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(54) APPARATUS FOR BRAIN FIBER BUNDLE MICROSCOPY

VORRICHTUNG FÜR FASERBÜNDELMIKROSKOPIE DES GEHIRNS

APPAREIL DE MICROSCOPIE À FAISCEAU DE FIBRES DE CERVEAU

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Description

BACKGROUND

Field of the Present Disclosure

[0001] The disclosure relates to animal brain imaging. Particularly, the disclosure relates to brain imaging on wake behaving animals.

Background Art

[0002] Brain imaging on small animals may be implemented through different methods but only a few of them enable researchers to study selected regions of the central nervous systems with a spatial and time resolution sufficient to image the function of neural structures.

[0003] Indeed, magnetic resonance imaging and scanner imaging methods generally result in low resolution images only enabling to access functional information relating to activated brain regions. Methods using electrodes directly inserted into the brain for analyzing brain electrical sensitivity are as far hindered by a severe precision requirement in positioning the electrodes and by a complex interpretation of the resulting electric signals.

[0004] Microscopy methods have proven useful in brain imaging. Brain slices microscopy on deceased animals is well known but *in vivo* microscopy on a living animal is a recent subject. Historically, *in vivo* microscopy could not analyze deep-brain regions as the technique lacks satisfactory resolution or because it requires over-invasive surgery. The Applicant has described an approach for functional fiber-optic imaging of the intact mouse brain (Vincent et al., Live imaging of neural structure and function by fibred fluorescence microscopy, EMBO reports Sept. 2006). The Applicant showed that fibered fluorescence microscopy which uses a small-diameter fiber-optic probe to provide real-time images has a spatial resolution enabling to image various neural structures in the living animal. This method has been useful in many physiological studies requiring the *in situ* functional imaging of tissues in a living anaesthetized animal.

[0005] Recently, a growing need to obtain images on freely moving animals and to make available chronic studies has emerged. Freely moving animal imaging requires high stability for images acquisition. Stanford University researchers have developed a bundle microscopy technology mounted on a mouse skull using an adapted helmet that enables freely moving studies (High speed, miniaturized fluorescence microscopy in freely moving mice. Benjamin Flusberg et al. Nature Methods, October 2008). However, this technology requires large coring in the mouse's brain and thereby prohibits deep-brain insertion. Additionally, the considerable helmet weight bans a truly free movement and the images resolution level limits the precision of the technology. Recently, the Applicant disclosed (Maskos et al., Functional fibered fluorescence imaging in freely moving mouse, poster No. 598.8 disclosed during the 38th annual meeting of the Society for Neurosciences 2008) the use of a minimally invasive probe securely fixed to the head with dental cement for fiber-optic microscopy imaging of neuronal networks in behaving animals. However, in order to acquire images on an extended period for chronic studies, there is a need to recalibrate the imaging system, therefore requiring to extract the probe out of the brain of the animal and to place it back. According to the current method, extracting the probe presents risk of breaking the tip of the bundle, thereby excluding reusing the same animal to carry out the study and involving incompatible maintenance costs to polish the broken probe.

[0006] US 2009/0048610 discloses a system for positioning fibers in the brain of a patient.

[0007] The Applicant proposes hereinunder an intracranial implant for positioning a fiber bundle probe in the brain of an animal. The Applicant also proposes a fiber bundle probe adapted to said implant, a stereotactic device to manipulate said implant and probe, and a method for brain fiber bundle microscopy.

SUMMARY OF THE CLAIMED SUBJECT MATTER

[0008] The invention is defined in appended independent claims 1 and 6.

[0009] In at least one aspect, embodiments disclosed herein relate to an intracranial implant to position a fiber bundle to a specified region of a brain of an animal. The implant includes a base support to be fixed to a skull of the animal over an orifice drilled in the skull and a hollow conduit arranged through the base support to guide the fiber bundle to the brain of the animal through the drilled orifice. The implant includes a first locking member arranged on the base support, to cooperate with a ferrule of the fiber bundle, the first locking member configured to lock the fiber bundle to the specified region of the brain of the animal.

[0010] Other aspects and advantages of the disclosure will be apparent from the following description and the appended claims.

BRIEF DESCRIPTION OF DRAWINGS

[0011]

Figure 1A and Figure 1B illustrate respectively a top view and a longitudinal section of an implant with a cap according to an embodiment of the present disclosure.

Figure 2 illustrates a perspective view of a transverse section of an implant according to an embodiment of the present disclosure.

Figure 3A and Figure 3B illustrate front and rear perspective views of a ferrule to be arranged on a distal portion of a fiber bundle according to an embodiment

of the present disclosure.

Figure 4A and Figure 4B illustrate lateral views of a fiber bundle probe according to an embodiment of the present disclosure.

Figure 5 illustrates schematically a transverse section of a fiber bundle probe according to an embodiment of the present disclosure.

Figures 6A, 6B and 6C illustrate respectively a lateral view, a transverse section and a top view of a fiber bundle probe according to an embodiment of the present disclosure cooperating with an implant according to an embodiment of the present disclosure.

Figure 7A and Figure 7B are enlargement views of the marked areas highlighted in Figure 6B.

Figure 8 is a perspective view of a transverse section of a fiber bundle probe according to an embodiment of the present disclosure cooperating with an implant according to an embodiment of the present disclosure.

Figure 9 is a perspective view of a transverse section of a fiber bundle probe according to an embodiment of the present disclosure cooperating with an implant according to an embodiment of the present disclosure.

Figure 10 is a perspective view of a stereotactic device according to an embodiment of the present disclosure manipulating an implant according to an embodiment of the present disclosure.

Figure 11 is perspective view of a stereotactic device according to an embodiment of the present disclosure positioning a fiber bundle probe according to an embodiment of the present disclosure in an implant according to an embodiment of the present disclosure.

Figure 12 is a drawing illustrating a fiber bundle probe according to an embodiment of the present disclosure inserted in an implant according to an embodiment of the present disclosure installed on a skull of a mouse.

Figure 13 illustrates schematically a transverse section of a fiber bundle probe according to an embodiment of the present disclosure.

Figure 14 illustrates schematically a transverse section of a fiber bundle probe according to an embodiment of the present disclosure.

Figure 15 illustrates schematically a transverse section of a fiber bundle probe according to an embodiment of the present disclosure.

Figures 16A and 16B illustrate top and bottom perspective views of a polishing system according to an embodiment of the present disclosure.

DETAILED DESCRIPTION

[0012] Specific embodiments of the present disclosure will now be described in detail with reference to the accompanying Figures. Like elements in the various Figures may be denoted by like numerals.

[0013] Embodiments of the present disclosure relate to an intracranial implant to position a fiber bundle in a determined region of the brain of an animal, to a fiber bundle probe for brain fiber bundle microscopy, to a stereotactic device to manipulate an implant and a fiber bundle probe within a stereotactic frame and to a method for brain fiber bundle microscopy.

[0014] For example, the animal may be a transgenic mouse engineered to express specifically Green Fluorescent Proteins in several brain areas. A proximal tip of the fiber bundle may be connected to a system for confocal fluorescence microscopy imaging and a distal tip of the fiber bundle may be inserted in the brain of the animal.

[0015] In a method according to the present disclosure, the mouse may be anaesthetized and its head may be held in a stereotactic frame in order to drill an orifice in the skull of the animal and to precisely install an implant on the skull of the animal over said orifice.

[0016] Figure 1A and 1B illustrate views of the implant according to an embodiment of the present disclosure. The implant 1 comprises a base support 11 to be fixed to the skull of the animal, an hollow conduit 12 arranged through the base support 11 and a first locking member 100 arranged on the base support 11 remote from the hollow conduit 12. Figures 1 further shows a cap comprising an axis plug 14 having a body, that may be inserted in the hollow conduit 12, and a head surrounded by a helmet 15 for maintaining the axis plug 14 in the hollow conduit 12. The cap may be adapted to the implant I to avoid dirt to enter the hollow conduit 12, for example when the implant 1 is not used.

[0017] In the embodiment described on Figure 1A and 1B, the first locking member 100 may include a cylindrical pin 13, generally perpendicular to the base support 11, comprising a portion integral to said base support 11. As shown on Figure 9, the pin 13 may be locked into a second locking member 26 arranged on a ferrule mounted on the fiber bundle 24 when the fiber bundle 24 is inserted in the hollow conduit 12 of the implant 1.

[0018] In another embodiment described on Figure 2. the first locking member 100 may comprise a screw 16 perpendicular to the base support 11 having a first portion 161 arranged in the base support and a second portion 164 around which a locking cylinder 17 is concentrically

arranged. The locking cylinder 17 may be fixed in translation with regard to a longitudinal axis of the screw and free to rotate around said axis. The first portion 161 may comprise a first threading 162 cooperating with a second threading 112 of the base support 11 to adjust the position of the screw in a direction perpendicular to the base support 11. When the screw is threaded, the locking cylinder 17 may translate with regard to the longitudinal axis of the screw 16. As shown on Figure 8, the first locking member comprising the screw 16 and the cylinder 17 is to be locked on the second locking member 26 of the ferrule arranged on the fiber bundle 24 using a locking screw 27 mounted on the second locking member 26, when the fiber bundle 24 is inserted in the hollow conduit 12 of the implant 1.

[0019] According to this embodiment, when the fiber bundle is inserted in the hollow conduit 12 of the implant and the second locking member of the ferrule arranged on the fiber bundle is fastened to the locking cylinder 17 of the first locking member to block the bundle on a determined position, it may be possible to adjust the position of the fiber bundle by adjusting the position of the locking cylinder 17. The first locking member may further comprise a toroid spring 18 concentrically arranged around the screw 16 at one end of the locking cylinder 17. The spring 18 enables compensation for play by pushing the screw 16 in the thread 112 and the locking cylinder 17 on the collar 163.

[0020] In another embodiment (not shown on Figure 2), the first locking member may comprise a pin having a first portion arranged in the base support, said first portion being fixed in translation with regard to a longitudinal axis of the pin and free to rotate around said axis, and a second portion comprising a first threading cooperating with a second threading of a locking cylinder concentrically arranged around said second portion. A toroid spring may also be added for compensation of play as previously. This embodiment may also enable the adjustment of the position of the locking cylinder with regard to the base support.

[0021] Adjusting the position of the fiber bundle probe by screwing the screw 16 may be done without requiring to hold the head of the mouse in a stereotactic frame. Thereby, it may easily be done after the fiber bundle has been locked. When the fiber bundle is inserted in the brain of the animal, the brain tends to contract and it may occur that, in order to stay on a determined region of the brain to image, the fiber bundle positioning may be adjusted because of brain re-inflating.

[0022] One advantage of a locking mechanism comprising the first and second locking members is that it may block the fiber bundle on a determined region of the brain to image, preventing the fiber bundle to rotate around its longitudinal axis and to move in the hollow conduit where the fiber bundle is to be inserted. It may lead to increase stability for image acquisition, enabling the acquisition of images from a freely moving animal. Arranging the first locking member remote from the hollow conduit 12 where the fiber bundle is to be inserted may ease the fastening of the fiber bundle by reducing the required fastening torque. It may enable to avoid excessive constraint on the fiber bundle which may lead to equipment damages.

[0023] When the orifice has been drilled in the skull of the animal, the base support 11 of the implant may be fixed to the skull of the animal for the hollow conduit 12 to emerge onto the drilled orifice. Fixing the base support may be performed using for example micro-screws and dental cement.

[0024] As shown on Figure 10, the implant 1 may be manipulated with a stereotactic device 3 comprising a rod 31 connected to the stereotactic frame, and a groove 32 comprising screws 33 to fasten an object placed in the groove 32. The stereotactic device 3 is an interface that enables to manipulate the implant within the stereotactic frame. The implant 1 may placed on the skull of the animal horizontally with regard to an horizontal axis defined by the head of the animal in the stereotactic frame. As the skull of a mouse is curved, an amount of glue may be applied on the surface of the base support 11 in contact with the skull to compensate for slope.

