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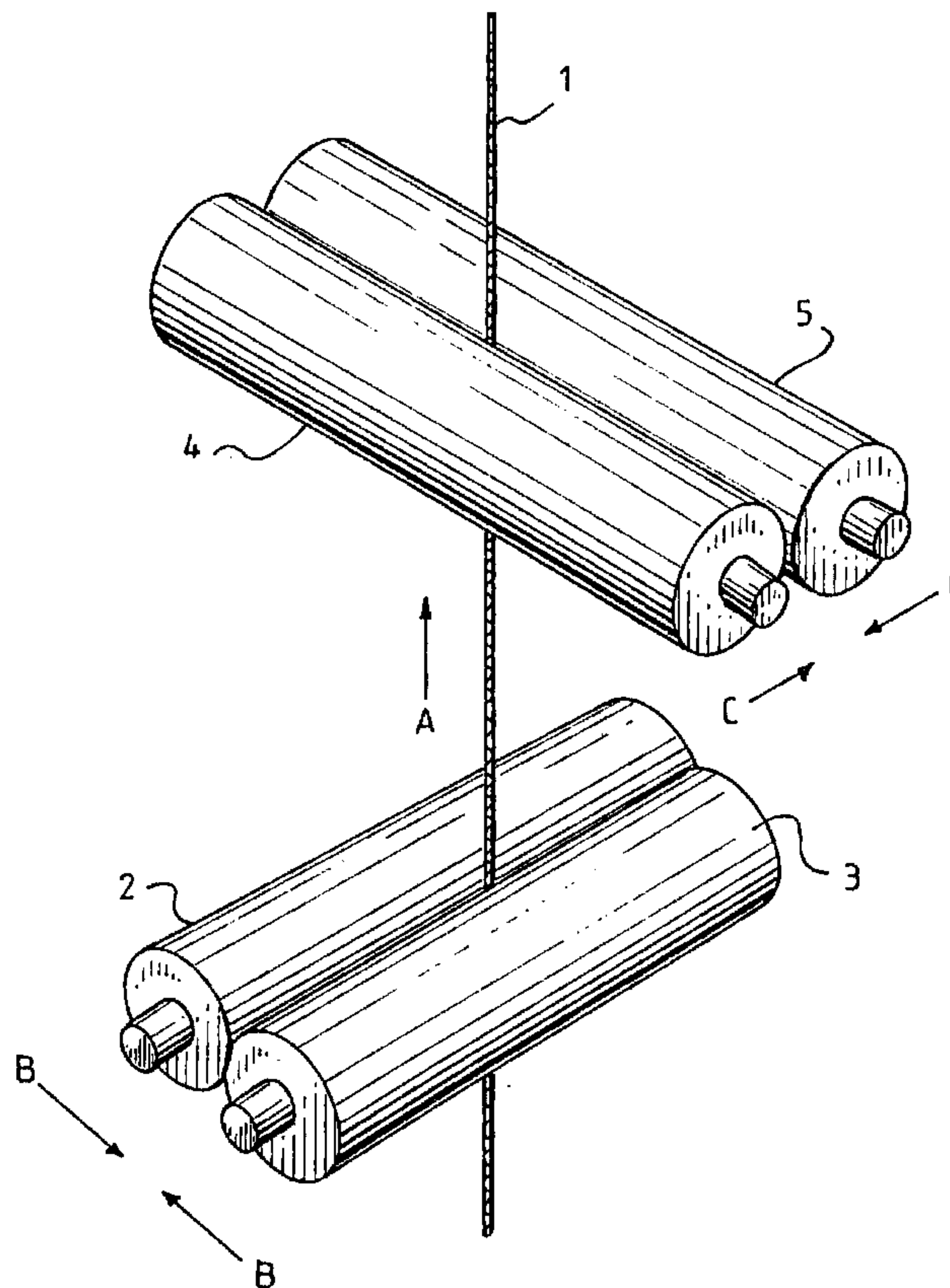
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(54) Titre : METHODE ET APPAREIL PERMETTANT DE LAMINER ET D'ENROBER OU DE REMPLIR DES JONCTIONS

(54) Title: METHOD AND APPARATUS FOR CALENDERING AND COATING/FILLING SUTURES



(57) **Abrégé/Abstract:**

The present invention provides a method for filling a suture comprising passing the suture lengthwise through a filling head. The filling head has a contacting region in which the suture is contacted by a filling agent substantially continuously supplied to the filling head as the suture passes therethrough.

ABSTRACT

The present invention provides a method for filling a suture comprising passing the suture lengthwise through a filling head. The filling head has a contacting region in which the suture is contacted by a filling agent substantially continuously supplied to the filling head as the suture passes therethrough.

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METHOD AND APPARATUS FOR CALENDERING AND
COATING/FILLING SUTURES

BACKGROUND OF THE INVENTION

This application is a divisional application of co-pending Canadian Application Serial No. 2,059,245 filed January 13, 1992.

10 1. Field of the Invention

This invention pertains to a method and apparatus for mechanically treating sutures, and especially to a method and apparatus for calendering multifilament surgical sutures.

2. Background of the Art

20 An important consideration in performing surgery is the "hand" or "feel" of the suture being used to close wounds, which is reflected at least in part by the knot tie-down and run-down characteristics of the suture. "Tie-down characteristics" refers to the facility with which a surgeon can tie a knot, and the ability of the suture to remain knotted without spontaneously unravelling. "Run-down characteristics" refers to the ability of a surgeon to make one or more "throws" of a knot in the suture and have it run down a suture to the knot site. Generally, hand or feel of a suture and tie-down characteristics relate to the lubricity and stiffness of the suture: lubricity facilitates the tying of a knot whereas stiffness makes tying a tight knot more difficult and increases the probability of kinking
30 of the suture and/or unravelling of the knot.

Both multifilament sutures and monofilament sutures are known in the art. Multifilament sutures, such as braided or twisted sutures, have better softness and flexibility than monofilament sutures and can be more easily

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knotted. However, multifilament sutures can have a rougher surface or "grabiness" than monofilament sutures and a significant percentage of dead space or interstices between the filaments. The dead space can be reduced by impregnating the multifilament suture with a filler material. Filler material can help lubricate the suture fibers and enhance flexibility.

10 Coatings improve the knot run down characteristics of a suture, although they also tend to increase stiffness. Another source of stiffness arises from the commonly employed process of "heat setting" or "hot stretching" the suture, such as described in U.S. Patent Nos. 3,322,125, 3,257,702, 3,379,552, and 3,838,524, for example. It has been proposed to improve the flexibility of heat set sutures by flexing the suture as disclosed in U.S. Patent Nos. 3,839,524 and 3,257,702.

20 Known materials for filling or coating sutures are described in U.S. Patent Nos. 3,322,125, 3,379,552, 3,867,190, 3,942,532, 4,047,533, 4,532,929, 4,201,216, and 4,711,241, for example.

 However, the uniformity of the filling or coating remains as an important concern in the fabrication of sutures. Non-uniformity can hamper the effectiveness of the filler and coating, and an apparatus and method which addresses this issue is needed.

SUMMARY OF THE INVENTION

30 One feature of the present invention is the suture filling method and apparatus. The suture is filled by passing the calendered suture lengthwise through a region in which the suture is contacted by a filling agent which is substantially continuously applied to the filling head as the suture passes therethrough. The filling agent is

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supplied by a metering pump. The filling process is optimized for any given multifilament braided suture by a computer program based upon the denier of the suture, pump capacity, suture velocity, desired or target fill level and calculating and setting a pump speed based on the foregoing parameters.

There is also disclosed a method and apparatus for treating a multifilament surgical suture. A compressive force is applied to the suture in a first linear direction generally transverse to the longitudinal orientation of the suture. The compressive force is of sufficient predetermined magnitude so as to expand the diameter of the suture in a direction orthogonal to the direction in which the compressive force is applied. Preferably a second application of compressive force is administered to the suture in a direction generally transverse to that of the first compressive force as well as transverse to the longitudinal direction of the suture. The second compressive force is substantially equal in magnitude to the first compressive force so that the suture returns to its original round configuration.

The apparatus for implementing this method includes at least one pair of rollers which are biased towards each other to apply a compressive force to a suture which is passed between them. A second pair of rollers is oriented at angle (preferably 90°) to the first set of rollers and transverse to the longitudinal extension of the suture. The second pair of rollers is positioned such that a suture, passing between both the first pair of rollers and the second pair of rollers, will be alternately compressed in a first direction, then in a second direction at an angle to the first direction. The application of compressive force expands the diameter of the suture in a direction

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orthogonally to the application of force. Thus, with two pairs of rollers, the suture will be expanded in two directions, thereby opening up the filaments to make the suture more receptive to the application of fillers, coating materials, and the like.

10 In a particularly preferred embodiment, braided synthetic absorbable sutures coated with a lubricant coating to enhance knot run down are calendered in accordance with the invention and thereafter are filled with a storage stabilizing agent. Calendering the braided synthetic absorbable suture prior to filling is believed to open up the braid structure to permit the storage stabilizing agent to penetrate substantially all interstices of the suture. In alternative embodiments, braided absorbable or non-absorbable sutures are calendered in order to facilitate coating of the suture with one or more lubricant coatings and/or fillers, such as the aforementioned storage
20 stabilizing agent, containing one or more therapeutic agents or growth factors.

BRIEF DESCRIPTION OF THE DRAWINGS

Fig. 1 is a diagrammatic illustration of a calendering apparatus;

Fig. 2 is a perspective view of the calendering apparatus;

Fig. 3 is an exploded perspective view of the upper calendering portion;

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1 Fig. 4 is a partially cutaway sectional view of
the spring mounting of the calender apparatus;

 Fig. 5 is an elevational view of the suture
filling apparatus of the present invention;

5 Fig. 6 is a partially cutaway perspective view of
the filling head;

 Fig. 7 is a flowchart of a computer program for
controlling the filling method of the present invention.

