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- *before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments (Rule 48.2(h))*

(54) Title: NEUROSURGICAL DEVICE AND METHOD

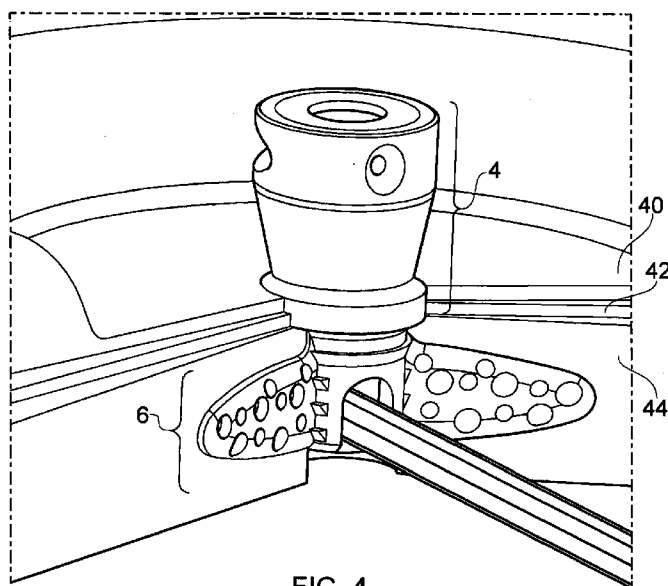


FIG. 4

(57) Abstract: A skull mountable, implantable percutaneous fluid delivery device (2; 52; 82; 02) is described for use in delivering fluids to target sites in the brain. The device (2; 52; 82; 102) includes a subcutaneous base portion (6; 56; 86) comprising one or more ports for supplying fluid to one or more implanted catheter devices (18). A percutaneous portion (4; 54; 84; 104) of the device comprises an extracorporeal surface (10), the one or more ports of the subcutaneous base portion (6; 56; 86; 106) being accessible from the extracorporeal surface (10) of the percutaneous portion (4; 54; 84; 104). The subcutaneous base portion (6; 56; 86) is at least partially insertable into a complementary recess formed in a bone (44; 140) and comprises one or more anchoring features comprising at least one radially protruding wing (24; 62; 88; 124) for directly anchoring the subcutaneous base portion (6; 56; 86; 106) to the bone (44; 140).

Neurosurgical Device and Method

The present invention relates to drug delivery apparatus and in particular to improved neurological drug delivery apparatus comprising a skull mountable percutaneous fluid delivery device.

The drug treatment of a number of neuro-degenerative disorders, hereditary neurological disorders, brain tumours and other diseases of the nervous system are compromised by the presence of the blood brain barrier which prevents the transfer of drugs from the vascular system or cerebrospinal fluid into the brain substance. Examples of drugs which do not adequately cross the blood brain barrier include protein molecules such as neurotrophins, monoclonal antibodies, viral particles for delivery of gene therapy, as well as a number of cytotoxic drugs for the treatment of tumours. It has been described previously how such drugs can be delivered to the brain by direct infusion into the parenchyma via one or more indwelling catheter. For example, a guide tube and catheter system is described in US6609020. A catheter with a small external diameter that can be precisely positioned in the brain is described in WO2003/077785. Percutaneous access ports have also been described in WO2008/062173 and WO2011/098769.

The percutaneous fluid delivery devices described in WO2011/098769 comprise a subcutaneous base portion that can be inserted into a recess formed in bone. One or more features on the base portion act to grip the bone and thereby secure the device to the subject. Although such a device performs well, it has been found that detachment of the device may occur when implanted in certain animal models. The present invention thus relates to an improvement to the percutaneous fluid delivery device of WO2011/098769.

According to a first aspect of the invention, an implantable percutaneous fluid delivery device is provided that comprises;

a subcutaneous base portion comprising one or more ports for supplying fluid to one or more implanted catheter devices, and

a percutaneous portion comprising an extracorporeal surface, the one or more ports of the subcutaneous base portion being accessible from the extracorporeal surface of the percutaneous portion,

wherein the subcutaneous base portion is at least partially  
5 insertable into a complementary recess formed in a bone and comprises one or more anchoring features for directly anchoring the subcutaneous base portion to the bone,

characterised in that the one or more anchoring features comprise at least one radially protruding wing.

10

The present invention thus relates to an implantable percutaneous fluid delivery device or port unit for use in delivering fluid, such as therapeutic agents, to selected targets within the body. The implantable percutaneous fluid delivery device has one or more outlets or ports that are separately connectable to one or  
15 more implanted catheter devices. The implantable percutaneous fluid delivery device is particularly suited for use in delivering therapeutic agents to targets within the brain using one or more associated implanted intraparenchymal catheter devices.

