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(71) Applicant: THE GENERAL HOSPITAL CORPORATION [US/US]; 55 Fruit Street, Boston, MA 02114 (US).

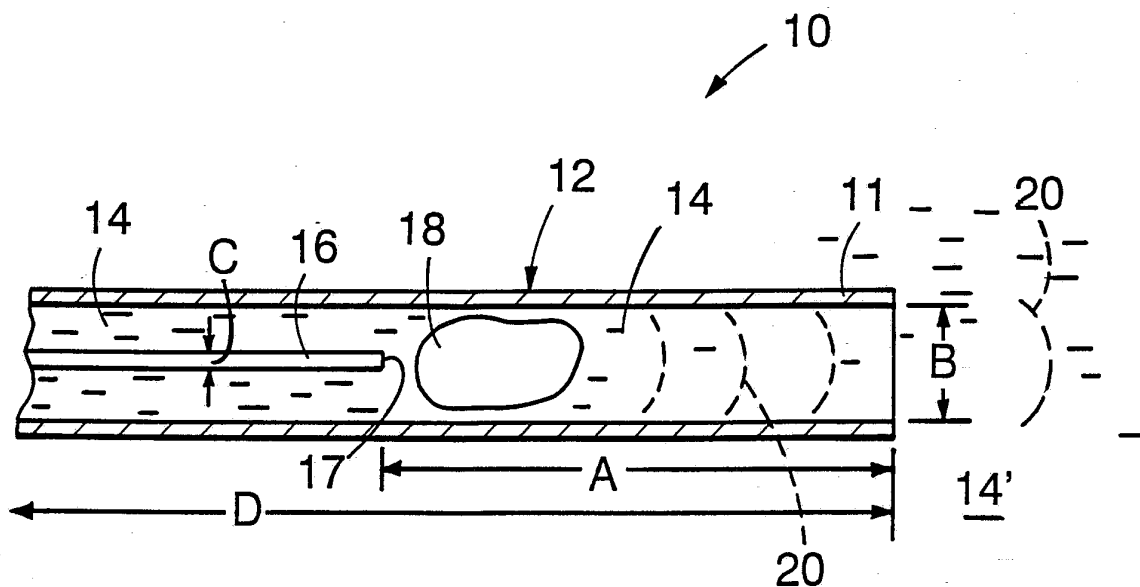
(72) Inventors: DE LA TORRE, Ralph ; 1682 Beacon Street, Brookline, MA 02146 (US). GREGORY, Kenton, W. ; 23200 Stafford Hill Drive, West Linn, OR 97068 (US).

(74) Agent: CLARK, Paul, T.; Fish & Richardson, 225 Franklin Street, Boston, MA 02110-2804 (US).

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(54) Title: APPARATUS AND METHOD FOR VASODILATION



(57) Abstract

A method and apparatus for dilating blood vessels in vasospasm through the use of high frequency waves, e.g., hydraulic or acoustic waves. The invention is suitable to treat any vasospasm, including any vasospasm intractable to medication; including cerebral vasospasm, which currently is not susceptible to any mechanical or chemical treatments. The apparatus (10) for dilating blood vessels includes a catheter (12) having a fluid-filled lumen, a wave generator (16) arranged within the catheter lumen for generating a wave front (20) that propagates through the fluid (14) in the lumen and is transmitted from the distal end (11) of the catheter to propagate through the fluid in the blood vessel, and an energy source connected to the wave generator to provide energy to produce the wave front.

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APPARATUS AND METHOD FOR VASODILATION

Background of the Invention

This invention relates to a method and apparatus
5 for dilating blood vessels in vasospasm.

Vasospasm is an abnormal and often persistent
contraction of an artery that reduces the caliber of the
artery and may critically reduce blood flow. Vasospasm
can produce a partial or complete obstruction in arteries
10 that otherwise appear completely normal. Greater or
lesser amounts of dynamic or spastic constriction at the
point of a fixed obstruction can create a severe
reduction of flow even where the fixed obstruction itself
would be clinically benign.

