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(72) Inventor; and
(71) Applicant : **PEPOSE, Jay** [US/US]; 1125 Templeton Place, Town And Country, MO 63017 (US).

(72) Inventor; and
(75) Inventor/Applicant *(for US only)*: **DANTA, Randall** [US/US]; 32 Discovery, Suite 200, Irvine, CA 92618 (US).

(74) Agent: **DELANEY, Karoline, A.**; Knobbe Martens Olson & Bear, LLP, 2040 Main Street, 14th Floor, Irvine, CA 92614 (US).

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[Continued on next page]

(54) **Title**: DEVICE AND METHOD FOR ADMINISTERING EYE MEDICATIONS

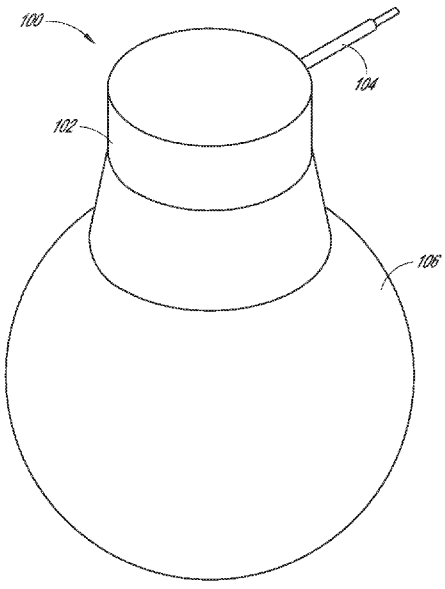

FIG. 1B

(57) **Abstract**: The present application describes devices and methods that use direct absorption to deliver mydriatic medications transclerally or transcorneally into the eye in order to enlarge the pupil of the eye of a patient. This may be done in preparation for ocular surgery, for examination, for treatment of malignant glaucoma, or other purposes. The mechanism of direct absorption may be assisted by electrorepulsion, magnetic repulsion, or ultrasonic excitation.

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DEVICE AND METHOD FOR ADMINISTERING EYE MEDICATIONS

BACKGROUND

Field of the Invention

[0001] This disclosure relates generally to the field of administering substances to tissue. More particularly, this application is directed to methods and apparatus for administering mydriatic medications to the eye.

Description of the Related Art

[0002] During ophthalmic medical procedures it may be necessary to deliver a medicament to the eyeball. The requirements for delivering medication to the eyeball vary depending on the particular medicinal purpose. For example, concentration levels of a medicament may be needed in the vitreous fluid of the interior of the eyeball to treat a particular affliction. However, for other pathological conditions, it may be efficacious to deliver and distribute medication over the entire surface of a sclera or to intraocular tissues. Yet another procedure may require an anesthetic compound to be carried or transmitted into the corneal tissue prior to a surgical procedure, such as keratotomy. Therefore, a given medical condition may require the delivery of a medicament over a widespread area, or conversely may need to be concentrated onto a smaller area.

[0003] One traditional method of delivering a medicament to the surface of the eye, either for treating a disorder or to aid in diagnosis, is through the use of eye drops. Generally, the lower eyelid is held away from the bulbar conjunctiva and a drop of the medication is introduced into the pocket or cul-de-sac formed between the eyelid and the bulbar conjunctiva. During this procedure, one must take care to avoid touching the eye with the dropper or one's fingers to reduce the risk of contamination. Through this procedure, numerous types of drug may be delivered to the eye, such as, antibiotics, corticosteroid, or antihistamines. Additionally, eye drops may be used to administer drugs which control glaucoma and which either dilate or constrict the pupil. For example, an ophthalmologist during an eye examination may drop tropicamide or phenylephrine onto the eye in order to dilate the pupil. By doing this the ophthalmologist will be able to fully view the crystalline lens and retina check for any signs of pathology. Additionally, a surgeon may use topical

drops to induce ocular anesthesia instead of performing a local retrobulbar or peribulbar anesthetic block with a needle. Furthermore, in cataract surgery, a physician may place a number of similar drops onto the surface of the eye in order to dilate the pupil so that most of the lens is visible, thereby facilitating the surgical procedure under direct observation.