20 The implantable percutaneous fluid delivery device comprises a subcutaneous base portion comprising one or more ports for supplying fluid to one or more implanted catheter devices. The term subcutaneous as used herein is intended to define a location below the outer surface of the skin. As described below, the subcutaneous base portion is preferably implantable below all of the skin. A  
25 percutaneous portion is also provided as part of the device that extends from the subcutaneous base portion and comprises an extracorporeal surface. As would be understood by those skilled in the art, when implanted a percutaneous device crosses the skin to provide a connection between the inside and outside of the body. The one or more ports of the subcutaneous base portion are accessible from  
30 the extracorporeal surface of the percutaneous portion; in other words, the extracorporeal surface (i.e. a surface accessible from outside of the body) provides fluidic access to the one or more outlet ports of the subcutaneous base portion of

the device. It should be noted that the subcutaneous base portion and percutaneous portion may be formed together or may be formed as separate components that are attached together before use.

- 5 The subcutaneous base portion of the device of the first aspect of the present invention has one or more anchoring features for directly anchoring the subcutaneous base portion to the bone. In particular, the one or more anchoring features comprise at least one radially protruding wing. The provision of such a radially protruding wing has been found to stabilise the device and allow more  
10 secure attachment to bone. This is especially advantageous when implanting the device in thin skull bones that are covered in muscle. The device is thus preferably used for non-human subjects, such as primates.

Any number of radially protruding wings may be provided. Advantageously, the  
15 device comprises a plurality of radially protruding wings. Preferably, three or more radially protruding wings are provided. In a preferred embodiment, three radially protruding wings are provided; these may be spaced apart from one another by approximately 120 degrees. Alternatively, three radially protruding wings may be provided that are spaced apart by approximately 90 degrees.

20 The device may comprise a subcutaneous base portion having a central hub for press fit attachment to a hole formed in the skull. The central hub may include any of the features described in WO2011/098769. In addition, said at least one radially protruding wing preferably extends from the central hub. The central hub may be  
25 approximately cylindrical. The central hub may have a radius. Each wing preferably extends radially from the hub by a distance greater than half the radius of the hub. Each wing may radially extend from the hub by a distance that is greater than the radius of the hub. Each wing may radially extend from the hub by at least 0.5mm, more preferably by at least 1mm, more preferably by at least  
30 2mm, more preferably by at least 3mm or more preferably by at least 4mm.

The radially protruding wings may be of any suitable shape. Advantageously,

each radially protruding wing has a rounded distal end or tip. Some or all of the radially protruding wings may comprise an aperture for receiving a bone screw. The wing may then be secured to the skull by a screw. This may aid attachment to the subject prior to the osseointegration of the device. Each wing may curve  
5 upwards (i.e. away from the subject) as it extends radially. The distal end of each wing may sit on the surface of the bone. For example, the distal end of each wing may sit on the surface of the bone adjacent the aperture in the bone that is formed to receive the central hub.

10 Each radially protruding wing may comprise one or more apertures to promote osseointegration. Each radially protruding wing preferably comprises a plurality of apertures extending through the wing to promote osseointegration. For example, each radially protruding wing may comprise a substrate (e.g. a sheet of metal) with one or more holes formed therein. Alternatively, each radially protruding  
15 wing may be formed from a mesh (e.g. a “chicken wire” type structure) or from a porous material. Such structures allow bone to grow through the apertures to anchor the device to the bone.

Advantageously, at least part of the subcutaneous base portion comprises a  
20 coating or surface texture to promote osseointegration. The coating or surface texture may be applied to the at least one radially protruding wing and/or to any central hub.

When implanted, at least part (and preferably most) of the subcutaneous base  
25 portion is located below the outer surface of a bone. The device preferably includes a feature or features that allow the depth of insertion of the device into an appropriate recess formed in a bone to be predefined. Advantageously, the subcutaneous base portion comprises a protruding lip or step(s) for engaging the outer surface of a bone around the periphery of a recess formed in that bone. Such  
30 a lip thus sits on the outermost bone surface when inserted and, as well as setting the depth of insertion, also allows the device to be implanted in a hole that passes all the way through a bone.

The device may be made using any suitable manufacturing technique. For example, by machining, selective laser sintering or 3D printing.

- 5 The invention also extends to a device as described above in combination with at least one neurosurgical catheter.

The invention also extends to a device as described above in combination with a fluid connector for attachment to the extracorporeal surface to provide fluid access  
10 to said one or more ports.

The invention also extends to a method of neurosurgery. The method may include the steps of forming a recess in the skull of a subject and implanting a device as described above in said recess. The surgically formed recess may be shaped to  
15 receive the device. The implantation technique described in WO2011/098769 is preferably used.

As explained above, the present invention is an improvement to the device that is described in WO2011/098769. The whole contents of WO2011/098769 are thus  
20 incorporated herein by reference. The device of the present invention may thus further comprise any feature described in WO2011/098769.