15 Vasospasm can occur spontaneously; or it may occur
as the result of certain pharmacological stimuli, such
as, for example, ergonovine testing; or of mechanical
stimuli such as contact with a surgical instrument or a
diagnostic or therapeutic catheter, for example as a
20 complication of percutaneous transluminal catheter
angioplasty (PTCA); or of environmental stimuli.
Raynaud's phenomenon and Prinzmetal angina are two
additional forms of vasospasm. Furthermore, certain
maladies such as subarachnoid hemorrhage can also lead to
25 vasospasm. In particular, cerebral vasospasm, which is
caused by subarachnoid hemorrhage, and ophthalmic artery
vasospasm may cause severe consequences if not treated
promptly.

Various medications have been tested for the
30 relief of vasospasms and are only partially effective.
For example, vasospasm in coronary vasculature has been
treated with calcium channel blockers. However, for some
unknown reason that relates to the pharmacological and
anatomical differences between cerebral and coronary
35 vasculature, these drugs are ineffective against cerebral

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vasospasm. In addition, mechanical treatment such as balloon angioplasty is also ineffective against cerebral vasospasm.

Other non-chemical treatments, e.g., laser
5 irradiation-induced dilation of the vessels, of vasospasm
have likewise been relatively unsuccessful or plagued
with various problems. For example, laser irradiation-
induced dilation of blood vessels is cumbersome, may
10 damage surrounding healthy tissue, does not use standard
catheter guide wire techniques, and provides a narrow
margin between the laser energy needed to cause
vasodilation and that needed to perforate the vessel
wall. Moreover, in those laser techniques using low
15 level constant wave laser radiation, vasospasm resumes as
soon as the radiation ceases.

Furthermore, mechanical dilation treatments, such
as balloon angioplasty, are generally ineffective
because, vasospasm generally resumes after the balloon is
removed, and these treatments are very difficult in
20 arteries that are hard to catheterize, e.g., the
ophthalmic artery.

Summary of the Invention

This invention features dilation of blood vessels
in vasospasm through the use of high frequency (on the
25 order of microseconds) waves, e.g., hydraulic or acoustic
waves, and offers several advantages over known laser
irradiation- or chemical-induced dilation. These
advantages include greater safety by preventing damage to
the blood vessel walls by the wave generator, e.g., a
30 laser pulse, increased maneuverability, dilation over a
concentric catheter guide wire, and an increased range of
energy levels that may be safely used for therapy. In
addition, the invention is successful for treating
cerebral vasospasm, which currently is not known to be
35 susceptible to any mechanical or chemical treatments.

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Furthermore, based upon animal studies done to date, we have found that vasospasm does not resume after treatment according to the invention. The method of the invention is suitable for any vasospasm, including any vasospasm intractable to medication, either functionally, or time limited.

The invention features an apparatus for dilating a fluid-filled blood vessel in vasospasm including a catheter having a lumen containing a fluid, a wave generator arranged within the catheter lumen for generating a wave front that propagates through the fluid in the lumen and is transmitted from the distal end of the catheter to propagate through the fluid in the blood vessel, and an energy source connected to the wave generator to provide energy to produce the wave front.

The wave generator of the invention may be a laser beam, e.g., a pulse, when the energy source is a laser. In preferred embodiments, this pulse has a duration of from about 10 nanosec to about 300 μ sec and is of a wavelength of less than about 600 nm or greater than about 1000 nm. The laser may be, e.g., a holmium, ultra violet, or pulsed-dye visible laser.

The wave generator also may be a spark generator, ultrasound agitator, or piezoelectric agitator.

When the distal end of the catheter is open, the wave front is transmitted from the distal end of the catheter by exiting the catheter and passing into the vessel. When the distal end of the catheter is sealed with a membrane, the wave front is transmitted from the distal end of the catheter via the membrane.

In any of these embodiments, the wave may be, e.g., a hydraulic or acoustic wave.

In a preferred embodiment, the invention also features an apparatus for dilating a fluid-filled blood vessel in vasospasm that includes a catheter having a

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lumen containing a fluid, a laser energy conducting filament arranged axially within the catheter lumen, the distal end of the filament being positioned at a distance from the distal end of the catheter such that laser energy emitted from the filament generates a cavitation bubble within the catheter lumen that generates a wave front that propagates through the fluid in the lumen and is transmitted from the distal end of the catheter to propagate through the fluid in the blood vessel, and a laser energy source connected to the conducting filament to provide laser energy to produce the wave front.