[0025] Referring again to Figure 1, the hollow conduit 12 may comprise a tube perpendicular to the base support 11 and may comprise an under part 121 extending beneath the base support 11. The under part 121 may enter the orifice drilled in the skull of the animal. In an embodiment, the under part 121 has a length adapted to penetrate in the brain of the animal. As the skull of a mouse is curved and the base support is installed horizontally, the length necessary to penetrate the brain may not be the same when the base support 11 is placed on different parts of the mouse's skull. In an embodiment, the length of the under part 121 is adapted for penetrating the brain when the base support 11 is fixed horizontally in any position of the mouse's skull. In another embodiment, the length of the under part 121 is adapted for penetrating the brain when the base support is fixed horizontally in at least one position on the skull of the mouse. In another embodiment, the length of the under part 121 is adapted for not entering the brain of the animal when the base support is fixed horizontally in any position of the mouse's skull.

[0026] The base support 11 may have a parallepipedic shape. Advantageously, the base support 11 may have a trapezoid based right prism shape, as shown on Figure 6A. In this embodiment, the face of greater surface of said trapezoid based right prism is laid on the skull of the animal. As glue may be spread below said face and on the bevelled edges of the trapezoid prism, the base support 11 is accurately fixed on the mouse's skull. As shown on Figure 1B, a base 111 of the trapezoid prism of the base support 11 close to the hollow conduit may advantageously be truncated for enabling an operator manipulating the base support 11 from aside to easily see the under part 121 of the hollow conduit 12. Thereby, the operator may accurately calibrate the stereotactic frame

by easily targeting the bones of the skull of the mouse with the under part 121 of the implant mounted on the stereotactic device 3.

[0027] When the implant 1 is positioned on the skull of the animal for the hollow conduit 12 to emerge onto the drilled orifice, the fiber bundle 24 may be inserted in the brain of the animal through the hollow conduit 12 of the implant 1. Figure 12 illustrates a mouse 4 on the head of which an implant 1 receiving a fiber bundle probe 2 is installed.

[0028] As shown on Figure 11, the fiber bundle may be manipulated with the stereotactic device 3. The stereotactic device 3 is an interface that enables to manipulate the implant 1 and the fiber bundle within the stereotactic frame. The stereotactic device 3 may adapted to successively hold the fiber bundle and the implant in collinear directions.

[0029] A fiber bundle probe 2 according to an embodiment of the present disclosure is represented on Figures 4A and 4B. The fiber bundle probe 2 may comprise a fiber bundle 24 for transporting light and a ferrule arranged around a distal portion of the fiber bundle 24. A portion of the fiber bundle 24 may be sheathed in a sheath 21. The ferrule may comprise an handling part 25 for manipulating the fiber bundle into the hollow conduit 12 of the implant 1 and a second locking member 26 for cooperating with the first locking member 13 of the intracranial implant, to lock the fiber bundle on a determined region of the brain of the animal, when the distal tip of the fiber bundle 24 is inserted in the brain of the animal through the hollow conduit 12 of the implant 1. The distal tip of the fiber bundle to be inserted in the brain of the animal may be stripped and not covered by the ferrule. As shown on figures 3A and 3B, the handling part 25 may comprise an hollow canal 29 for the fiber bundle 24 to be mounted in. The handling part 25 may extend longitudinally along the distal portion of the fiber bundle 24 and the second locking member 26 may extend laterally to the handling part 25, perpendicularly to said handling part 25.

[0030] The stereotactic device 3 may be adapted to hold the fiber bundle 24 by fastening the handling part 25 of the fiber bundle probe in the groove 32. The stereotactic device 3 may be adapted to hold the implant 1 by fastening the first locking member of the implant. The surface of the groove 32 may be adapted to successively hold the fiber bundle probe 2 and the implant 1 in collinear directions. The surface of the groove 32 may be any if a U-shaped groove or a V-shaped groove (not shown on Figures 10-11).

[0031] As shown on Figures 3A and 3B, the second locking member 26 of the ferrule may comprise two halves 28 forming an arch for the first locking member 13 to fit into, when the distal tip of the fiber bundle 24 may be inserted in the brain of the animal through the hollow conduit 12 of the implant 1. One half of the second locking member may comprise the locking screw 27 arranged in a hole 281. The locking screw 27 enables to block the first locking member 13 within the second locking member halves 28 on a determined region of the brain to image, when the distal tip of the fiber bundle 24 is inserted in the brain of the animal through the hollow conduit 12 of the implant 1. Figure 6C is a top view of a fiber bundle probe inserted in an implant and shows how the first locking member may fit into the halves 28 of the second locking member 26 in accordance with the present embodiment.

[0032] Figure 5 illustrates schematically a transverse section of a fiber bundle probe according to an embodiment of the present disclosure. The fiber bundle may initially comprise a coating 22 and a sheath 21 wrapping the fiber bundle 24. In order to obtain a fiber bundle probe 2, the sheath 21 may be removed on a first distal part extending from a sheath removing section 211, located in the distal portion around which the ferrule is to be arranged, to the distal tip of the fiber bundle to be inserted in the brain of the animal. The coating 22 may further be removed on a second distal part extending till the distal tip of the fiber bundle to be inserted in the brain of the animal. The second distal part may be smaller than the first distal part. A guiding sheath 23, of a specified diameter adapted to the diameter of the hollow conduit 12, may further be arranged on the fiber bundle 24. The guiding sheath 23 may extend from the sheath removing section 211 and may cover a guiding portion of the fiber bundle 24 to be inserted in the hollow conduit 12 of the implant while leaving the distal tip of the fiber bundle to be inserted in the brain of the animal uncovered. The guiding sheath 23 may be fixed to the fiber bundle 24 using glue. The ferrule may be fixed to the guiding sheath 23 using glue.

[0033] Figure 7B is an enlargement of the highlighted area marked C on Figure 6B which shows a lateral section of a fiber bundle probe 2 inserted in an implant 1. Figure 7B illustrates a lateral section of a piece of the guiding portion of the fiber bundle 24, sheathed in the guiding sheath 23, inserted in the hollow conduit 12 of the implant. As shown on Figure 7B, the distal tip of the fiber bundle may be stripped and the guiding sheath may not extend till the distal tip of the fiber bundle to be inserted in the brain of the animal.

[0034] Figure 7A is an enlargement of the highlighted area marked B on Figure 6B. Figure 7A illustrates a lateral section of a piece of the fiber bundle probe 2. As shown on Figure 7A, the hollow canal 29 in which the fiber bundle is mounted may comprise an upper part 291 of an inner diameter adapted to the sheath 21, a middle part 292 of a diameter adapted to the guiding sheath 23 and a lower part 293 of a diameter superior to the diameter of the hollow conduit. This enables the fiber bundle to be inserted in the hollow conduit 12. The upper part 291 may cover a portion of the fiber bundle 24 wrapped with the sheath 21 and extends till the sheath removal section 211. The middle part 292 may cover a portion of the fiber bundle 24 covered with the guiding sheath 23. Advantageously, the ferrule is fixed to the fiber bundle by using

glue at the level of the middle part 292. The lower part 293 may cover a portion of the fiber bundle covered by the guiding sheath 23 that is to be inserted in the hollow conduit 12 of the implant. This may protect the guiding portion of the fiber bundle to be inserted in the hollow conduit 12.

[0035] When the fiber bundle is positioned on the determined region of the brain to image, the first and second members may be locked for blocking the fiber bundle probe on the determined region and the animal may be woken-up and unrestrained from the stereotactic frame.

[0036] As shown on Figure 6A, 6B, 6C, 8 and 9, the first locking member of the implant cooperates with the second locking member of the fiber bundle probe. As previously described, the first locking member either being a pin 13 or a locking cylinder 17 mounted on a screw 16 may fit into the arch formed by the halves 28 of the second locking member 26 and may be blocked by the locking screw 27 mounted on one half of the second locking member 26. This may enable a high stability for image acquisition and may permit taking the fiber bundle out of the brain of the mouse while limiting risks of equipment damages. This enables chronic experiments to be carried out on extended period of time.

[0037] The fiber bundle probe may further comprise a rigid jacket 241 arranged at the distal tip of the fiber bundle 24. The rigid jacket 241 may be formed of a metallic material, for example stainless steel. The rigid jacket 241 may have a generally cylindrical shape and comprise a lumen adapted for the fiber bundle 24 to fit into. An external diameter of the rigid jacket 241 may be inferior to a external diameter of the guiding sheath 23. The external diameter of the rigid jacket 241 may be of around 400 to 500 μm. At a distal portion of the guiding sheath 23, an inner diameter of the guiding sheath 23 may be configured to enable the rigid jacket 241 to fit into the lumen of the guiding sheath 23. The rigid jacket may enable to strengthen the tip of fiber bundle against lateral and frontal shocks thereby easing handling and re-polishing operations by the end user.

[0038] In an embodiment illustrated on Figure 13, the rigid jacket 241 may extend to the end of the distal tip of the fiber bundle 24. In an embodiment illustrated on Figure 14, the rigid jacket 241 and the distal tip of the fiber bundle 24 may further be beveled. In an embodiment illustrated on Figure 15, the rigid jacket 241 may extend beyond the end of the distal tip of the fiber bundle to cover a miniaturized objective 242 arranged at the end of the distal tip of the fiber bundle. The miniaturized objective 242 may be of a cylindrical shape and have a diameter substantially equal to the diameter of the fiber bundle. The miniaturized objective 242 may be a gradient index lens and may be connected coaxially to the fiber bundle 24, for example by using adhesive means. Alternatively, the miniaturized objective 242 may include other elements, such as conventional lenses, filters, or diffractive elements. The rigid jacket 241 may enable to strengthen the connection between the fiber bundle 24 and the miniaturized objective 242.

[0039] Figures 16A and 16B illustrate a fiber bundle probe 2 inserted into a polishing tool 5. The polishing tool 5 comprises a polishing support 51, a polishing hollow conduit (not shown on Figures 16A and 16B) arranged through the polishing support 51, a polishing locking member 52, arranged on the polishing support to cooperate with the ferrule of the fiber bundle probe 2 when the distal tip of the fiber bundle is inserted into the polishing hollow conduit and a supplementary locking mechanism 53 to lock the fiber bundle probe 2 on the polishing base support 51. The polishing base support 51 may be configured for the distal tip of the fiber bundle to protrude out of a polishing face 54 when the fiber bundle probe 2 is locked on the polishing support 51. The polishing of the fiber bundle may be performed by rubbing the protruding tip of the fiber bundle over a rigid surface. An insertion face 55 of the polishing support 51 may form an angle with the polishing face 54 thereby enabling to polish the distal tip of the fiber bundle with a bevel. The polishing conduit and the polishing locking member may be arranged to reproduce the configuration of the intracranial implant. Therefore, the polishing tool 5 may hold the fiber bundle in a position identical to the position it may have when inserted in the intracranial implant. This enables, in an embodiment in which the fiber bundle is originally beveled in a determined direction, to keep said direction when re-polishing the fiber bundle with the polishing tool.

[0040] While the disclosure has been described with respect to a limited number of embodiments, those skilled in the art, having benefit of this disclosure, will appreciate that other embodiments can be devised which do not depart from the scope of the disclosure as disclosed herein. Accordingly, the scope of the disclosure be limited only by the attached claims.

Claims

1. An intracranial implant (1) to position a fiber bundle of a fiber bundle probe to a specified region of a brain of an animal, wherein the fiber bundle probe further comprises a ferrule arranged on a distal portion of the fiber bundle, the intracranial implant (1) comprising:

   a base support (11) to be fixed to a skull of the animal over an orifice drilled in the skull;
   a hollow conduit (12) arranged through the base support (11) to guide the fiber bundle to the brain of the animal through the drilled orifice;
   a first locking member (100) arranged on the base support (11), to cooperate with the ferrule of the fiber bundle probe, the first locking member (100) being configured to lock the fiber bundle to the specified region of the brain of the animal **characterized in that** the first locking

member (100) comprises a pin (13) substantially perpendicular to the base support (11).

2. The intracranial implant (1) according to claim 1, wherein the first locking member (100) is arranged on the base support (11) remote from the hollow conduit (12).

3. The intracranial implant (1) according to claim 1, wherein a portion of the pin (13) is integral to the base support (11).

4. The intracranial implant (1) according to claim 1, wherein the pin (13) further comprises:

a first portion (161) arranged in the base support (11) comprising a first threading (162) cooperating with a second threading (112) of the base support (11), the first portion (161) being configured to adjust the position of the pin (13) in a direction substantially perpendicular to the base support (11); and
a second portion (164) comprising a locking cylinder (17) concentrically arranged thereon, wherein the locking cylinder (17) is fixed in translation with regard to a longitudinal axis of the pin (13) and free to rotate around the longitudinal axis.

