



(51) International Patent Classification:
A61K 9/22 (2006.01)

(21) International Application Number:
PCT/IB2011/050860

(22) International Filing Date:
1 March 2011 (01.03.2011)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
61/308,998 1 March 2010 (01.03.2010) US

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(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PE, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

(84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LR, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

- with international search report (Art. 21(3))
- with amended claims (Art. 19(1))

(54) Title: DRUG DELIVERY DEVICE

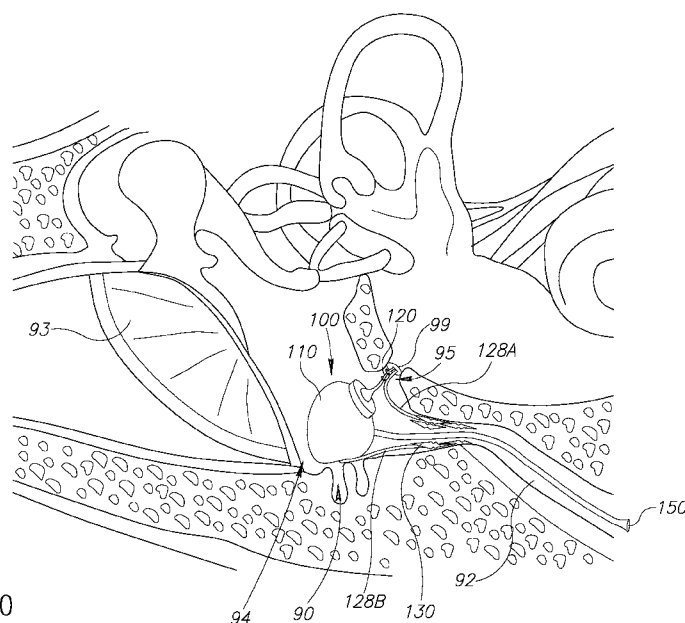


Figure 10

(57) Abstract: A drug delivery device comprising a drug reservoir coupled with a delivery element arranged to deliver the drug from the reservoir to a specified location; and an anchoring element arranged to anchor and support the drug reservoir in a vicinity of the specified location and the delivery element at the specified location. The anchoring element is attachable to a cavity and has a collapsed state arranged to enable insertion of the anchoring element into the cavity in a minimally invasive procedure; and an operative state arranged to affix the anchoring element to the cavity. The anchoring element is arranged to change from the collapsed state to the operative state upon fulfillment of a specified condition.

DRUG DELIVERY DEVICE

CROSS REFERENCE TO RELATED APPLICATIONS

[0001] This application claims the benefit of U.S. Provisional Patent Application 61/308,998 filed on March 1st, 2010, which is incorporated herein by reference.

BACKGROUND

1. TECHNICAL FIELD

[0002] The present invention relates to the field of drug delivery, and more particularly, to an implantable drug delivery device.

2. DISCUSSION OF RELATED ART

[0003] Various methods of drug delivery into body cavities are known. These shall be exemplified below for the middle ear cavity. Intratympanic delivery involves depositing the therapeutic agent in the middle ear, relying primarily on diffusion through the round window membrane (RWM) for access to the scala tympani. Intratympanic delivery must rely solely on diffusion through the round window and for dispersion throughout the scala tympani. Therefore, access to the apical regions of the scala tympani can be limited, and large concentration gradients may develop. Also, the RWM presents a physical barrier to delivery. A great deal of variability of condition and thickness of the membrane across population has been observed, limiting dosage control from patient to patient.

[0004] Additionally, cavities in the body are usually open, and present a challenge to maintain an appropriate concentration of the drug in proximity to the application area, e.g. the RWM. In the inner ear for example, drug may be drained into other regions in the middle ear and be removed altogether through the Eustachian tube.

[0005] For intratympanic delivery, multiple passive and active drug delivery approaches are being explored, with applications ranging from protection from noise-induced hearing loss to delivery of regenerative compounds aimed at alleviating sensorineural hearing loss. This research is often aimed at establishing extended release profiles with controllable and predictable kinetics using compounds within the middle ear. In the following, examples of passive drug delivery to the cochlea will be described for several principal approaches: biodegradable polymers, hydrogel-based systems, and nanoparticles. In addition, examples of active intratympanic delivery are described using a variety of components and devices, including microcatheters, microwicks, and osmotic pumps. Here, we define active as any device used for intratympanic dosing of therapeutics, although in some cases, these devices by themselves do not provide a mechanism for changing dosing.

[0006] Passive drug delivery systems are designed to deliver drug compounds with specific kinetic profiles using local triggers for release, such as hydrolysis in the in vivo environment, or in response to local stimuli such as temperature or pH. Drug may be dispersed within a matrix or contained within a reservoir encapsulated by a shell of bulk polymer, depending upon the specific application.

[0007] Active intratympanic drug delivery was explored for streptomycin ablation treatment of vertigo associated with Meniere's disease and Sakata's study of

dexamethasone treatment for tinnitus. The methods for and uses of intratympanic drug delivery are sufficiently numerous that review articles have been dedicated to the topic, for example: "Inner ear drug delivery for auditory applications" by Leary Swan et al. (Advanced drug delivery reviews 60 (2008) 1583-1599, and "Drug delivery for treatment of inner ear disease: Current state of knowledge" by McCall et al. (Ear & Hearing 2010; 31; 156-165).

[0008] Anatomical variations can significantly alter the pathway from the delivery site to the round window. These include extraneous or false membranes, fibrous tissue and fatty plugs, and may be present in as high as one third of all patients. In addition, there is a need for better characterization of pharmacokinetics in both the inner and middle ear. While substantial progress has been made on this front, particularly by Salt and Plontke, the inability to define consistent and accurate methods (or the lack of broad acceptance of such methods) for withdrawal and analysis of fluid samples taken from the inner ear during preclinical animal studies substantially impedes progress. Certainly most reported clinical results do not include measurements of drug concentration at the round window or other quantities like middle ear fluid clearance rate that might be used to infer an approximate concentration. Even in preclinical animal experiments, measurement of cochlear concentrations is difficult. The need for continued development of improved methods for quantifying drug concentration in both the middle and inner ear is clear. Combined approaches, for example Hashimoto's combination of hearing test and subsequent morphologic examination of hair cell death appear promising. Ultimately it appears as though wide acceptance of a particular device or method may require the

development of measurement techniques that provide data which permits evaluation of drug delivery and treatment outcome against a pharmacokinetic model.

[0009] Additional approaches are: (i) Round Window Microcatheters (μ -CathTM and e-CathTM) developed by IntraEAR and later acquired by Durect in 1999, currently used for local drug delivery to the middle or inner ear for tinnitus by Neurosystec, (ii) Silverstein MicroWickTM for treatment of Meniere's related vertigo by perfusion of gentamicin, (iii) an implantable Alzet osmotic pump provides the means for continuous sustained delivery in a very small volume with simple form factor, (iv) various intracochlear drug delivery methods and cochlear prosthesis-based delivery.

[0010] WIPO Publication No. 2010143181, which is incorporated herein by reference in its entirety, discloses an electrode, and a minimally-invasive auditory implant system employing the electrode, for treating hearing disorders by electrically stimulating tissues in the middle ear. The electrode employs a structure which switches between narrow and spread shapes, facilitating the electrode insertion into the site, securing the electrode against vibration or permanent movement, and optimizing the current density.

BRIEF SUMMARY

[0011] Embodiments of the present invention provide a drug delivery device comprising: a drug reservoir coupled with a delivery element arranged to deliver the drug from the reservoir to a specified location; and an anchoring element arranged to anchor and support the drug reservoir in a vicinity of the specified location and the delivery element at the specified location, wherein the anchoring element is attachable to a cavity and has at least two states: a collapsed state arranged to enable insertion of the anchoring element

into the cavity in a minimally invasive procedure; and an operative state arranged to affix the anchoring element to the cavity, wherein the anchoring element is arranged to change from the collapsed state to the operative state upon fulfillment of a specified condition.

[0012] These, additional, and/or other aspects and/or advantages of the present invention are: set forth in the detailed description which follows; possibly inferable from the detailed description; and/or learnable by practice of the present invention.

BRIEF DESCRIPTION OF THE DRAWINGS

[0013] The present invention will be more readily understood from the detailed description of embodiments thereof made in conjunction with the accompanying drawings of which:

Figure 1 is a schematic illustration of a drug delivery device positioned in the middle ear, according to some embodiments of the invention;

Figures 2A and **2B** are schematic illustrations of an anchoring element of the drug delivery device in collapsed an operative states, according to some embodiments of the invention;

Figures 3A and **3B** are schematic illustrations of the drug delivery device in collapsed an operative states, according to some embodiments of the invention;

Figures 4A to **4C** are schematic illustrations of toroidal drug delivery devices, according to some embodiments of the invention;

Figures 5A and **5B** are schematic illustrations of the drug delivery device with hooked protrusions in the anchoring element, in collapsed an operative states, according to some embodiments of the invention;

Figures 6 and 7 are schematic illustrations of toroidal drug delivery devices in the paranasal sinuses, according to some embodiments of the invention;

Figure 8 is a schematic illustration of the drug delivery device with hooked protrusions in the anchoring element, in the operative state in the hypotympanum, according to some embodiments of the invention;

Figures 9 and 10 are schematic illustrations of filling methods of the drug delivery device, according to some embodiments of the invention;

Figures 11A-11D are schematic illustrations of an ellipsoidal drug delivery device in collapsed and operative states and in the paranasal sinuses, according to some embodiments of the invention;

Figure 12 is a high level schematic block diagram illustrating components of the drug delivery device, according to some embodiments of the invention; and

Figure 13 is a high level schematic flowchart illustrating a method of delivering a drug to a specified location, according to some embodiments of the invention.

DETAILED DESCRIPTION

[0014] Before explaining at least one embodiment of the invention in detail, it is to be understood that the invention is not limited in its application to the details of construction and the arrangement of the components set forth in the following description or illustrated in the drawings. The invention is applicable to other embodiments or of being practiced or carried out in various ways. Also, it is to be understood that the phraseology and terminology employed herein is for the purpose of description and should not be regarded as limiting.

[0015] **Figure 1** is a schematic illustration of a drug delivery device **100** positioned in the middle ear, according to some embodiments of the invention; **Figures 2A** and **2B** are schematic illustrations of an anchoring element **130** of drug delivery device **100** in collapsed and operative states (**101** and **102**, respectively), according to some embodiments of the invention; and **Figures 3A** and **3B** are schematic illustrations of drug delivery device **100** in collapsed and operative states (**101** and **102**, respectively), according to some embodiments of the invention.

[0016] Drug delivery device **100** comprises a drug reservoir **110** (e.g. compressible, elastic and water-tight) coupled with a delivery element **120** arranged to deliver the drug from reservoir **110** to a specified location **99**. Drug reservoir **110** may be elastic (e.g. have an outer elastic chassis) to the extent that drug is excreted under pressure from drug reservoir **110** through delivery element **120**. Drug delivery device **100** may further comprise a control unit **140** arranged to control delivery element **120**, and an anchoring element **130**.

[0017] Anchoring element **130** is attachable to a cavity **90** and has at least two states: a collapsed state **131** arranged to enable insertion of anchoring element **130** into cavity **90** in a minimally invasive procedure; and an operative state **132** arranged to affix anchoring element **130** to cavity **90**. Cavity **90** may comprise a bone cavity with epithelial tissue, a cartilage cavity or any other cavity which is stiff enough to support and allow anchoring of anchoring element **130**. Anchoring element **130** is arranged to change (e.g. self-expand) from collapsed state **131** to operative state **132** upon fulfillment of a specified condition. Anchoring element **130** may have a form that attaches to cavity **90** upon expansion to the operative state.