The invention will now be described, by way of example only, with reference to the accompanying drawings in which:  
25

Figure 1 shows a percutaneous fluid delivery device of the present invention,

Figure 2 is an alternative view of the device of figure 1,

30 Figure 3 illustrates the device when implanted as viewed from the exterior of the subject,

Figure 4 is a cut-away view of the device when implanted,

Figure 5 shows a first variant of the device of figure 1,

5 Figure 6 shows a further variant of the device of figure 1,

Figure 7 shows a screw anchored variant of the device of figure 1, and

Figure 8 shows the device of figure 7 when screwed in place.

10

Referring to figures 1 and 2, an implantable percutaneous fluid delivery device 2 of the present invention is illustrated.

The device 2 comprises a percutaneous portion 4 and a subcutaneous base portion  
15 6. The percutaneous portion 4 includes a transcutaneous region 8 that is roughened to promote skin adhesion and an extracorporeal surface 10. The side walls of the extracorporeal surface 10 are smooth to allow cleaning. A septum seal 12 is accessible via a top surface 14. The septum seal 12 provides fluidic access to ports provided in the subcutaneous base portion 6 that are also connected to a  
20 four-lumen supply tube 16. The supply tube 16 is further connected to four intracranial fluid delivery catheters 18 via a fluid hub 20. The device 2 may be formed as a single piece or from multiple parts and may include any of the internal or external configurations that are described in detail in WO2011/098769.

25 The present invention relates to the improved subcutaneous base portion 6. The base portion 6 comprises a central hub 22 that comprises broaching fins or ribs 23 for engaging and gripping a complementary hole formed in the bone of a subject. The central hub 22 also includes three radially protruding wings 24. In other words, the device has a longitudinal axis L that is typically arranged to be  
30 approximately perpendicular to the surface of the bone, when implanted. The wings 24 extend outwardly from the central hub 22 in directions perpendicular to the longitudinal axis L (i.e. they extend radially). The bone recess that is formed

in the subject prior to implantation of the device will thus include a central aperture for receiving the central hub 22 and three radially extending slots corresponding to the size and spacing of the radially protruding wings 24. Each of the radially protruding wings 24 also comprises multiple apertures 26. These  
5 apertures 26 help promote osseointegration (i.e. bone can grow through the apertures thereby securing the device in place). Although three equidistantly spaced wings are shown, it should be noted that a different number of wings could be provided and the radial spacing could be altered as required.

10 The implantable percutaneous fluid delivery device may be used as part of the drug delivery apparatus described in WO2011/098769. For example, the percutaneous fluid delivery device may be connected to one or more implantable intracranial catheters.

15 Referring to figure 3, there is provided an illustration of how the device will sit in the skin (i.e. dermis 40) after the graft has taken. It should be noted that the sunken area is where the hypodermal layers have been removed and the dermal layer has adhered to the periosteum.

20 Figure 4 shows a sectioned view of the device implanted into the model's skull. The dermis 40, periosteum 42 and bone 44 are shown. Again, it can be noted how the bone is shown following a period of healing. During surgical implantation, burred and/ or drilled bone fragments are preferably packed back in around the implanted device to maximise rate of recovery.

25

Figure 5 shows an implantable percutaneous fluid delivery device 52 that has a similar structure to the device described above with reference to figures 1 to 4. The device 52 comprises a percutaneous portion 54 and a subcutaneous base portion 56. The percutaneous portion 54 is similar to the percutaneous portion 4  
30 described above, although the transcutaneous region 58 is longer than that described above to reduce dermal growth over the device.



The subcutaneous base portion 56 comprises a central hub 60 and three protruding wings 62 (noting that only two of the wings 62 are illustrated in the cross-sectional view of figure 5). The central hub 60 is approximately cylindrical and has a central longitudinal axis L and a radius r. The wings 62 protrude radially from the hub 60 and have a radial length w. As explained above, it is preferred the distance w that the wings extend from the hub is greater than half the radius r of the hub. In this example, the wings 62 extend from the hub 60 by a distance w that is slightly larger than the radius r. In this example, the three wings 62 are spaced 90° apart from each other around the hub, with a supply tube exiting the hub 60 at the position 64 shown as hatched outline in figure 5. Although small broaching fins 66 are also provided to aid press-fit attachment to the hole formed in the skull, the three wings 62 provide stabilisation of the device within the bone.

Figure 6 shows an implantable percutaneous fluid delivery device 82 that has a similar structure to the devices described above with reference to figures 1 to 5. The device 82 also includes a percutaneous portion 84 and a subcutaneous base portion 86. The device 82 has a central hub 90 and three protruding wings 88. Each wing 88 lies in a plane that includes the longitudinal axis L. The wings 88 do not extend the full length of the subcutaneous base portion 86. Instead, the lower ends of the wings 88 are set back from the distal (lower) end of the subcutaneous base portion 86. Similarly, the upper ends of the wings 88 are set back from the proximal (upper) end of the subcutaneous base portion 86.