5. The intracranial implant (1) according to claim 1, wherein the pin (13) further comprises:

a first portion arranged in the base support (11), the first portion being fixed in translation with respect to a longitudinal axis of the pin (13), wherein the first portion is free to rotate around the longitudinal axis; and
a second portion comprising a first threading cooperating with a second threading of a locking cylinder concentrically arranged around said second portion, the second portion being configured to adjust the position of the locking cylinder in a direction substantially perpendicular to the base support (11).

6. A fiber bundle probe (2) useful in brain fiber bundle microscopy to cooperate with an intracranial implant (1) according to claim 1, comprising:

a fiber bundle (24) for transporting light having a distal tip to be inserted in the brain of an animal through the intracranial implant (1); and
a ferrule arranged on a distal portion of the fiber bundle (24) for transporting light, said ferrule comprising

- a handling part (25) extending along the distal portion of the fiber bundle (24), to manipulate the fiber bundle into the intracranial implant (1); **characterized in that** the ferrule comprises:
- a second locking member (26) extending laterally to the handling part (25) and comprising two halves (28) forming an arch for the first locking member (100) of the intracranial implant (1) to fit into, when the distal tip of the fiber bundle (24) for transporting light is inserted in the brain of the animal through the hollow conduit (12) of the intracranial implant (1).

7. The fiber bundle probe (2) according to claim 6, wherein a screw is arranged in a half of the second locking member (26) to block the first locking member (100) within the second locking member halves (28) on the determined region of the brain to image, when the distal tip of the fiber bundle (24) is inserted in the brain of the animal through the hollow conduit (12) of the intracranial implant (1).

8. The fiber bundle probe (2) according to claim 6, wherein a portion of the fiber bundle (24) to be inserted in the hollow conduit (12) of the intracranial implant (1) is sheathed with a guiding sheath (23), said guiding sheath (23) being of a specified diameter adapted to the diameter of the hollow conduit (12) and fixed to the fiber bundle (24).

9. The fiber bundle probe (2) according to claim 8, wherein the guiding sheath (23) extends to the distal portion around which the ferrule is arranged, the ferrule being fixed to the guiding sheath (23).

10. The fiber bundle probe (2) according to claim 6 wherein the distal tip of the fiber bundle (24) to be inserted in the brain of the animal is beveled.

11. The fiber bundle probe (2) according to any of claims 6 to 10, wherein the distal tip of the fiber bundle (24) to be inserted in the brain of the animal is covered with a rigid jacket (241).

12. The fiber bundle probe (2) according to claim 11, wherein the rigid jacket (241) extends beyond the end of the distal tip of the fiber bundle (24) to cover a miniaturized objective (242) arranged at the end of said distal tip.

Patentansprüche

1. Intrakranielles Implantat (1) zum Positionieren eines Faserbündels einer Faserbündelsonde in einem spezifizierten Gebiet eines Gehirns eines Tiers, wobei die Faserbündelsonde ferner eine Muffe umfasst, die an einem distalen Abschnitt des Faserbün-

dels angeordnet ist, wobei das Implantat umfasst:

einen Basisträger (11), der an einem Schädel des Tiers über einer in dem Schädel gebohrten Öffnung zu befestigen ist;
eine hohle Röhre (12), die durch den Basisträger angeordnet ist, um das Faserbündel durch die gebohrte Öffnung zu dem Gehirn des Tiers zu führen;
ein erstes Verriegelungselement (100), das an dem Basisträger angeordnet ist, um mit der Muffe der Faserbündelsonde zusammenzuwirken, wobei das erste Verriegelungselement dafür konfiguriert ist, das Faserbündel in dem spezifizierten Gebiet des Gehirns des Tiers zu verriegeln, **dadurch gekennzeichnet, dass** das Verriegelungselement einen Stift (13) umfasst, der im Wesentlichen senkrecht zu dem Basisträger (11) ist.

2. Intrakranielles Implantat nach Anspruch 1, wobei das erste Verriegelungselement fern von der hohlen Röhre an dem Basisträger angeordnet ist.

3. Implantat nach Anspruch 1, wobei ein Abschnitt des Stifts einteilig mit dem Basisträger ist.

4. Implantat nach Anspruch 1, wobei der Stift ferner umfasst:

einen ersten Abschnitt (161), der in dem Basisträger angeordnet ist, der ein erstes Gewinde (162) umfasst, das mit einem zweiten Gewinde (112) des Basisträgers zusammenwirkt, wobei der erste Abschnitt dafür konfiguriert ist, die Stellung des Stifts in einer Richtung im Wesentlichen senkrecht zu dem Basisträger einzustellen; und
einen zweiten Abschnitt (164), der einen Verriegelungszylinder (17) umfasst, der konzentrisch daran angeordnet ist, wobei der Verriegelungszylinder in Bezug auf die Translation hinsichtlich einer Längsachse des Stifts befestigt und um die Achse frei drehbar ist.

5. Implantat nach Anspruch 1, wobei der Stift ferner umfasst:

einen ersten Abschnitt, der in dem Basisträger angeordnet ist, wobei der erste Abschnitt in Bezug auf die Translation hinsichtlich einer Längsachse des Stifts befestigt ist und wobei der erste Abschnitt um die Achse frei drehbar ist; und
einen zweiten Abschnitt, der ein erstes Gewinde umfasst, das mit einem zweiten Gewinde eines Verriegelungszylinders, der um den zweiten Abschnitt konzentrisch angeordnet ist, zusammenwirkt, wobei der zweite Abschnitt dafür konfiguriert ist, die Position des Verriegelungszylinders in einer Richtung im Wesentlichen senkrecht zu dem Basisträger einzustellen.

6. Faserbündelsonde (2), die in der Gehirnfaserbündelmikroskopie verwendet werden kann, um mit einem intrakraniellen Implantat nach Anspruch 1 zusammenzuwirken, wobei die Faserbündelsonde umfasst:

ein Faserbündel (24) zum Transportieren von Licht, das eine distale Spitze aufweist, die durch das intrakranielle Implantat in das Gehirn eines Tiers einzuführen ist; und
eine Muffe, die in einem distalen Abschnitt des Faserbündels zum Transportieren von Licht angeordnet ist, wobei die Muffe umfasst:

- ein Handhabungsteil (25), das entlang des distalen Abschnitts des Faserbündels verläuft, um das Faserbündel in das intrakranielle Implantat zu manipulieren;
dadurch gekennzeichnet, dass die Muffe ferner umfasst:
- ein zweites Verriegelungselement (26), das quer zu dem Handhabungsteil verläuft und zwei Hälften umfasst, die einen Bogen bilden, damit das erste Verriegelungselement des intrakraniellen Implantats hineinpasst, wenn die distale Spitze des Faserbündels zum Transportieren von Licht durch die hohle Röhre des intrakraniellen Implantats in das Gehirn des Tiers eingeführt wird.

7. Faserbündel nach Anspruch 6, wobei in einer Hälfte des zweiten Verriegelungselements eine Schraube angeordnet ist, um das erste Verriegelungselement innerhalb der zweiten Hälften des Verriegelungselements in einem vorgegebenen Gebiet des Gehirns zu arretieren, um abzubilden, wenn die distale Spitze des Faserbündels durch die hohle Röhre des Implantats in das Gehirn des Tiers eingeführt wird.

8. Faserbündelsonde nach Anspruch 6, wobei ein Abschnitt des Faserbündels, der in die hohle Röhre des Implantats einzuführen ist, mit einer Führungshülle (23) umhüllt ist, wobei die Führungshülle einen spezifizierten Durchmesser aufweist, der an den Durchmesser der hohlen Röhre angepasst ist, und an dem Faserbündel befestigt ist.

9. Faserbündel nach Anspruch 8, wobei die Führungshülle zu dem distalen Abschnitt verläuft, um den die Muffe angeordnet ist, wobei die Muffe an der Führungshülle befestigt ist.

10. Faserbündel nach Anspruch 6, wobei die distale

Spitze des Faserbündels, die in das Gehirn des Tiers einzuführen ist, abgephast ist.

11. Faserbündel nach einem der Ansprüche 6 bis 10, wobei die distale Spitze des Faserbündels, die in das Gehirn des Tiers einzuführen ist, mit einem starren Mantel bedeckt ist.

12. Faserbündel nach Anspruch 11, wobei der starre Mantel über das Ende der distalen Spitze des Faserbündels hinaus verläuft, um ein Miniaturobjektiv, das an dem Ende der distalen Spitze angeordnet ist, zu bedecken.

Revendications

1. Implant intracrânien (1) permettant de positionner un faisceau de fibres d'une sonde à faisceau de fibres dans une région spécifiée du cerveau d'un animal, dans lequel la sonde à faisceau de fibres comprend en outre un manchon agencée sur une partie distale du faisceau de fibres, l'implant comprenant :

un support de base (11) à fixer au crâne de l'animal sur un orifice foré dans le crâne ;
un conduit creux (12) disposé à travers le support de base pour guider le faisceau de fibres jusqu'au cerveau de l'animal à travers l'orifice foré ;
un premier élément de verrouillage (100) disposé sur le support de base, destiné à coopérer avec le manchon de la sonde à faisceau de fibres, le premier élément de verrouillage étant configuré pour bloquer le faisceau de fibres sur la région spécifiée du cerveau de l'animal **caractérisé en ce que** l'élément de verrouillage comprend une goupille (13) sensiblement perpendiculaire au support de base (11).

2. Implant intracrânien selon la revendication 1, dans lequel le premier élément de verrouillage est disposé sur le support de base à distance du conduit creux.

3. Implant selon la revendication 1, dans lequel une partie de la goupille fait partie intégrante du support de base.

4. Implant selon la revendication 1, dans lequel la goupille comprend en outre :

une première partie (161) agencée dans le support de base comprenant un premier filetage (162) coopérant avec un second filetage (112) du support de base, la première partie étant configurée pour ajuster la position de la goupille dans une direction sensiblement perpendiculaire au support de base ; et
une seconde partie (164) comprenant un cylindre de verrouillage (17) disposé de manière concentrique sur celle-ci, dans lequel le cylindre de verrouillage est fixé en translation relativement à un axe longitudinal de la goupille et libre de pivoter autour de l'axe.

5. Implant selon la revendication 1, dans lequel la goupille comprend en outre :

une première partie disposée dans le support de base, la première partie est fixée en translation relativement à un axe longitudinal de la goupille et la première partie est libre de pivoter autour de l'axe ; et
une seconde partie comprenant un premier filetage coopérant avec un second filetage d'un cylindre de verrouillage disposé de manière concentrique autour de ladite seconde partie, la seconde partie étant configurée pour ajuster la position du cylindre de verrouillage dans une direction sensiblement perpendiculaire au support de base.

6. Sonde de faisceau de fibres (2) utile en microscopie cérébrale par faisceau de fibres pour coopérer avec un implant intracrânien selon la revendication 1, ladite sonde comprenant :

un faisceau de fibres (24) pour transporter la lumière ayant une pointe distale à insérer dans le cerveau d'un animal à travers l'implant intracrânien ; et
un manchon disposé sur une partie distale du faisceau de fibres pour transporter la lumière, ledit manchon comprenant :

- une partie de manipulation (25) s'étendant le long de la partie distale du faisceau de fibres, pour manipuler le faisceau de fibres dans l'implant intracrânien ; **caractérisé en ce que** le manchon comprend en outre
- un second élément de verrouillage (26) s'étendant latéralement jusqu'à la partie de manipulation et comprenant deux moitiés formant un arc à l'intérieur duquel s'ajustera le premier élément de verrouillage de l'implant intracrânien, lorsque la pointe distale du faisceau de fibres pour transporter la lumière est insérée dans le cerveau de l'animal à travers le conduit creux de l'implant intracrânien.

7. Faisceau de fibres selon la revendication 6, dans lequel une vis est agencée dans une moitié du second élément de verrouillage pour bloquer le premier élément de verrouillage à l'intérieur des moitiés du second élément de verrouillage sur la région céré-

brale à imager déterminée, lorsque la pointe distale du faisceau de fibres est insérée dans le cerveau de l'animal à travers le conduit creux de l'implant.