[0018] Anchoring element **130** is arranged to anchor and support drug reservoir **110** in a vicinity of specified location **99** and to anchor and support delivery element **120** at specified location **99**. Specified location **99** may be within a second cavity **95**. Second cavity **95** may be the same cavity as cavity **90** or an adjacent cavity. Second cavity **95** may be a bone cavity with epithelial tissue, a cartilage cavity or any other cavity to which drug may be delivered.

[0019] **Figures 1 and 8-10** illustrates drug delivery device **100** in the inner ear (comprising malleus **71**, incus **72**, stapes **73** at oval window, vestibular organ **74**, cochlea **75** and its basis **76**), e.g. arranged to deliver the drug to the round window as specified location **99**. In embodiments, anchoring element **130** may be arranged to be attachable to Eustachian tube **92** or hypotympanum **94**. In the first case, anchoring element **130** may be cylindrical, or comprise a cylindrical network (or mesh) that attaches to the circumference of an orifice or a lumen of Eustachian tube **92**. In the second case, anchoring element **130** may have a form that attaches to hypotympanum **94** upon expansion to the operative state, such as a conical form comprising a membrane **129** spun by bracings **128** interconnected at a common basis **127** (**Figures 2A, 2B**).

[0020] Drug delivery device **100** may be part of a drug delivery system (not shown) comprising additionally an applicator **149** (illustrated schematically in **Figure 12**) arranged to introduce (releasably deploying) drug delivery device **100** to a vicinity of specified location **99** (e.g. within hypotympanum **94**) and deliver anchoring element **130** in collapsed state **131** to cavity **90**.

[0021] Applicator **149** may be further arranged to deliver anchoring element **130** in collapsed state **131** to cavity **90** and transfer anchoring element **130** to operative state **132**

upon releasing anchoring element **130** from applicator **149**. Applicator **149** may actuate the transition anchoring element **130** from collapsed **131** to operative state **132**.

[0022] Applicator **149** may be any standard endoscopic equipment, for example, a balloon arranged to facilitate a transition of anchoring element **130** from collapsed state **131** to operative state **132**. Applicator **149** may further comprise an endoscopic visualization channel.

[0023] Either drug reservoir **110** in its operative state **111** or delivery element **120** is arranged to fit into the hypotympanum.

[0024] **Figures 4A to 4C** are schematic illustrations of toroidal drug delivery devices **100**, according to some embodiments of the invention; and **Figures 6 and 7** are schematic illustrations of toroidal drug delivery devices **100** in paranasal sinuses **96**, according to some embodiments of the invention.

[0025] Drug reservoir **110** may be ellipsoidal. Alternatively, drug reservoir **110** may be toroidal (**Figures 4A, 4B, 4C**) to allow fluid communication through an axial hollow **126** in the toroid. Anchoring element **130** may be integrated in the toroidal drug reservoir **110** (e.g. **Figure 4C**). Toroidal drug reservoir **110** may be positioned within a fluid conducting cavity, such as Eustachian tube **92** or sinuses **96**. The dimensions and sizes of drug reservoir **110** may be adapted to the intended position thereof. Toroidal drug reservoir **110** may have integrated anchoring element **130**, or anchoring element **130** may support drug reservoir **110** internally, at hollow **126**. For example, positioned in Eustachian tube **92**, anchoring element **130** may position drug reservoir **110** to keep Eustachian tube **92** in fluid communication with the inner ear through hollow **126** and in place in respect to specified location **99**.

[0026] Drug reservoir **110** may be formed to fit into hypotympanum **94**, or sinus **96** and comprise a conduit **122** arranged to deliver the drug from drug reservoir **110** to specified location **99**. Anchoring element **130** may comprise supporting elements **121** arranged to support conduit **122**. Supporting elements **121** may be connected to an extension **128A** of anchoring element **130** (e.g. of bracing **128**). **13**. Conduit **12** may comprise a stricture (not shown) that is arranged to limit a rate of delivery of the drug therethrough to specified location **99**. The width of the stricture may be controlled by control unit **140** or externally.

[0027] **Figures 5A and 5B** are schematic illustrations of drug delivery device **100** with hooked protrusions **133** in anchoring element **130**, in collapsed and operative states (**101**, **131** and **102**, **132** respectively), according to some embodiments of the invention; and

[0028] **Figure 8** is a schematic illustration of drug delivery device **100** with hooked protrusions **133** in anchoring element **130**, in operative state **102** in hypotympanum **94**, according to some embodiments of the invention.

[0029] Anchoring element **130** may comprise a plurality of elongated protrusions **133** fixated at one end **133A** and arranged to spread apart at their free ends **133B** in operative state **132**. Free ends **133B** of protrusions **133** may be hooked to enhance attachment of anchoring element to cavity **90** (such as hypotympanum **94**).

[0030] In still another embodiment (**Figures 11A – 11D**), anchoring element **130** may comprise a plurality of flexible ellipses **134** interconnected at two common apices **134A** to define a spheroid, that is prolate in collapsed state **131** (**Figure 11A**) and oblate in operative state **132** (**Figure 11B**). **Figures 7A, 7B** illustrate drug delivery device **100** within sinuses **96**.

[0031] Anchoring element **130** may be made of a shape memory alloy that is pre-formed to an operative state shape. Anchoring element **130** may be made of a super elastic metal, such as nitinol or elginoy. Anchoring element **130** may then be inserted in collapsed state **131** and expand to the pre-formed shape upon the specified condition, for example body warmth or reaching a specified body temperature.

[0032] Anchoring element **130** in operative state **132** may be arranged to receive, support and fixate drug reservoir **110**.

[0033] Delivery element **120** may comprise a tip **123** arranged to deliver the drug to specified location **99**. Tip **123** may be porous or spongeous, to optimize drug delivery.

[0034] Delivery element **120** may be arranged to fit into round window niche **95**, and may comprise a sealing element **124** in proximity to tip **123** (**Figures 4A, 4B, 8, 11A, 11B**) arranged to seal round window niche **95** to prevent leakage of the drug out of round window niche **95**. Sealing element **124** may comprise one or more silicon discs (**Figure 8**), and may be structurally integrated in tip **123A** (**Figure 4C**).

[0035] Drug delivery device **100** may further comprise an electroporation unit **123B** (**Figures 11A, 11B**) comprising one or more electrodes **123C**, arranged to enhance a permeability of a membrane at specified location **99**, for example of the round window. Electroporation unit **123B** may be integrated with tip **123** form a functional tip **123D** for delivering the drug.

[0036] The drug itself may be is selected from any anti inflammatory drugs, N-Methyl-D-aspartate (NMDA) antagonists, anti-oxidant drugs, nerve growth factors, cyto-toxic drugs, and cyto-static drugs. The drug may be selected to treat an ear disease, such as Tinnitus, Meniere's disease, Sudden hearing loss, etc.

[0037] The drug may be selected to facilitate ion current, and drug delivery device **100** may further comprise a stimulation electrode (not shown) in galvanic contact with the drug.

[0038] **Figures 9 and 10** are schematic illustrations of filling methods of drug delivery device **100**, according to some embodiments of the invention.

[0039] Drug reservoir **110** may be fillable through ear drum **93** (**Figure 9**), or through any other soft tissue near the location of drug reservoir **110** by filling device **150**. In embodiments, drug reservoir **110** may be fillable endoscopically, e.g. through Eustachian tube **92** (**Figure 10**) or through sinuses **96** or the nasal cavity.

[0040] Filling device **150** may comprise a syringe (**Figure 9**), e.g. with a needle, or a drug-loading/refilling catheter (**Figure 10**).

[0041] Anchoring element **130** may comprise a proximal barrel shaped mesh having extension **128** supporting delivery element **120** (e.g. conduit **122**) and extension **128B** arranged to support drug reservoir **110** in place.

[0042] Drug delivery device **100** may comprise retrieval elements (not shown) connected e.g. to anchoring element **130** of drug reservoir **110** and arranged to allow endoluminal retrieval of drug delivery device **100** as a whole, or drug reservoir **110** on itself, e.g. by an endoscopic intervention. For example, the retrieval elements may transfer anchoring element **130** from operative state **132** back to collapsed state **131** before retrieval. The retrieval elements may comprise retrieval handles arranged to engage a retrieval apparatus provided with means of transitioning anchoring element **130** from operative state **132** back to collapsed state **131** and its subsequent disposition into a generally elongated sheath.

[0043] **Figure 12** is a high level schematic block diagram illustrating components of drug delivery device **100**, according to some embodiments of the invention. Control unit **140** may comprise an internal power source **141**, or may be arranged to inductively receive power by an inductive element **142** (an implantable energy conversion unit), e.g. by an attached coil **145**, from an external (extra-corporeal) power source **141A**.

[0044] Control unit **140** may be internal or external (**140A**), or device **100** may comprise both internal control unit **140** and external control unit **140A**. In case only external control unit **140A** is used, inductive element may be connected to reservoir **110** and inductive power supply therethrough may actuate drug delivery. External power may be delivered to drug delivery device **100** in mechanical, electromagnetic or magnetic forms. Control unit **140** may comprise a controller (e.g. an electronic processor embedded in PCB) arranged to manage drug delivery and power use of device **100**.

[0045] Control unit **140** may further comprise a pump (not shown) arranged to deliver the drug through delivery element **120**.

[0046] **Figure 13** is a high level schematic flowchart illustrating a method **200** of delivering a drug to a specified location, according to some embodiments of the invention. Method **200** comprises the following stages: inserting the drug in a reservoir connected to an anchoring element in a collapsed state to a vicinity of the specified location (stage **205**); attaching the anchoring element in a cavity in the vicinity of the specified location (stage **210**), by transforming the anchoring element from the collapsed to an operative state (stage **215**); and releasing the drug from the reservoir (stage **220**).

[0047] Method **200** may further comprise pre-forming the anchoring element in the operative state (stage **214**), for example from a super-elastic metal such as nitinol, or elginoy.

[0048] Method **200** may further comprise controlling the drug release **220** from the reservoir (stage **222**), externally (e.g. by a mechanical or electromagnetic signal, or internally, e.g. by reshaping of the reservoir upon a specified conditions, such as a body temperature).

[0049] Method **200** may further comprise sealing a second cavity that surrounds the specified location (**224**), to prevent drug leakage and allow a better control of the delivered amount of drug and the delivery location, and furthermore allow using smaller amounts of drug.

[0050] Method **200** may further comprise re-filling the reservoir without removing the anchoring element from the cavity (stage **226**), for example endoscopically or through neighboring soft tissue, such as the ear drum in case of drug delivery to the inner ear, or nose cartilage in case of drug delivery to the paranasal sinuses.

[0051] Method **200** may further comprise integrating the anchoring element in the reservoir (stage **228**), for example when the reservoir is toroidal with the anchoring element as its external layer.

[0052] In the above description, an embodiment is an example or implementation of the invention. The various appearances of "one embodiment", "an embodiment" or "some embodiments" do not necessarily all refer to the same embodiments.

[0053] Although various features of the invention may be described in the context of a single embodiment, the features may also be provided separately or in any suitable

combination. Conversely, although the invention may be described herein in the context of separate embodiments for clarity, the invention may also be implemented in a single embodiment.

[0054] Furthermore, it is to be understood that the invention can be carried out or practiced in various ways and that the invention can be implemented in embodiments other than the ones outlined in the description above.

[0055] The invention is not limited to those diagrams or to the corresponding descriptions. For example, flow need not move through each illustrated box or state, or in exactly the same order as illustrated and described.

[0056] Meanings of technical and scientific terms used herein are to be commonly understood as by one of ordinary skill in the art to which the invention belongs, unless otherwise defined.