Although figure 6 is for illustration purposes only and is not drawn to scale, the radial tips of the wings 88 are located approximately 5.5mm from the longitudinal axis L. The lower and upper ends of the wings 88 are also set back approximately 2mm and 1mm respectively from the lower and upper ends of the subcutaneous base portion 86. It should, of course, be noted that these dimensions are provided for the purpose of illustrating the invention and should not be seen as limiting the size of devices that may be provided in accordance with the present invention. Providing wings as illustrated in figure 6 has been found to be advantageous as it allows the device 82 to be implanted in areas of the skull with larger curvatures;

i.e. it ensures the wings do not penetrate the skin or dig deeper into the skull when the skull curves away from the hub.

Referring to figures 7 and 8, a further implantable percutaneous fluid delivery  
5 device 102 is illustrated.

The device 102 includes a percutaneous portion 104 and a subcutaneous base  
portion 106. The percutaneous portion 104 is similar to those described above  
with reference to figures 1 to 6. The subcutaneous base portion 106 comprises a  
10 central hub 122 with fins or ribs 123 for engagement with a bone recess. Three  
wings 124 protrude from the central hub 122. The wings 124 are radially spaced  
apart by 90° and a supply tube exit 110 (shown in hatched outline in figures 7 and  
8) is provided radially opposite one of the wings 124. Each wing 124 has a  
proximal end attached to the central hub 122. The distal end of each wing 124  
15 includes an aperture 130 for securing the wing 124 to the bone of the subject with  
a bone screw 132. A plurality of holes 134 are provided near the proximal end of  
each wing 124 to promote osseointegration.

Figure 7 shows the device 102 and bone screws 132 prior to use, whilst figure 8  
20 illustrates the device 102 and bone screws 132 after implantation in a subject. The  
bone 140, temporal fascia 142 and dermis 144 are also illustrated in figure 8. It can  
be seen that the central hub 122 and proximal ends of each wing 124 lie within a  
recess formed with the bone 140. Each wing 124 is shaped to curve upwardly  
towards the surface of the bone layer and to have a distal end (comprising the  
25 aperture 130) that sits on the surface of the bone. This allows attachment of the  
device to the bone 140 using bone screws 132, thereby immediately securing the  
device to the subject. Osseointegration can then occur on a slower time scale to  
further secure the device in place, but the screws 132 allow the device to be used  
immediately after implantation and stabilise the device whilst osseointegration  
30 takes place.

Claims

1. An implantable percutaneous fluid delivery device, comprising;  
a subcutaneous base portion comprising one or more ports for  
5 supplying fluid to one or more implanted catheter devices, and  
a percutaneous portion comprising an extracorporeal surface, the  
one or more ports of the subcutaneous base portion being accessible from the  
extracorporeal surface of the percutaneous portion,  
wherein the subcutaneous base portion is at least partially  
10 insertable into a complementary recess formed in a bone and comprises one or  
more anchoring features for directly anchoring the subcutaneous base portion to  
the bone,  
characterised in that the one or more anchoring features comprise  
at least one radially protruding wing.  
15
2. A device according to claim 1, comprising a plurality of radially  
protruding wings.
3. A device according to any preceding claim, comprising three or more  
20 radially protruding wings.
4. A device according to any preceding claim, comprising three radially  
protruding wings.
- 25 5. A device according to claim 4, wherein the radially protruding wings are  
spaced apart from one another by approximately 120 degrees.
6. A device according to any preceding claim, wherein the subcutaneous base  
portion comprises a central hub for press fit attachment to a hole formed in the  
30 skull, said at least one radially protruding wing extending from the central hub.
7. A device according to any preceding claim, where each radially protruding

wing has a rounded distal end.

8. A device according to any preceding claim, wherein each radially protruding wing comprises one or more apertures to promote osseointegration.

5

9. A device according to claim 8, wherein each radially protruding wing comprises a plurality of apertures extending through the wing to promote osseointegration

10 10. A device according to any preceding claim, wherein at least part of the subcutaneous base portion comprises a coating or surface texture to promote osseointegration.

11. A device according to any preceding claim, comprising a lip to set the  
15 depth of insertion of the device into a bone recess.

12. Neurosurgical apparatus comprising a device according to any preceding claim and at least one neurosurgical catheter.

20 13. Neurosurgical apparatus comprising a device according to any one of claims 1 to 11 and a fluid connector for attachment to the extracorporeal surface to provide fluid access to said one or more ports.

25 14. A method of neurosurgery, comprising the steps of forming a recess in the skull of a subject and implanting a device according to any one of claims 1 to 11 in said recess, the recess being shaped to receive the device.