10 DETAILED DESCRIPTION OF PREFERRED EMBODIMENTS

 The present invention is primarily directed to the
treatment of braided surgical sutures to facilitate and
promote substantially uniform and complete coating and/or
filling of the suture. In the preferred embodiment braided
15 synthetic absorbable sutures are calendered prior to filling
with a storage stabilizing agent, preferably a mixture
containing glycerol, in order to promote substantially
complete penetration of the filler throughout the braid
structure.

20 However, the calendering method and apparatus may
also find application to coating and/or filling of
absorbable or non-absorbable sutures. To facilitate
understanding the invention, possible suture materials and
braid constructions, coatings and fillers, possibly
25 containing one or more therapeutic agents or growth factors,
will be discussed prior to describing in detail the
preferred calendering apparatus and method and the preferred
method for calendering braided synthetic absorbable sutures
prior to filling with a stabilizing agent.

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1 Suture Material and Construction

As stated, the calendering method and apparatus finds particular application to the treatment of braided multifilament surgical sutures. The term "braid" means a
5 substantially symmetrical strand formed by crossing a number (at least three) of individual strands composed of one or more filaments diagonally in such manner that each strand passes alternatively over and under one or more of the others. The braid may include a core section composed of
10 one or more filaments around which the braid is externally fabricated, although such core may be excluded, if desired. The braid may be of traditional construction (so-called "hollow" or "tubular" braid) or may be of spiroid construction, with or without a core. Preferred braid
15 constructions of the traditional type are disclosed and claimed in United States Patents No. 5,019,093 issued May 28, 1991.

The braided suture can be fabricated from a wide
20 variety of natural and synthetic fibrous materials such as any of those heretofore disclosed for the construction of sutures. Such materials include non-absorbable as well as partially and fully bio-absorbable (i.e., resorbable) natural and synthetic fiber-forming polymers. Non-
25 absorbable materials which are suitable for fabricating the braided suture of this invention include silk, polyamides, polyesters, polypropylene, silk, cotton, linen, etc. Carbon fibers, steel fibers and other biologically acceptable inorganic fibrous materials can also be employed. Bio-
30 absorbable resins from which the suture can be fabricated include those derived from glycolic acid, glycolide, lactic

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1 acid, lactide, dioxanone, epsilon-caprolactone, trimethylene
carbonate, etc., and various combinations of these and
related monomers. Sutures prepared from resins of this type
are known in the art, e.g., as disclosed in U.S. Patent Nos.
5 2,668,162; 2,703,316; 2,748,987, 3,225,766; 3,297,033;
3,422,181; 3,531,561; 3,565,077; 3,565,869; 3,620,218;
3,262,948; 3,636,956; 3,736,646; 3,772,420; 3,773,919;
3,792,010; 3,797,499; 3,839,297; 3,867,190; 3,787,284;
3,982,543; 4,047,533; 4,060,089; 4,137,921; 4,157,437;
10 4,234,775; 4,237,920; 4,300,565; and 4,523,591; U.K. Patent
No. 779,291; D.K. Gilding et al., "Biodegradable polymers
for use in surgery - -polyglycolic/poly(lactic acid) homo-
and copolymers: 1, Polymer, Volume 20, pages 1459-1464
(1979), and D.F. Williams (ed), Biocompatibility of Clinical
15 Implant Materials, Vol. II, Ch. 9: "Biodegradable Polymers"
(1981).

Filling Agent

When a multifilament suture is fabricated from a
material which is susceptible to hydrolysis, e.g., any of
20 the absorbable resins previously mentioned, prior patents
teach that extreme care must be taken to rigorously exclude
moisture from contacting the suture during storage or to
otherwise preserve the suture from excessive hydrolytic
attack which would compromise its in vitro strength to the
25 point where the suture would no longer be serviceable.

Thus, according to U.S. Patent Nos. 3,728,839 and
4,135,622, the in vivo strength of polyglycolic acid
surgical elements such as sutures undergoes significant
deterioration on long term standing in the package even on
30 exposure of the contents to very small amounts of water for
very short periods of time, e.g., 20 minutes or less, just

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1 prior to packaging due to the tendency of a moisture
impervious package to seal the moisture in with the suture.
To prevent or minimize the extent of hydrolytic degradation
of an absorbable suture during storage, U.S. Patent Nos.
5 3,728,839 and 4,135,622 disclose removing substantially all
moisture from the suture before sealing the package. This
approach to improving the suture's storage stability, while
effective, is in practice difficult and expensive to carry
out. Prior to sealing the suture within its moisture
10 impervious package, it is essential that the suture be "bone
dry", a condition achieved by heating the suture for a
sufficient period to remove essentially all water therefrom,
e.g., 180-188° for 1 hour under a 26 inch vacuum. However,
once the water is removed, the suture cannot be allowed to
15 contact a moisture-containing environment even for a limited
duration since as previously noted, the patents teach that
even brief exposure to moisture can cause severe
deterioration of suture in vivo strength. It therefore
becomes necessary following the water removal step to
20 temporarily store the suture in a dry area, i.e., an
environment which is essentially free of moisture, where the
possibility of contact with moisture is largely eliminated.
These operations for improving the storage stability of an
absorbable suture are time consuming, expensive and
25 constitute a relatively complex solution to the storage
stability problem.

In an entirely different approach to improving the
storage stability of an absorbable suture, one that avoids
the foregoing drawbacks associated with the method of U.S.
30 Patent Nos. 3,728,839 and 4,135,622, the storage stability

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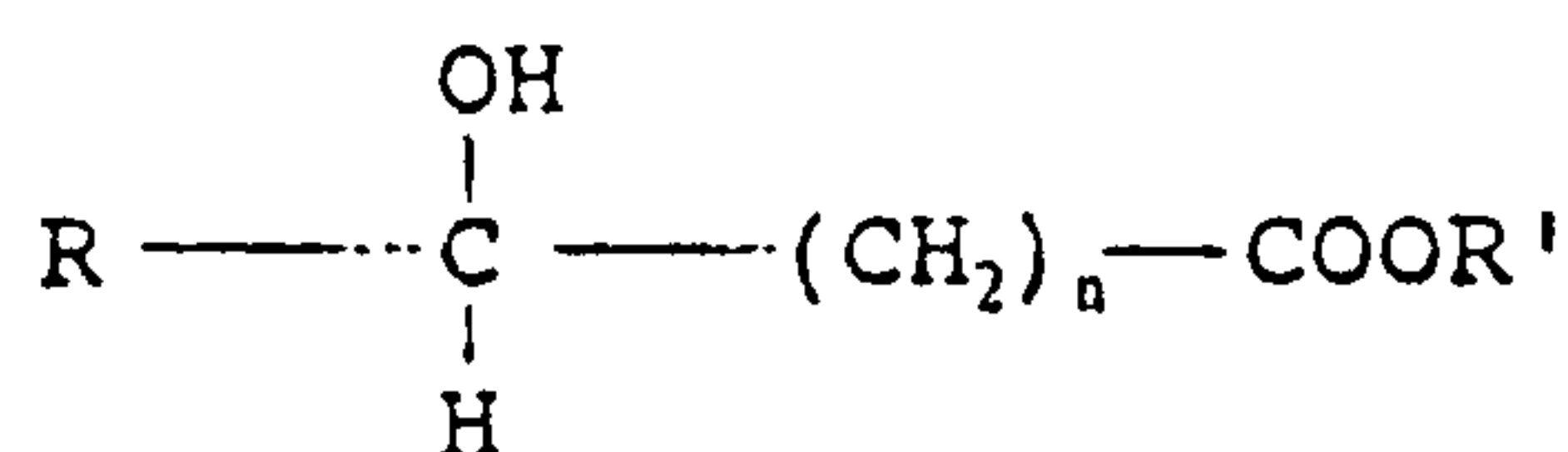
1 of an absorbable braided suture which is susceptible to
hydrolysis is improved by applying to the suture a storage
stabilizing amount of a filler material containing at least
one water soluble liquid polyhydroxy compound and/or ester
5 thereof. In addition to imparting an enhanced degree of
storage stability to the suture, practice of this embodiment
of the present invention confers other benefits as well.
So, for example, a braided suture which has been filled with
a storage stabilizing amount of, e.g., glycerol, exhibits
10 better flexibility and "hand" characteristics than the
untreated suture. Moreover, since the polyhydroxy compounds
are generally capable of dissolving a variety of medico-
surgically useful substances, they can be used as vehicles
to deliver such substances to a wound or surgical site at
15 the time the suture is introduced into the body.

The useful storage stabilizing agents are
generally selected from the water soluble, liquid
polyhydroxy compounds and/or esters of such compounds,
preferably those having no appreciable toxicity for the body
20 at the levels present. The expression "liquid polyhydroxy
compound" contemplates those polyhydroxy compounds which in
the essentially pure state are liquids, as opposed to
solids, at or about ambient temperature, e.g., at from about
15°C to about 40°C. The preferred polyhydroxy compounds
25 possess up to about 12 carbon atoms and where the esters are
concerned, are preferably the monoesters and diesters.
Among the specific storage stabilizing agents which can be
used with generally good results are glycerol and its mono-
and diesters derived from low molecular weight carboxylic
30 acids, e.g., monoacetin and diacetin (respectively, glyceryl
monoacetate and glyceryl diacetate), ethylene glycol,

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1 diethylene glycol, triethylene glycol, 1,3-propanediol,
 trimethylolethane, trimethylolpropane, pentaerythritol,
 sorbitol, and the like. Glycerol is especially preferred.
 Mixtures of storage stabilizing agents, e.g., sorbitol
 5 dissolved in glycerol, glycerol combined with monoacetin
 and/or diacetin, etc., are also useful.