[0057] While the invention has been described with respect to a limited number of embodiments, these should not be construed as limitations on the scope of the invention, but rather as exemplifications of some of the preferred embodiments. Other possible variations, modifications, and applications are also within the scope of the invention. Accordingly, the scope of the invention should not be limited by what has thus far been described, but by the appended claims and their legal equivalents.

CLAIMS

What is claimed is:

1. A drug delivery device comprising:

a drug reservoir coupled with a delivery element arranged to deliver the drug from the reservoir to a specified location; and

an anchoring element arranged to anchor and support the drug reservoir in a vicinity of the specified location and the delivery element at the specified location, wherein the anchoring element is attachable to a cavity and has at least two states:

a collapsed state arranged to enable insertion of the anchoring element into the cavity in a minimally invasive procedure; and

an operative state arranged to affix the anchoring element to the cavity,

wherein the anchoring element is arranged to change from the collapsed state to the operative state upon fulfillment of a specified condition.

2. The drug delivery device of claim 1, wherein the specified location is within a second cavity.
3. The drug delivery device of claim 2, wherein the second cavity is the round window niche.
4. The drug delivery device of claim 3, wherein the delivery element is arranged to fit into the round window niche.

5. The drug delivery device of claim 4, further comprising a sealing element arranged to seal the round window niche to prevent leakage of the drug out of the round window niche.
6. The drug delivery device of claim 2, wherein the second cavity is a sinus.
7. The drug delivery device of claim 1, wherein the cavity is at least one of: the Eustachian tube, the hypotympanum, and a sinus.
8. The drug delivery device of claim 1, wherein the drug reservoir is arranged, in its operative state, to fit into the hypotympanum.
9. The drug delivery device of claim 8, wherein the drug reservoir is fillable through the ear drum.
10. The drug delivery device of claim 1, wherein the drug reservoir is fillable endoscopically.
11. The drug delivery device of claim 10, wherein the drug reservoir is fillable through the Eustachian tube.
12. The drug delivery device of claim 1, further comprising a control unit arranged to control the delivery element.
13. The drug delivery device of claim 12, wherein the control unit comprises a power source.
14. The drug delivery device of claim 12, wherein the control unit is internal and arranged to inductively receive power.
15. The drug delivery device of claim 14, wherein the control unit comprises a coil arranged to inductively receive power.

16. The drug delivery device of claim 14, further comprising an external power source arranged to inductively provide power to the control unit.
17. The drug delivery device of claim 14 or 15, further comprising an external control unit arranged to provide power inductively to the internal control unit that is arranged to control the drug delivery.
18. The drug delivery device of claim 12, wherein the control unit comprises a pump arranged to deliver the drug through the delivery element.
19. The drug delivery device of claim 1, wherein the specified condition is reaching a specified body temperature.
20. The drug delivery device of claim 1, wherein the anchoring element comprises a shape memory alloy pre-formed to an operative state shape.
21. The drug delivery device of claim 1, wherein the delivery element comprises a conduit.
22. The drug delivery device of claim 21, wherein the anchoring element comprises a supporting element arranged to support the conduit.
23. The drug delivery device of claim 21, wherein the conduit comprises a stricture arranged to limit a rate of delivery of the drug therethrough.
24. The drug delivery device of claim 1, wherein the anchoring element in the operative state is cylindrical.
25. The drug delivery device of claim 1, wherein the anchoring element in the operative state is conical.
26. The drug delivery device of claim 25, wherein the anchoring element in the operative state is arranged to receive, support and fixate the drug reservoir.

27. The drug delivery device of claim 1, wherein the drug delivery element is arranged to fit into the hypotympanum.
28. The drug delivery device of claim 1, wherein the anchoring element comprises a plurality of elongated protrusions fixated at one end and arranged to spread apart at their free ends in the operative state.
29. The drug delivery device of claim 28, wherein the free ends of the protrusions are hooked.
30. The drug delivery device of claim 1, wherein the anchoring element comprises a plurality of flexible ellipses interconnected at two common apices to define a spheroid that is prolate in the collapsed state and oblate in the operative state.
31. The drug delivery device of claim 1, wherein the drug reservoir is toroidal to allow fluid communication through an axial hollow in the toroid.
32. The drug delivery device of claim 1, wherein the anchoring element is integrated in the toroidal drug reservoir.
33. The drug delivery device of claim 1, wherein the drug reservoir is ellipsoidal.
34. The drug delivery device of claim 1, wherein the drug reservoir has a collapsed empty state and an operative filled state.
35. The drug delivery device of claim 1, wherein the delivery element comprises a tip arranged to deliver the drug to the specified location.
36. The drug delivery device of claim 1, wherein the tip is porous.
37. The drug delivery device of claim 1, wherein the tip is spongy.
38. The drug delivery device of claim 1, wherein the anchoring element is self expanding, from the collapsed state to the operative state.

39. The drug delivery device of claim 1, wherein the anchoring element comprises a mesh.
40. The drug delivery device of claim 1, wherein the anchoring element comprises nitinol.
41. The drug delivery device of claim 1, further comprising an electroporation unit arranged to enhance a permeability of a membrane at the specified location.
42. The drug delivery device of claim 1, wherein the drug is selected to facilitate ion current, and further comprising a stimulation electrode in galvanic contact with the drug.
43. The drug delivery device of claim 1, wherein the drug is selected to treat an ear disease.
44. The drug delivery device of claim 1, wherein the drug is selected from: anti inflammatory drugs, NMDA antagonists, anti-oxidant drugs, nerve growth factors, cyto-toxic drugs, and cyto-static drugs.
45. The drug delivery device of claim 1, further comprising retrieval elements arranged to allow endoscopic retrieval of the drug delivery device.
46. A drug delivery system comprising the drug delivery device of any of claims 1 to 45 and an applicator arranged to introduce the drug delivery device to a vicinity of the specified location.
47. The drug delivery system of claim 46, wherein the applicator is further arranged to deliver the anchoring element in the collapsed state to the cavity and transfer the anchoring element to the operative state upon releasing the anchoring element from the applicator.

48. The drug delivery system of claim 46, wherein the applicator comprises a balloon arranged to facilitate a transition of the anchoring element from the collapsed state to the operative state.
49. The drug delivery system of claim 46, wherein the applicator further comprises an endoscopic visualization channel.
50. A method of delivering a drug to a specified location, comprising:
- inserting the drug in a reservoir connected to an anchoring element in a collapsed state to a vicinity of the specified location;
 - attaching the anchoring element in a cavity in the vicinity of the specified location, by transforming the anchoring element from the collapsed to an operative state; and
 - releasing the drug from the reservoir.
51. The method of claim 50, further comprising pre-forming the anchoring element in the operative state.
52. The method of claim 50, wherein the releasing is carried out controllably.
53. The method of claim 50, further comprising sealing a second cavity that surrounds the specified location.
54. The method of claim 50, further comprising re-filling the reservoir without removing the anchoring element from the cavity.
55. The method of claim 50, further comprising integrating the anchoring element in the reservoir.

AMENDED CLAIMS
received by the International Bureau on 14 August 2011 (14.08.2011)

What is claimed is:

1. A drug delivery device comprising:

a drug reservoir coupled with a delivery element arranged to deliver the drug from the reservoir to a specified location within a second cavity; and

an anchoring element attachable to a first cavity in a vicinity of the specified location and arranged to anchor and support the drug reservoir in the first cavity, and the delivery element at the second cavity, wherein the anchoring element is and has at least two states:

a collapsed state arranged to enable insertion of the anchoring element into the first cavity in a minimally invasive procedure; and

an operative state arranged to affix the anchoring element to the first cavity,

wherein the anchoring element is arranged to change from the collapsed state to the operative state upon fulfillment of a specified condition.

2. The drug delivery device of claim 1, wherein the first cavity is the Eustachian tube or the hypotympanum, the second cavity is the round window niche, and the drug is selected to treat an ear disease.
3. The drug delivery device of claim 2, wherein the drug reservoir is fillable through the ear drum or through the Eustachian tube.

4. The drug delivery device of claim 2, further comprising a sealing element arranged to seal the round window niche to prevent leakage of the drug out of the round window niche.
5. The drug delivery device of claim 1, further comprising a control unit arranged to control the delivery element and drug delivery therefrom with power supplied by an internal power source or by a coil arranged to inductively receive power from an external source.
6. The drug delivery device of claim 1, wherein the anchoring element is made of a shape memory alloy pre-formed to an operative state shape.
7. The drug delivery device of claim 6, wherein the anchoring element comprises a nitinol mesh.
8. The drug delivery device of claim 1, wherein the delivery element comprises a conduit and wherein the anchoring element comprises a supporting element arranged to support the conduit.
9. The drug delivery device of claim 8, wherein the conduit comprises a stricture arranged to limit a rate of delivery of the drug therethrough.
10. The drug delivery device of claim 1, wherein the anchoring element in the operative state is cylindrical or conical.
11. The drug delivery device of claim 1, wherein the anchoring element comprises a plurality of elongated protrusions fixated at one end and arranged to spread apart at their free ends in the operative state.

12. The drug delivery device of claim 1, wherein the anchoring element comprises a plurality of flexible ellipses interconnected at two common apices to define a spheroid that is prolate in the collapsed state and oblate in the operative state.
13. The drug delivery device of claim 1, wherein the drug reservoir is toroidal to allow fluid communication through an axial hollow in the toroid, and the anchoring element is integrated in the toroidal drug reservoir.
14. The drug delivery device of claim 1, wherein the delivery element comprises a porous or spongy tip arranged to deliver the drug to the specified location.
15. The drug delivery device of claim 1, further comprising an electroporation unit arranged to enhance a permeability of a membrane at the specified location.
16. The drug delivery device of claim 1, wherein the drug is selected to facilitate ion current, and further comprising a stimulation electrode in galvanic contact with the drug.
17. The drug delivery device of claim 1, wherein the drug is selected from: anti-inflammatory drugs, NMDA antagonists, anti-oxidant drugs, nerve growth factors, cyto-toxic drugs, and cyto-static drugs.
18. The drug delivery device of claim 1, further comprising retrieval elements arranged to allow endoscopic retrieval of the drug delivery device.
19. A drug delivery system comprising the drug delivery device of any of claims 1 to 18 and an applicator arranged to introduce the drug delivery device to a vicinity of the specified location.
20. The drug delivery system of claim 19, wherein the applicator is further arranged to deliver the anchoring element in the collapsed state to the cavity and transfer the

anchoring element to the operative state upon releasing the anchoring element from the applicator.

21. The drug delivery system of claim 21, wherein the applicator comprises a balloon arranged to facilitate a transition of the anchoring element from the collapsed state to the operative state.
22. The drug delivery system of claim 21, wherein the applicator further comprises an endoscopic visualization channel.
23. A method of delivering a drug to a specified location, comprising:
 - inserting the drug in a reservoir connected to an anchoring element in a collapsed state to a vicinity of the specified location;
 - attaching the anchoring element in a cavity in the vicinity of the specified location, by transforming the anchoring element from the collapsed to an operative state; and
 - releasing the drug from the reservoir.
24. The method of claim 23, further comprising pre-forming the anchoring element in the operative state.
25. The method of claim 23, wherein the releasing is carried out controllably.
26. The method of claim 23, further comprising sealing a second cavity that surrounds the specified location.
27. The method of claim 23, further comprising re-filling the reservoir without removing the anchoring element from the cavity.
28. The method of claim 23, further comprising integrating the anchoring element in the reservoir.