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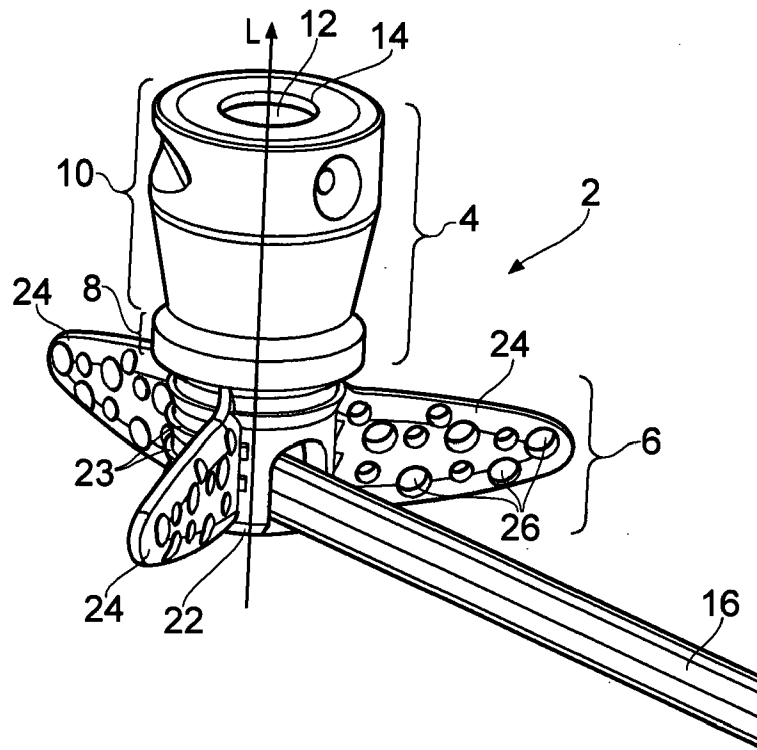


