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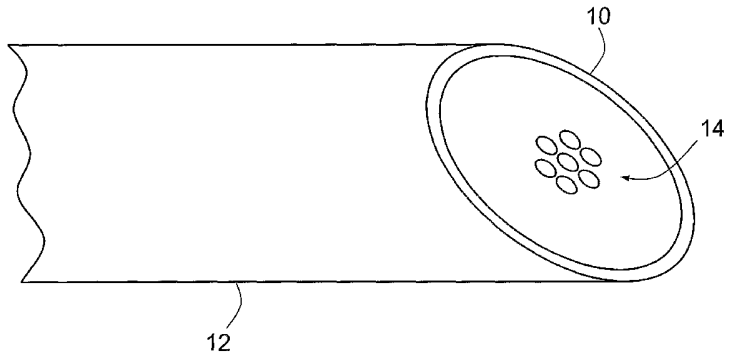
(54) **Title:** FIBRE BUNDLE FOR CONTACT ENDOMICROSCOPY



(57) **Abstract:** A fibre optic bundle (12,32) for use in contact endoscopy or microscopy, comprising a pointed forward tip (10,30) for insertion into a specimen (23,42), the forward tip (10,30) having at least a portion that is oriented obliquely to the longitudinal axis of the bundle (12,32). The forward tip (10,30) may be, for example, flat and oblique.

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FIBRE BUNDLE FOR CONTACT ENDOMICROSCOPY

RELATED APPLICATION

This application is based on and claims the benefit of the filing date of Australian application no. 2005900254 filed 21 January 2005, the content of which is incorporated herein by reference in its entirety.

FIELD OF THE INVENTION

The present invention relates to a fibre bundle for contact microscopy or endomicroscopy.

BACKGROUND OF THE INVENTION

Existing confocal endomicroscopes depend on the contact of a viewing window with the tissue to stabilise the tissue under observation and minimise motion artefacts and to provide a smooth optical interface during the acquisition of images.

One variation of bundle microscopy used by Mauna Kea Technologies (a French company) is to eliminate the window and the lens and to make the tip of the bundle directly touch the tissue to be imaged. This principle was first described by Kapany in 1965 for *in vivo* reflection images of microvasculature with broad-field illumination carried by the same fibre.

Hirano, Yamashita, and Miyakawa (in *Brain Research*, April 1996) report visualising hippocampal cells *in vivo* during anoxia by means of a fibre-optic plate microscope system comparable to that Kapany's system but with an angle polished tip and using fluorescence. US Patent No. 3,556,085 (Nagashige Takahashi) discloses an angle polished tip bundle, but in Takahashi's system illumination is transmitted to the observational field by

a separate bundle of fibres and his system includes a relay lens train within the bundle.

The application of fluorescence and the greater discrimination and sensitivity of confocal systems has greatly extended its range. The x-y resolution in this imaging mode is determined by the inter-core spacing at the contact face, following standard information theory.

Available core/cladding glass combinations can achieve numerical apertures (NAs) of 0.4-0.5, which defines a resolution limit of 4-5 micron. Useful images, however, can be obtained with bundles of 300 microns diameter containing fewer than 10,000 fibres.

SUMMARY OF THE INVENTION

According to a first broad aspect, the present invention provides a fibre optic bundle for use in contact endoscopy or microscopy, comprising:

a pointed forward tip for insertion into a specimen, having at least a portion that is oriented obliquely to the longitudinal axis of the bundle.

The forward tip may be formed flat but oblique, conically, or otherwise, to facilitate passage through a specimen or other sample and/or contact with the specimen.

Thus, the bundle can be used like a needle, to facilitate insertion of the bundle into, for example, tissue. The forward tip is preferably polished.

In one embodiment, the forward tip is at an angle to the longitudinal axis and hence to the propagation direction of incoming excitation light such that the excitation light is not totally internally reflected at an interface

defined by the forward tip and the specimen back into the fibre optic bundle.

The fluorescence of fibre polymer coatings and tip potting materials eliminate current "soft-wound" bundles from this application, but as the bundle is often pushed into tissue like a hypodermic syringe, the stiffness provided by the fused bundle may be a desirable feature.

Angle polishing the tip is very easy to do and facilitates its penetration into tissue.