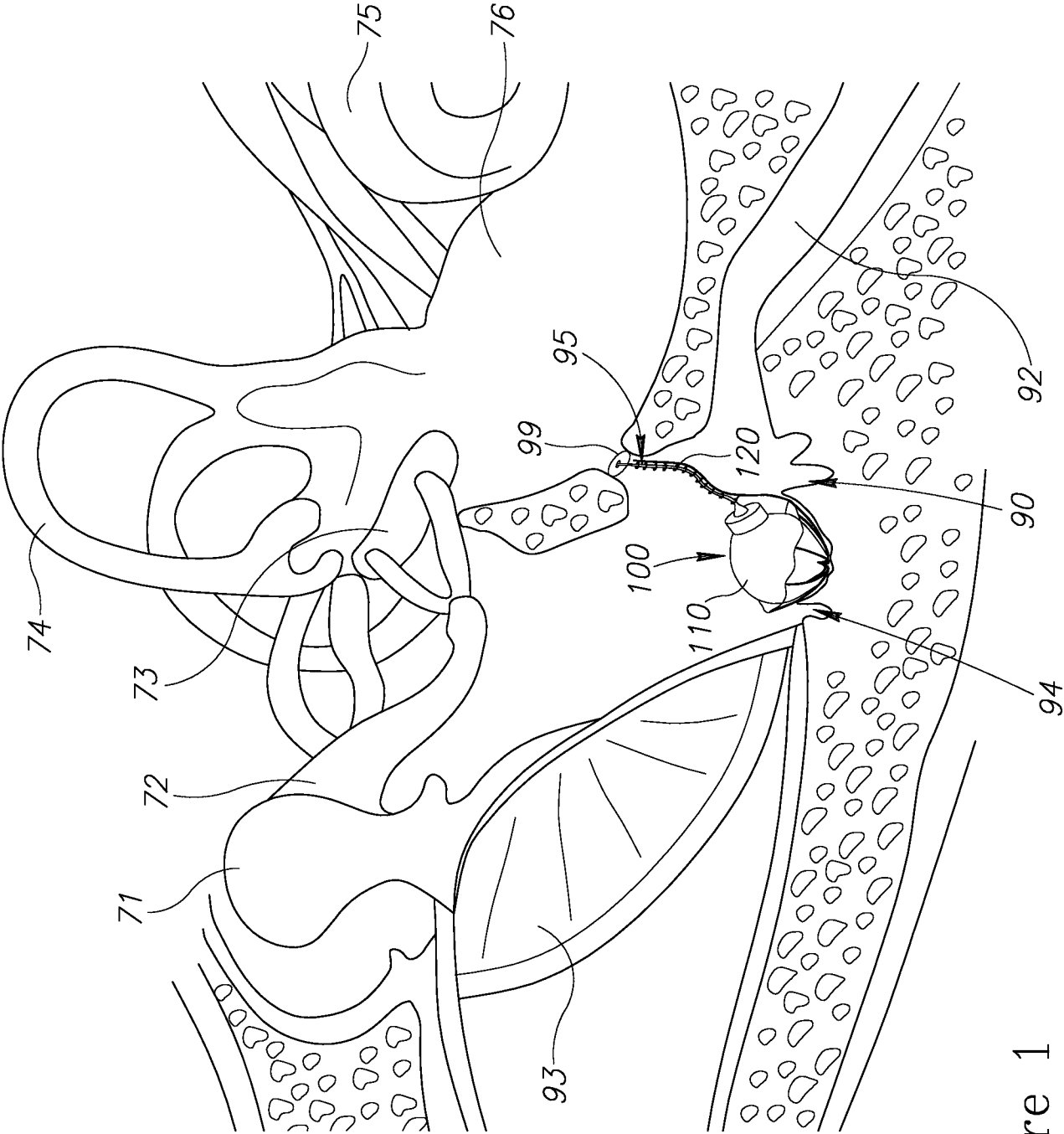


Figure 1

130 (132)

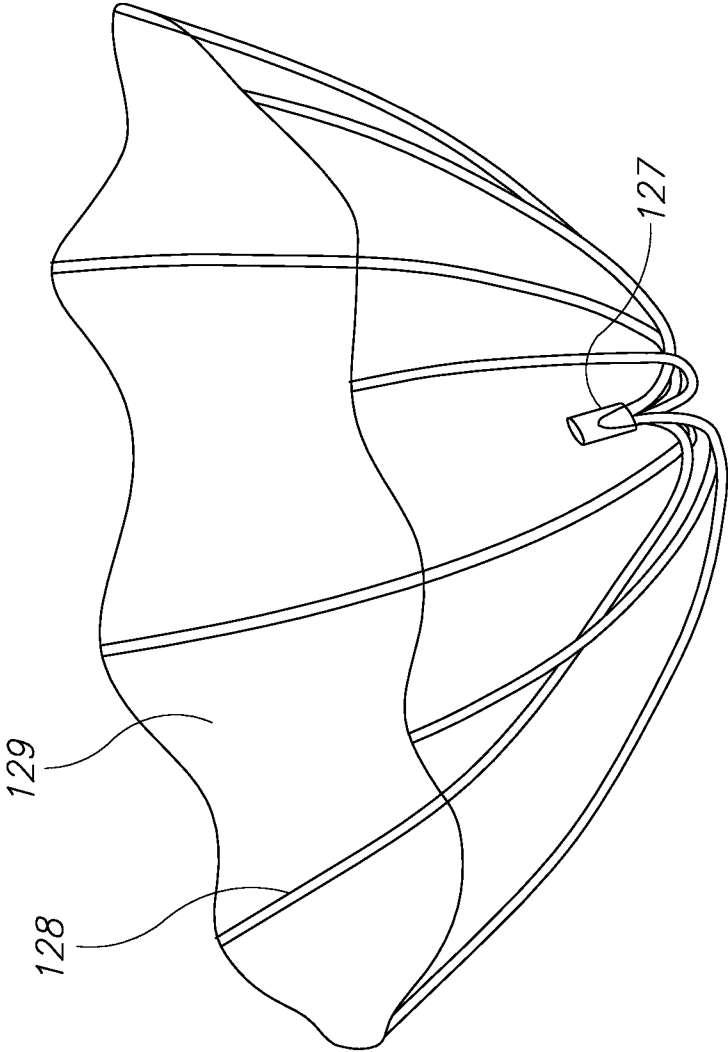


Figure 2B

130 (131)