The invention also features a method of dilating a fluid-filled blood vessel in vasospasm by propagating a wave front that induces vasodilation through a fluid in a blood vessel in need of dilation without generating a shock wave or cavitation bubble within the blood vessel.

Furthermore, the invention features a method of dilating a fluid-filled blood vessel in vasospasm by inserting a catheter into a blood vessel in vasospasm, the catheter having a lumen containing a fluid, generating a wave front in the fluid in the catheter, propagating the wave front through the fluid in the catheter, transmitting the wave front from the distal end of the catheter, and propagating the transmitted wave front through the fluid in the blood vessel to induce vasodilation.

The wave front used in this method may be generated by a laser pulse that forms a cavitation bubble within the catheter without forming a laser breakdown-induced shock wave. In addition, the wave may be generated by other wave generators noted above.

The fluid through which the wave front propagates may be, e.g., blood, a crystalloid solution such as saline or lactated Ringer's solution, or a colloid solution. When a laser is used, the fluid may be any

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solution that absorbs the incident laser energy. This fluid is in the catheter and, when it is something other than blood, may be infused into the blood vessel in vasospasm prior to dilation.

- 5 Other features and advantages of the invention will be apparent from the following description of the preferred embodiments thereof, and from the claims.

Detailed Description

The drawings are first briefly described.

10 Drawings

Fig. 1 is a schematic of the vasodilator of the invention.

Fig. 2 is a schematic of a close-ended vasodilator.

15 Dilation

- The invention utilizes a wave front transmitted from the end of a catheter to bring about dilation of a vessel in spasm. This wave front is created by a wave generator, e.g., a laser pulse, a spark generator, an
20 ultrasound or piezoelectric agitator, or any other mechanism that can vaporize or displace the fluid rapidly enough to create a wave front. For example, a laser pulse may be used to produce a cavitation bubble, i.e., a vapor bubble, which expands to displace a certain fluid
25 volume in a column inside the catheter. Any short laser pulse can be calibrated to give the appropriate dilatory wave, and the laser energy is adjusted so that a laser-induced breakdown of the fluid does not occur.

- Therefore, essentially no shock wave is created according
30 to the invention. Only a hydraulic or acoustic wave is formed, which is on the order of 100 times slower than a shock wave generated by a laser-induced breakdown. The physical characteristics of this macroscopic hydraulic or acoustic wave are significantly different from a
35 microscopic shock wave.

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This displaced fluid serves to create a transient pressure increase or wave front that propagates coaxially down the catheter and is transmitted into the occluded artery. In one embodiment, the catheter is open-ended, and the wave front is transmitted from the distal end of the catheter merely by exiting the catheter and passing into the fluid filling the artery. In other embodiments, the catheter is close-ended, and the wave front strikes a membrane, e.g., a highly pliable polymer film, that transmits the wave energy to the fluid in the occluded vessel to generate a transmitted wave that continues on the outside of the catheter and propagates through the occluded vessel.

In each embodiment, no destructive shock wave or cavitation bubble is generated inside the exposed blood vessel. The only effect on the blood vessel is from the wave that is generated within the confines of the catheter and then propagates through the fluid within the vessel and dilates it for some distance beyond the distal end of the catheter.

Structure

Fig. 1 shows a laser-catheter device 10 that may be used to generate wave fronts according to the invention. The device includes a catheter 12 with an inner diameter B and a length D. This catheter is filled with a fluid 14, e.g., blood, a crystalloid solution such as saline, or a colloid solution. In general, this fluid may be any solution capable of absorbing the incident laser energy. An optical fiber 16, with a diameter C, is located within catheter 12. The tip 17 of fiber 16 is located at a distance A from the distal end 11 of catheter 12. When a pulse of laser energy is generated by a laser (not shown), it is transmitted through fiber 16 and creates a cavitation, or vaporization, bubble 18 in fluid 14. This bubble generates a wave front

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(represented by dashed lines in the Figures) that propagates through the liquid towards the distal end of the catheter.