In certain embodiments, the forward tip is at an angle to the longitudinal axis and hence to a propagation direction of incoming excitation light such that said excitation light is totally internally reflected at an interface defined by the forward tip and the specimen back into the fibre optic bundle. This allows evanescent wave fluorescence microscopy, as incident light directed towards the specimen is totally internally reflected back into the bundle. Fluorescent molecules in close proximity to the tip (less than 1 micron from the surface) are influenced and excited by the evanescent EM field. Fluorescence at such distances is also coupled back into the cores. Hence a confocal evanescent contact mode of microscopy is possible for angles more acute than the critical angle.

It is envisaged that this approach would provide sub-micron z resolution.

Fat droplets or other structures of higher refractive index (RI) within the specimen could also be imaged, such as by coupling the light out from the core. Various detection methods for this light could be envisaged

including detection via adjacent fibres.

Alternatively, the forward tip may be concave or convex so that one part of the forward tip is operating within a critical angle for total internal reflection at an interface defined by the forward tip and the specimen, and another part of the forward tip is not operating within the critical angle. This will typically produce two regions of non-critical angle contact at the tip/specimen interface, separated by a boundary critical angle contact (and hence maximum sensitivity for evanescent wave fluorescence microscopy or the like). That boundary will differ according to the refractive index of the specimen, with two benefits: a greater range of specimen refractive indices are accommodated, and useful information may be ascertainable from the form and location of the boundary.

It should be noted that the z resolution for flat-ended fibre bundle contact microscopy is quoted by Mauna Kea Technologies as 15 microns. This figure would appear to be defined by the distances on the tissue side of the bundle tip plane, so it is not directly comparable with the normal ratio between x-y resolution and optical sectioning ability. In fact it appears to be half this value, which is exactly as should be expected for the NA of the bundle being used.

The anamorphic distortion/aspect ratio introduced by the elliptical profile of the oblique tip should not be too extreme but images may require interpretation. Making images isomorphic using scan ratio changes or by means of software adjustment is relatively easy but may not be necessary, or in fact best for interpretation.

The bundle may further comprise an optical coupler for

coupling return light out from one or more fibre cores of the fibre optic bundle.

In one embodiment, the forward tip has a roughened finish.

The bundle may further comprise a periodic structure of lines or discrete regions provided on the forward tip.

The bundle may further comprise a thin layer of a biologically compatible metal provided on the forward tip, as a thin uniform layer, as thin lines or strips, or as discrete uniform structures

The forward tip may comprise a Bragg grating reflector for light in the fibre optic bundle, such as formed of the aforementioned periodic structures or thin layer of a biologically compatible metal.

According to a second aspect, the invention provides a method of performing contact endoscopy, comprising introducing a fibre optic bundle with a pointed leading tip into a specimen.

The method may further comprise providing the leading tip as a flat and oblique leading tip. Alternatively, the leading tip may be provided as a conical leading tip.

The method may further comprise providing the leading tip at an angle to a propagation direction of incoming excitation light to totally internally reflect the excitation light at an interface defined by the leading tip and the specimen back into the fibre optic bundle.

Alternatively the method may further comprise providing the leading tip at an angle to a propagation direction of

incoming excitation light to avoid totally internally reflecting the excitation light at an interface defined by the leading tip and the specimen back into the fibre optic bundle.

According to this aspect, the leading tip may be polished. Also, the method may include roughening the leading tip (whether after previous polishing or otherwise).

The method may further comprise obtaining return light from those optic fibres in the fibre optic bundle with respective forward tips distal to an exit core tip of an excitation light optic fibre.

The method may further comprise introducing a hypodermic syringe (or equivalent structure) into the specimen and passing the fibre optic bundle down the hypodermic syringe, in order to facilitate correctly locating the leading tip at a desired location in the specimen.

According to a third aspect, the invention provides a method of performing contact endoscopy or microscopy, comprising placing a fibre optic bundle with a pointed leading tip against a specimen.

According to a fourth aspect, the invention provides an endoscope or microscope for use in contact endoscopy or microscopy, comprising: a fibre optic bundle having a pointed forward tip for inserting into or placing against a specimen, the forward tip having at least a portion that is oriented obliquely to the longitudinal axis of the bundle. The fibre optic bundle of this aspect may have any of the features of the fibre optic bundle of the first aspect of the invention described above.