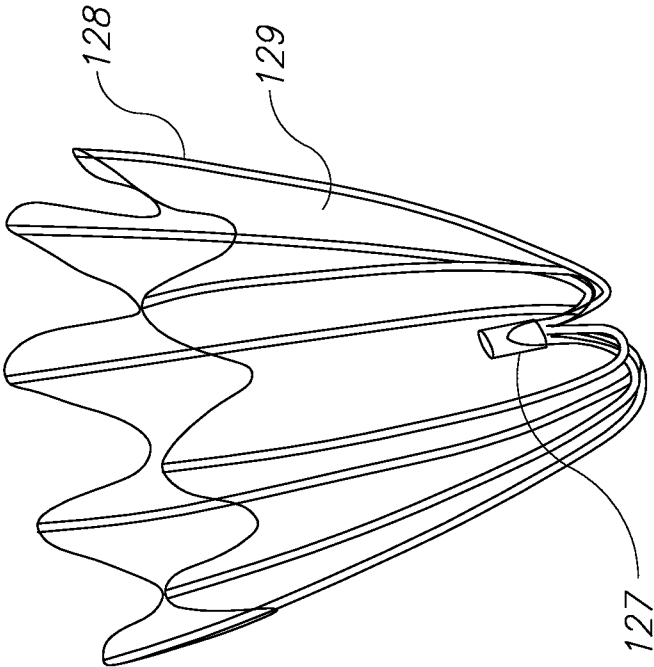


Figure 2A

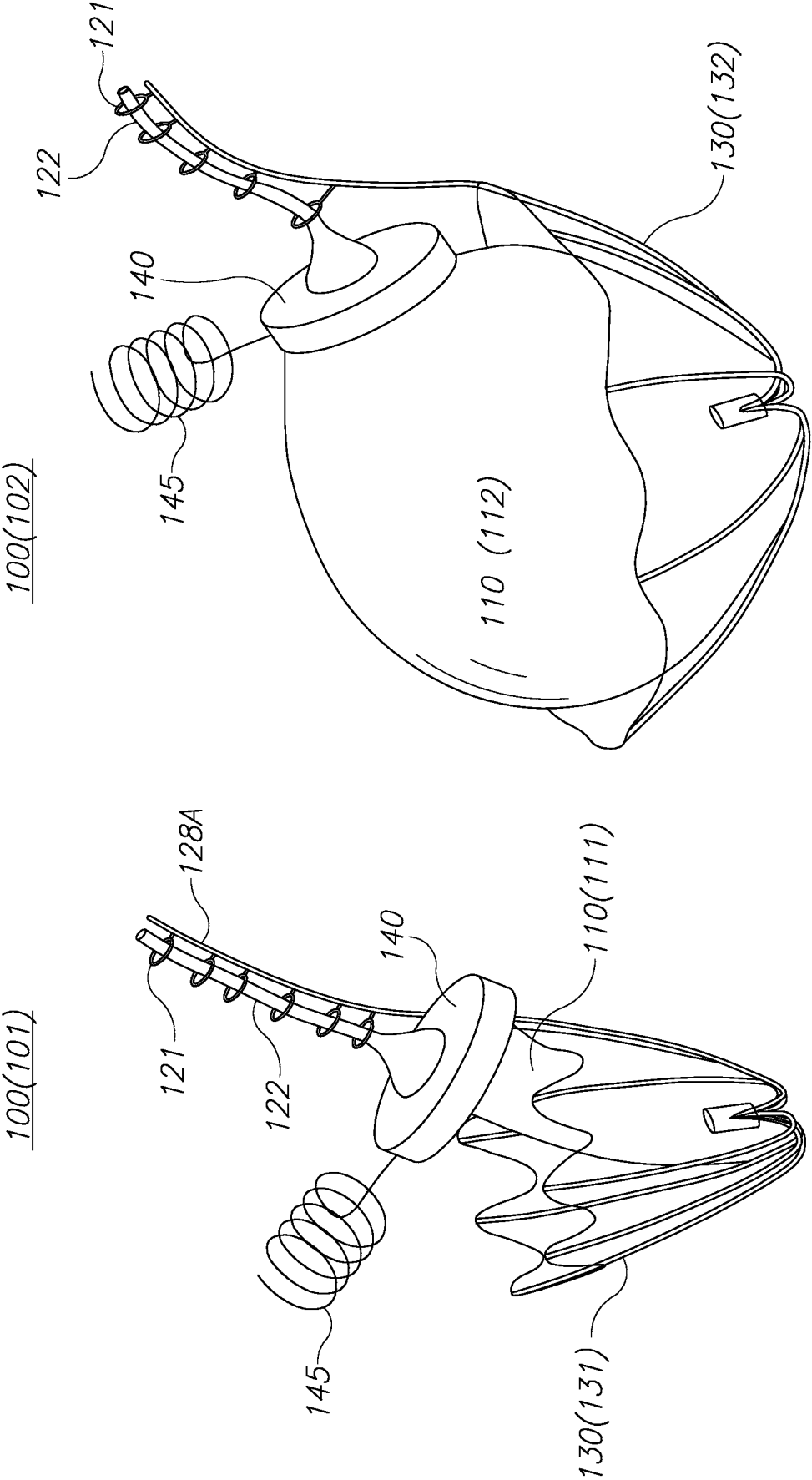


Figure 3B

Figure 3A

4/12

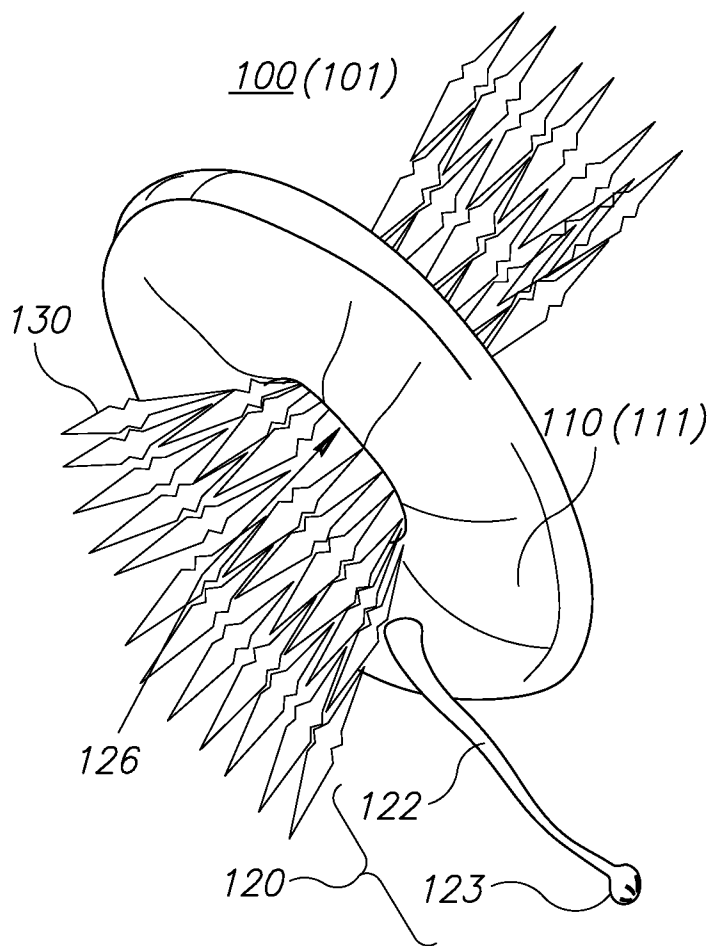


Figure 4A

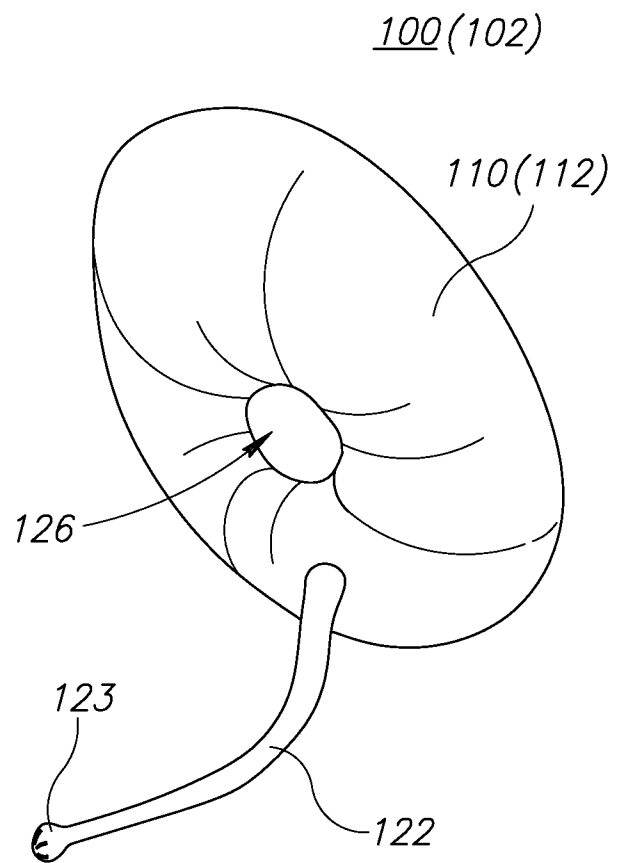


Figure 4B

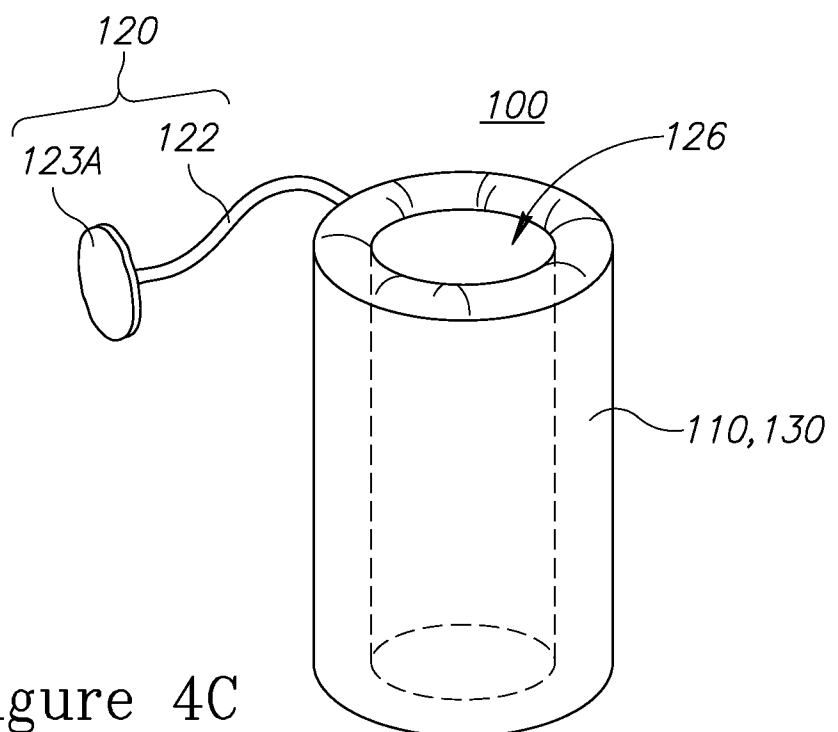


Figure 4C

5/12

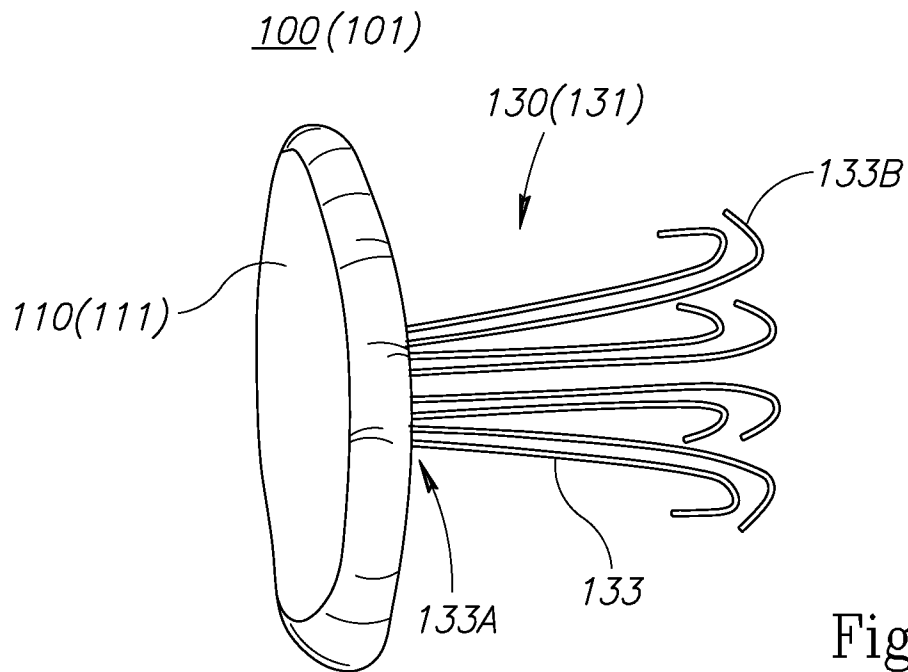


Figure 5A

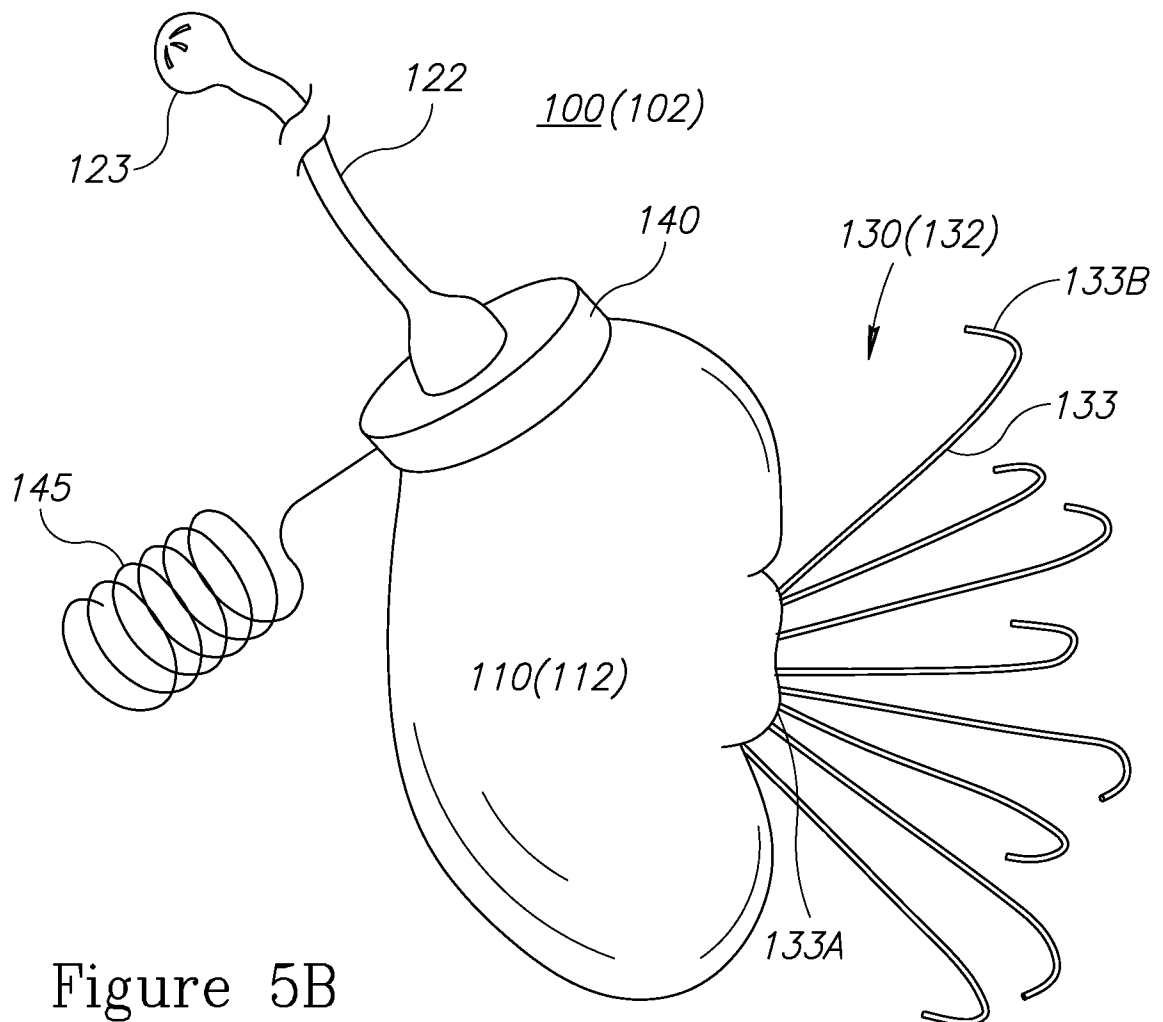


Figure 5B

6/12

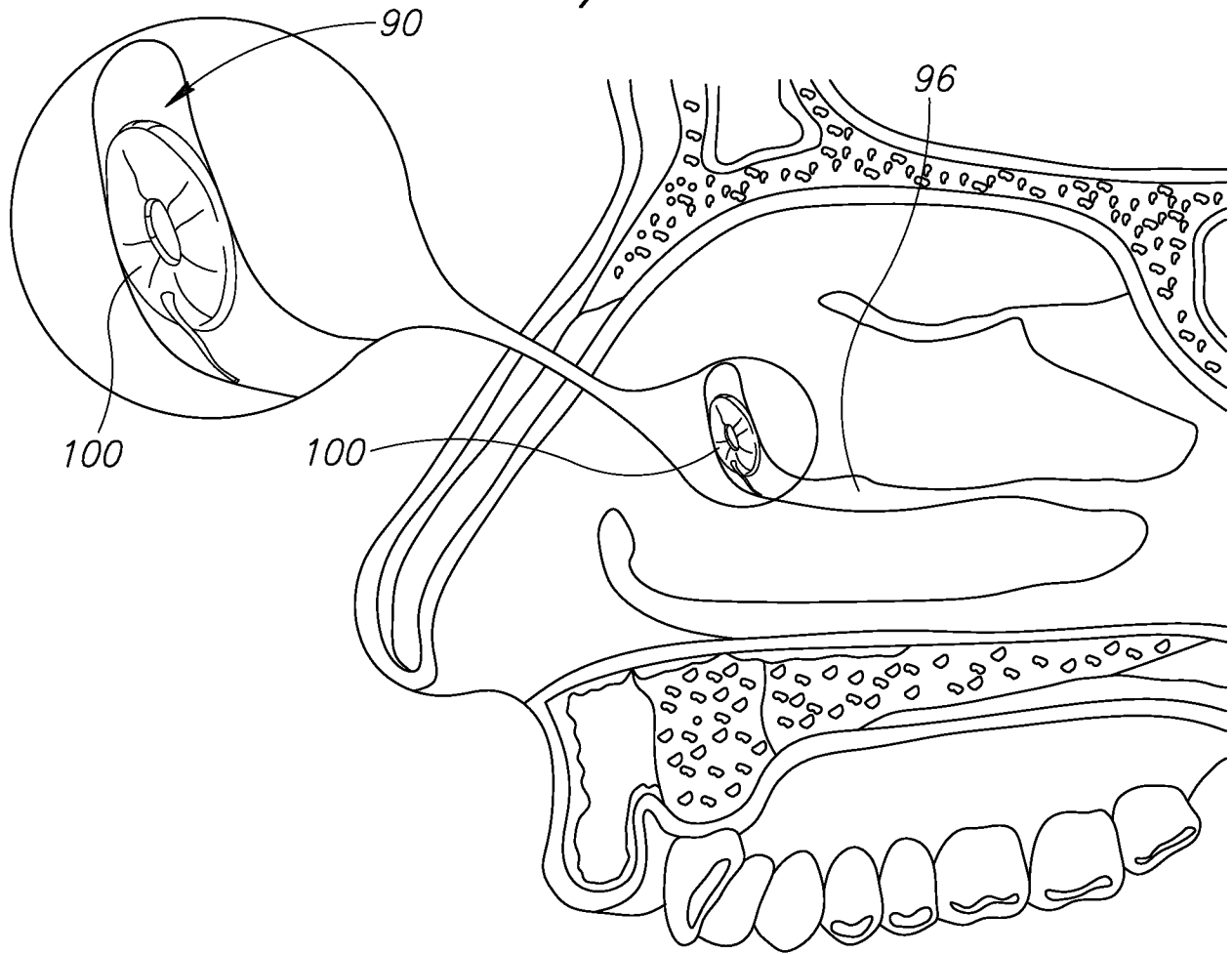


Figure 6

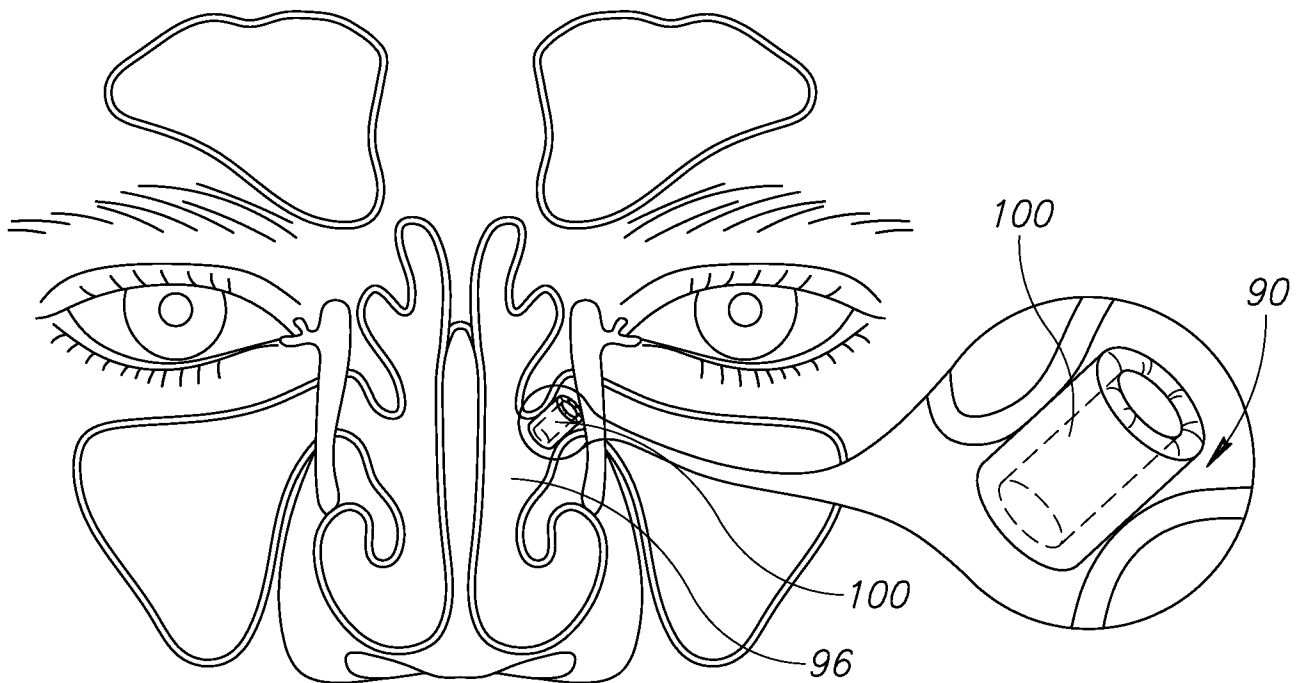


Figure 7

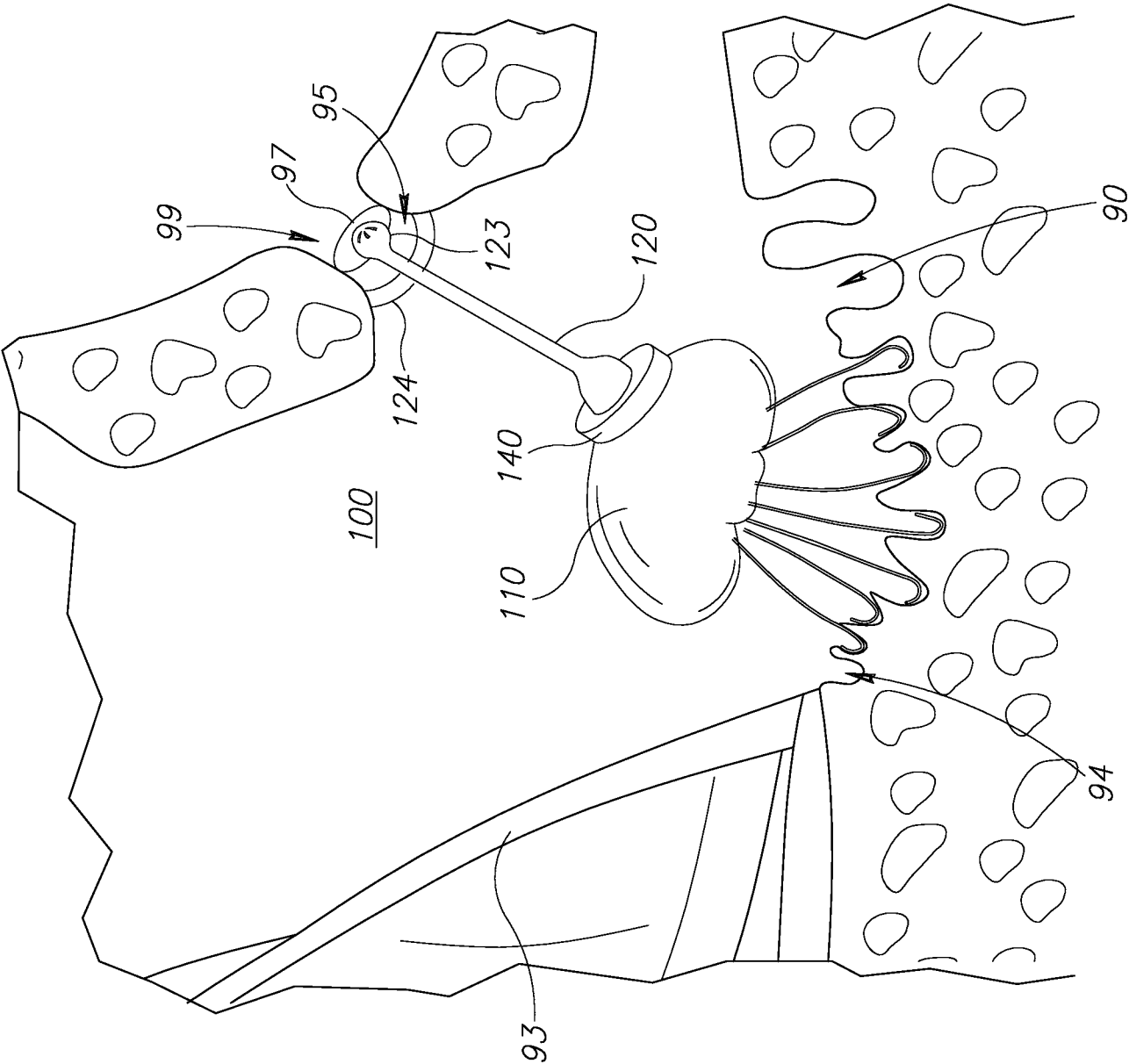


Figure 8

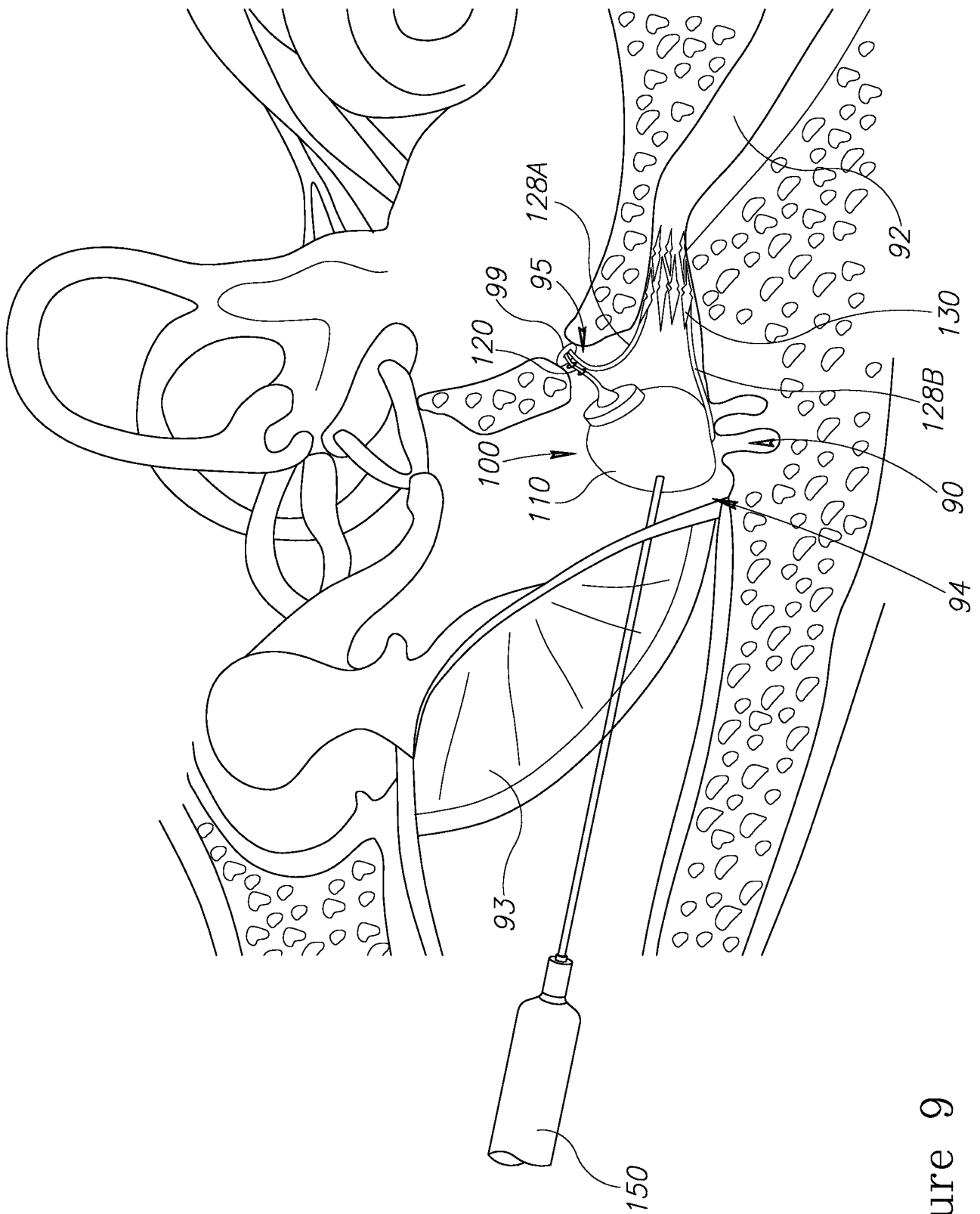


Figure 9

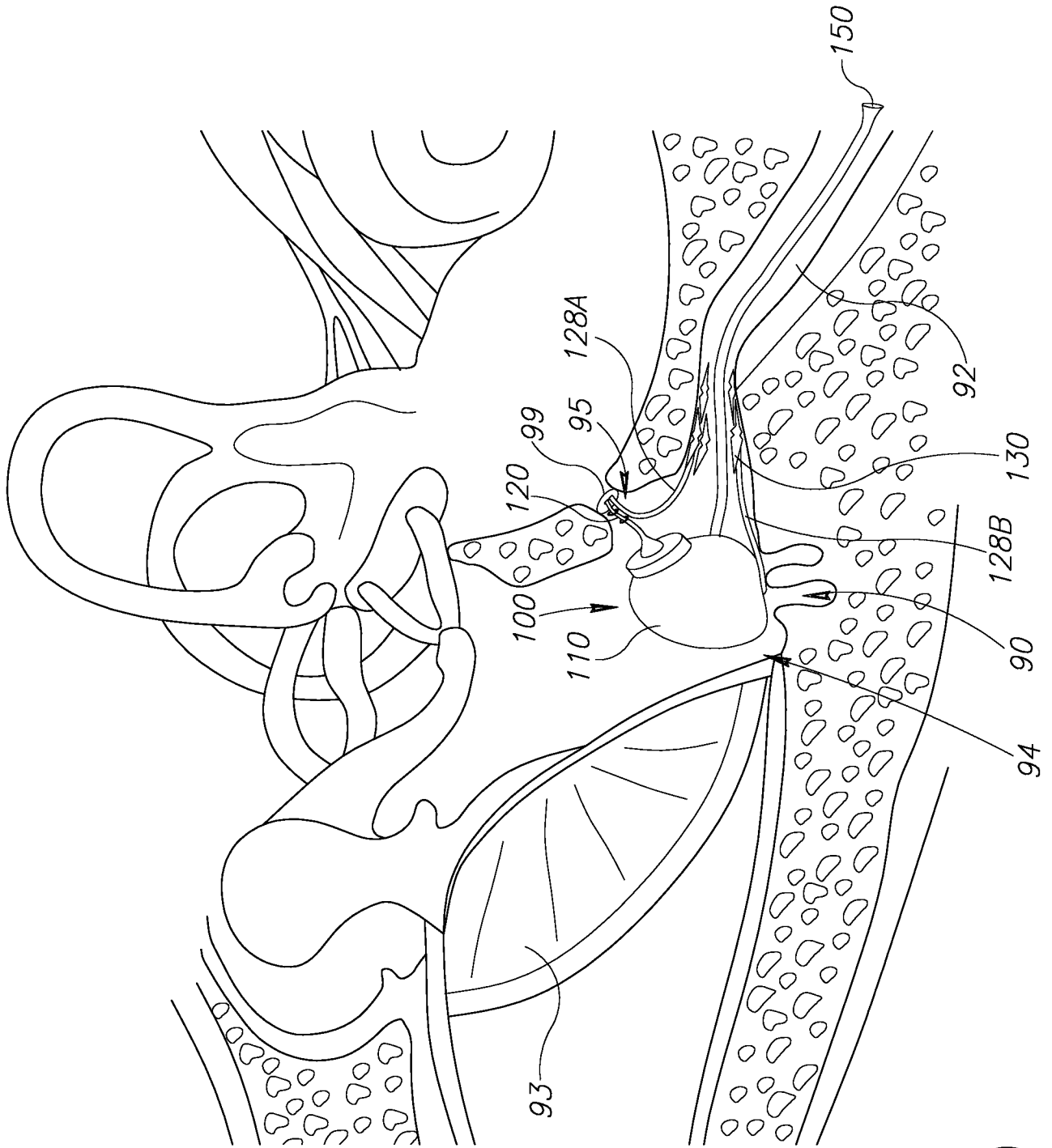


Figure 10

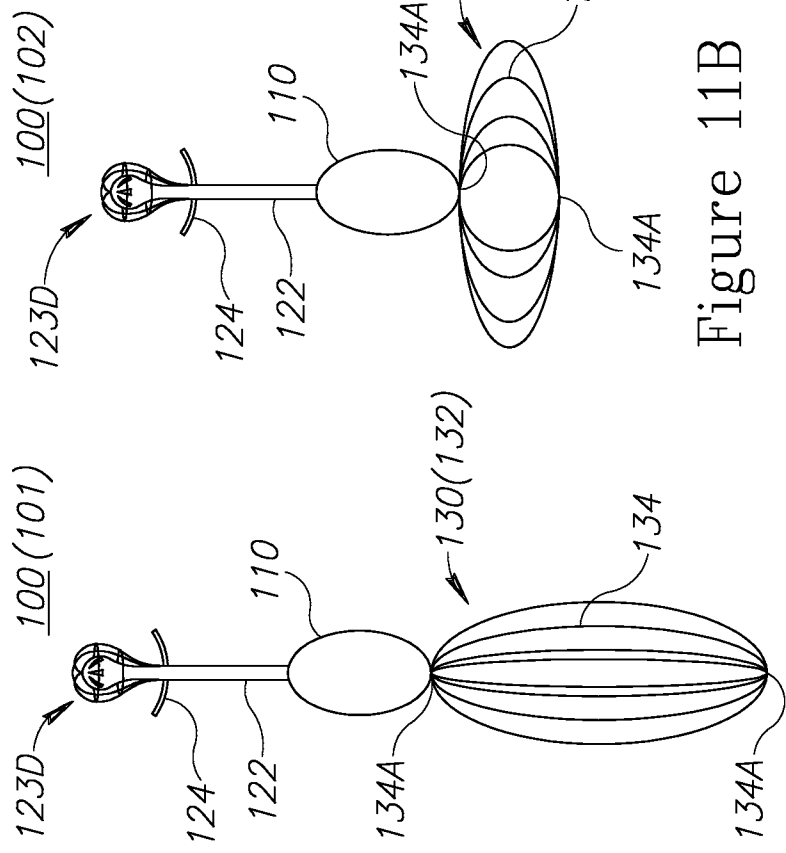


Figure 11B

Figure 11A

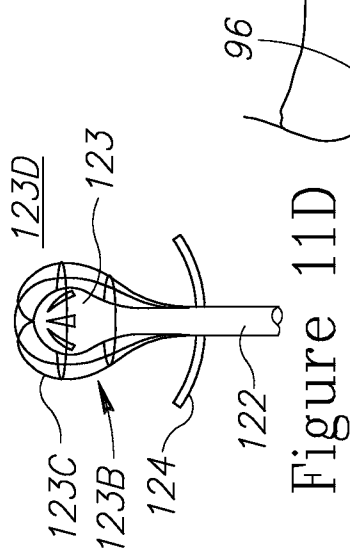


Figure 11D

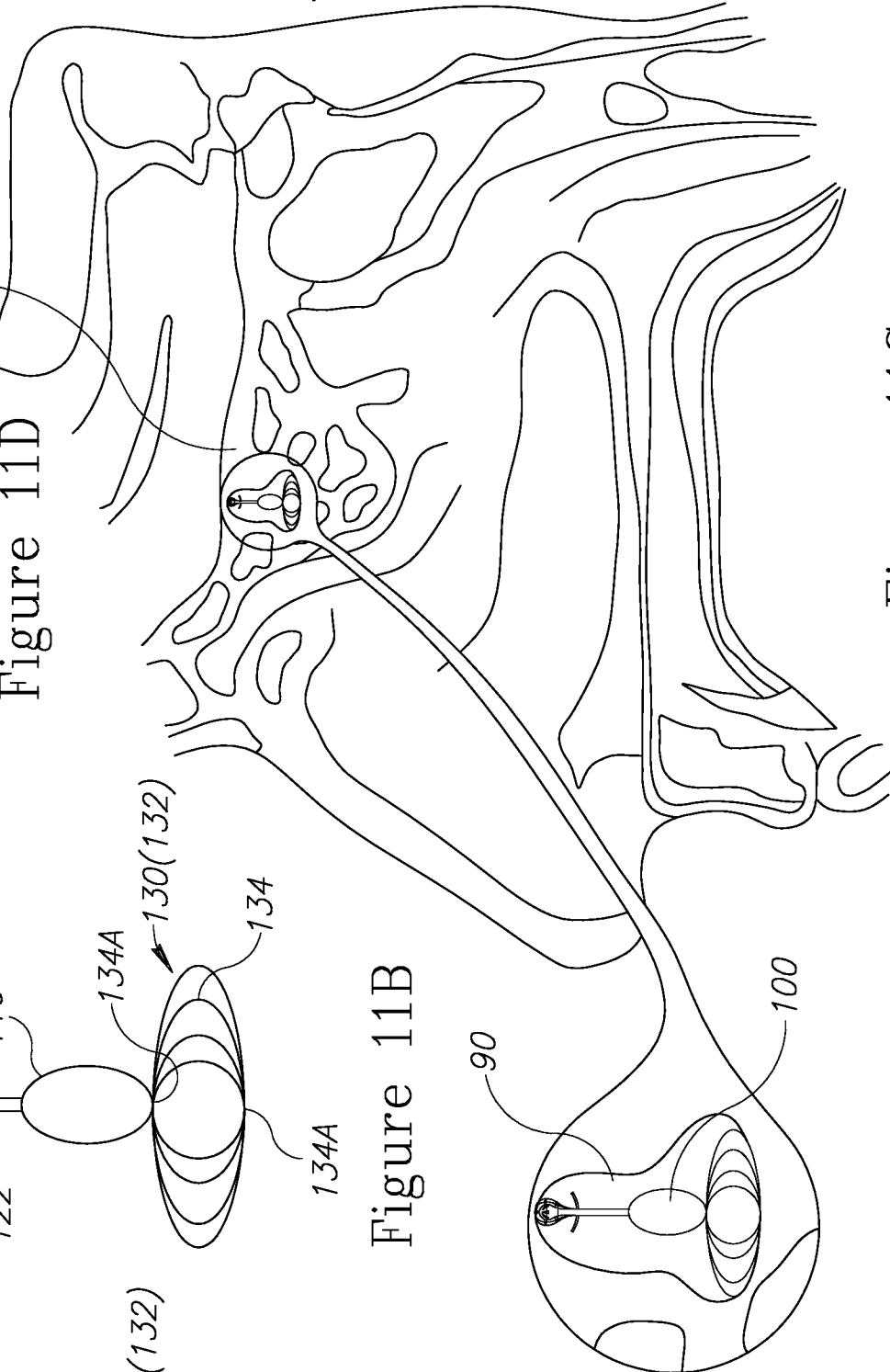


