in the handpiece but is longitudinally adjustable relative thereto. Extension or

retraction of the mandrel 106 relative to the housing 102 regulates its longitudinal position relative to the length of the plastic nozzle 110 in the retracted position.

5 The fit between the plastic nozzle 110 and the mandrel 106 must permit relative movement therebetween, whereby the aperture 112 in the nozzle 110 can be positioned for the acceptance of the retinal tissue 120 and subsequent discharge of the tissue 120.

10 The nozzle 110 is molded of elastic plastic, for example fluorinated ethylene propylene, so as to have a curvature at the tip 118 thereof in order to slide under the retina 68 into the subretinal "space" 80. Because of its elasticity, the curved nozzle tip 118, when retracted, will straighten out over the mandrel 106 so as to deposit implant tissue at the  
15 target area behind the retina 68.

Advancement and retraction of the sleeve 108 and nozzle 110 is controlled by the rigid toggle link 114 and spring element 115 on the handpiece 102. When the spring element 115 of the toggle mechanism is pressed toward the  
20 handpiece 102, the sleeve 108 and the nozzle 110 are driven forwardly, relative to the mandrel 106, by the rigid toggle link 114. When pressure on the spring element 115 of the toggle mechanism is released, the sleeve 108 and the nozzle 110 thereon is retracted over the mandrel 106, biasing  
25 the retinal tissue 120 to the desired location.

In preparation for the use of tool of the invention, the surgeon first places an incision in the pars plana 70 of the eye 50. A small incision is then made in, for example, the macular region 84 of the retina 68. If necessary, abnormal  
30 tissue is removed from the subretinal "space" 80 between the retina 68 and the RPE 77. The nozzle 110 of the instrument 100, with the retinal tissue 120 enclosed in the curved nozzle tip 118 thereof, is inserted through the incision in the pars plana 70 and through the incision in the  
35 retina 68 until the tip of the nozzle 118 is orientated adjacent the target area in the subretinal "space" 80.



Slight pressure on the spring element 115 of the instrument 100 then releases the toggle lock 130 from the pin 132 allowing the spring element 115 and rigid link 114 of the toggle mechanism to effect retraction of the nozzle 110 and deposition of the retinal tissue 120. It is to be noted that the handpiece 102 and mandrel 106 of the instrument 100 are not required to move incident to deposition of the retinal tissue 120 allowing the surgeon to precisely position the tissue.

From the forgoing, it should be apparent that the instrument of the present invention accepts retinal tissue in an efficient manner and thereafter precisely implants the tissue into the eye. The surgeon has only to keep his hand still and exert a slight pressure on the spring element 115 of the instrument 100 to release the toggle lock 130 conditioning the instrument 100 itself to effect retraction of the nozzle 110 and placement of the implant on the target.

While the preferred embodiment of the invention has been disclosed, it should be appreciated that the invention is susceptible of modification without departing from the scope of the following claims:

I CLAIM

1. An instrument for implanting retinal tissue into the human eye comprising:

an elongated mandrel;

5 a tubular nozzle telescoped over said mandrel and having an open end for the discharge of retinal tissue and an aperture in a sidewall thereof spaced from said open end for the acceptance of retinal tissue, and

10 a nozzle control connected to said nozzle and to said mandrel, movement of said control relative to said mandrel effecting movement of said nozzle relative to said mandrel whereby said mandrel biases the retinal tissue through the open end of said nozzle.