To prevent or minimize run-off or separation of
 the storage stabilizing agent from the suture, a tendency to
 which relatively low viscosity compounds such as glycerol
 10 are especially prone, it can be advantageous to combine the
 agent with a thickener. Many kinds of pharmaceutically
 acceptable non-aqueous thickeners can be utilized including
 water-soluble polysaccharides, e.g., hydroxypropyl
 methylcellulose (HPMC), and the other materials of this type
 15 which are disclosed in European Patent Application
 O 267 015, polysaccharide gums such as guar, xanthan, and
 the like, gelatin, collagen, etc. An especially preferred
 class of thickeners are the saturated aliphatic
 hydroxycarboxylic acids of up to about 6 carbon atoms and
 20 the alkali metal and alkaline earth metal salts and hydrates
 thereof. Within this preferred class of compounds are those
 corresponding to the general formula



25 wherein R is hydrogen or methyl, R' is a metal selected from
 the group consisting of alkali metal and alkaline earth
 metal and n is 0 or 1, and hydrates thereof. Specific
 examples of such compounds include salts of lactic acid such
 30 as calcium lactate and potassium lactate, sodium lactate,

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1 salts of glycolic acid such as calcium glycolate, potassium
glycolate and sodium glycolate, salts of 3-hydroxy propanoic
acid such as the calcium, potassium and sodium salts
thereof, salts of 3-hydroxybutanoic acid such as calcium,
5 potassium and sodium salts thereof, and the like. As stated
hereinabove, hydrates of these compounds can also be used.
Calcium lactate, especially calcium lactate pentahydrate, is
a particularly preferred thickener.

Where a thickener is utilized, it will be
10 incorporated in the filling composition in at least that
amount required to increase the overall viscosity of the
storage stabilizing agent to the point where the agent no
longer readily drains away from the suture in a relatively
short period. In the case of a preferred storage
15 stabilizing agent-thickener combination, namely, glycerol
and calcium lactate, the weight ratio of glycerol to calcium
lactate can vary from about 1:1 to about 10:1 and preferably
is from about 6:1 to 8:1.

If necessary or desirable, the storage stabilizing
20 agent together with optional thickener can be dissolved in
any suitable non-aqueous solvent or combination of solvents
prior to use. To be suitable, the solvent must (1) be
miscible with the storage stabilizing agent and optional
thickener, if present (2) have a sufficiently high vapor
25 pressure to be readily removed by evaporation, (3) not
appreciably affect the integrity of the suture and (4) be
capable of wetting the surface of the suture. Applying
these criteria to a preferred storage stabilizing agent,
glycerol, advantageously in admixture with a preferred
30 thickener, calcium lactate, lower alcohols such as methanol
and ethanol are entirely suitable solvent carriers. When a

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1 solvent is utilized in the preparation of the stabilizing
agent, e.g., methanol, such solvent can be employed in
amounts providing a solution concentration of from about 20%
to about 50%, preferably about 30% to about 45%, by weight
5 of the storage stabilizing agent including any optional
thickener.

Preparing the storage stabilizing agent for
application to the suture is a relatively simple procedure.
For example, in the case of a mixture of glycerol and
10 calcium lactate, the desired amount of glycerol is first
introduced to a suitable vessel followed by the addition
thereto of the desired amount of calcium lactate. If no
solvent is to be used, the mixture is then thoroughly mixed.
Where a solvent such as methanol is employed, the solvent is
15 added to the mixture of glycerol and calcium lactate and the
solution is then thoroughly mixed to dissolve the compounds.

Application of the storage stabilizing agent to
the suture can be carried out in any number of ways. Thus,
for example, the suture can be submerged in the storage
20 stabilizing agent or solution thereof until at least a
storage stabilizing amount of agent is acquired or otherwise
retained by the suture, even after the optional removal of
any excess agent and/or accompanying solvent (if present)
such as by drainage, wiping, evaporation, etc. In many
25 cases, contact times on the order of from just a few
seconds, e.g., about 10 seconds or so, to several hours,
e.g., about 2 hours and even longer, are sufficient to
impart a substantial improvement in the storage stability of
the treated suture compared to the same suture which has not
30 been treated with storage stabilizing agent.

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1 The foregoing method of contacting the suture with
the storage stabilizing agent can be conducted continuously
or in batch. Thus, a running length of the suture can be
continuously passed through a quantity of stabilizing agent
5 at a velocity which has been previously determined to
provide the necessary degree of exposure, or contact time,
of the suture with the storage stabilizing agent. As the
suture emerges from the storage stabilizing agent, it can be
passed through a wiper or similar device to remove excess
10 agent prior to the packaging operation. Preferably, the
suture is passed through a coating head supplied by a
metering pump with a constant supply of filling solution,
with the suture emerging from the coating head and passing
through an evaporation oven to remove the filling solution
15 solvent prior to any further surface contact, i.e., with
rollers, etc. In a batch operation, a quantity of suture is
merely submerged within the storage stabilizing agent for
the requisite period of time with any excess agent being
removed from the suture if desired.

20 Alternatively, the storage stabilizing agent and
solutions thereof can be applied to the suture by spraying,
brushing, wiping, etc. such that the suture receives and
retains at least a storage stabilizing amount of the agent.

 Yet another procedure which can be used to apply
25 the storage stabilizing agent involves inserting suture in a
package containing an effective amount of the agent such
that intimate contact between the suture and the agent is
achieved.

 Whatever the contacting procedure employed, it is
30 necessary that the suture being treated acquire a storage
stabilizing amount of the storage stabilizing agent. In

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1 general, amounts from about 2 to about 25, and preferably
from about 5 to about 15, weight percent of storage
stabilizing agent(s) (exclusive of any solvent) by weight of
the suture contacted therewith is sufficient to provide
5 significantly improved storage stability compared to that of
the untreated suture.

As previously pointed out, a filled braided suture
component in accordance with the invention need not be
packaged and maintained under the very dry conditions
10 required for prior synthetic absorbable sutures. Instead,
it is preferred that the filled sutures be equilibrated so
that the level of moisture or other stabilizing agent
solvent is sufficient to result in an appropriate viscosity
level for the stabilizing agent and thickener in order to
15 keep the stabilizing agent on the suture. In the preferred
embodiment of a braided suture filled with a mixture of
glycerol and calcium lactate, the moisture level may be
equilibrated to as low as about 0.2% by weight of the
suture, and is preferably above 0.3% or, even more
20 preferably, above 0.5% by weight of the suture.

Indeed, it has been found that a braided suture
filled with a glycerol/calcium lactate composition tends to
undergo undesirable changes if exposed to a very dry
environment. More particularly, if such a filled suture is
25 exposed to a very dry environment, the surface of the suture
may accumulate a flaked or powdered substance which could
possibly interfere with, or render more difficult, the
removal of the suture from its package. Exposure of sutures
filled with a glycerol stabilizing agent to vacuum has been
30 found to adversely decrease the level of glycerol filler,
possibly by vaporizing the glycerol. Equilibrating the

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1 filled suture, such as in a dew point controlled
environment, so that the suture contains a relatively high
moisture level, e.g., in excess of 0.2% and preferably in
excess of 0.5% by weight of the suture, prevents such
5 accumulation of flaked or powdered substances which might
otherwise result were the suture exposed to an extremely dry
environment. Conversely, the presence of too much moisture
can also have deleterious effects, such as causing the
glycerol filling to run. Therefore, it is preferable to
10 control the moisture level within a range having preset
upper and lower limits.

Therapeutic Agents and/or Growth Factors

It is also within the scope of the invention to
15 impregnate the braided suture of this invention with, or
otherwise apply thereto, one or more medico-surgically
useful substances, e.g., those which accelerate or
beneficially modify the healing process when the suture is
applied to a wound or surgical site. So, for example, the
20 braided suture herein can be provided with a therapeutic
agent which will be deposited at the sutured site. The
therapeutic agent can be chosen for its antimicrobial
properties, capability for promoting wound repair and/or
tissue growth or for specific indications such as
25 thrombosis. Antimicrobial agents such as broad spectrum
antibiotics (gentamicin sulphate, erythromycin or
derivatized glycopeptides) which are slowly released into
the tissue can be applied in this manner to aid in combating
clinical and sub-clinical infections in a surgical or trauma
30 wound site.

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1 To promote wound repair and/or tissue growth, one
or more biologically active materials known to achieve
either or both of these objectives can be applied to the
braided suture. Such materials include any of several Human
5 Growth Factors (HGFs), magainin, tissue or kidney
plasminogen activator to cause thrombosis, superoxide
dismutase to scavenge tissue damaging free radicals, tumor
necrosis factor for cancer therapy, colony stimulating
factor, interferon, interleukin-2 or other lymphokine to
10 enhance the immune system, and so forth.