Figure 11C

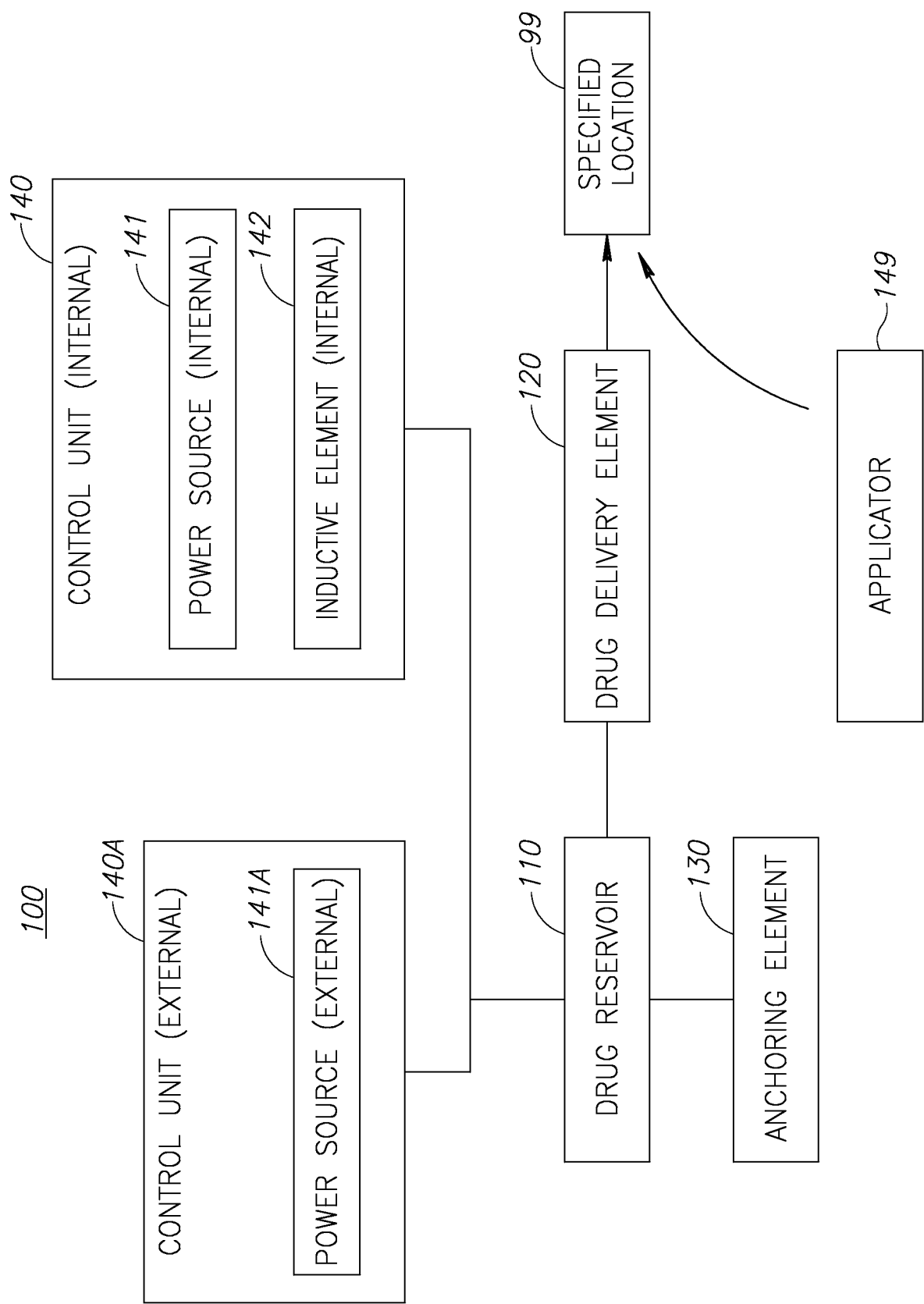


Figure 12

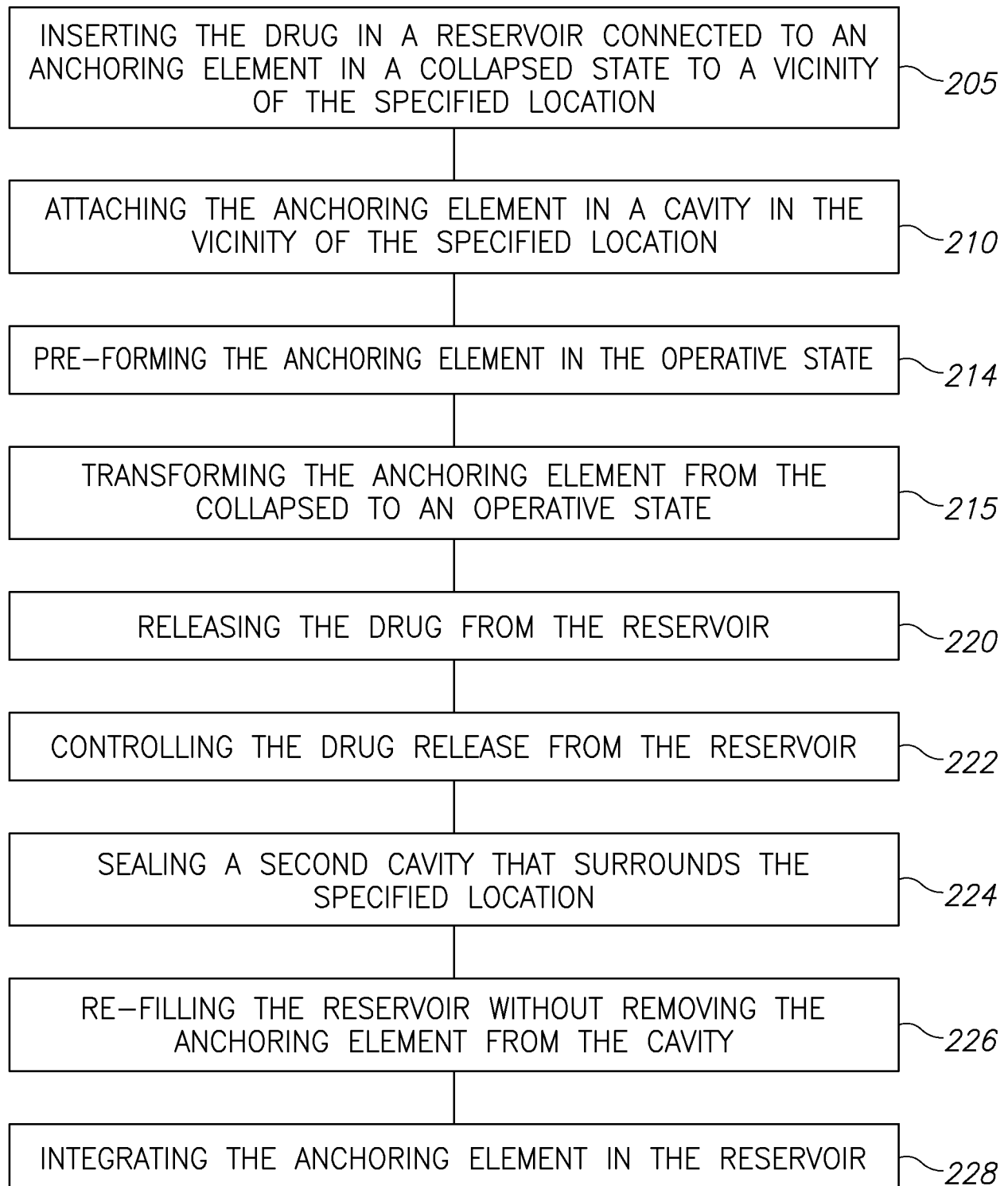
*12/12*200

Figure 13

INTERNATIONAL SEARCH REPORT

International application No.

PCT/IB 11/50860

A. CLASSIFICATION OF SUBJECT MATTER

IPC(8) - A61K 9/22 (2011.01)

USPC - 604/891.1

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)

USPC: 604/891.1

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

USPC: 128/897, 898, 899; 604/19, 48, 93.01, 104, 131, 288.01, 890.1, 891.1 (keyword limited; terms below)

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

PubWEST(PGPB, USPT, EPAB, JPAB); Google

Search Terms Used: drug, deliver\$3, nitinol, shape memory, anchor\$3, window niche, hypotympanum, eustachian, coil, inductive\$2, rf, radiofrequency, processor, microprocessor, control, mesh, ear, permeability, membrane