[0004] Unfortunately, with the administration of medication through the use of an eyedropper there is the possibility of contamination, especially when multiple individuals use the same dropper. Furthermore, one may inadvertently contact the dropper with one's finger and thereby transmit any bacteria located on ones finger to the dropper and consequently to the eye.

[0005] Also, with drops it is difficult to achieve a desired concentration of medication within the eye. This is due to the tendency of drops to spread out into a thin layer, and the nature of the eye to wipe away surface films by blinking. Most of medication in a topical drop runs out of the conjunctival cul-de-sac onto the lid rather than remaining on the ocular surface where it can penetrate into the eye. The remainder of the drop applied to the ocular surface becomes diluted in the tears, lowering its concentration and absorption. In addition, some drug may be absorbed by the conjunctival or episcleral blood vessels or lymphatics, further reducing drug contact time. This may necessitate reapplication of drops several times to reach an effective level in a reasonable period of time. Medicated eyedrops often do not remain in long contact with the eye where it can lead to subconjunctival or intraocular absorption as intended. Rather, the medicated eyedrop quickly is pumped by blinking from the tear film down the nasolacrimal duct, where it can be absorbed into the bloodstream, sometimes leading to unwanted systemic side effects. Acute hypertension, tachycardia, or cardiac arrhythmias are reported examples of potentially serious systemic side effects following administration of topical epinephrine or phenylephrine drops to the eye to induce dilation.

[0006] At times, medication may be required within the vitreous body of the eye, but the eyedropper only delivers medication to the surface of the eye and the medication passes inefficiently through the layers of the eye. The passage of medicament into the vitreous body may take a long period of time and be impaired by the barrier of the outer layers of the eye or the lens within the eye and hence reduce the effectiveness of eyedropper medicament delivery.

[0007] When a drug needs to be delivered to tissues or fluids within the eye, it is typical to utilize an injection. This is usually performed by inserting a needle into the tissue surrounding the eye or through the sclera of the eye. As a drug is injected into either region, it may be directed into the vitreous body or other surrounding tissue or other portions of the eye.

[0008] The use of a hypodermic needle, however, also has its disadvantages. Injection of a medicament is invasive, inconvenient and sometimes risky, due to the sharpness of the needle. As the physician inserts the needle into the surrounding tissues, a minor increase in the force applied may inadvertently result in a perforated eyeball, choroidal or subretinal hemorrhage, detached retina, or intraocular inflammation with numerous associated problems. Additionally, many individuals are uneasy about the use of needles for any type of injection and more so when it involves inserting a needle close to or into the eye. In addition, the ocular surface is not sterile and normally harbors a variety of microbial flora. Unlike injections into the epidermis, it is difficult to sterilize the eye by wiping with alcohol or other surface disinfectant. Thus, bacteria can be transmitted into the eye during an intraocular injection, resulting in intraocular infection (e.g., endophthalmitis). Intraocular infection can lead to permanent blindness in some cases. Making incisions or using needles to inject medications into the eye may not be practical in certain situations, such as prior to application of the laser interface for femtosecond cataract surgery, since pressure from application of the interface to the opened globe may lead to fluid to leaking from the anterior chamber and interfere with proper, efficient docking of the laser interface.

[0009] One alternate method for applying drugs to the eye is through direct absorption in which medication is brought into contact with the eye, possibly using a reservoir. Direct absorption is especially useful for the cornea, which has virtually no blood supply and is easily accessible for topical application. Direct absorption can achieve higher concentrations of medication than possible using eye drops. The reservoir can be configured to maintain a concentration of medication over a selected region of the eye. It may be possible to configure the reservoir with split chambers to provide multiple medications either side by side or concentric. It may be possible to support the reservoir on the sclera and provide a vaulted portion containing medication targeted to the cornea. It may also be possible to support the device on the cornea, with a vaulted portion containing medication

targeted to the sclera. It may also be possible to support the reservoir on another device, such as the applanation cone or suction ring of a femtosecond laser.

[0010] It may also be possible to enhance penetration and absorption of medication through the use of an electric charge, a magnetic field, or ultrasound.