BRIEF DESCRIPTION OF THE DRAWING

In order that the invention may be more clearly ascertained, embodiments will now be described, by way of example, with reference to the accompanying drawing, in which:

Figure 1 is an isomorphic view of an angle polished fibre bundle tip according to an embodiment of the present invention;

Figure 2 is a cross sectional view of the angle polished tip bundle of figure 1;

Figure 3 is a view of a fibre bundle with a conical tip according to another embodiment of the present invention;

Figure 4 is a view of an endoscopic system according to another embodiment of the present invention being used to test meat; and

Figures 5A and 5B are views of further embodiments of respective angle polished fibre bundle tips according to the present invention with, respectively, concave and convex forward tips.

DETAILED DESCRIPTION

Figure 1 is an isomorphic view of an angle polished fibre bundle tip 10 of a bundle 12 according to an embodiment of the present invention, showing the cores 14 of the constituent fibres. The tip 10 is essentially in the form of a planar ellipse.

Figure 2 is a cross sectional view of the forward end of the bundle 12 with its angle-polished tip 10. Light, represented by arrows 27, 28, 29, travels along one of the cores 14 (in this example, representative fibre core 21) and reaches the interface 22 between the angle-polished bundle tip 10 and a specimen in the form of tissue 23. At angles close to the critical angle for total internal

refection (TIR), the EM energy penetrates a substantial distance 24 into the lower RI material of the tissue before it returns into the glass 25 and traverses across the bundle to be absorbed by the black glass outer layer 26.

Figure 3 is a view of a conical tip 30 of a fibre bundle 32 according to another embodiment of the present invention, operating on the same principle.

Figure 4 is a view of an endoscopic system 40 according to another embodiment of the present being used to test a sample of meat 42.

Figures 5A and 5B are isomorphic views of further embodiments of respective angle polished fibre bundle tips 50 and 60 according to the present invention. These fibre bundle tips 50 and 60 are similar to the tip 10 of figure 1, except that the tip 50 of figure 5A is concave and the tip 60 of figure 5B is convex. This means that one part of the forward tip in each case is operating within a critical angle for total internal reflection at the interface between the forward tip and a specimen, and another part of the forward tip is not operating within the critical angle.

The concavity of fibre bundle tip 50 and convexity of fibre bundle tip 60 are ellipsoid, but could be of other forms (including cylindrical or paraboloidal). Further, the degree of concavity or convexity may be selected according to intended application. For example, it may be desirable to employ a higher degree of concavity or convexity with a specimen that has a greater range of refractive indices.

Modifications within the scope of the invention may be readily effected by those skilled in the art. It is to be understood, therefore, that this invention is not limited to the particular embodiments described by way of example hereinabove.

In the claims that follow and in the preceding description of the invention, except where the context requires otherwise owing to express language or necessary implication, the word "comprise" or variations such as "comprises" or "comprising" is used in an inclusive sense, that is, to specify the presence of the stated features but not to preclude the presence or addition of further features in various embodiments of the invention.

Further, any reference herein to prior art is not intended to imply that such prior art forms or formed a part of the common general knowledge.

THE CLAIMS DEFINING THE INVENTION ARE AS FOLLOWS:

1. A fibre optic bundle for use in contact endoscopy or microscopy, comprising:

a pointed forward tip for insertion into a specimen, said forward tip having at least a portion that is oriented obliquely to said longitudinal axis of said fibre optic bundle.

2. A fibre optic bundle as claimed in claim 1, wherein said forward tip is flat and oblique.

3. A fibre optic bundle as claimed in claim 1, wherein said forward tip is conical.

4. A fibre optic bundle as claimed in any one of claims 1 to 3, wherein said forward tip is at an angle to said longitudinal axis and hence to a propagation direction of incoming excitation light such that said excitation light is totally internally reflected at an interface defined by said forward tip and said specimen back into said fibre optic bundle.

5. A fibre optic bundle as claimed in any one of claims 1 to 3, wherein said forward tip is at an angle to said longitudinal axis and hence to a propagation direction of incoming excitation light such that said excitation light is not totally internally reflected at an interface defined by said forward tip and said specimen back into said fibre optic bundle.

6. A fibre optic bundle as claimed in any one of claims 1 to 3, wherein said forward tip is concave or convex so that one part of said forward tip is operating within a critical angle for total internal reflection at an

interface defined by said forward tip and said specimen, and another part of said forward tip is not operating within said critical angle.