This wave front 20 then can either exit the catheter, in the open-ended embodiments, or, as shown in Fig. 2, strike a membrane 11' that seals the distal end 11 of catheter 12. Fig. 1 shows that in the open-ended catheter, the transmitted wave front 20 is the same wave front 20 inside the catheter. Fig. 2 shows that in the sealed-end catheter, the transmitted wave front 20' differs from, but corresponds to wave front 20 inside the catheter. In both cases, the transmitted wave front propagates through the fluid 14' that surrounds the catheter and fills the vessel to be dilated. In other embodiments, the optic fiber 16 is replaced by another wave generator to create wave fronts 20.

Use of the Catheter Wave Front Generator

The dimensions and energy of the wave front are determined by selecting the dimensions A and B of the catheter and, in the laser system, dimension C of the optic fiber, as well as the duration and intensity of the laser pulse. In non-laser embodiments, energy levels of the spark from a spark gap or the ultrasound agitation may be selected by standard techniques to achieve the desired dimensions and energy levels.

In particular, the high frequency (preferably on the order of 75 to 100 μ sec) wave fronts may be created via a pulsed-dye laser set to deliver a light pulse with a 15 mJ pulse of 1 μ sec duration into a 200 micron fiber. This light is directed into a fluid, e.g., blood, contained well within a catheter inserted in the body (e.g., A = 25-30 mm or more). Preferably, the laser pulse is from about 10 nanosec to about 300 μ sec in duration and is at a wavelength of less than about 600 nm or greater than about 1000 nm. The preferred lasers for

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use in the invention are holmium, ultra violet, and pulsed-dye visible lasers. The preferred pulse duration for a holmium laser is about 250 μ sec.

5 In addition, the wave front can be created through the use of an entirely extracorporeal laser delivery system, with only the catheter being inserted into the occluded artery, i.e., the dimension A being the length of the catheter section inserted into the body.

10 The method of using this catheter wave generator is as follows. The catheter is advanced in a blood vessel in the body to an area of vasospasm. Once the catheter is set, a wave front of short duration is launched down the center of the catheter and either exits the catheter, or is transmitted via a membrane at the end
15 of the catheter, into the occluded vessel to effect dilation. This procedure is repeated as necessary until the full length of spasm has been dilated.

For example, a Tracker-18 Target Therapeutics (San Jose, California) catheter has been used successfully,
20 but smaller, more maneuverable catheters may also be used. In addition, larger catheters have also been used successfully, and the proper size may be easily determined by those skilled in the art depending on the application.

25 Animal Studies

We studied intraluminal high frequency waves in the form of hydraulic waves as a means of reversing arterial vasospasm in the rabbit model. Vasospasm was induced in 10 New Zealand white rabbit carotid arteries
30 in vivo by application of extravascular whole blood retained in a silicon cuff. The hydraulic wave consisted of a wave front propagated in an overdamped mode with a single oscillation (average velocity 30-40 m/s; BW 200 μ sec; repetition rate 2 Hz). This wave front was created

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in the carotid arteries with a 3 Fr laser catheter delivered via the femoral artery and coupled to a pulsed-dye laser. Carotid artery diameters were assessed by angiography and measurements made from cut films.

- 5 Baseline diameters decreased by 37.5% following application of blood. Following delivery of the hydraulic wave, arterial diameter increased by a mean of 48% over spasm diameter, with no reversion to spasm diameters. Such waves delivered to control vessels not
10 in spasm had minimal effect on their diameter (mean change of 5.3%). Scanning electron microscopy revealed no evidence of perforations or other endothelial damage. These experiments demonstrate that high frequency intraluminal wave fronts, e.g., hydraulic waves, can
15 rapidly reverse arterial vasospasm without loss of structural or endothelial integrity of arterial walls.

Therapy

- This system can be used for the treatment of any vasospasm including cerebral vasospasm, ophthalmic
20 vasospasm, acute closure in post PTCA patients, as well as any spasm intractable to medication, either functionally, or time limited.

Other embodiments are within the following claims.