8. Sonde de faisceau de fibres selon la revendication 6, dans laquelle une partie du faisceau de fibres à insérer dans le conduit creux de l'implant est gainée d'une gaine de guidage (23), ladite gaine de guidage étant d'un diamètre spécifié adapté au diamètre du conduit creux et fixée au faisceau de fibres.

9. Faisceau de fibres selon la revendication 8, dans lequel la gaine de guidage s'étend jusqu'à la partie distale autour de laquelle le manchon est disposé, le manchon étant fixé à la gaine de guidage.

10. Faisceau de fibres selon la revendication 6, dans lequel la pointe distale du faisceau de fibres à insérer dans le cerveau de l'animal est biseautée.

11. Faisceau de fibres selon l'une quelconque des revendications 6 à 10, dans lequel la pointe distale du faisceau de fibres à insérer dans le cerveau de l'animal est couverte d'une enveloppe rigide.

12. Faisceau de fibres selon la revendication 11, dans lequel l'enveloppe rigide s'étend au-delà de l'extrémité de la pointe distale du faisceau de fibres pour couvrir un objectif miniaturisé au niveau de l'extrémité de ladite pointe distale.

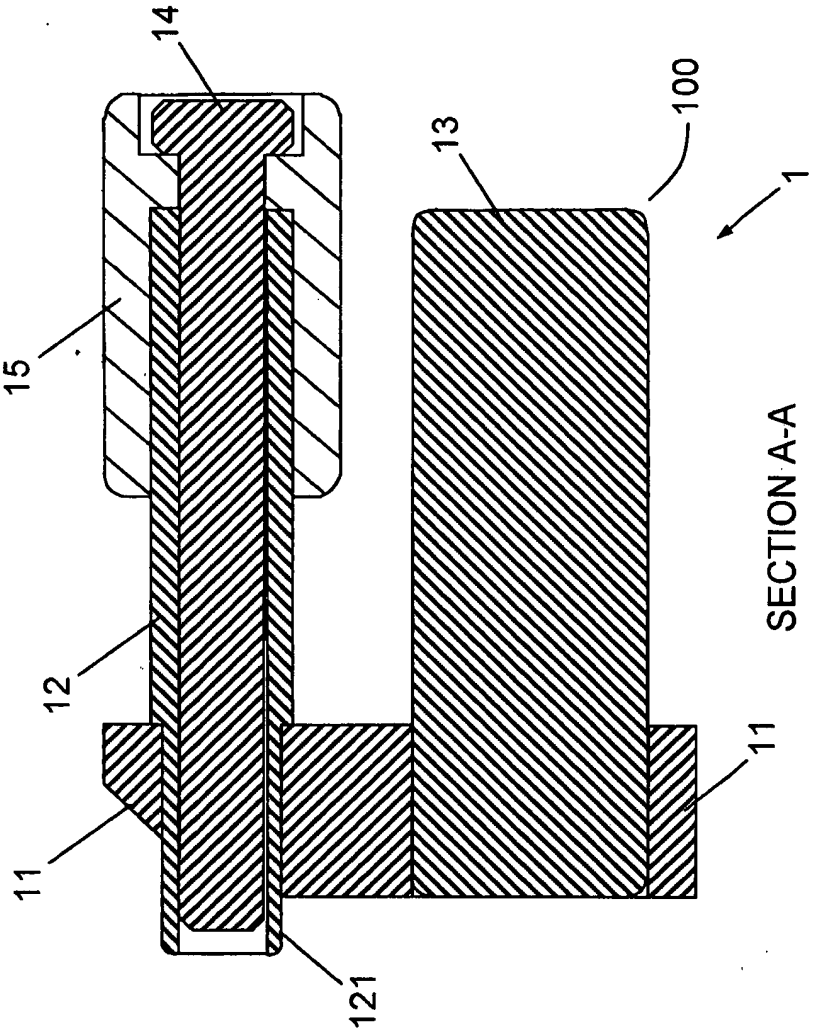

FIG.1B

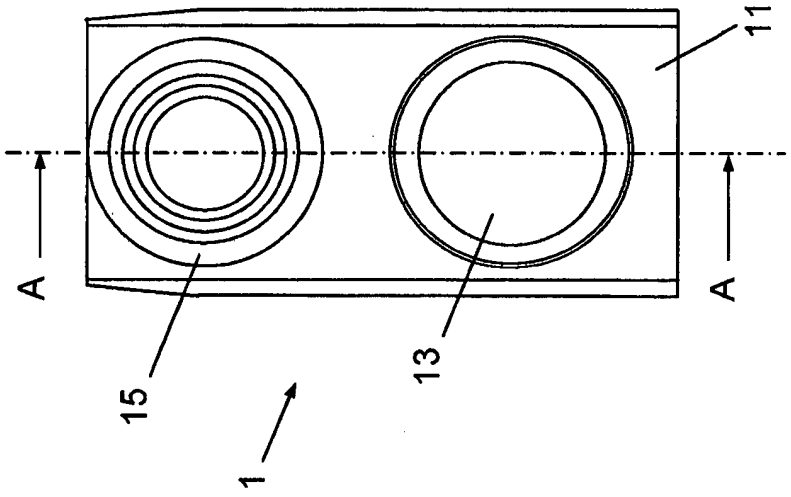

FIG.1A

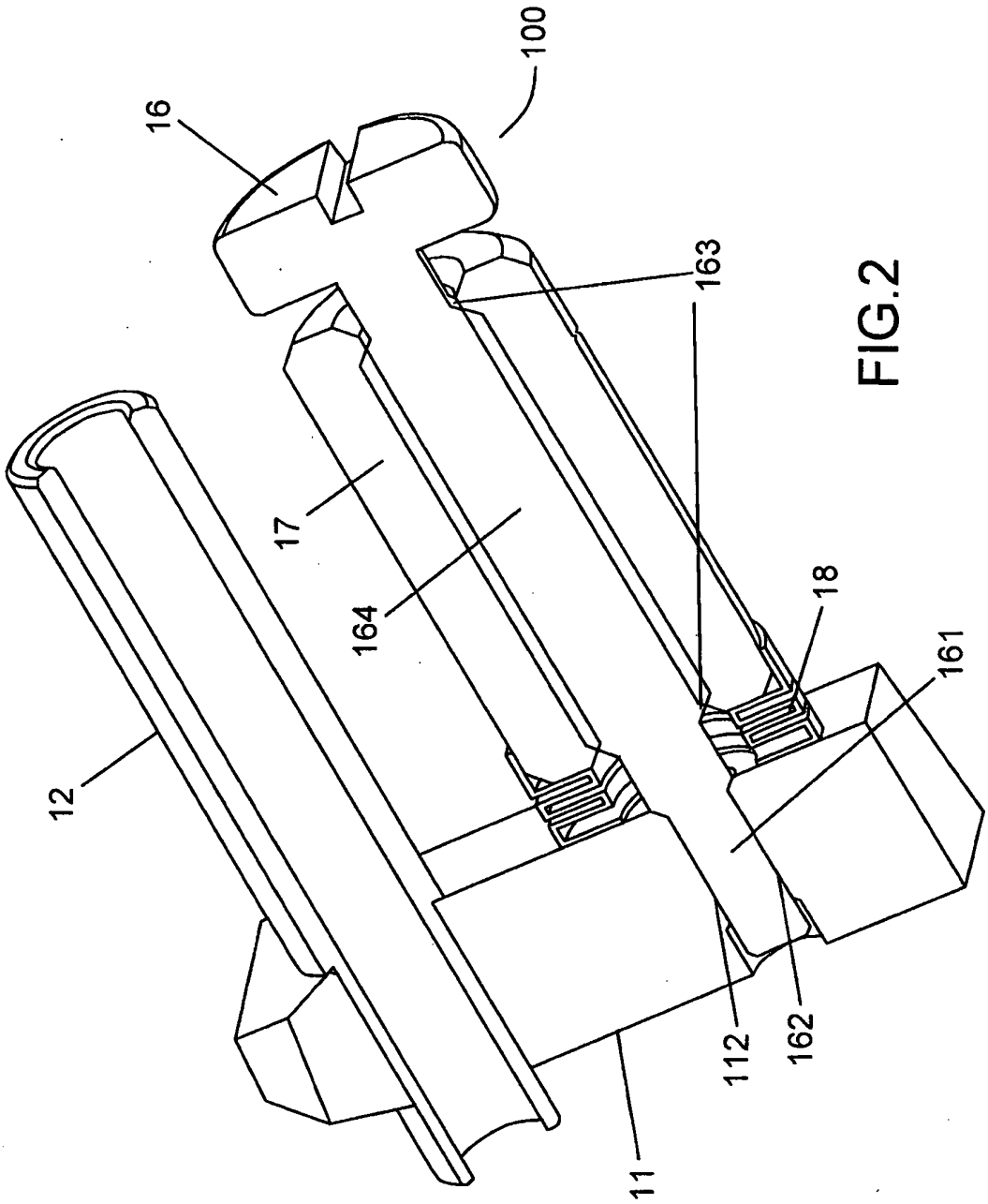

FIG.2

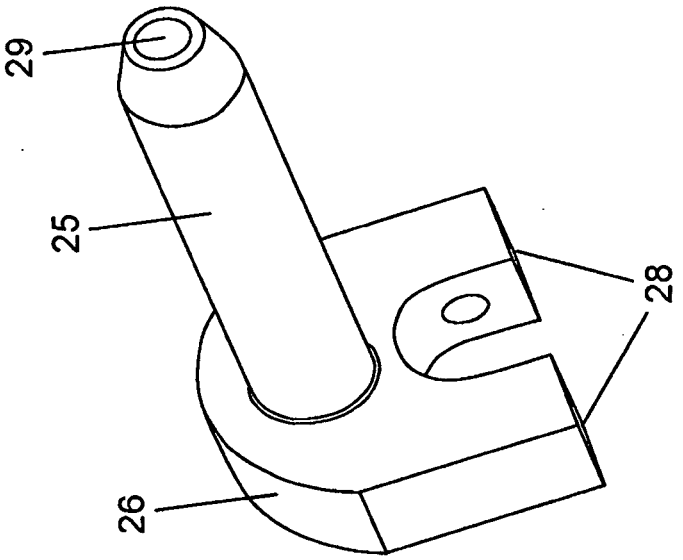

FIG.3B

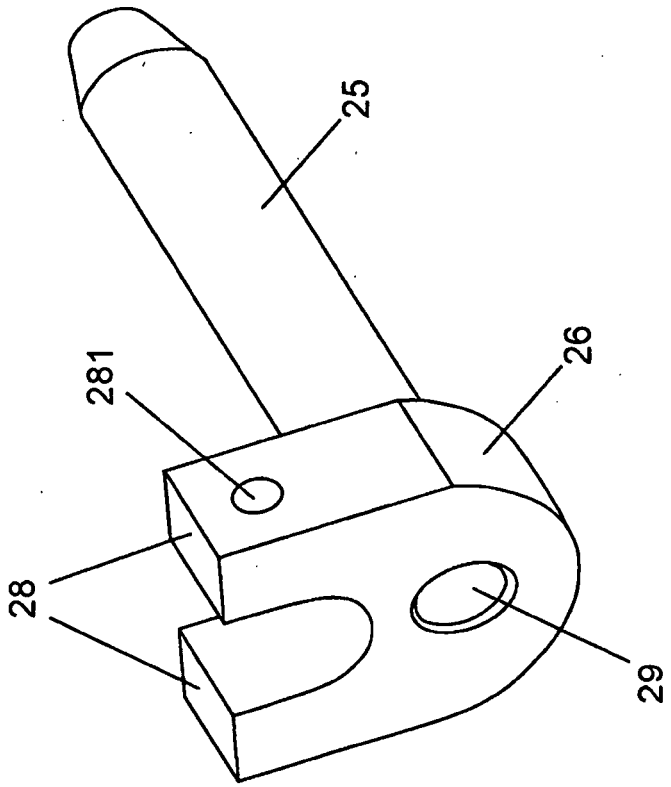

FIG.3A