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 2008/0319424 A1 (MUNI et al) 25 December 2008 (25.12.2008) fig 5B, 6D, 6E, table 1, para [0077], [0095], [0106], [0134], [0136], [0138], [0147]-[0148], [0153], [0177]	1-2, 6-7, 9-11, 19-23, 28-29, 31-38, 40, 43-45, 50-52, 54-55
Y		3-5, 8, 12-18, 24-27, 30, 39, 41-42, 53
Y	US 6,685,697 B1 (ARENBERG et al) 03 February 2004 (03.02.2004) Abstract, col 35, ln 43-57	3-5, 8, 27
Y	US 2008/0009836 A1 (FIERING et al) 10 January 2008 (10.01.2008) fig 2B, para [0066], [0069]	12-18
Y	US 2008/0154250 A1 (MAKOWER et al) 26 June 2008 (26.06.2008) fig 2I, 3B, 3D, para [0139], [0148]	5, 24-26, 39, 53
Y	US 2009/0253914 A1 (RIINA et al) 22 October 2009 (22.10.2009) fig 40-43	30
Y	US 2005/0043680 A1 (SEGAL et al) 24 February 2005 (24.02.2005) para [0017]	41, 42

☐ Further documents are listed in the continuation of Box C.

* 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

19 June 2011 (19.06.2011)

Date of mailing of the international search report

28 JUN 2011

Name and mailing address of the ISA/US

Mail Stop PCT, Attn: ISA/US, Commissioner for Patents
P.O. Box 1450, Alexandria, Virginia 22313-1450

Facsimile No. 571-273-3201

Authorized officer:

Lee W. Young

PCT Helpdesk: 571-272-4300

PCT OSP: 571-272-7774

INTERNATIONAL SEARCH REPORT

International application No.

PCT/IB 11/50860

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.:
because they relate to subject matter not required to be searched by this Authority, namely:
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.: 46-49
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 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.