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Claims

1. An apparatus for dilating a fluid-filled blood vessel in vasospasm comprising
a catheter comprising a lumen containing a fluid,
5 a wave generator arranged within said catheter lumen for generating a wave front that propagates through the fluid in said lumen and is transmitted from the distal end of said catheter to propagate through the fluid in the blood vessel, and
10 an energy source connected to said wave generator to provide energy to produce said wave front.
2. The apparatus of claim 1, wherein said wave generator is a laser beam and said energy source is a laser.
- 15 3. The apparatus of claim 2, wherein said laser beam is in the form of a pulse comprising a duration of from about 10 nanosec to about 300 μ sec.
4. The apparatus of claim 3, wherein said laser pulse is of a wavelength of less than about 600 nm or
20 greater than about 1000 nm.
5. The apparatus of claim 2, wherein said laser is a holmium, ultra violet, or pulsed-dye visible laser.
6. The apparatus of claim 1, wherein said distal end of said catheter is open and said wave front is
25 transmitted from the distal end of said catheter by exiting the catheter and passing into the vessel.
7. The apparatus of claim 1, wherein said distal end of said catheter is sealed with a membrane and said

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wave front is transmitted from the distal end of said catheter via said membrane.

8. The apparatus of claim 1, wherein said wave generator is a spark generator, an ultrasound agitator,
5 or a piezoelectric agitator.

9. The apparatus of claim 1, wherein said fluid is blood, a crystalloid solution, or a colloid solution.

10. The apparatus of claim 1, wherein said wave is a hydraulic or acoustic wave.

10 11. An apparatus for dilating a fluid-filled blood vessel in vasospasm comprising
a catheter comprising a lumen containing a fluid,
a laser energy conducting filament arranged
axially within said catheter lumen, the distal end of
15 said filament being positioned at a distance from the distal end of said catheter such that laser energy emitted from said filament generates a cavitation bubble within said catheter lumen that generates a wave front that propagates through the fluid in said lumen and is
20 transmitted from the distal end of said catheter to propagate through the fluid in the blood vessel, and
a laser energy source connected to said conducting filament to provide laser energy to generate said wave front.

25 12. The apparatus of claim 11, wherein said laser energy emitted from said filament is in the form of a pulse comprising a duration of from about 10 nanosec to about 300 μ sec.

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13. The apparatus of claim 11, wherein said laser energy emitted from said filament is of a wavelength of less than about 600 nm or greater than about 1000 nm.