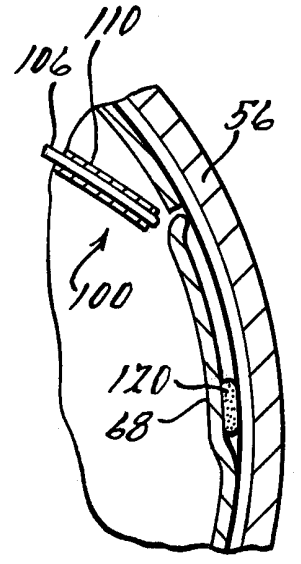
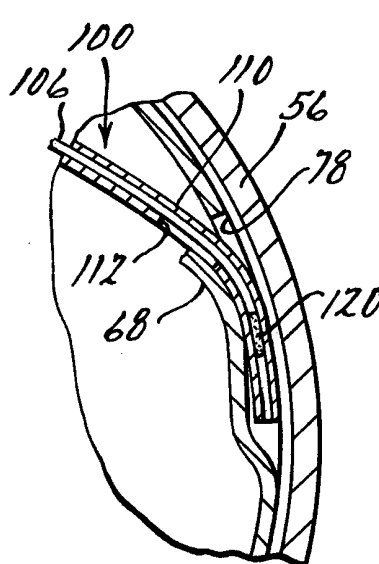
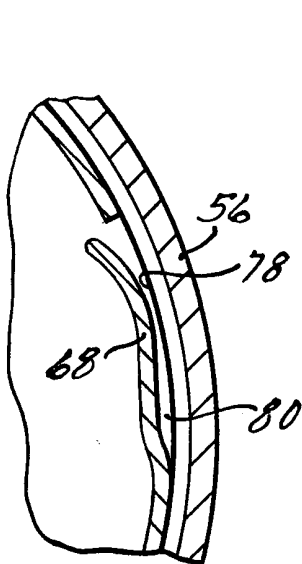
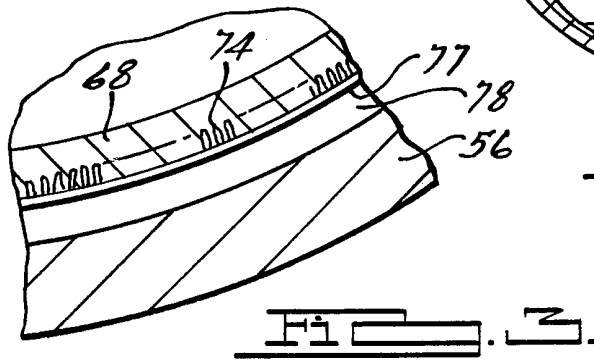
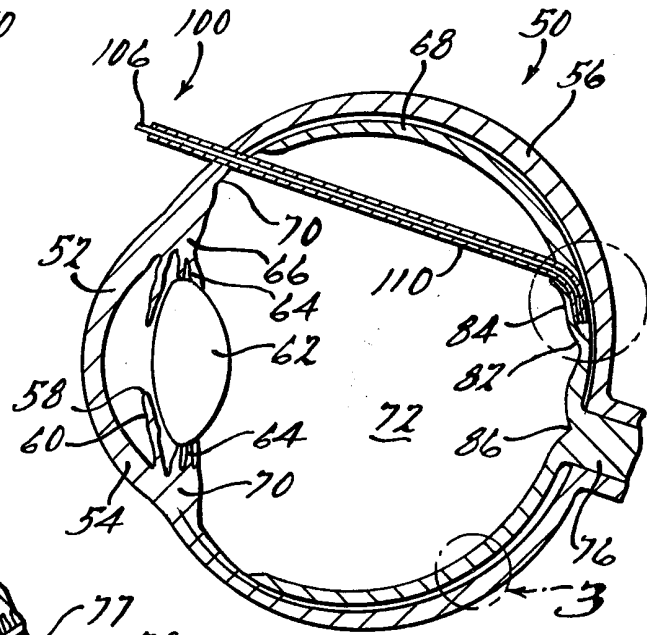
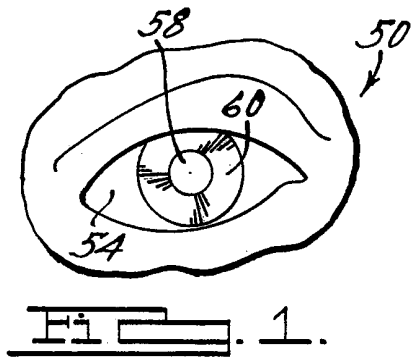
2. The instrument of claim 1 wherein said mandrel is supported by a handpiece and said nozzle control comprises a toggle mechanism having one end connected to said nozzle and an opposite end connected to said handpiece.

3. An instrument for implanting retinal tissue into the human eye comprising:

an elongated mandrel;

5 a tubular nozzle telescoped over said mandrel having an open end for the discharge of retinal tissue and an aperture in a sidewall thereof spaced from said open end for the acceptance of retinal tissue; and

10 a nozzle control linkage connected to said nozzle and to said mandrel, movement of said control linkage in one direction relative to said mandrel effecting movement of said nozzle relative to said mandrel to a position wherein the aperture in said nozzle is spaced from an end portion of said mandrel for the acceptance of retinal tissue, movement of said control linkage in an  
15 opposite direction effecting retraction of said nozzle over said mandrel whereby the end portion of said mandrel biases said retinal tissue through the open end of said nozzle.