 The term "Human Growth Factor" or "HGF" embraces
those materials, known in the literature, which are referred
to as such and include their biologically active loosely
related derivatives. The HGFs can be derived from naturally
15 occurring sources including human and non-human sources,
e.g., bovine sources, and are preferably produced by
recombinant DNA techniques. Specifically, any of the HGFs
which are mitogenically active and as such are effective in
stimulating, accelerating, potentiating or otherwise
20 enhancing the wound healing process can be usefully applied
to the suture herein, e.g., hEGF (urogastrone), TGF-beta,
IGF, PDGF, FGF, etc. These and other useful HGFs and
closely related HGF derivatives, methods by which they can
be obtained and methods and compositions featuring the use
25 of HGFs to enhance wound healing are variously disclosed,
inter alia, in U.S. Patent Nos. 3,883,497, 3,917,824,
3,948,875, 4,338,397, 4,418,691, 4,528,186, 4,621,052,
4,743,679, 4,717,717, 4,861,757, 4,874,746 and 4,944,948.
European Patent Application Nos. 46,039, 128,733, 131,868,
30 136,490, 147,178, 150,572, 177,915 and 267,015, PCT
International Applications WO 83/04030, WO 85/003698,

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1 WO 85/01284 and WO 86/02271 and UK Patent Applications GB 2
092 155 A, 2 162 851 A and GB 2 172 890 A, and, "Growth
Factors in Wound Healing", Lynch et al., J. Clin. Invest.,
Vol. 84, pages 640-645 (August 1989). Of the known
5 HGFs, hEGF, TFG-beta, IGF, PDGF and FGF are preferred,
either singly or combination.

In a preferred embodiment of a braided suture, a
filling composition comprising a surgical wound healing
10 enhancing amount of at least one HGF and as carrier therefor
at least one water soluble, liquid polyhydroxy compound
and/or ester thereof is applied to the suture. The carrier
protects the HGF component of the filling composition from
excessive degradation or loss of biopotency during storage
15 and as disclosed above, when the suture is fabricated from
an absorbable resin which is susceptible to hydrolysis, the
carrier improves the storage stability of the suture as
well. In addition to the carrier, the HGF can contain a
thickener such as any of those previously mentioned in order
20 to reduce the tendency of carrier run-off.

The filling composition can contain one or more
additional components which promote or enhance the wound
healing effectiveness of the HGF component. Thus, e.g.,
25 site-specific hybrid proteins can be incorporated in the
filling composition to maximize the availability of the HGF
at the wound site and/or to potentiate wound healing. See
e.g., Tomlinson (Ciba-Geigy Pharmaceuticals, West Sussex,
U.K.), "Selective Delivery and Targeting of Therapeutic
30 Proteins", a paper presented at a symposium held June 12-14,
1989 in Boston, MA. The HGFs can also be associated with

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1 carrier proteins (CPs), e.g., in the form of CP-bound
HGF(s), to further enhance availability of the HGF(s) at a
wound site as disclosed in "Carrier Protein-Based Delivery
of Protein Pharmaceuticals", a paper of BioGrowth, Inc.,
5 Richmond, CA presented at the aforementioned symposium.
The HGFs can also be incorporated in liposomes to
provide for their release over an extended period.
Lactate ion can be present to augment the wound healing
activity of the HGF. Protectants for the HGF can
10 also be utilized, e.g., polyoxyethylene glycols,
acetoxypheoxy polyethoxy, ethanols, polyoxyethylene
sorbitans, dextrans, albumin, poly-D-alanyl peptides
and N-(2-hydroxypropyl)-methacrylamide (HPMA).

15 The amounts of HGF, carrier and optional
component(s) such as thickener, site-specific hybrid
protein, carrier protein, etc., identified above can vary
widely and in general will be at least that amount of a
particular component which is required to perform its
20 respective function in an effective way. Those skilled in
the art employing known or conventional procedures can
readily determine optimum amounts of each component for a
particular filling composition and particular braided suture
filled therewith.

25 In general, the HGF(s) can be present in the total
composition at a level ranging from about 0.1 to about
25,000 micrograms per gram of such composition, preferably
from about 0.5 to about 10000 micrograms per gram of
composition and most preferably from about 1 to about 5000
30 micrograms per gram of composition.

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1 Application of the HGF-containing composition to
the braided suture of this invention can be carried out by
any suitable technique, e.g., by any of the procedures
described above for applying a storage stabilizing agent to
5 the suture.

Suture Coating

It is also advantageous to apply one or more
coating compositions to a braided suture component where
10 particular functional properties are desired. For example,
the suture can be coated with a material which improves its
surface lubricity and/or knot tie-down characteristics.
Coating materials for sutures are known and include non-
bioabsorbable substances such as silicone, beeswax, or
15 polytetrafluoroethylene, as well as absorbable substances
such as homopolymers and/or copolymers of glycolide and
lactide, polyalkylene glycols, and higher fatty acids or
salts or esters thereof. Other suitable materials which
impart either or both characteristics have been proposed in
20 United States Patents 3,867,190; 3,942,532; 4,047,533;
4,452,973; 4,624,256; 4,649,920; 4,716,203; and 4,826,945.
Preferred bioabsorbable coating compositions can be obtained
by copolymerizing in accordance with known procedures (1) a
polyether glycol selected from the group consisting of
25 relatively low molecular weight polyalkylene glycol, e.g.,
one corresponding to the general formula $\text{HO}(\text{RO})_y\text{H}$ wherein R
is an alkylene group of from 2-4 carbon atoms and y is an
integer of from about 100-350, and polyethylene oxide-
polypropylene oxide block copolymer, e.g., one corresponding
30 to the general formula $\text{H}(\text{OCH}_2\text{CH}_2)_x(\text{OC}_3\text{H}_6)_y(\text{OCH}_2\text{CH}_2)_z\text{OH}$ wherein x

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1 is an integer of from about 45-90, y is an integer of from
about 60-85 and z is an integer of from about 45-90 with (2)
a mixture of lactide monomer and glycolide monomer or a
preformed copolymer of lactide and glycolide, the weight
5 ratio of (1) to (2) preferably ranging from about 4:1 to
about 1:4 and more preferably from about 2:1 to about 1:2.
The ratio of lactide to glycolide in the monomer mixture or
in the copolymer of these monomers preferably varies from
about 65-90 mole percent lactide and 10-35 mole percent
10 glycolide. Polyether glycols which can be used to prepare
the bioabsorbable coating composition advantageously include
polyethylene glycols having molecular weights of about
3,500-25,000 and preferably from about 4,000-10,000 and
polyethylene oxide-polypropylene oxide block copolymers
15 having molecular weights of from about 5,000-10,000 and
preferably from about 7,500 to about 9,000, e.g., those
disclosed in U.S. Patent Nos. 2,674,619, 3,036,118,
4,043,344 and 4,047,533 and commercially available as the
*Plurionics (BASF-Wyandotte). Where preformed copolymers of
20 lactide and glycolide are employed in preparing the
bioabsorbable coating compositions, they may be prepared as
described in U.S. Patent No. 4,523,591. The amounts of
bioabsorbable coating composition to be applied to the
suture, e.g., by coating, dipping, spraying or other
25 appropriate techniques, will vary depending upon the
specific construction of the suture, the size and the
material of this construction. In general, the coating
composition applied to an unfilled suture will constitute
from about 1.0 to about 3.0 percent by weight of the coated
30 suture, but the amount of coating add on may range from as
little as about 0.5 percent, by weight, to as much as 4.0

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*Trade-mark

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1 percent or higher. For a preferred filled (i.e. containing
a storage stabilizing agent) braided suture, amounts of
coating composition will generally vary from about 0.5% to
2.0% with as little as 0.2% to as much as 3.0%. As a
5 practical matter and for reasons of economy and general
performance, it is generally preferred to apply the minimum
amount of coating composition consistent with good surface
lubricity and/or knot tie-down characteristics and this
10 level of coating add on is readily determined experimentally
for any particular suture.

Suture Calendering

In accordance with the invention, it has been
found to be desirable to calender the braided suture prior
15 to coating and/or filling in order to facilitate penetration
of the coating or filler into the interstices of the braid
suture.

Referring to Fig. 1, a braided suture 1 is moved
axially in the direction indicated by arrow A. The suture
20 is first passed between two cylindrical calendering rollers
2 and 3, each of which has a smooth, polished surface. The
rollers are rotatably mounted in a calendering apparatus
(not shown) such that one of the rollers is fixed with
respect to translational movement whereas the other of the
25 two rollers is biased, for example by a spring means,
towards the fixed roller. The biasing force may be set to
any desired predetermined magnitude. Alternatively, both
rollers may be biased towards each other.

30 The rollers 2 and 3 are parallel to each other,
but transverse to the axial orientation of suture 1. They

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1 apply a mechanical compression force to the suture in a
direction as shown by arrows B.

When the suture 1 passes between rollers 2 and 3,
it is compressed radially inward in direction B, but it
5 expands laterally in the transverse direction, which opens
up the braid structure. After passing between the first
pair of rollers 2 and 3, suture 1, without turning or
twisting, then preferably passes between a second pair of
calendering rollers 4 and 5 which operate in the same manner
10 as rollers 2 and 3, except that the second pair of rollers
are oriented transversely to the first pair of rollers 2 and
3, as well as transversely to the suture 1. Thus, rollers 4
and 5 compress the suture laterally in a direction C which
is transverse to direction B. The suture braids are then
15 opened in a direction transverse to C and the suture is
caused to return to its original, substantially round
configuration. Preferably, the upper and lower roller pairs
are positioned so that the suture rests against the surface
of the fixed roller and is contacted and compressed by the
20 action of the spring-loaded roller pressing against the
suture and fixed roller.

Having passed between both pairs of rollers, the
braids are uniformly opened to a predetermined extent, which
facilitates application of filler material and/or coating
25 material.

Figs. 2 and 3 respectively illustrate a
perspective view of the calendering apparatus and an
exploded perspective view of the upper portion 11 of the
apparatus 10 for calendering sutures. Fig. 4 is a partially
30 cut away detailed view of the spring mounting of the
apparatus of the present invention.

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1 Referring to Fig. 2, adapter plate 20 provides a
means for mounting the apparatus to any appropriate
receiving surface. Bolts 21 disposed through apertures in
the adapter plate 20 secure the adapter plate 20 to the
5 receiving surface.