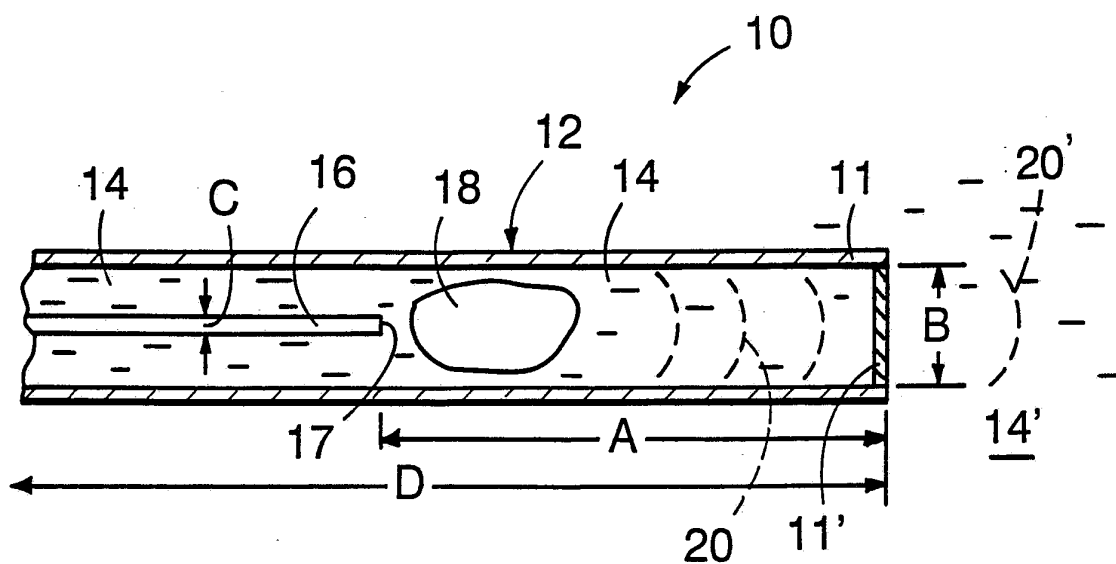
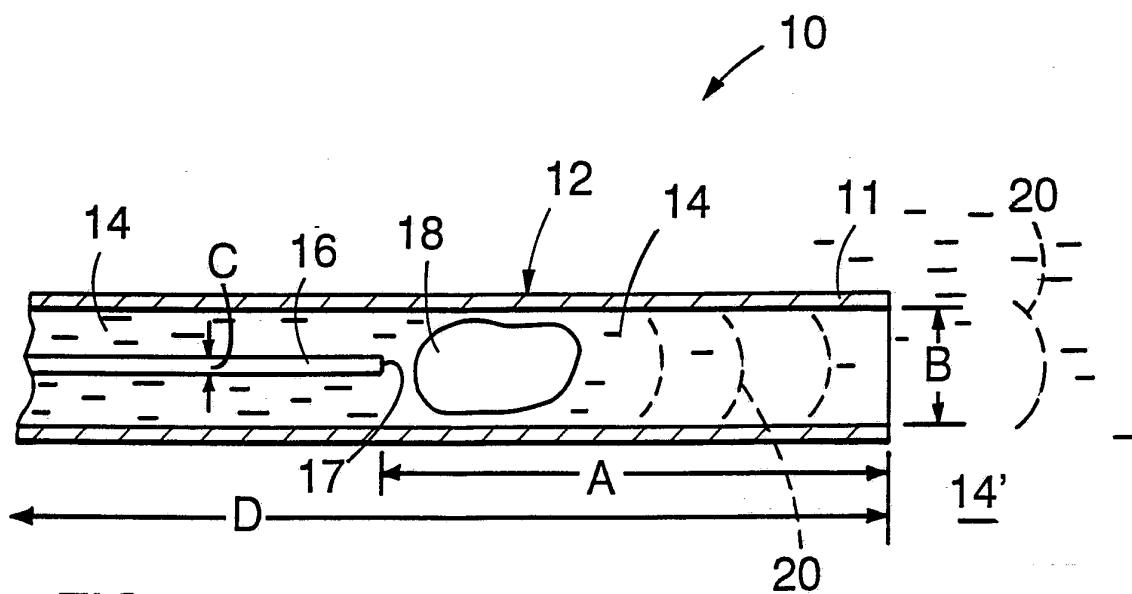
14. The apparatus of claim 11, wherein said laser energy source is a holmium, ultra violet, or pulsed-dye visible laser.

15. The apparatus of claim 11, wherein said distal end of said catheter is open and said wave front is transmitted from the distal end of said catheter by exiting the catheter and passing into the vessel.

16. The apparatus of claim 11, wherein said distal end of said catheter is sealed with a membrane and said wave front is transmitted from the distal end of said catheter via said membrane.

17. The apparatus of claim 11, wherein said wave is a hydraulic or acoustic wave.

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SUBSTITUTE SHEET

INTERNATIONAL SEARCH REPORT

International application No.
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A. CLASSIFICATION OF SUBJECT MATTER

IPC(5) :A61B 17/00

US CL :128/24AA; 128/24.1, 395; 606/2, 15, 191

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. : 128/24AA, 24.1, 395; 606/2, 2.5, 13-16, 128, 191, 194

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.
<u>X,E</u> Y	US, A, 5,152,768 (Bhatta) 06 October 1992, See entire document.	<u>1,6,8-10</u> 11-15,17
<u>X</u> Y	US, A, 5,041,121 (Wondrazek et al.) 20 August 1991, See entire document.	1-3,6,9-10, 11- <u>12,15,17</u> 4-5,13-14
Y,P	US, A, 5,059,200 (Tulip) 22 October 1991, See entire document.	4-5,13-14
X	SU, A, 1,475,680 (Golov) 30 April 1989, See entire document.	1,6,8
X	DT, A, 3,600,713 (Schmidt) 17 July 1986, See entire document.	1,2,7

☒ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

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Date of the actual completion of the international search 24 NOVEMBER 1992	Date of mailing of the international search report 07 JAN 1993
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INTERNATIONAL SEARCH REPORT

International application No.
PCT/US92/08380

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
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