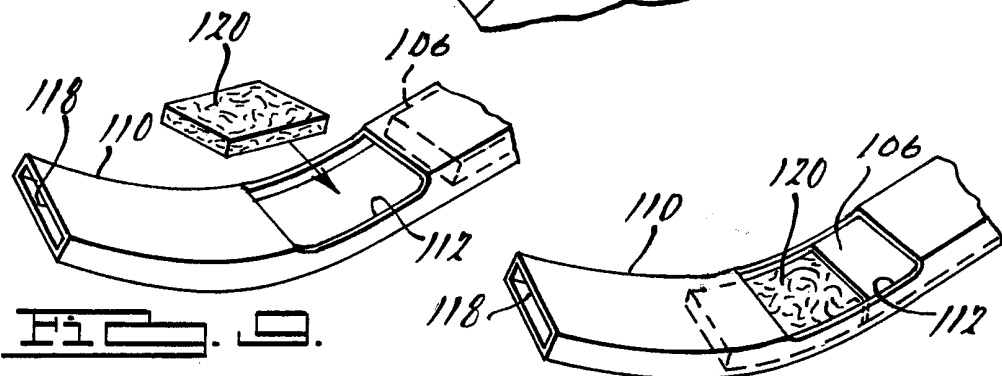
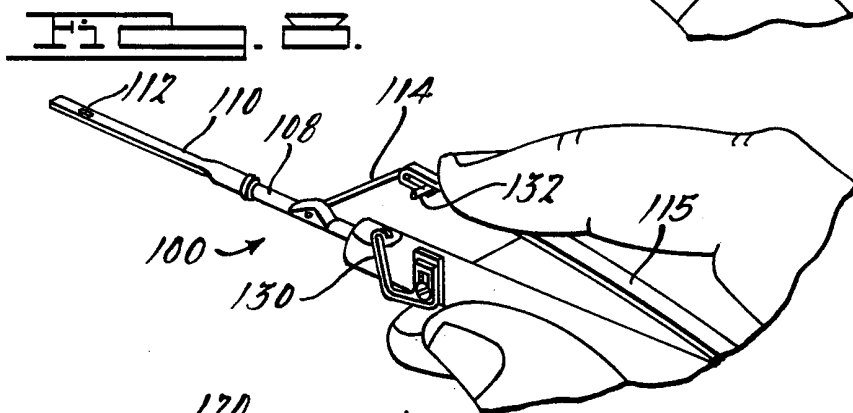
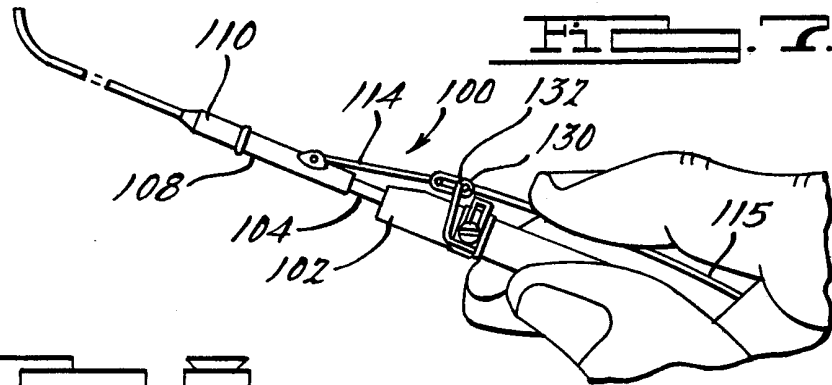


FIG. 10.

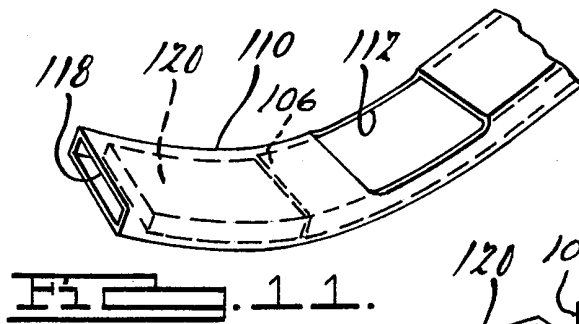
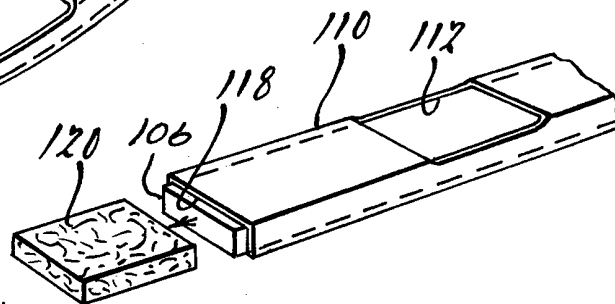


FIG. 12.



## INTERNATIONAL SEARCH REPORT

International application No.

PCT/US00/12556

**A. CLASSIFICATION OF SUBJECT MATTER**

IPC(7) :A61B 17/00

US CL :606/107

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)

U.S. : Please See Extra Sheet.

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 practicable, 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.
A	US 5,817,075 A (GIUNGO) 06 October 1998.	1-3
A	US 5,468,246 A (BLAKE) 21 November 1995.	1-3
A	US 4,955,889 A (VAN GENT) 11 September 1990.	1-3



Further documents are listed in the continuation of Box C.



See patent family annex.

* Special categories of cited documents:		"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
"A"	document defining the general state of the art which is not considered to be of particular relevance	"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
"E"	earlier document published on or after the international filing date	"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
"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)	"&"	document member of the same patent family
"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		

Date of the actual completion of the international search

13 JULY 2000

Date of mailing of the international search report

02 AUG 2000

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# INTERNATIONAL SEARCH REPORT

International application No.

PCT/US00/12556

## B. FIELDS SEARCHED

Minimum documentation searched

Classification System: U.S.

604/15, 18, 51, 57-60, 93, 95, 158, 184, 187, 190, 205, 210, 239, 272, 289, 290, 294; 606/1, 107, 166, 167, 170;  
95, 158, 164, 187, 198, 205, 210, 239, 272, 289, 290, 294; 623/4-6