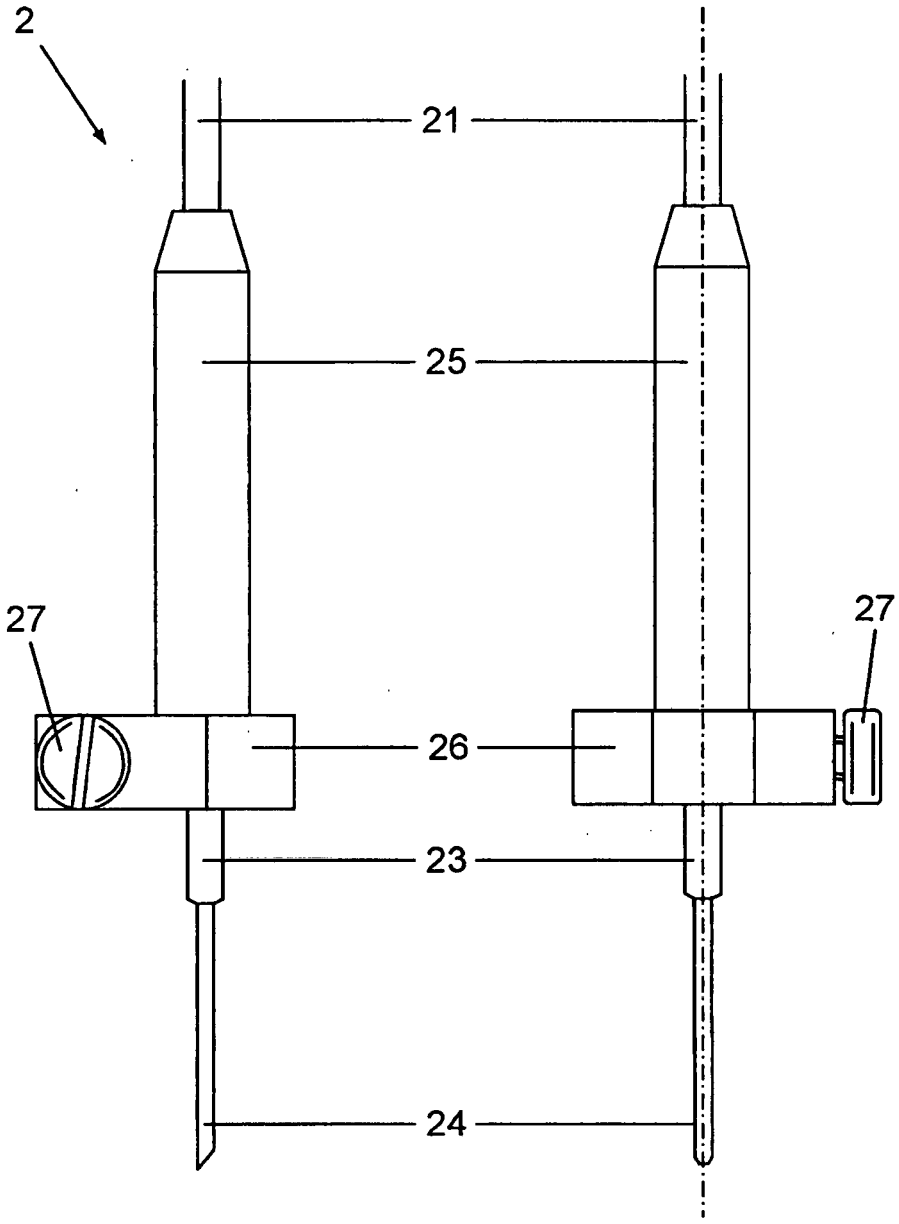

FIG.4A FIG.4B

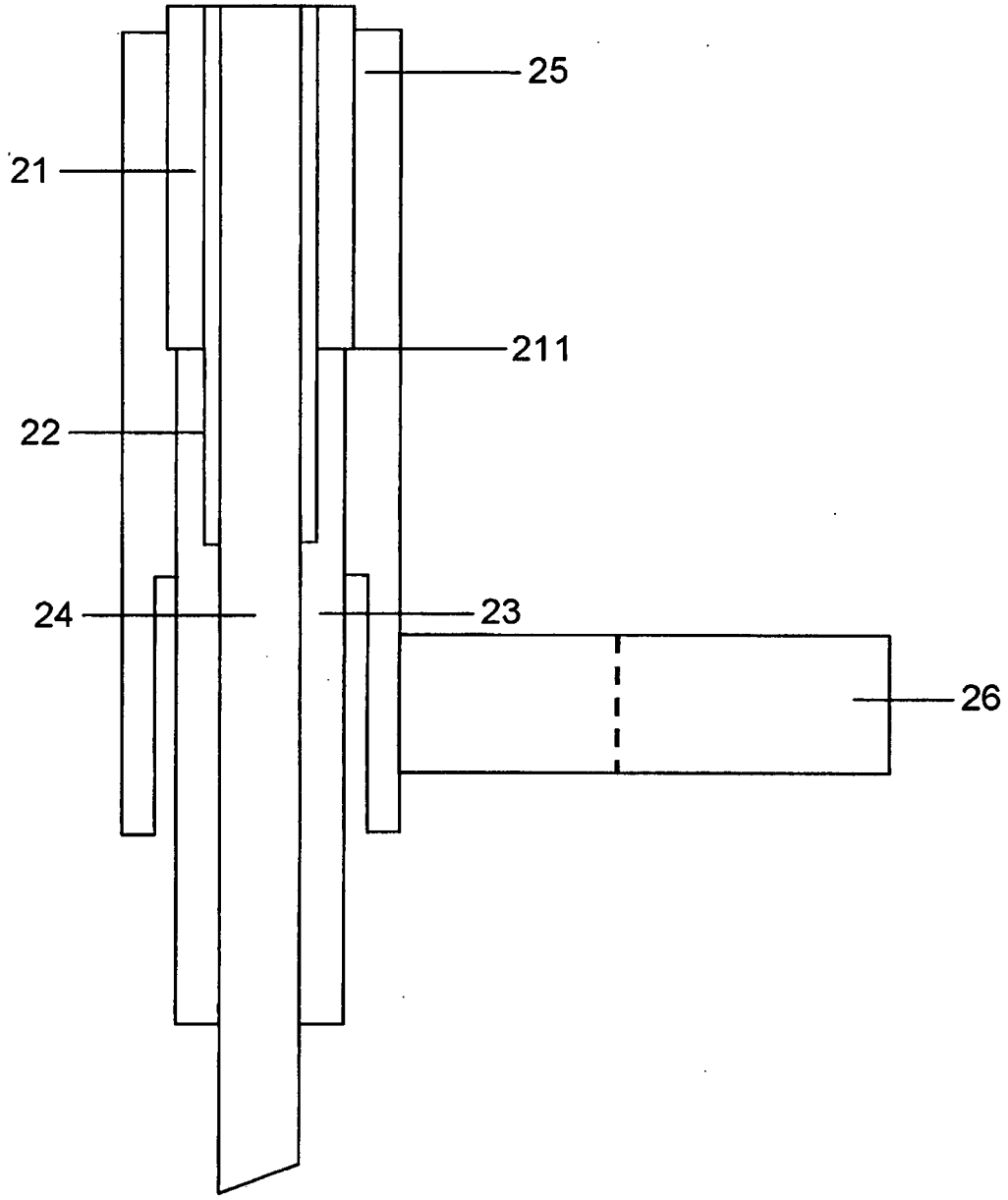

FIG.5

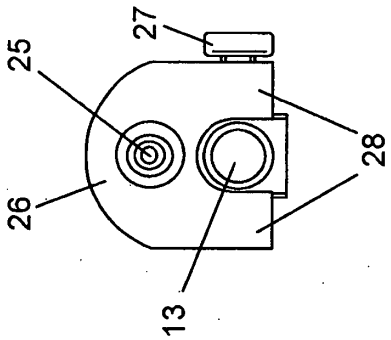

FIG.6C

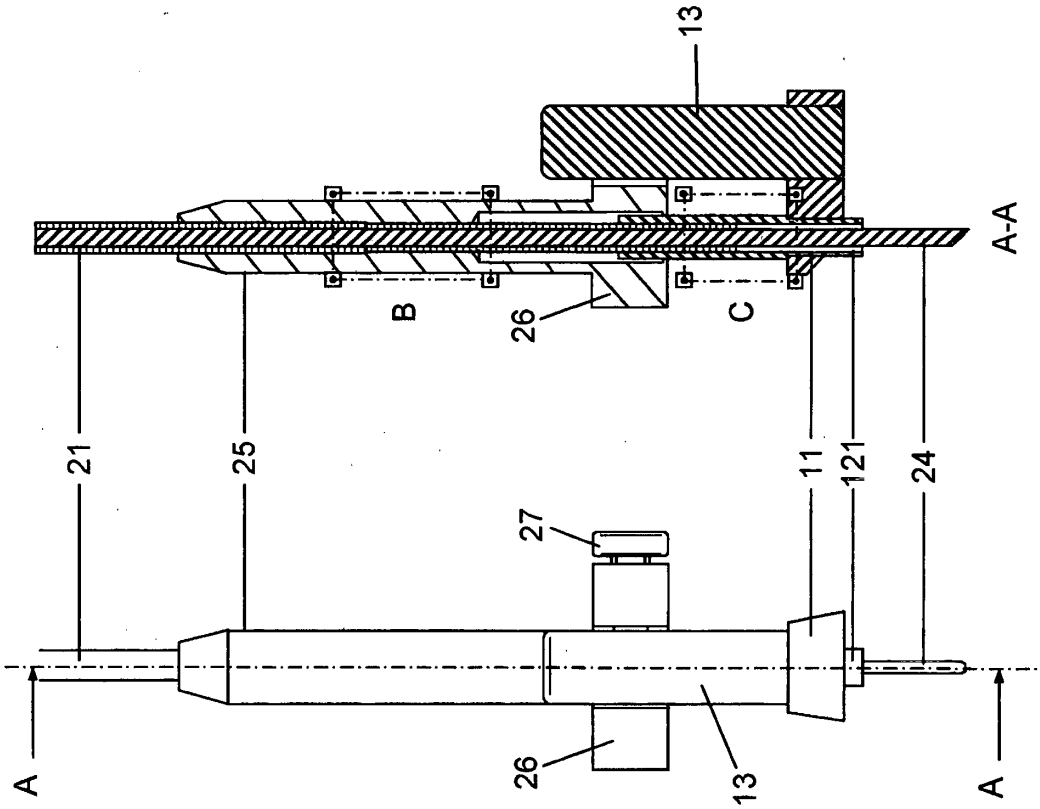

FIG.6B

FIG.6A

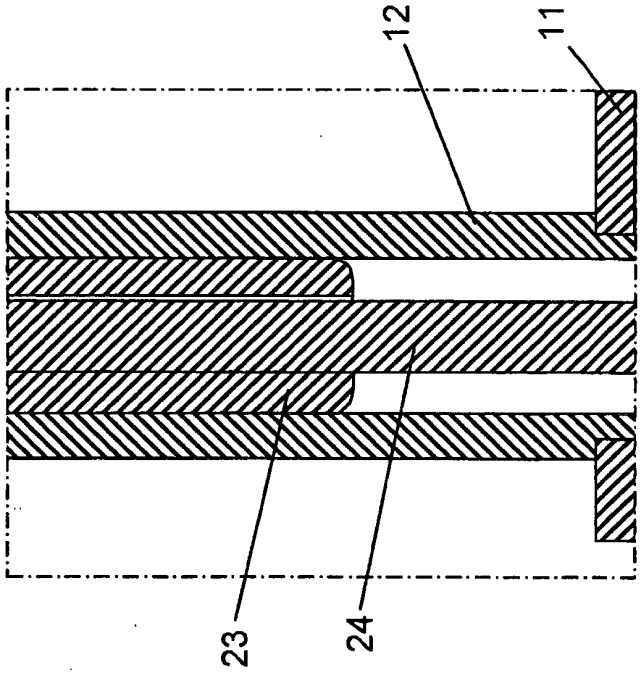

FIG.7B

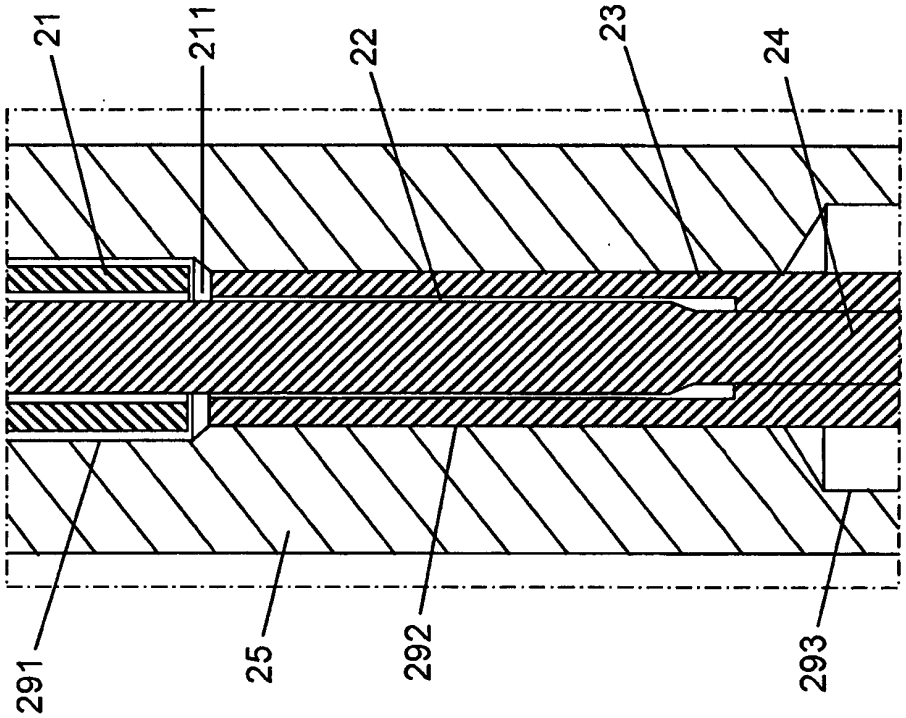

FIG.7A

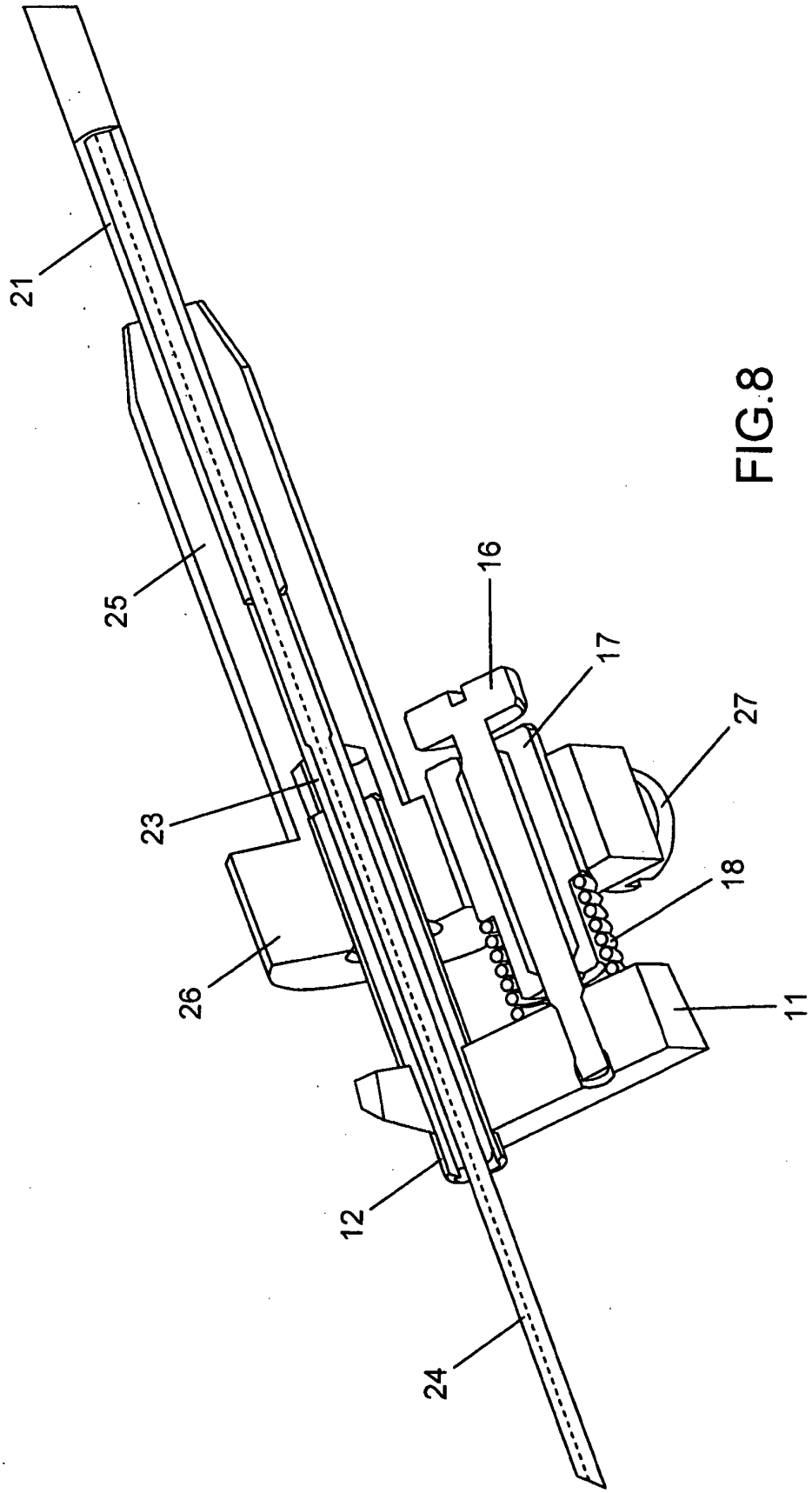

FIG.8

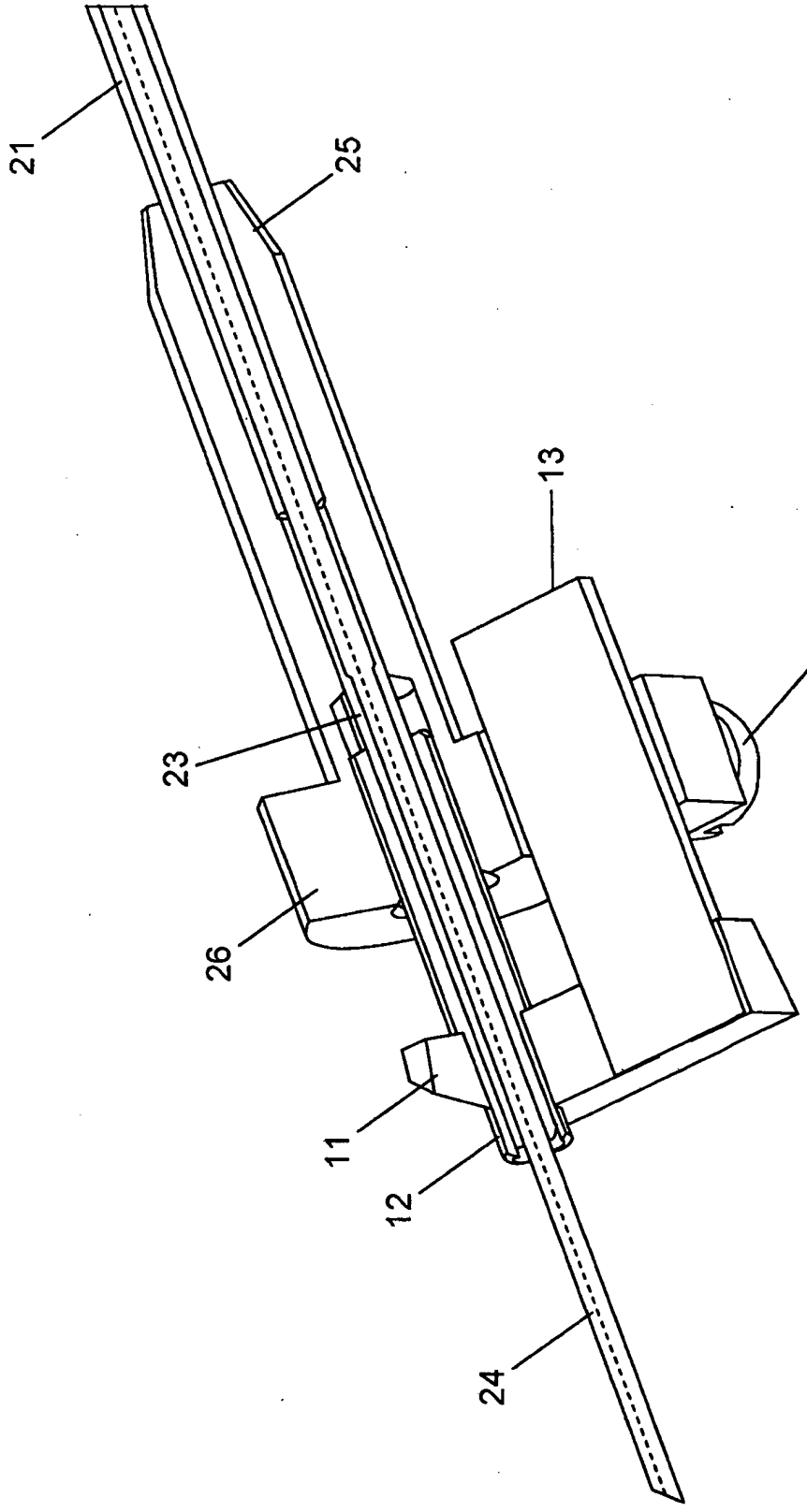

FIG.9

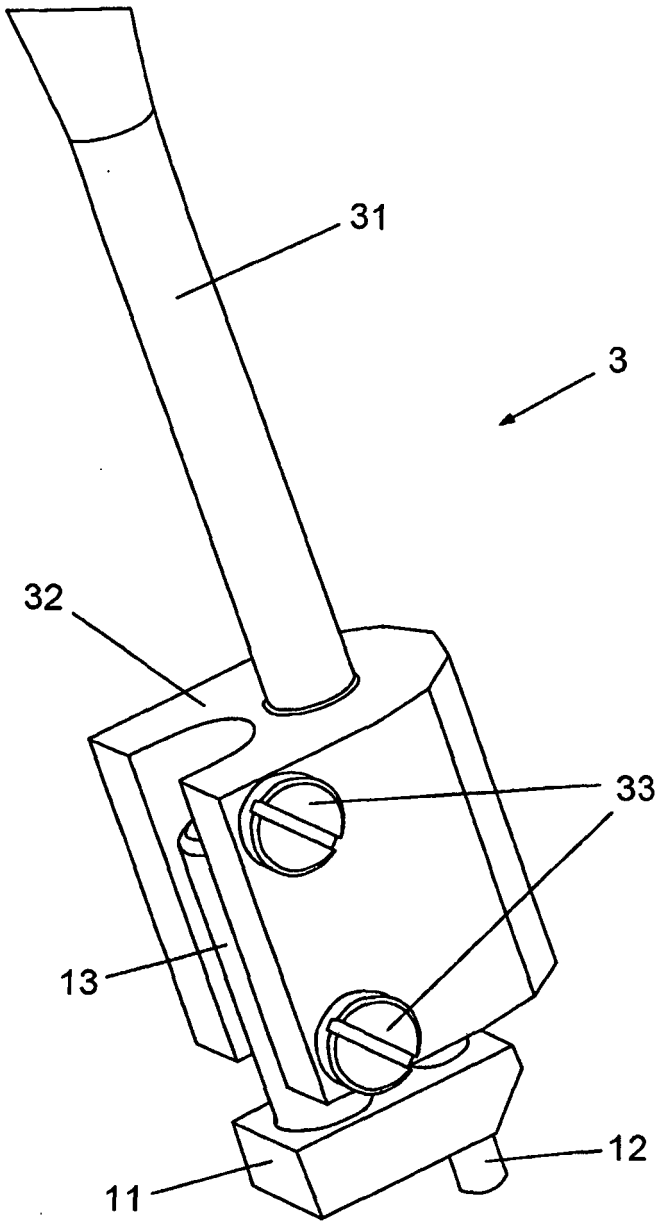

FIG.10

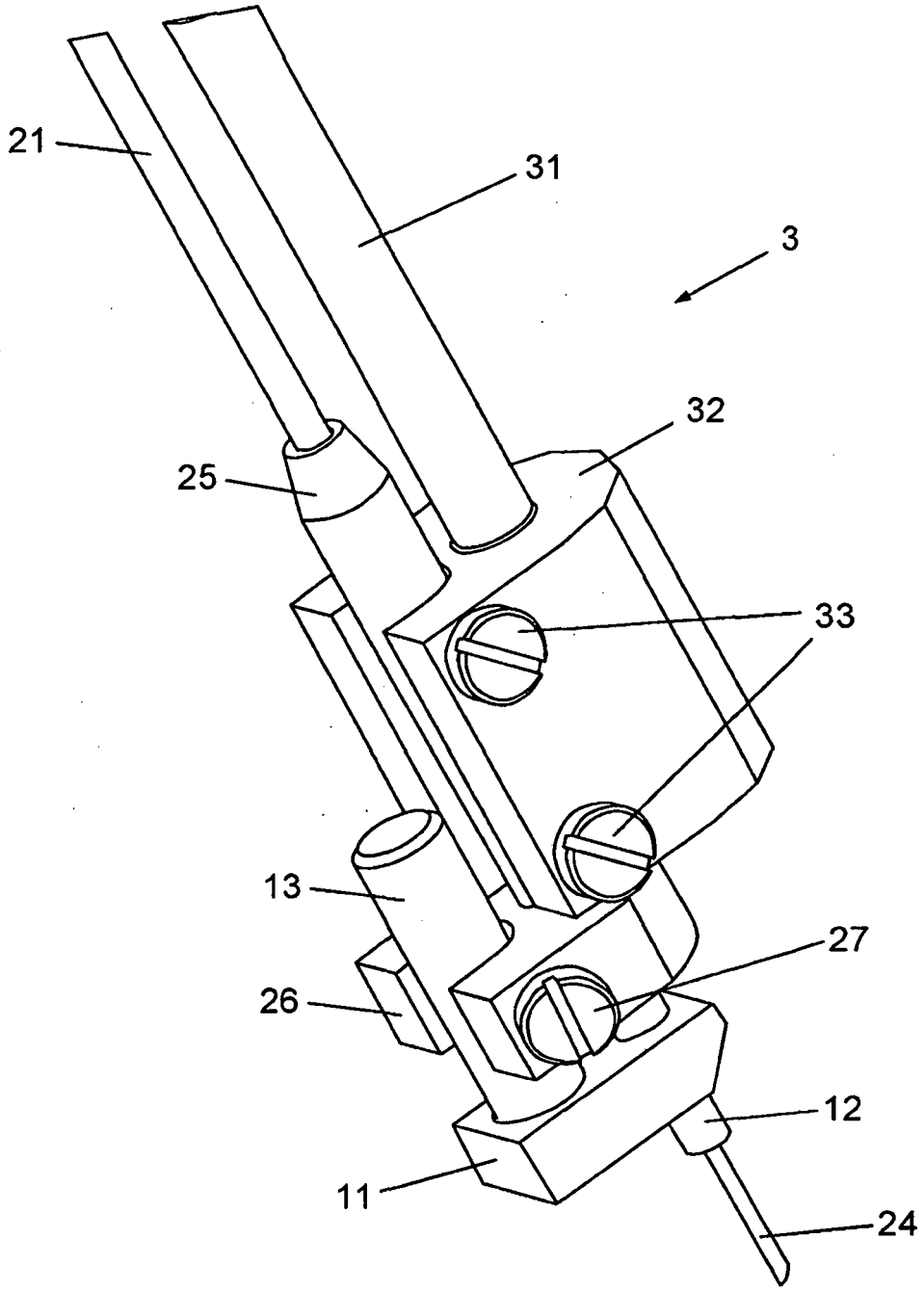

FIG.11

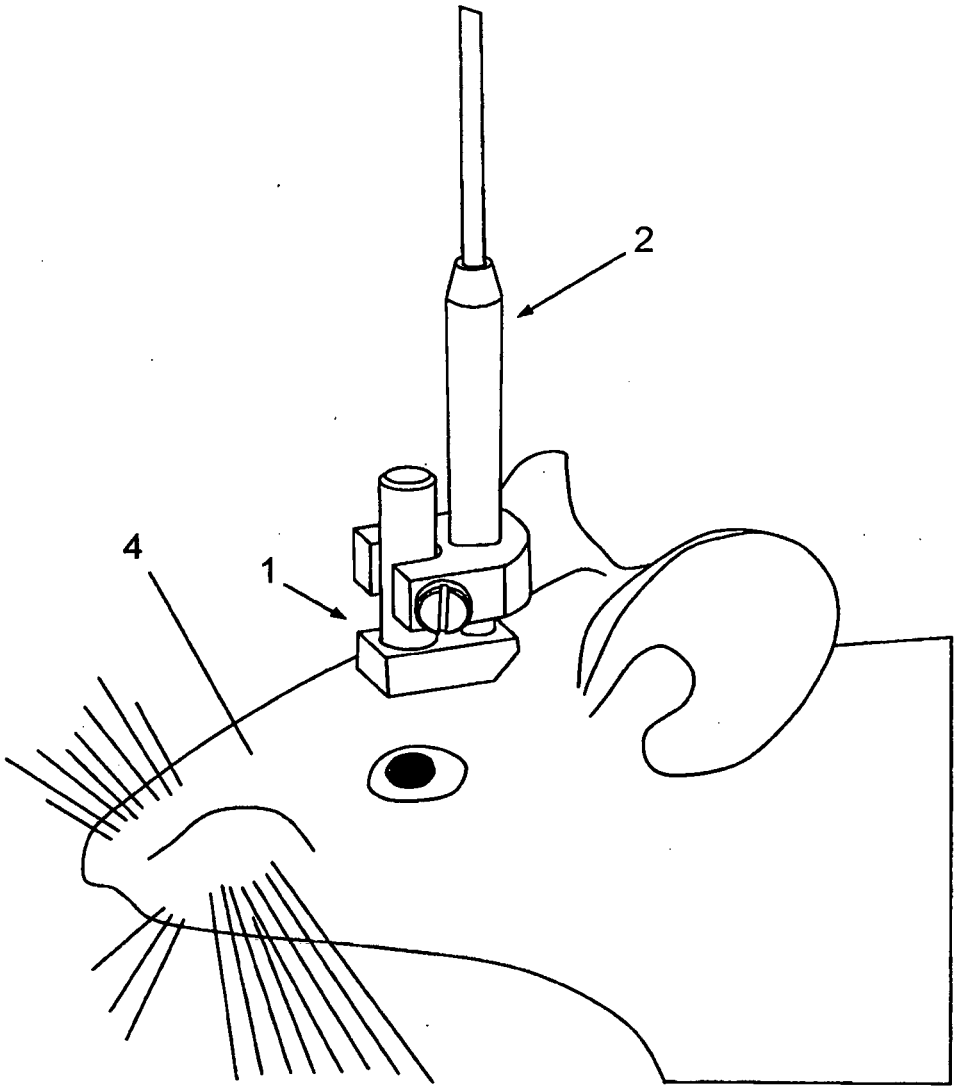

FIG.12

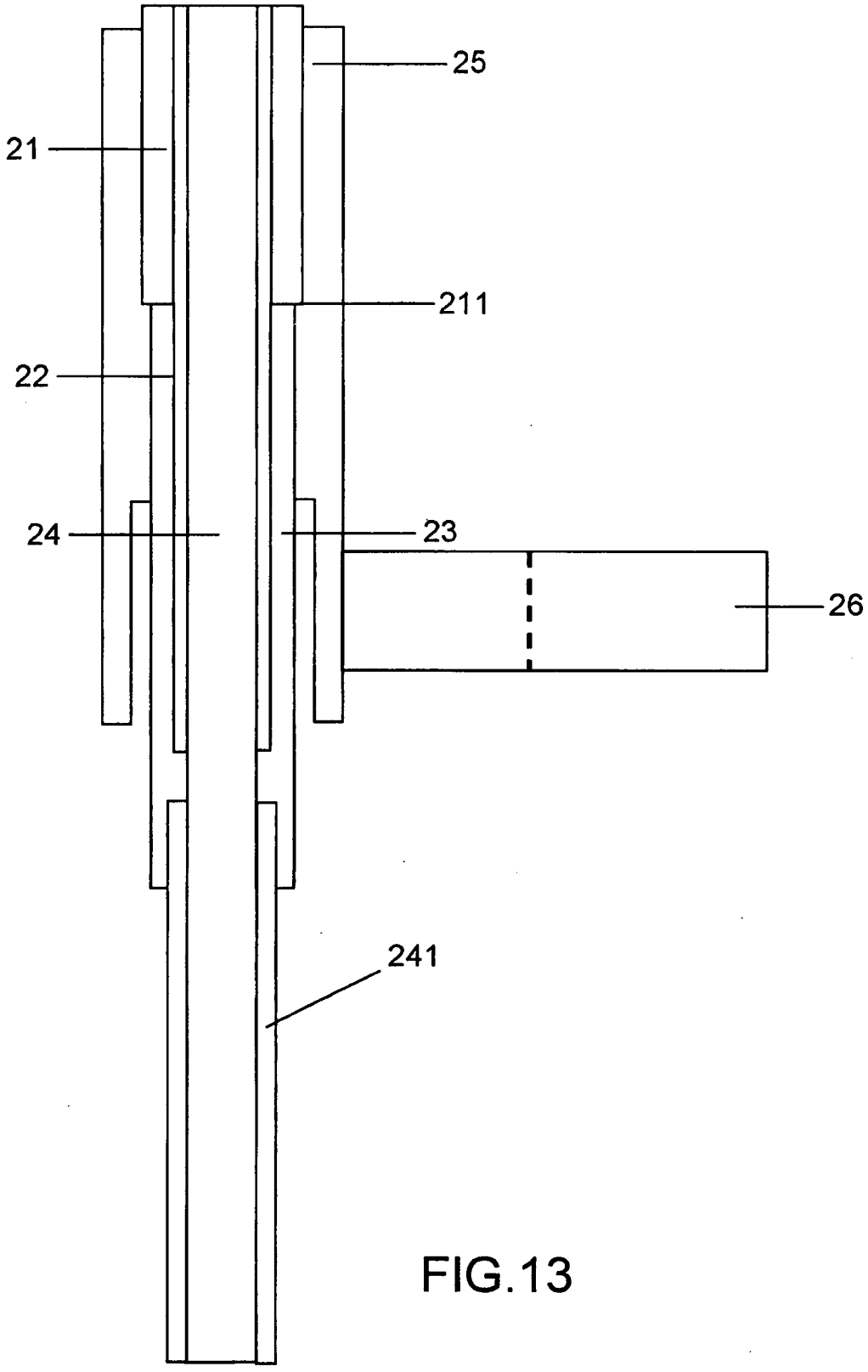

FIG.13

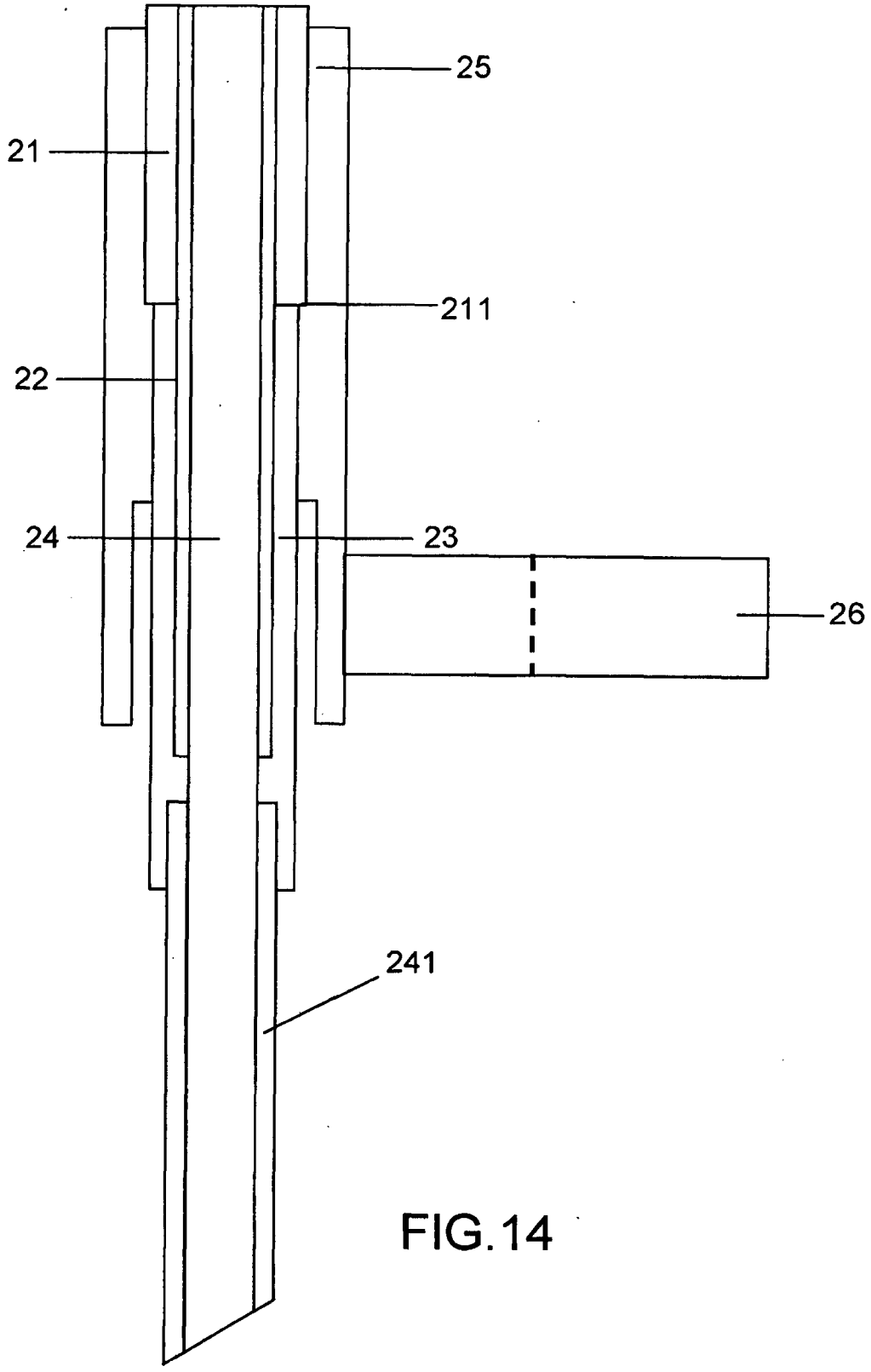

FIG.14

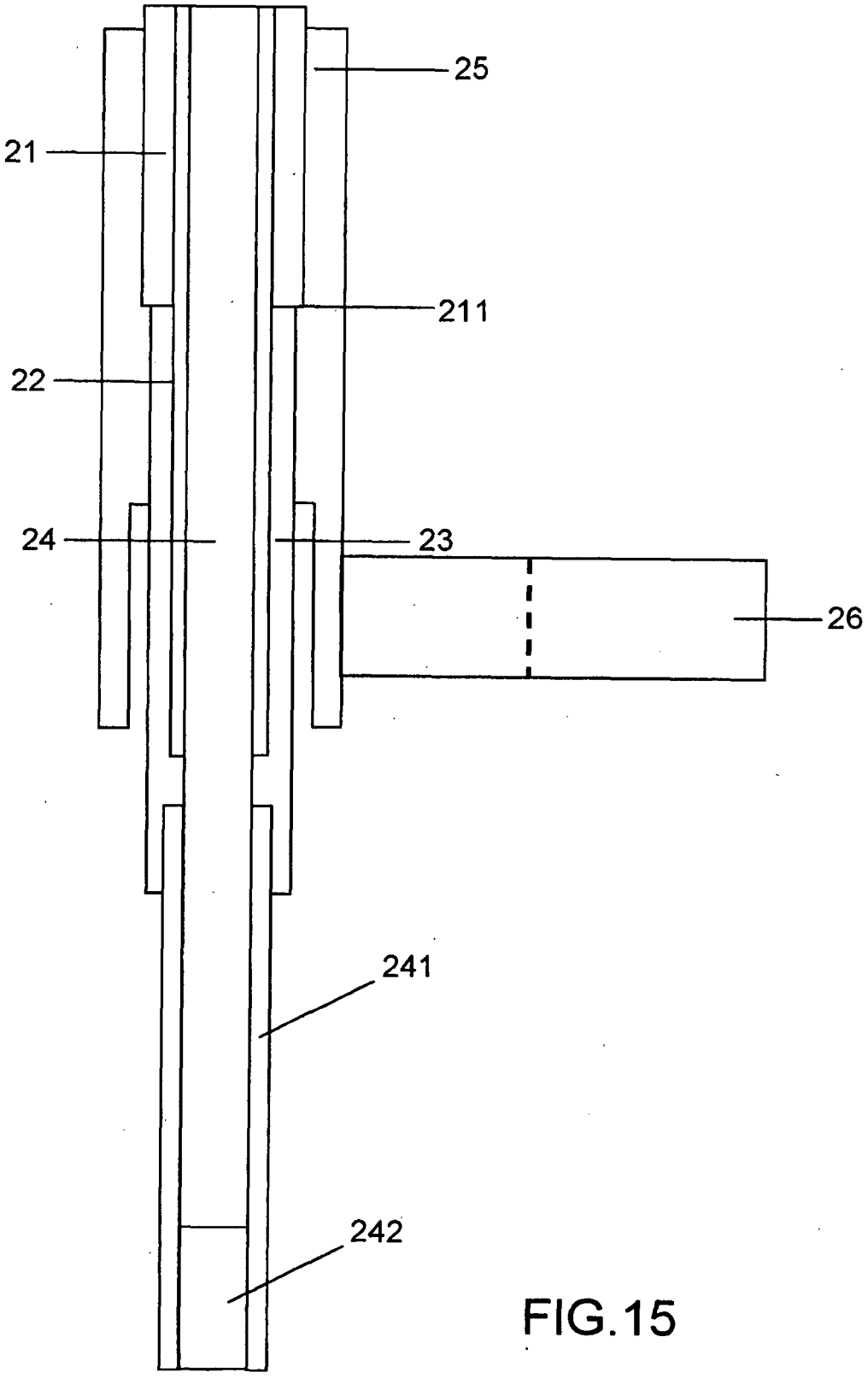