Upper calender fixture 11 includes a backplate 30,
and a fixed roller 50 rotatably mounted between left and
right guides 60 and 61 respectively. The fixed roller 50
has a platen 51 with a surface of sufficient smoothness not
10 to damage the suture. Bearing ends 52 fit into countersunk
holes 62 in the left and right guides. Slide plates 80 and
81 are slidably mounted within respective slots 63 and 64 in
the left and right guides. Floating roller 55 is rotatably
mounted between slide plates 80 and 81 and is parallel to
15 roller 50. Platen 56 of roller 55 has a surface of
sufficient smoothness so as not to damage a suture being
calendered. Surface smoothness for the calendering rollers
of the present invention is preferably a fine surface finish
in the range of about 4 to 16 microinches, and most
20 preferably about 8 microinches, (i.e. the root mean square
difference between the surface peaks and valleys) and can be
achieved by electropolishing, lapping, or superfinishing.

Since slide plates 80 and 81 are movable within
slots 63 and 64, floating roller 55 is movable toward and
25 away from fixed roller 50. Compression springs 90 urge the
floating roller 55 toward the fixed roller 50 by applying a
biasing force of predetermined magnitude. Springs 90 are
disposed around retainer rods 70 between front support plate
40 and respective slide plates 80 and 81. Retainer rods 70
30 are disposed through apertures 41 in the front support plate
40. Threaded ends 72 of the retainer rods are received into

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1 tapped holes 83 and 84 of the slide plates 80 and 81. The
spring size and type is chosen so as to apply an appropriate
biasing force. The biasing force must be sufficient
magnitude to compress the suture, but less than that which
5 would cause permanent damage to the suture.

In an attempt to qualify the amount of suture
compression during calendering, sutures of different sizes
were passed through one set of calender rolls, e.g. the
upper portion 11 of the calendering device. The average
10 diameter of the suture prior to application of the calender
rolls and the average diameter in the narrowest direction,
i.e. the direction of compression, were determined using an
optical microscope. The percentage of compression of the
suture is determined from the following formula: $\frac{D_1 - D_2}{D_1} \times 100$
15

wherein:

D_1 = average suture diameter before
calendering

20 D_2 = average suture diameter after
calendering (in one direction only)
as measured across the narrowest
direction, i.e. the direction in which
the compression force is applied.

25 An acceptable range of suture compression is from
about 0 to 20%. A preferred range of suture compression is
about 0 to 10%. Most preferred is a suture compression of
about 5%.

30 A helical compression spring 90 should be chosen
so as to apply biasing force to achieve suture compression

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1 within the above mentioned ranges. As stated, springs 90
are disposed around rods 70 between the inside surface of
plate 40 and slide plates 80 and 81. In a preferred
configuration with rollers 50 and 55 touching, the space
5 between plate 40 and slide plates 80 and 81 is slightly less
than about 2 inches, such as about $1\frac{1}{4}$ inches. In this
configuration, a spring which has been found to be suitable
has a free length of about 2" and a spring rate of 2.0
lbs./in.

10 The bottom portion of the fixture 12 is similar to
the top portion 11 except that it is mounted to the adapter
plate 20 in an orientation orthogonal to that of top portion
11. It has been found that most sutures can be calendered
at relatively high velocity, on the order of about 50 meters
15 per minute, which is conducive to calendering in line
immediately before the coating or filling operation, as
explained in more detail below. However, smaller size
sutures, e.g. sizes 6/0, 7/0 and 8/0, may require
calendering at a slower speed, on the order of about 25
20 meters per minute, to provide more gentle suture handling
and avoid filament breakage.

Filling

After the suture has been calendered it may be
25 filled with appropriate filling agents as described above by
passing the suture through a filling head. Filling heads
are applicators for applying a fluid medium to the running
length of an indefinite length work, such as a fiber or
thread. Such an apparatus is available from Bouligny
30 Company of Charlotte, North Carolina, and may include the
applicator head designated as part number 503-488 of the

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1 Bouligny Company. An example of such a filling head is
illustrated in Fig. 6. Filling solution may be continuously
delivered from a reservoir by means of a standard metering
pump.

5 In contrast to batch processes wherein the entire
length of a suture is immersed in a trough of filling
solution, use of the filling method of the present invention
possesses the advantage of efficient use of filling
solution. Only a small quantity of filling solution need be
10 prepared at any one time. Thus, the method of the present
invention enables the use of HGFs or other therapeutic
agents such as those discussed above, which may be
prohibitively expensive to formulate in solution in large
quantity.

15 Fig. 5 illustrates the preferred apparatus for
filling the suture in conjunction with the calendering
apparatus. Suture 1 is drawn off a winding roll (not shown)
and passes around roller 201 and up through calendering
portions 12 and 11. The suture 1 is then guided around
20 rollers 202, 203, 204 and 205, and passed vertically through
filling head 210.

Referring now to Fig. 6, filling head 210 includes
two wing portions 211 and 212 which define a V-shaped notch
216 through which the suture 1 is passed. A filler supply
25 tube 213 provides means for carrying filling solution from a
metering pump to the filling head 210. The filling solution
passes through aperture 214 so as to enter the V-shaped
notch region 216 along the corner edge defined by the
intersection of the inner surfaces of wing portions 211 and
30 212. The filling solution accumulates to some extent along
the interior walls of the V-shaped notch 216. As suture 10

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1 passes through V-shaped notch 216 it is wetted and filled by
the filling solution, which is substantially continuously
applied by means of the metering pump. The term
"substantially continuously" also includes the intermittent
5 application of filling solution to maintain a predetermined
minimum accumulation of filling agent in the filling head as
the suture continuously passes therethrough. The filling
head 210 can be fabricated from any material suitable for
the purpose described herein, such as metal or plastic.

10 Referring again to Fig. 5, excess filling solution
is collected and returned through a return conduit 213a to
the filling solution reservoir, further conserving filling
solution. After the suture is passed through the filling
head 210 it is passed into a vertical oven 207 wherein it is
15 heated so as to dry the suture. The oven is preferably
maintained at a temperature of about 84 degrees Centigrade.
The suture passes to the top of the oven without contacting
any surface until it passes around a driver roller at the
top of the oven. The filler dries rapidly in the heated
20 oven, so that the suture substantially dries in the time
required for the suture to travel to the top of the oven.
Optionally, the suture may be guided around roller 206 and
up again into oven 207 for as many multiple passes through
the oven 207 as is desired. After calendering tension may
25 be applied to the suture so as to produce up to about a 5%
stretch in the suture. The suture speed is held constant
throughout the procedure. After the final pass through the
oven 207, suture 1 is guided around rollers 208, 209, 221,
222, 223 and onto a winding spool (not shown) or other
30 suitable receiver.

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1 case CNC = .3966. For suture sizes 6/0, 7/0 and 8/0 the
 preferred filling solution has a ratio of glycerol to
 calcium lactate of about 10:1 is used, and for all other
 suture sizes the ratio preferably is about 6.5:1. Preferred
 5 values for the remaining parameters (other than denier)
 needed to determine the pump rate are set forth in Table 1.
 Variable pump capacity may be achieved with a single
 metering pump by providing a variable setting flow valve
 with recirculating loops. Thus, at less than maximum pump
 10 capacity at least some filling solution is returned to the
 reservoir instead of to the applicator head.

TABLE 1

15	Suture Size	VEL (Meters per Min.)	TARG (% suture weight)	CAP (cc per rev.)
	8/0	50	15	.02
	7/0	50	15	.02
	6/0	50	15	.02
	5/0	50	13	.08
	4/0	50	12	.08
20	3/0	50	12	.08
	2/0	50	12	.08
	0	50	12	.08
	1	50	12	.08
	2	50	12	.08
	3	50	12	.08

25 Denier of the suture material to be filled is
 measured and a metering pump rate is calculated for the
 suture material using equation (1) and the values set forth
 above.

30 In order to facilitate implementation of the
 filling operation in production, a computer program has been
 developed and may be used to reduce operator error. A flow

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1 chart of the program is shown in Fig. 7, the steps of which
are described below.

The user initiates the program and the computer
proceeds according to the following steps as shown in
5 Fig. 7.

Step 101 - Start of program

10 Step 102 - The computer asks the user the following
questions:

- 1) What is the size of the braid?
- 2) What is the braid lot number?
- 3) What is the denier of the braid?

15 Step 103 - The user inputs size, lot number, and denier
of the suture to be filled.

20 Step 104 - The computer then determines whether the
suture size specified by the user was 8/0.
If no, the program proceeds Step 108. If
yes, the program proceeds to Step 105.

25 Step 105 - The computer selects a pump capacity flow
valve setting of 0.02 cc per revolution, a
suture velocity of 50 meters per minute; a
target add on percentage of 15% fill; and a
drying oven temperature of 84°C.

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1 Step 106 - The computer determines whether the denier
input by the user in Step 103 was less than
33. If yes, then the program goes to Step
147 and the user is told that the denier does
5 not match the braid size, and that another
denier sample should be taken before
continuing. If no, then the program proceeds
to Step 107.

10 Step 107 - The computer determines whether the denier
input by the user in Step 103 was greater
than 50. If yes, the program moves to Step
147. If no, the program proceeds to Step 144
15 wherein pump rotations per minute (RPM) is
calculated using equation (1) and the
procedure advances to step 145.

Step 108 - The computer determines whether the size of
braid input by the user in Step 103 was 7/0.
20 If no, the program moves to Step 112. If
yes, the program advances to Step 109.