FIG. 1

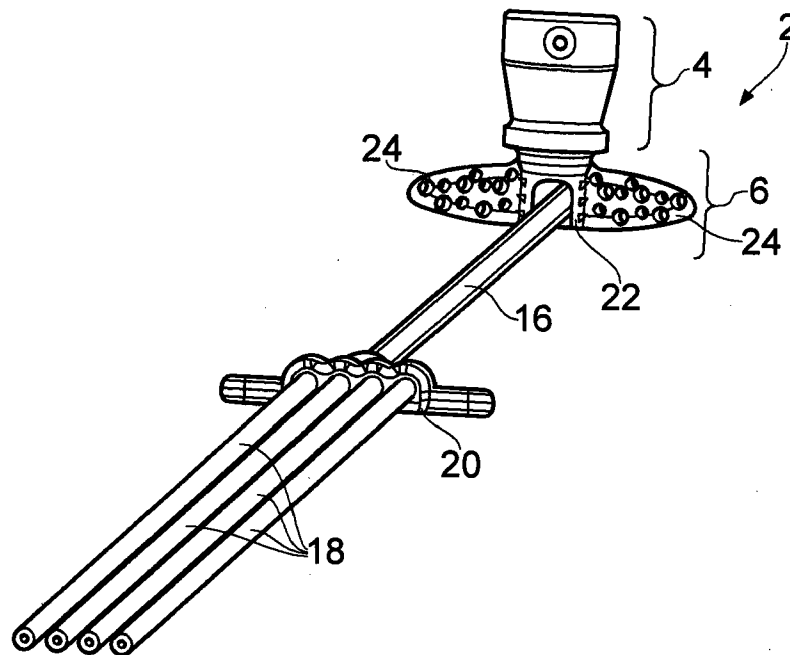


FIG. 2

2/4

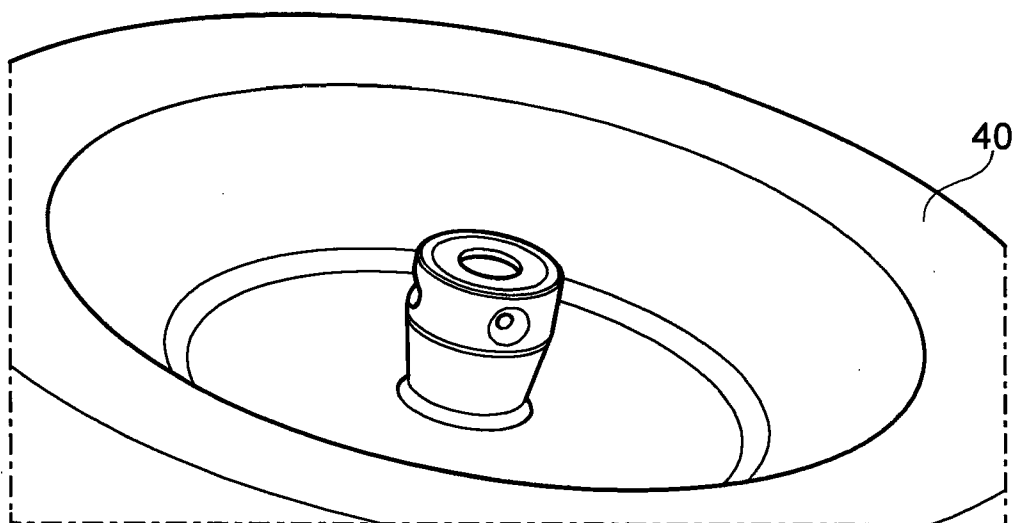


FIG. 3