[0011] One method used to enhance absorption of a drug to an eye is using an electric charge and is known as iontophoresis. At the most basic level, iontophoresis involves the application of an electromotive force to drive ionic chemicals through a tissue so that they can be absorbed by adjacent tissues and blood vessels. In general terms, this is performed by placing a first electrode containing an ionic medication solution in contact with a portion of the tissue which is to be phoresed. A second electrode is placed on a part of the body near to the first electrode, and a voltage is applied sufficient to cause current to pass through the tissue thereby completing the electrical circuit between the electrodes. As current flows, the ionized medication molecules migrate through the tissue under the influence of the second electrode. Examples of iontophoresis are disclosed in Chang, "Cell ***Poration*** and Cell Fusion Using an Oscillating Electric Field," Biophys J. Oct. 1989; 56(4): 641-652 and Weaver, "Electroporation: A General Phenomenon for Manipulating Cells and Tissues," Cell Biochem. Apr. 1993; 51(4):426-35.

[0012] A similar approach is taken with respect to ocular iontophoresis. Traditionally ocular iontophoretic apparatus comes in one of two types, either an eyecup device or an applicator probe. The traditional eyecup device is formed from a half-spherical element. Normally the interior of the element is hollow and an electrode extends from the top of the half-spherical element. During iontophoresis, the eyecup is filled with a medicament solution and placed on the eye. As the voltage from a power source is applied, current passes from the electrode within the half-spherical element and flows into the surface of the eye. For the case of cathodic iontophoresis, negatively charged medicament ions are repulsed from the cathodic electrode within the half-spherical element, thereby forcing the medicament into the eye of the patient. The oppositely charged ground electrode is applied elsewhere on the body, such as the skin of the forehead, thereby completing the circuit. For the case of positively charged medicament ions, anodic iontophoresis is utilized where the positively charged anodic electrode repulses the positively charged medicament into the ocular tissue.

[0013] In an alternative ocular iontophoretic device, an applicator probe may be used. An applicator probe has an electrode which extends into a probe end that is filled with a medicament. The probe end is placed on the patient's afflicted area and medicament migrates from the probe end into the patient's tissue as current is applied.

[0014] Conventional ocular iontophoretic apparatus have a number of problems. For example, an applicator probe device requires one to precisely and continuously hold the probe against the patient's eyeball. Unfortunately, if the entire eyeball has to be phoresed this procedure can take a long period of time. Additionally, if one applies too great a force, too high a current, or maintains contact for too long a period of time, the patient's eyeball can be burned leaving lesions on the eye surface and/or damaging the underlying intraocular tissues such as the retina or choroid, depending on the location of the probe. Furthermore, with the eyecup-type apparatus, there is a possibility that one may scratch the eyeball of the patient if the probe is too long or if placement is not accurate. Also medication which is placed within the eyecup may escape from beneath the edges of the eyecup due to conformability limitations of the eyecup and variations in the size and curvature of the eyeball. Additionally, contaminants, such as tears, saline, or other impurities may infiltrate the medicament thereby reducing the potency or pharmacological effectiveness of the medicament. The eyecup may be forced against the surface of the eye to reduce the effects of leaking and containment infiltration; however, the required force may damage the eye.

[0015] Perhaps the most significant problem with prior ocular iontophoretic devices is the unintentional delivery of medicament to the surrounding soft tissues, including the eyelid, socket, etc, instead of to the eyeball or sclera. This inadvertent drug delivery to the surrounding tissues is due to the sclera and other eyeball tissues being wetted with conductive saline or tears. The saline or tears has considerably lower electrical resistance than alternative transscleral pathways, resulting in the electrical current preferentially following a pathway to the surrounding soft tissues

[0016] Magnetic fields may be used to enhance penetration and absorption of drugs into tissue. Particular success has been found in administering long chain polynucleotides and polypeptides into mammalian tissue. Examples of use of magnetic fields are described in U.S. Patent Application Publication 2010/0249488.

[0017] Ultrasound may also be used to enhance penetration and absorption of drugs into tissue such as that described by Sundaram et al, An experimental and theoretical analysis of *ultrasound*-induced permeabilization of cell membranes, 2003, Biophysical Journal, vol. 84, p. 3087-101. US7,922,709, US7,758,561, US7,662,629, US7,612,033.