Step 109 - The computer selects the following settings:
Pump capacity = 0.02 cc/rev.
25 Suture velocity = 50 meters/min.
Target add on = 15% fill
Drying oven temp. = 84°C

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- 1 Step 110 - The computer determines whether the denier
size input by the user in Step 103 is less
than 40. If yes, the program proceeds to
Step 147. If no, the program advances to
5 Step 111.
- Step 111 - The computer determines whether the denier
size input by the user is above 60. If yes,
the program goes to Step 147. If no, the
10 program advances to Step 144.
- Step 112 - The computer determines whether the size of
the braid input by the user in Step 103 was
6/0. If no, the program goes to Step 116.
15 If yes, the program advances to Step 113.
- Step 113 - The computer selects the following settings:
Pump capacity = 0.02 cc/rev.
Suture velocity = 50 meters/min.
20 Target add on = 15% fill
Drying oven temp. = 84°C
- Step 114 - The computer determines whether the denier
input by the user in Step 103 is less than
25 50. If yes, the program goes to Step 147.
If no, the program proceeds to Step 115.
- Step 115 - The computer determines whether the denier
input by the user is above 160. If yes, the
30 program goes to Step 147. If no, the program
proceeds to Step 144.
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1 Step 116 - The computer determines whether the size of
the braid input by the user in Step 103 was
5/0. If no, the program goes to Step 120.
If yes, the program advances to Step 117.

5 Step 117 - The computer selects the following settings:
Pump capacity = 0.08 cc/rev.
Suture velocity = 50 meters/min.
Target add on = 13 % fill
10 Drying oven temp. = 84°C

Step 118 - The computer determines whether the denier
input by the user in Step 103 is less than
250. If yes, the program goes to Step 147.
15 If not, the program proceeds to Step 119.

Step 119 - The computer determines whether the denier
input by the user is above 340. If yes, the
program moves to Step 147. If no, the
20 computer proceeds to Step 144.

Step 120 - The computer determines whether the size of
the braid input by the user in Step 103 was
4/0. If no, the program goes to Step 124.
25 If yes, the program advances to Step 121.

Step 121 - The computer selects the following settings:
Pump capacity = 0.08 cc/rev.
Suture velocity = 50 meters/min.
30 Target add on = 12 % fill
Drying oven temp. = 84°C

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- 1 Step 122 - The computer determines whether the denier
input by the user in Step 103 is less than
350. If yes, the program goes to Step 147.
If no, the program advances to Step 123.
- 5 Step 123 - The computer determines whether the denier
input by the user is above 500. If yes, the
program goes to Step 147. If no, the program
advances to Step 144.
- 10 Step 124 - The computer determines whether the size of
the braid input by the user in Step 103 was
3/0. If no, the program moves to Step 128.
If yes, the program advances to Step 125.
- 15 Step 125 - The computer selects the following settings:
Pump capacity = 0.08 cc/rev.
Suture velocity = 50 meters/min.
Target add on = 12 % fill
- 20 Drying oven temp. = 84°C
- Step 126 - The computer determines whether the denier
input by the user in Step 103 is less than
500. If yes, the program moves to Step 147.
25 If no, the program advances to Step 127.
- Step 127 - The computer determines whether the denier
input by the user in Step 103 is above 900.
If yes, the program moves to Step 147. If
30 no, the program proceeds to Step 144.
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1 Step 128 - The computer determines whether the size of
the braid input by the user in Step 103 was
2/0. If no, the program goes to Step 132.
If yes, the program goes to Step 129.

5 Step 129 - The computer selects the following settings:
Pump capacity = 0.08 cc/rev.
Suture velocity = 50 meters/min.
Target add on = 12 % fill
10 Drying oven temp. = 84°C

Step 130 - The computer determines whether the denier
input by the user in Step 103 is less than
1,000. If yes, the program moves to Step
15 147. If no, the program goes to Step 131.

Step 131 - The computer determines whether the denier
input by the user in Step 103 is above 1,350.
If yes, the program moves to Step 147. If
20 no, the program advances to Step 144.

Step 132 - The computer determines whether the size of
the braid input by the user in Step 103 was
size 0. If no, the program goes to Step 136.
25 If yes, the program proceeds to Step 133.

Step 133 - The computer selects the following settings:
Pump capacity = 0.08 cc/rev.
Suture velocity = 50 meters/min.
30 Target add on = 12 % fill
Drying oven temp. = 84°C

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- 1 Step 134 - The computer determines whether the denier
input by the user in Step 103 is less than
1,400. If yes, the program moves to Step
5 135. If no, the program advances to Step
135.
- Step 135 - The computer determines whether the denier
input by the user is above 1,950. If yes,
10 the program goes to Step 147. If no, the
program goes to Step 144.
- Step 136 - The computer determines whether the size of
the braid input by the user in Step 103 was
size 1. If no, the program advances to Step
15 140. If yes, the program proceeds to Step
137.
- Step 137 - The computer selects the following settings:
20 Pump capacity = 0.08 cc/rev.
Suture velocity = 50 meters/min.
Target add on = 12 % fill
Drying oven temp. = 84°C
- Step 138 - The computer determines whether the denier
25 input by the user in Step 103 is less than
2,000. If yes, the program goes to Step 147.
If no, the program goes to Step 139.

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- 1 Step 139 - The computer determines whether the denier
input by the user is above 2,600. If yes,
the program goes to Step 147. If no, the
program goes to Step 144.
- 5 Step 140 - The computer determines whether the size of
the braid input by the user in Step 103 is
size 2. If no, the program goes to Step 146.
If yes, the program goes to Step 141.
- 10 Step 141 - The computer selects the following settings:
Pump capacity = 0.08 cc/rev.
Suture velocity = 50 meters/min.
Target add on = 12 % fill
15 Drying oven temp. = 84°C
- Step 142 - The computer determines whether the denier
input by the user in Step 103 is less than
3,000. If yes, the program goes to Step 147.
20 If no, the program goes to Step 143.
- Step 143 - The computer determines whether the denier
input by the user in Step 103 is above 3,500.
If yes, the program goes to Step 147. If no,
25 the program goes to Step 144.
- Step 144 - The computer calculates the pump speed in
rotations per minute in accordance with
equation (1) and proceeds to step 145.
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- 1 Step 145 - The user is informed by printout or by
monitor as to the lot number specified, the
appropriate braid speed, pump rate, pump
5 capacity setting, filling target percentage,
and temperature of the drying chamber. The
suture size, denier and filling solution
identification are also displayed. The
program thereafter runs to completion to Step
148.
- 10 Step 146 - This step is arrived at if the suture size
input by the user in Step 103 does not match
any of the designated suture sizes pre-
programmed in the computer. The user is
15 informed that he has chosen an incorrect size
designation. The program then moves to Step
148, which is the end.
- 20 Step 147 - The user is warned that the denier which he
has input in size 103 does not match the size
of braid which he has also input in 103. The
user is advised to take another denier sample
before continuing. The program then moves to
Step 148.
- 25 Step 148 - End of program.

The program may be expanded to accommodate
different size sutures, and the processing conditions for
30 any particular suture may readily be modified without
affecting the conditions for other size sutures. Although

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1 the program has been described in the context of printing
out processing conditions in terms of settings to be
adjusted by the user, it is contemplated that one or more
processing conditions could be set automatically by computer
5 control. Thus, the flow valve could be adjusted by
electromechanical controls to the appropriate position, the
godet or roller motor(s) could be automatically set to
achieve the appropriate braid speed including, if desired, a
stretch condition, the drying oven temperature could be set
10 automatically and the metering pump could be electronically
set to the appropriate RPM calculated from equation (1).

While many specifics have been described, it is
contemplated that a wide range of processes could be
developed which take advantage of the calendering and
15 coating/filling operations described herein. Thus, the
apparatus and computer program for filling may also be used
to advantage to coat sutures with a lubricant coating in
order to improve knot run down, irrespective whether the
suture is absorbable or non-absorbable and is or is not to
20 be filled. In this regard, numerous advantageous processes
are contemplated.

By way of example, the apparatus, method and/or
computer program described above for filling may be used to
coat absorbable or non-absorbable sutures, and the sutures
25 may be calendered prior to coating to improve coating
efficiency. By way of further example, absorbable or non-
absorbable sutures may be calendered and subsequently
filled. Because the filling may contain desirable
therapeutic agents and/or growth factors, filling may be
30 desirable for both absorbable or non-absorbable sutures in
order to administer such agents or growth factors. It has

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1 been found desirable to apply a lubricant coating, if any,
prior to calendering and filling, but it is also
contemplated that calendering and filling could precede the
coating operation.

5 Numerous variations and modifications of the
invention will occur to a person of ordinary skill in the
art or will be learned by or from experimentation with the
invention all within the scope of the appended claims.

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THE EMBODIMENTS OF THE INVENTION IN WHICH AN EXCLUSIVE PROPERTY OR PRIVILEGE IS CLAIMED ARE DEFINED AS FOLLOWS:

1. A method for filling a suture comprising passing the suture lengthwise through a filling head, said filling head having a contacting region in which the suture is contacted by a filling agent substantially continuously supplied to the filling head as the suture passes therethrough.

2. The method of claim 1, wherein said contacting region is a substantially V-shaped notch defined by two wing portions, said filling agent being supplied to said contacting region along the inner edge thereof.

3. The method of claim 1 or 2, wherein said filling agent comprises a storage stabilizing agent.

4. The method of claim 3, wherein said storage stabilizing agent comprises glycerol.

5. The method of claim 3, wherein said stabilizing agent contains a thickener.

6. The method of claim 5, wherein said thickener is calcium lactate.

7. The method of claim 1 or 2, wherein said filling agent comprises a therapeutic agent.

8. The method of claim 7, wherein said therapeutic agent is selected from the group consisting of antibiotics,

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human growth factors, magainin, tissue plasminogen activator, kidney plasminogen activator, superoxide dismutase, tumor necrosis factor, colony stimulating factor, interferon, and interleukin-2.