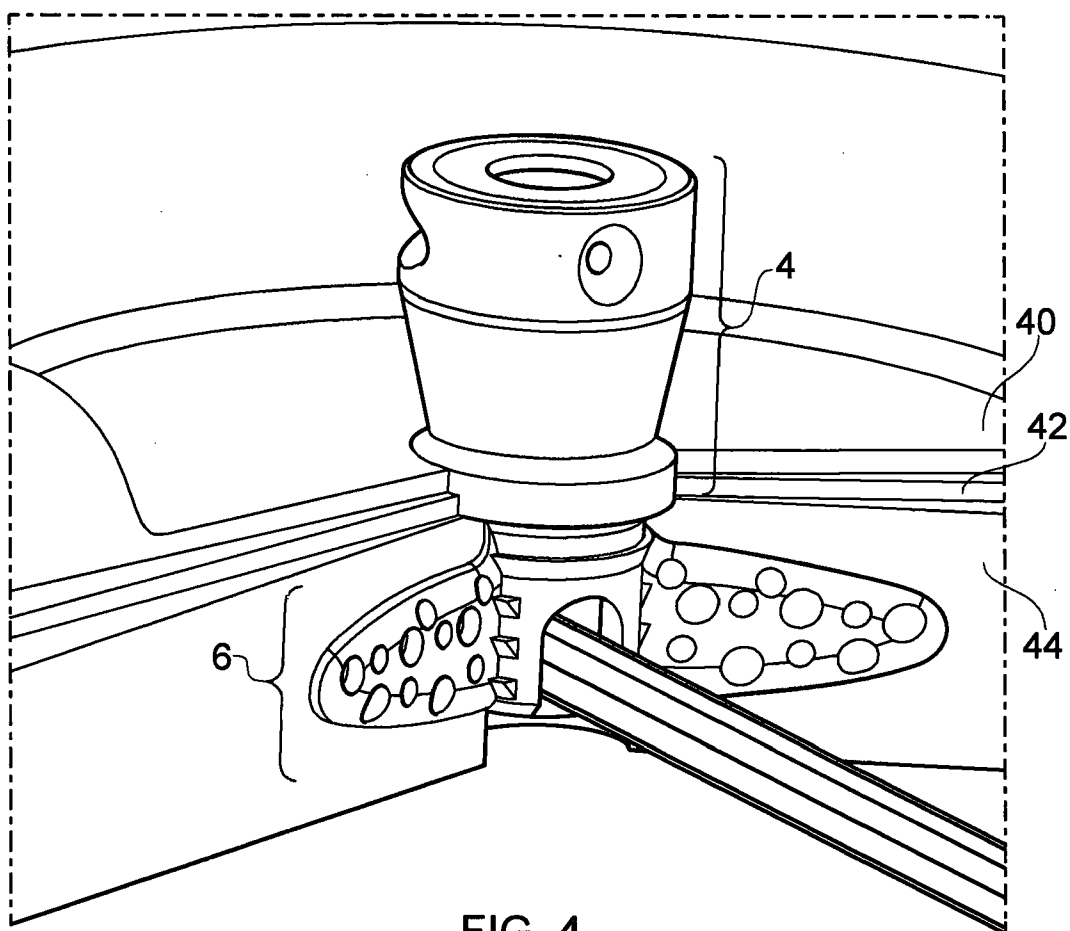
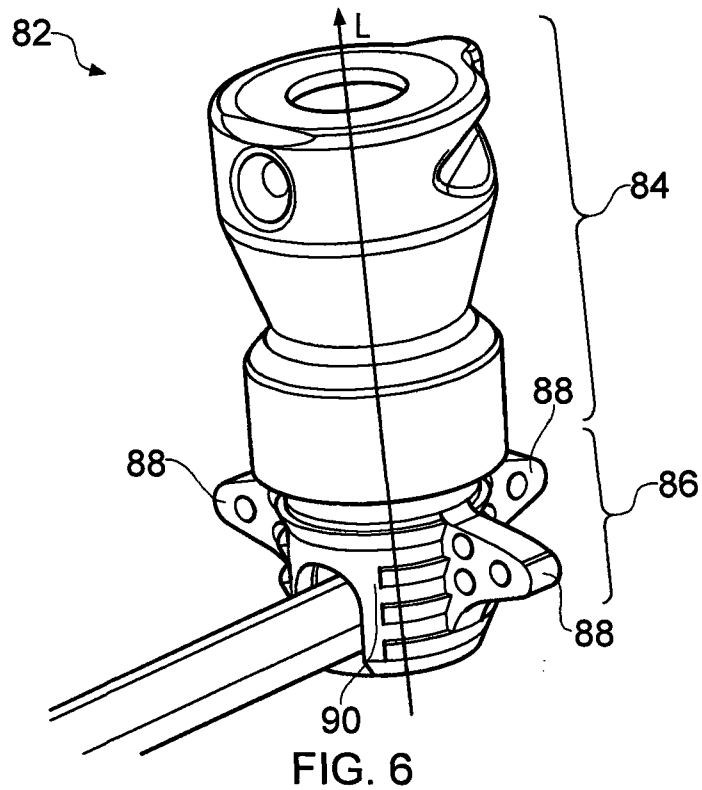
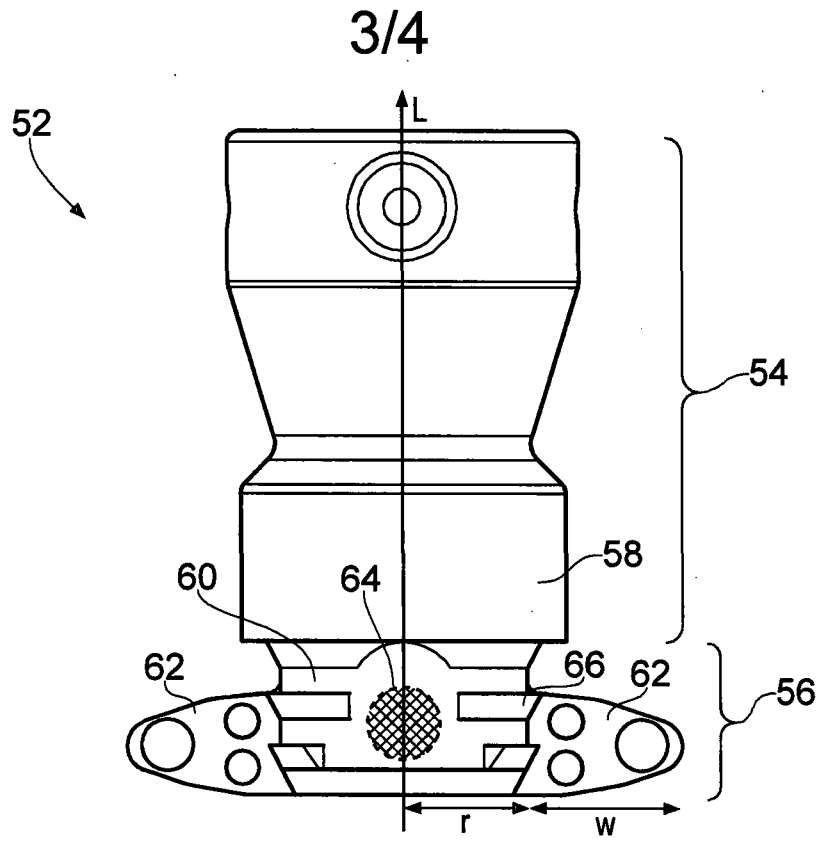