FIG.15

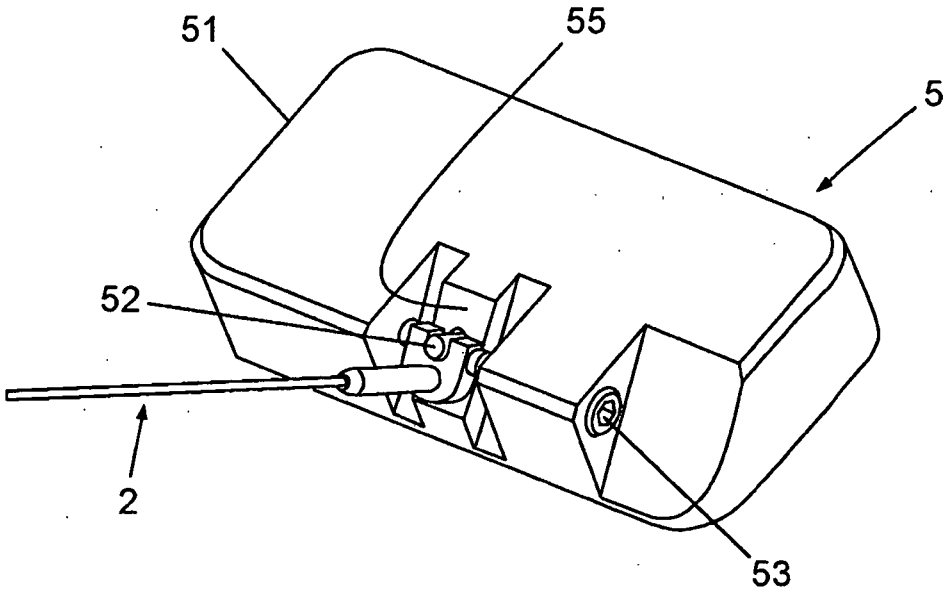

FIG.16A

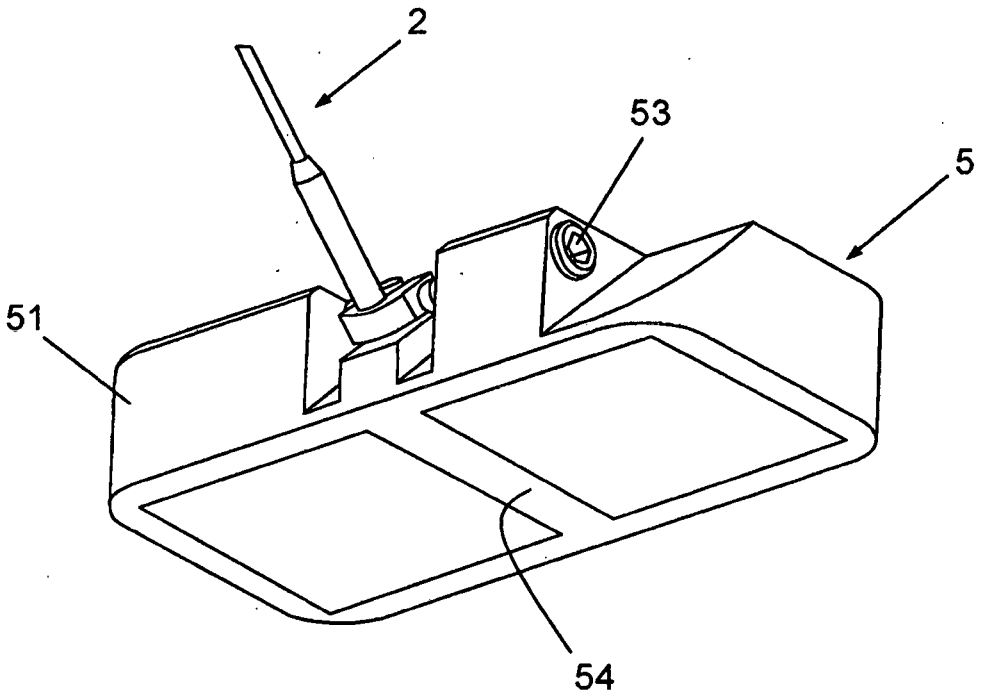

FIG.16B

REFERENCES CITED IN THE DESCRIPTION

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- **VINCENT et al.** Live imaging of neural structure and function by fibred fluorescence microscopy. *EMBO reports,* September 2006 **[0004]**
- **BENJAMIN FLUSBERG et al.** High speed, miniaturized fluorescence microscopy in freely moving mice. *Nature Methods,* October 2008 **[0005]**
- **MASKOS et al.** Functional fibered fluorescence imaging in freely moving mouse, poster No. 598.8. *38th annual meeting of the Society for Neurosciences,* 2008 **[0005]**

专利名称(译)	脑纤维束显微镜检查装置		