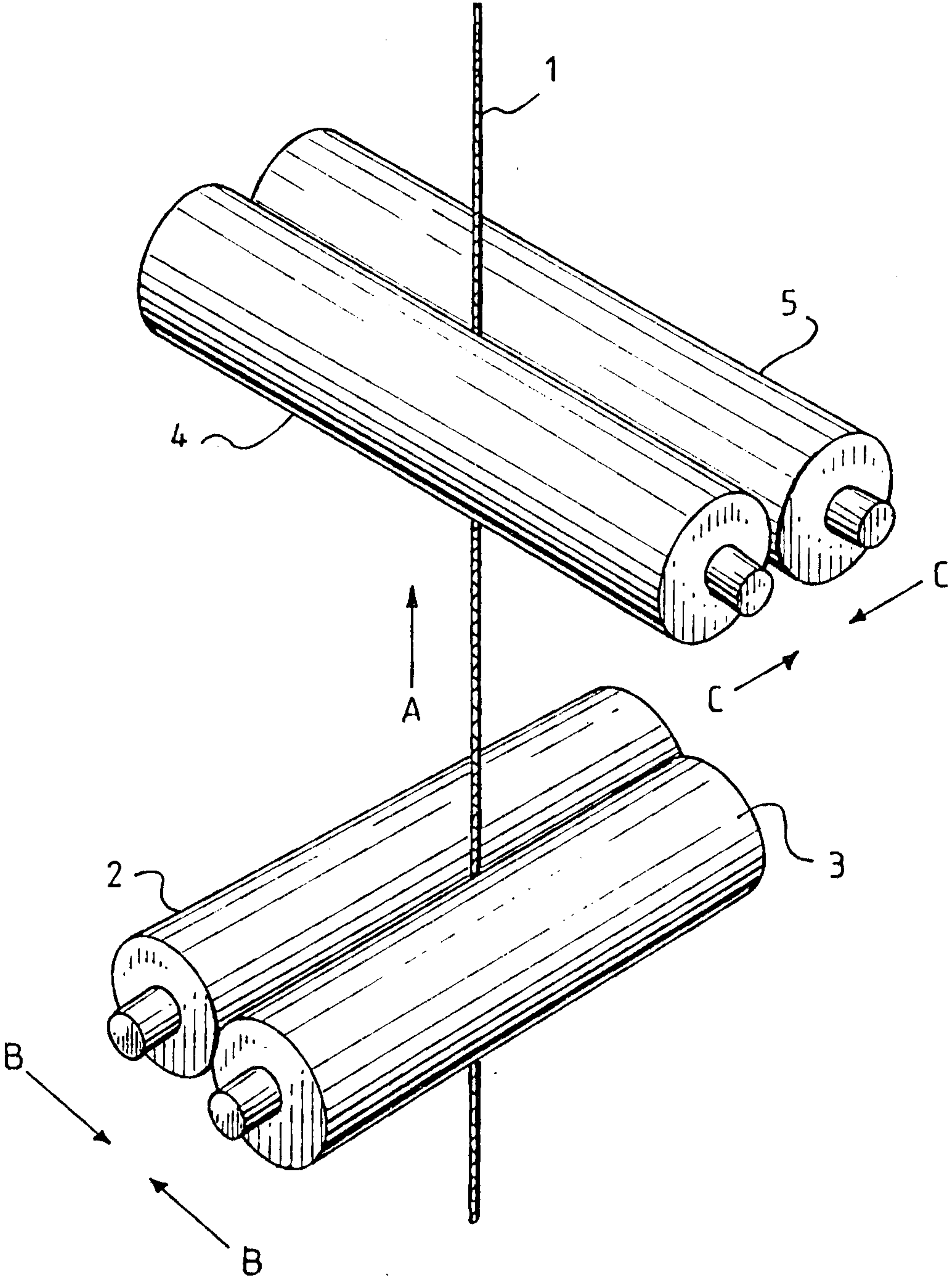
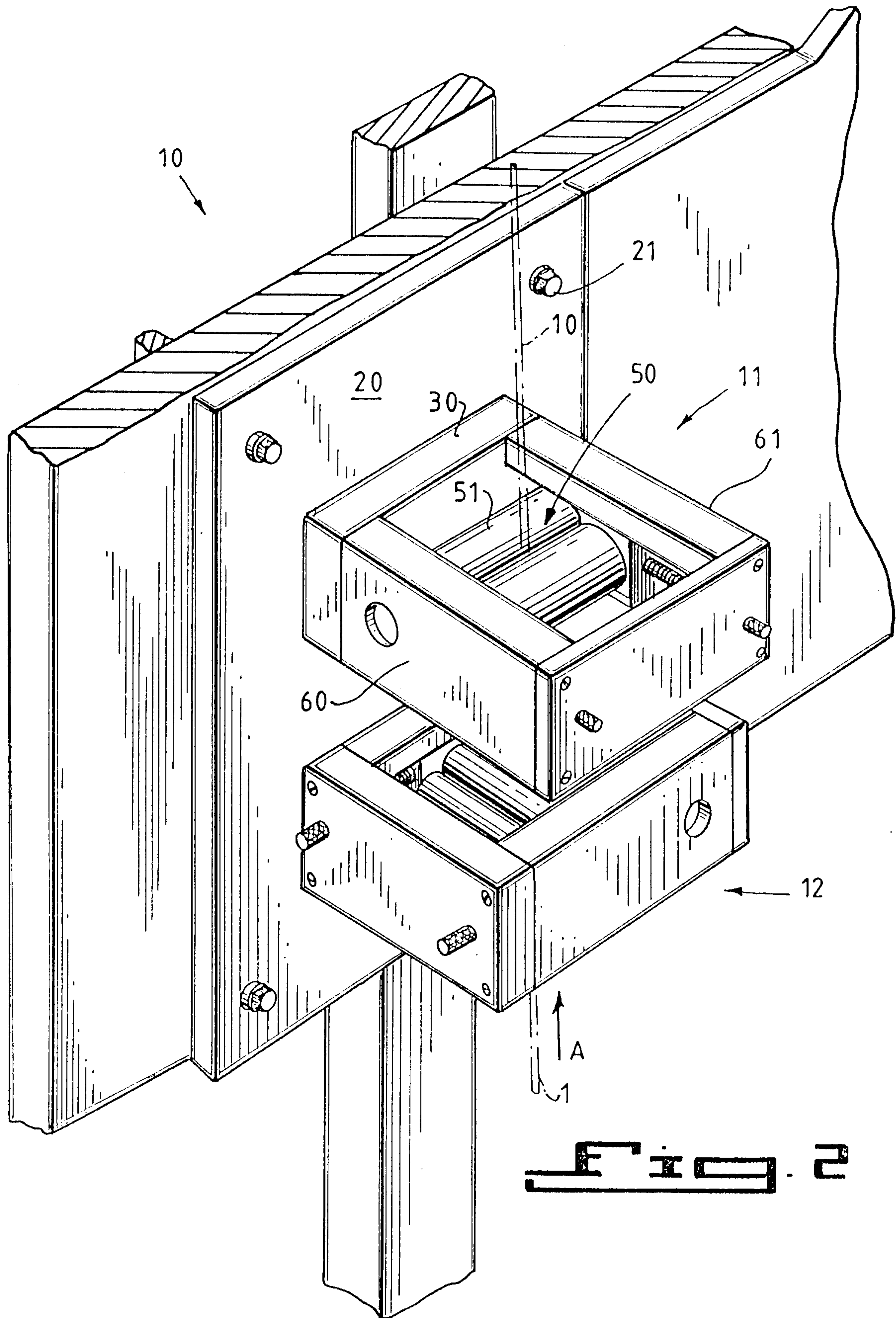