7. A fibre optic bundle as claimed in any one of the preceding claims, wherein said forward tip is polished.

8. A fibre optic bundle as claimed in any one of the preceding claims, further comprising an optical coupler for coupling return light out from one or more fibre cores of said fibre optic bundle.

9. A fibre optic bundle as claimed in any one of the preceding claims, wherein said forward tip has a roughened finish.

10. A fibre optic bundle as claimed in any one of the preceding claims, further comprising a periodic structure of lines or discrete regions provided on said forward tip.

11. A fibre optic bundle as claimed in any one of the preceding claims, further comprising a thin layer of a biologically compatible metal provided on said forward tip, as a thin uniform layer, as thin lines or strips, or as discrete uniform structures

12. A fibre optic bundle as claimed in any one of the preceding claims, wherein said forward tip comprises a Bragg grating reflector for light in said fibre optic bundle.

13. A method of performing contact endoscopy, comprising introducing into a specimen a fibre optic bundle with a pointed leading tip.

14. A method as claimed in claim 13, further comprising providing said leading tip as a flat and oblique leading tip.

15. A method as claimed in claim 13, further comprising providing said leading tip as a conical leading tip.

16. A method as claimed in any one of claims 13 to 15, further comprising providing said leading tip at an angle to a propagation direction of incoming excitation light to totally internally reflect said excitation light at an interface defined by said leading tip and said specimen back into said fibre optic bundle.

17. A method as claimed in any one of claims 13 to 15, further comprising providing said leading tip at an angle to a propagation direction of incoming excitation light to avoid totally internally reflecting said excitation light at an interface defined by said leading tip and said specimen back into said fibre optic bundle.

18. A method as claimed in any one of claims 13 to 17, wherein said leading tip is polished.

19. A method as claimed in any one of claims 13 to 18, including roughening said leading tip.

20. A method as claimed in any one of claims 13 to 19, further comprising obtaining return light from those optic fibres in said fibre optic bundle with respective forward tips distal to an exit core tip of an excitation light optic fibre.

21. A method as claimed in any one of claims 13 to 20, further comprising introducing a hypodermic syringe into

said specimen and passing said fibre optic bundle down said hypodermic syringe.

22. A method of performing contact endoscopy or microscopy, comprising placing a fibre optic bundle with a pointed leading tip against a specimen.

23. A method as claimed in claim 22, wherein said leading tip is flat and oblique.

24. An endoscope or microscope for use in contact endoscopy or microscopy, comprising:

a fibre optic bundle having a pointed forward tip for inserting into or placing against a specimen, said forward tip having at least a portion that is oriented obliquely to the longitudinal axis of said fibre optic bundle.