FIG. 4



4/4

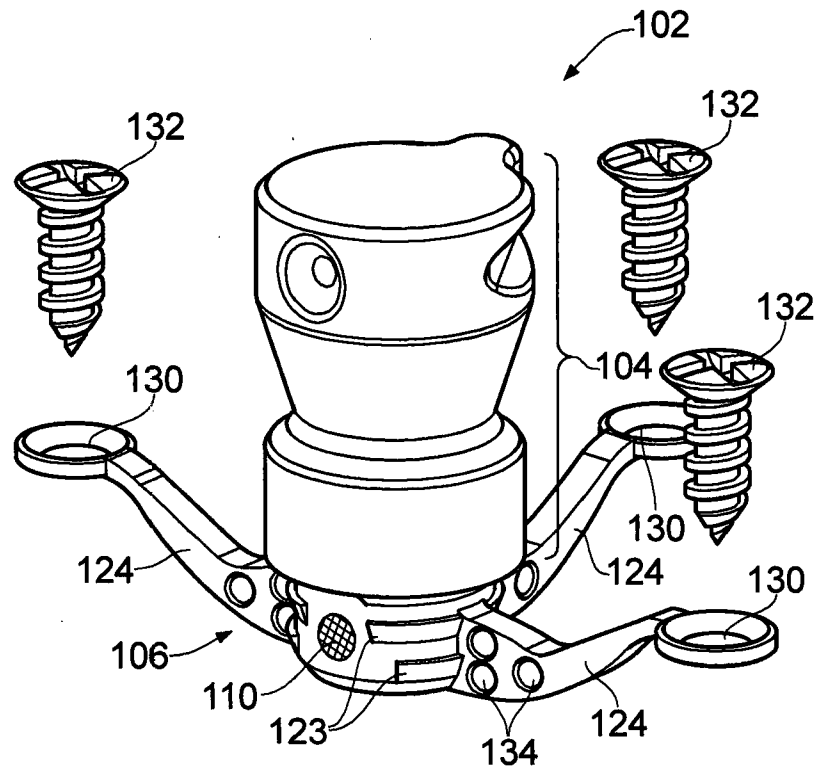


FIG. 7

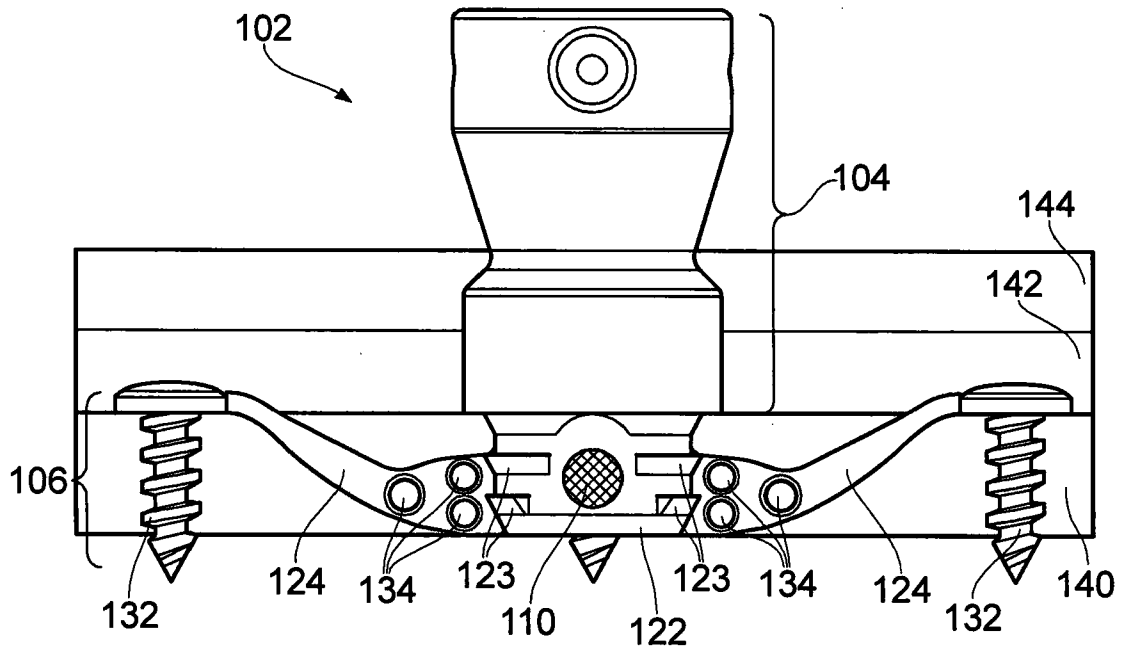


FIG. 8



## INTERNATIONAL SEARCH REPORT

International application No  
PCT/GB2013/052559

A. CLASSIFICATION OF SUBJECT MATTER  
INV. A61M39/02  
ADD.

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)  
A61M

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)

EPO-Internal, WPI Data

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 96/29953 A1 (FOX WILLIAM CASEY [US]) 3 October 1996 (1996-10-03) abstract claim 1 figures 1-6	1-13
X	US 2008/287910 A1 (PICHA GEORGE J [US]) 20 November 2008 (2008-11-20) abstract figures	1-13
X	EP 1 481 697 A1 (CODMAN & SHURTLEFF [US] JOHNSON & JOHNSON PROFESSIONAL [US]) 1 December 2004 (2004-12-01) abstract figures	1-13
	-/-	



Further documents are listed in the continuation of Box C.



See patent family annex.

\* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search

23 January 2014

Date of mailing of the international search report

31/01/2014

Name and mailing address of the ISA/

European Patent Office, P.B. 5818 Patentlaan 2  
NL - 2280 HV Rijswijk  
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Fax: (+31-70) 340-3016

Authorized officer

Türkavci, Levent

## INTERNATIONAL SEARCH REPORT

International application No

PCT/GB2013/052559

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	DE 201 15 120 U1 (DISETRONIC LICENSING AG [CH]) 7 March 2002 (2002-03-07) abstract figures -----	1-13

# INTERNATIONAL SEARCH REPORT

International application No.  
PCT/GB2013/052559

## Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.: 14  
because they relate to subject matter not required to be searched by this Authority, namely:  
see FURTHER INFORMATION sheet PCT/ISA/210
2. ☐ Claims Nos.:  
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fees, this Authority did not invite payment of additional fees.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

### Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.
- ☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.
- ☐ No protest accompanied the payment of additional search fees.

**FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210**

Continuation of Box II.1

Claims Nos.: 14

Rule 39.1(iv) PCT - Method for treatment of the human or animal body by surgery The method according to independent claim 14 defines a surgery method practised on the human body because it claims forming a recess in the skull. So the International Searching Authority is not required to perform a search regarding claim 14 (Rule 35 and 39.1 (iv) PCT).

# INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/GB2013/052559

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