公开(公告)号	EP2459101B1	公开(公告)日	2014-08-20
申请号	EP2010768547	申请日	2010-07-19
[标]申请(专利权)人(译)	莫纳基技术公司		
申请(专利权)人(译)	莫纳克亚TECHNOLOGIES		
当前申请(专利权)人(译)	莫纳克亚TECHNOLOGIES		
[标]发明人	BOULAROT NICOLAS CRESSANT ARNAUD		
发明人	BOULAROT, NICOLAS CRESSANT, ARNAUD		
IPC分类号	A61B1/00 A61B19/00 A61B5/00 A61B1/313 G02B23/26		
CPC分类号	A61B5/0084 A61B1/00154 A61B1/313 A61B5/0068 A61B5/0071 A61B5/6814 A61B5/6864 A61B5/6868 A61B5/6882 A61B90/11 A61B2503/40 A61B2560/063 A61B2562/0238 G02B23/26		
优先权	61/229677 2009-07-29 US		
其他公开文献	EP2459101A2 EP2459101B8		
外部链接	Espacenet		

摘要(译)

颅内植入物，用于将纤维束定位到动物大脑的特定区域。植入物可包括基部支撑件，其通过在颅骨中钻出的孔口固定到动物的颅骨上，中空导管布置成穿过基部支撑件以通过钻孔将纤维束引导到动物的脑部。锁定构件布置在基部支撑件上，以与纤维束的套圈配合，第一锁定构件构造成将纤维束锁定到动物的脑的指定区域。