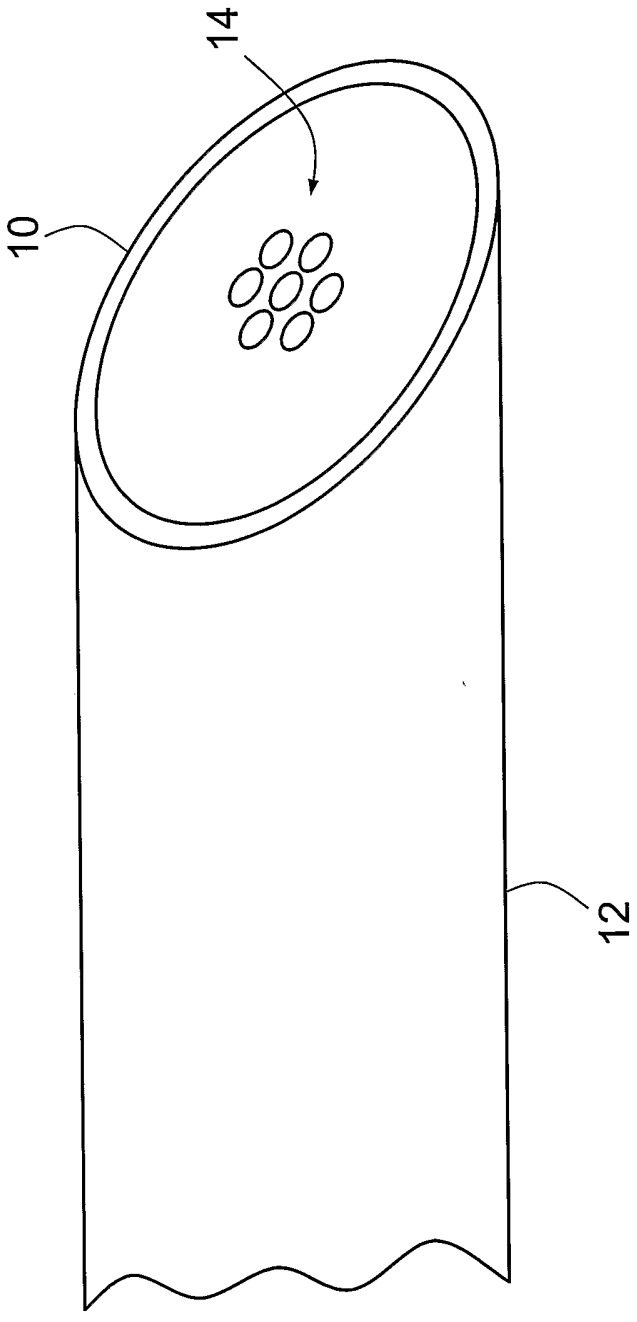

Figure 1

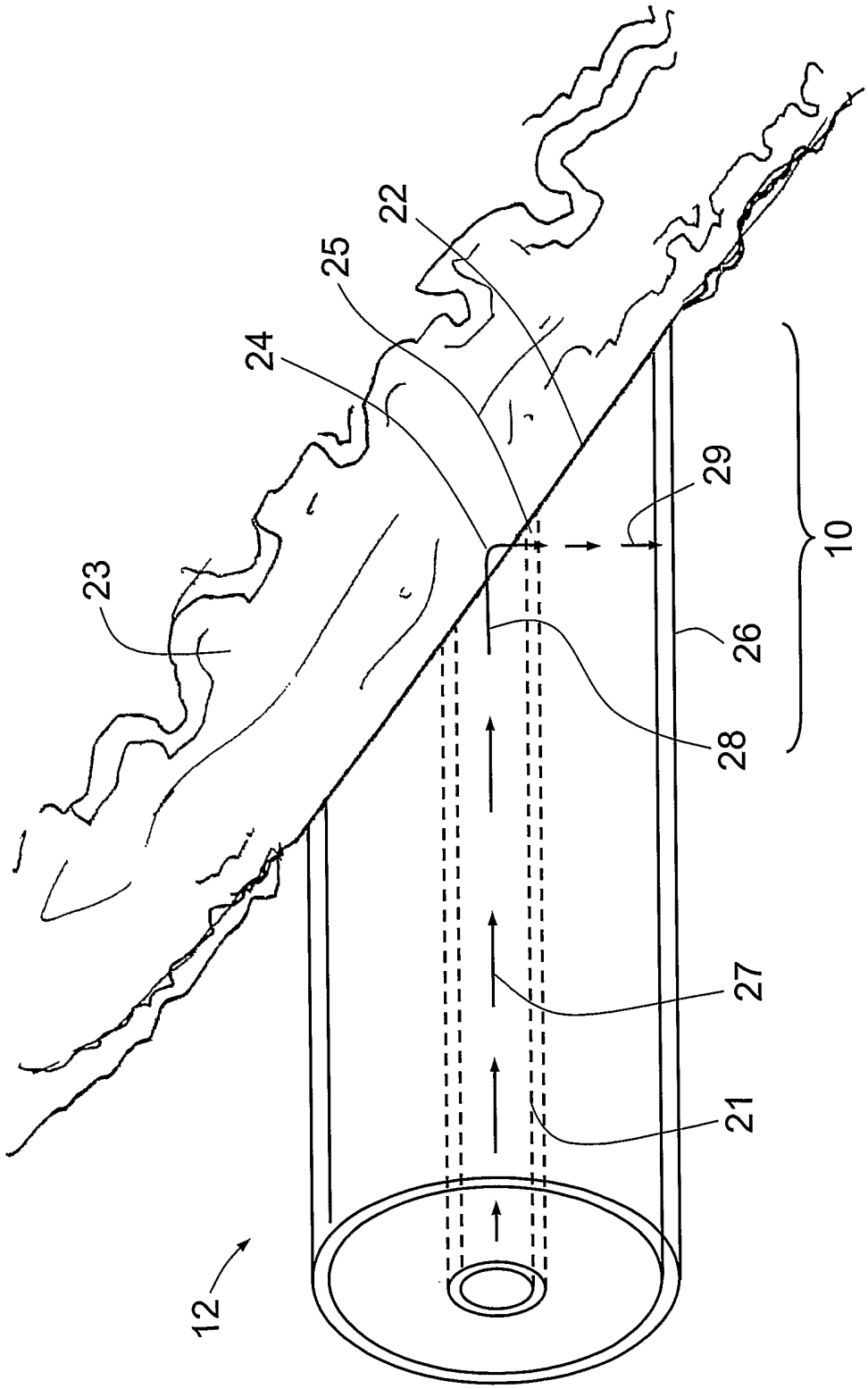

Figure 2

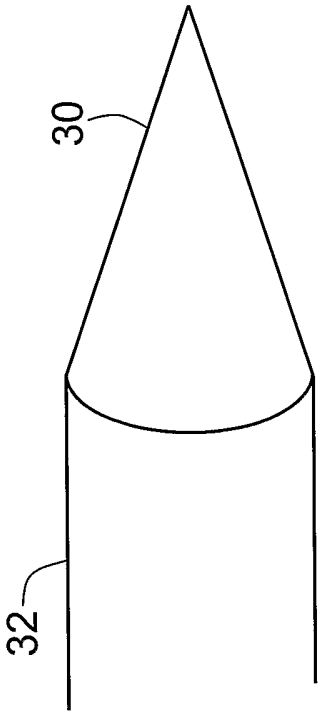

Figure 3

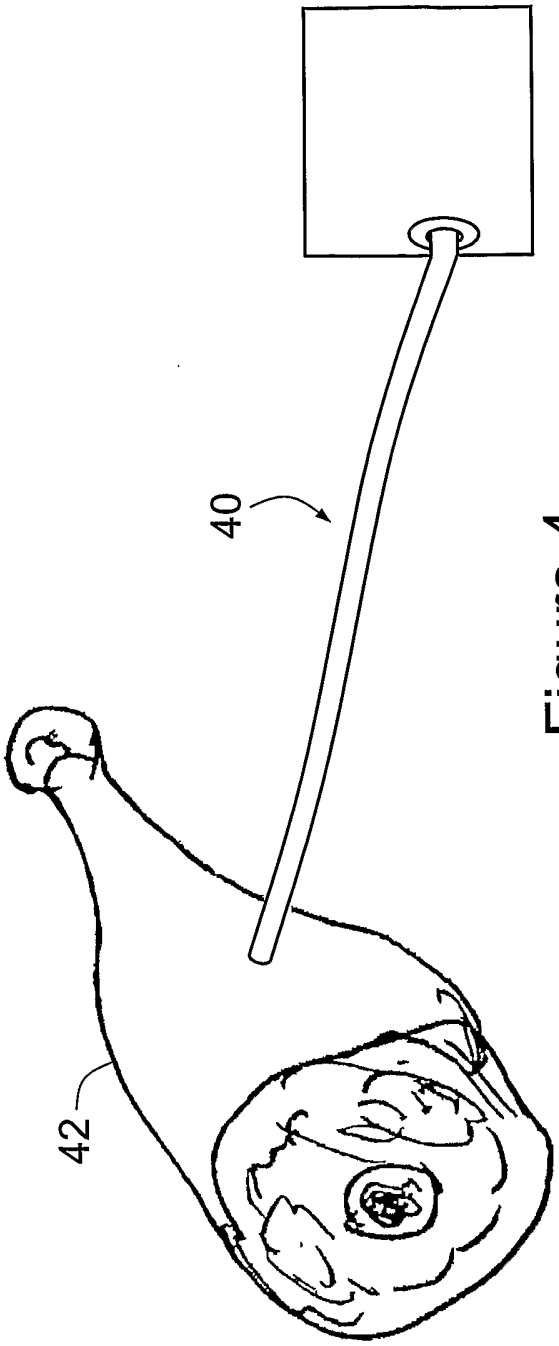

Figure 4

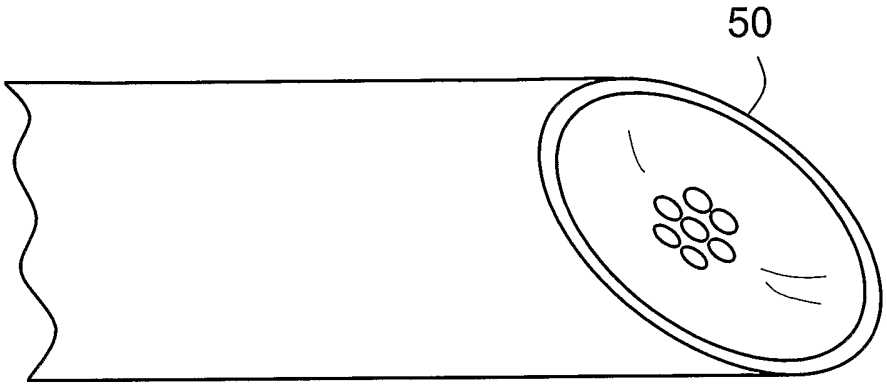

Figure 5A

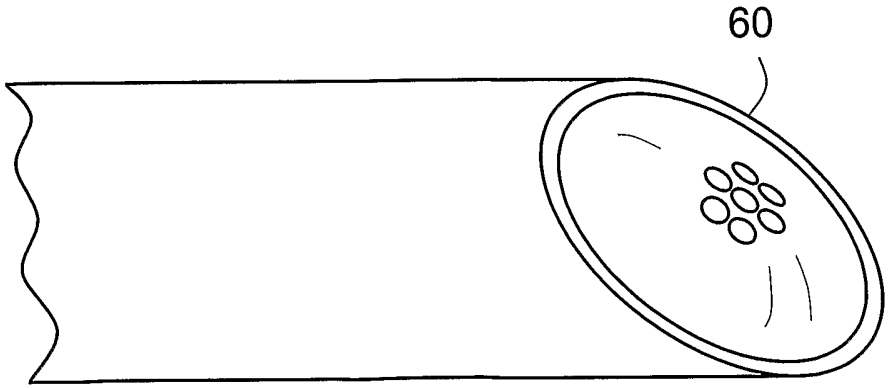

Figure 5B

INTERNATIONAL SEARCH REPORT

International application No.
PCT/AU2005/001954

A. CLASSIFICATION OF SUBJECT MATTER

Int. Cl. ***A61B 1/07*** (2006.01) ***G02B 6/04*** (2006.01)

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

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)
DWPI and keywords: fibre and optic and oblique and end and similar terms

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
	US 2004/0127776 A1 (WALKER et al.) 1 July 2004	
X	Paragraphs 35 and 36	1,2,4,7,8,13, 14,16,18,22-24
Y		3,9,15,19,21
	US 3556085 A (TAKAHASHI) 19 January 1971	