Fig. 1



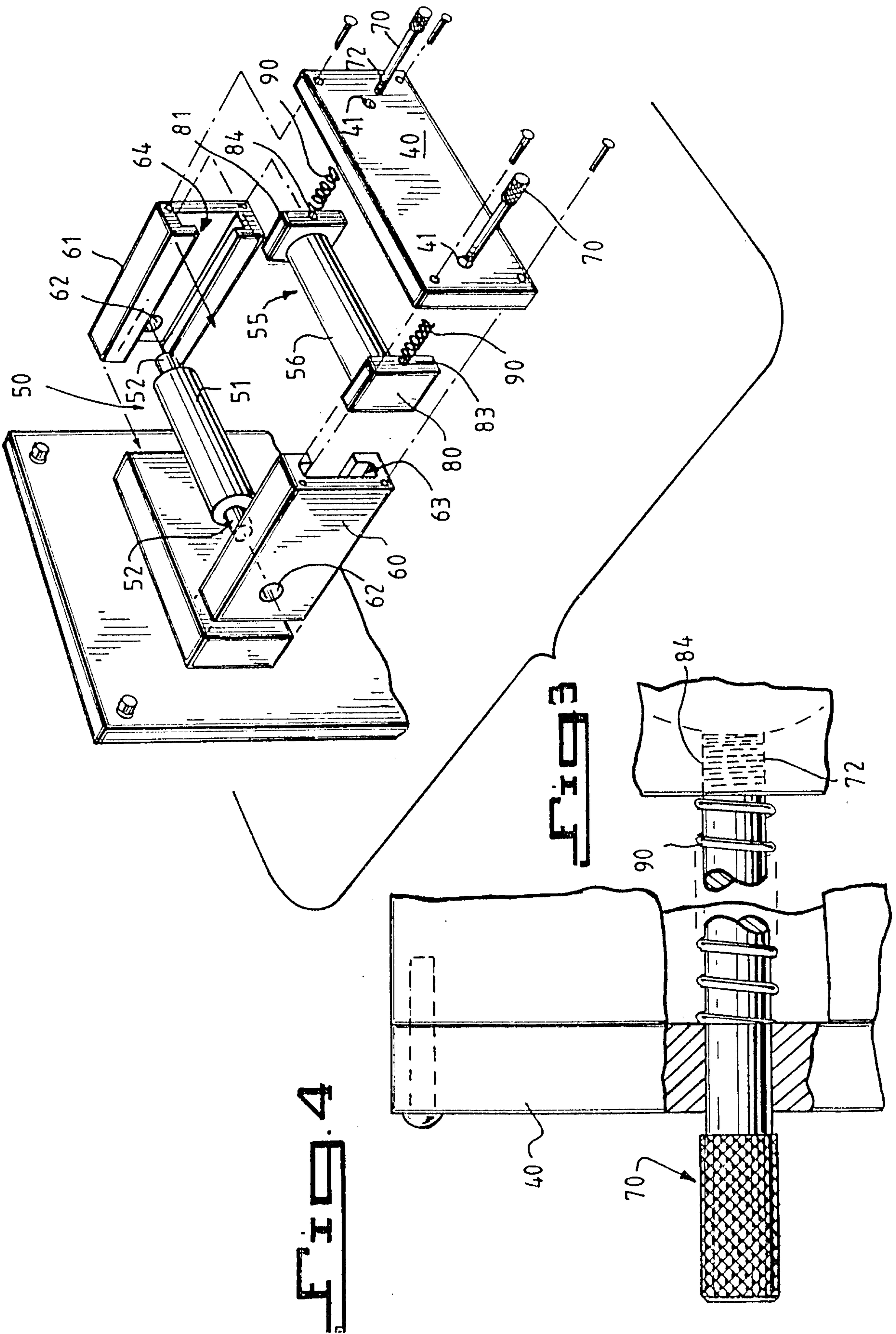
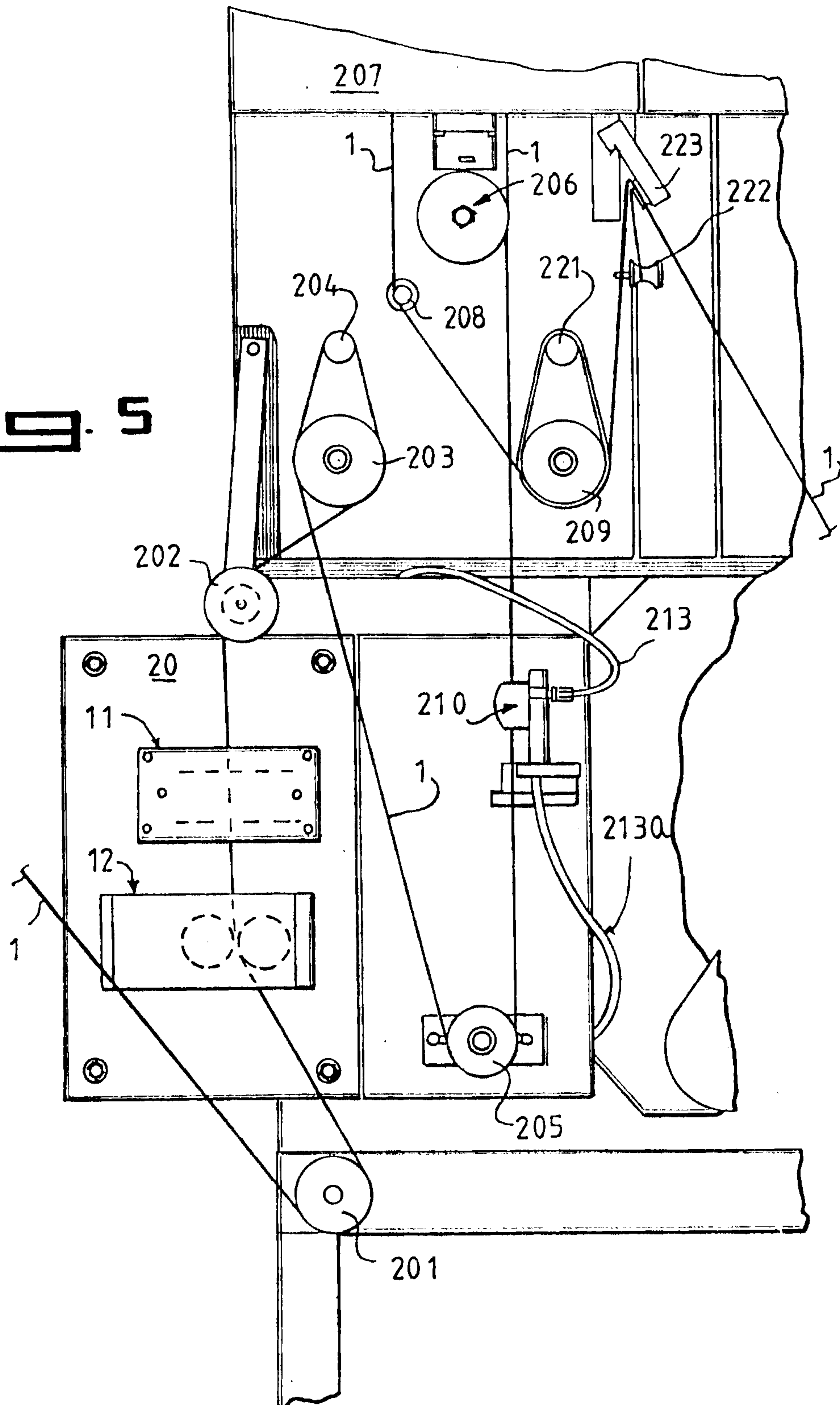


Fig. 5



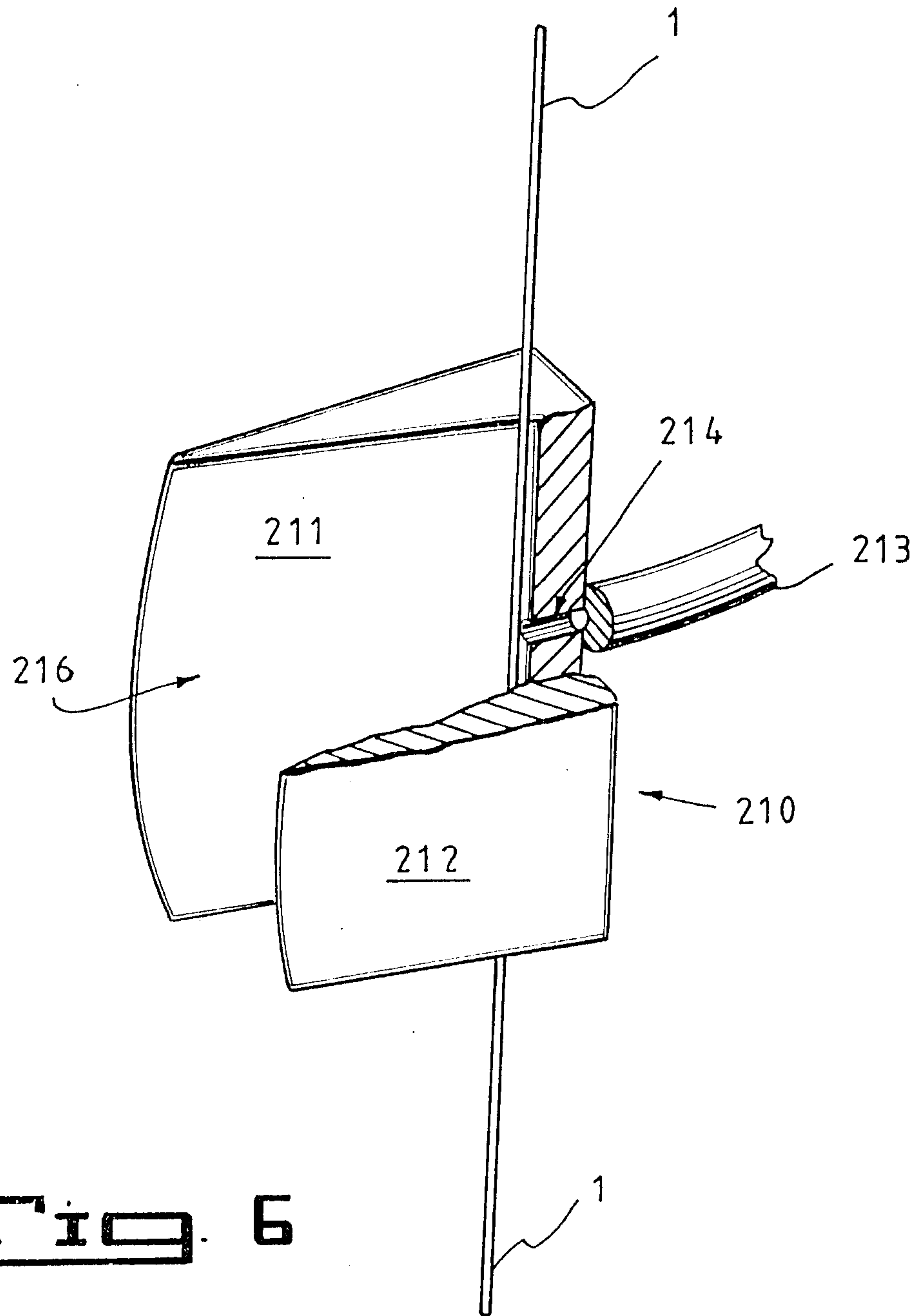


Fig. 6