X	Column 2 lines 16 to 20	1,2,4,7,8,13, 14,16,18,22-24
Y		3,9,15,19,21
	US 5554100 A (LEINER et al.) 10 September 1996	
X	Column 2 lines 45 to 59	1,2,7,8,13,14, 18,22-24
Y		3,9,15,19,21

[X] Further documents are listed in the continuation of Box C [X] See patent family annex

* Special categories of cited documents:

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"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
03 February 2006	9 FEB 2006
Name and mailing address of the ISA/AU AUSTRALIAN PATENT OFFICE PO BOX 200, WODEN ACT 2606, AUSTRALIA E-mail address: pct@ipaustralia.gov.au Facsimile No. (02) 6285 3929	Authorized officer D. Melhuish **DAVID MELHUISH** Telephone No : (02) 6283 2426

INTERNATIONAL SEARCH REPORT

International application No.
PCT/AU2005/001954

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 4615333 A (TAGUCHI) 7 October 1986 Column 5 lines 46 to 57	1,2,7,8,13,14, 18,22-24
Y		3,9,15,19,21
Y	WO 1991/006251 A1 (SURGILASE INC.) 16 May 1991 Page 8 last line to page 9 line 8	3,9,15,19,21
Y	WO 2001/026542 A1 (C.R. BARD, INC.) 19 April 2001 Page 5 lines 23 to 30	3,9,15,19,21

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No.
PCT/AU2005/001954

This Annex lists the known "A" publication level patent family members relating to the patent documents cited in the above-mentioned international search report. The Australian Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

Patent Document Cited in Search Report		Patent Family Member					
US	2004127776	AU	2003274980	WO	2004026363		
US	3556085						
US	5554100	US	5651759	US	5718664	US	6152872
US	4615333	DE	3503538				
WO	0126542	AU	13340/01	US	6308092		
WO	9106251						

Due to data integration issues this family listing may not include 10 digit Australian applications filed since May 2001.

END OF ANNEX