[0018] It would be an advantage, therefore, to provide an apparatus which may be used to effectively administer a controlled concentration of medicaments to a selected region of an eyeball over a short period of time, while preventing damage to the eye and inaccurate distribution of medicament to surrounding tissues, thereby minimizing systemic drug absorption and troubling drug related systemic side effects and also obviating the possibility of intraocular infections associated with injections.

SUMMARY OF THE INVENTION

[0019] Described herein are devices and methods to deliver mydriatic drugs into tissue (e.g., eye). Direct absorption is a non-invasive technique in which a quantity of a drug is held in contact with a tissue surface to promote drug penetration into the eye tissue. Furthermore, direct absorption can include optional addition of energy such as electricity (e.g., iontophoresis), magnetism, ultrasound, and/or light) to assist or promote surface penetration and cellular absorption of the drug. In some embodiments, the drug may be contained under a thin meniscus of elastomeric material vaulted over the cornea configured as a sclera contact lens. In some embodiments, the drug may be contained under a thin meniscus of elastomeric material configured as a contact lens vaulted over the sclera. In some embodiments, blinking helps to hold the thin meniscus configurations in place. In other embodiments, a larger reservoir is used, and blinking is precluded. In such embodiments, a portion of the reservoir may be configured to support a slight vacuum to hold the device in place. In some embodiments the vacuum may be produced to maintain contact between the device and the tissue by drawing air or liquid through a syringe or squeezing and releasing a bulb. In other embodiments, the vacuum may be produced by pressing the flexible portion of the reservoir into the eye and then releasing. In certain embodiments, direct absorption is aided by application of an electric current, magnetic field, or ultrasound energy.

[0020] In some embodiments, the device is configured to contain drug over the sclera and in contact with it. In some embodiments, the sponge is positioned over the sclera for example hydrogels or hydroxylated polyvinyl acetal sponges. In other embodiments, fluid resides over the sclera without the aid of sponges. In some embodiments, the device is configured with sponge over the sclera and fluid over the cornea. The area that is covered over the sclera could vary, and could range from 12.9 mm in diameter to greater than 18 mm.

[0021] In some embodiments, a syringe is used to apply the drugs. In some embodiments, the device is configured with a nipple through which drug may be applied into the chamber over the cornea. In other embodiments, the device is configured with a nipple through which drug may be applied into the chamber over the sclera. In some embodiments, the device is configured with a syringe pre-attached to the nipple. In other embodiments, a syringe is removable.

[0022] In some embodiments, a syringe is configured to create a vacuum to apply the device and maintain contact with the eye.

[0023] The device enhances drug penetration by increasing contact time on the sclera and cornea, and the vasoconstrictors reduce the egress of drugs from the conjunctival and episcleral vessels. Drugs may be selected that have further penetration enhancing characteristics. For example, they can be mixed within cationic, anionic or neutral liposomes, micelles, microemulsions, within micro- or nanoparticles or LGA or chitogan-coated micro or nanoparticles. They can be mixed in viscous or mucoadhesive excipients, such as hydroxyethyl cellulose, xan tham gum or gellan gum or in Durasite. The drugs can be complexed to cyclodextrins to increase aqueous solubility or to surfactants or co-solvents. Examples of vasoconstrictors are phenylephrine, epinephrine, etc.

[0024] Certain devices can use one or more medications alone or in combination, depending on the nature of the drug delivery to be provided. Adding a vasoconstrictor to a mydriatic drug enhances concentration and effectiveness. The agents may be used in the form of a gel or liquid. In the gel form, the agent may be first placed into a chamber, and then the chamber may be inverted and placed onto the eye of a patient. If used in the form of a liquid of low viscosity, the chamber is first placed onto the eye of a patient, and then agent is introduced into the chamber through a fill tube. A drain tube may be used to circulate

liquid, remove air bubbles, and maintain a slight negative pressure to maintain contact with the eye.

[0025] The reservoir may be fashioned as a single piece, or split into multiple parts each with a specific chemical content. Once in place, the device is held in place for a period of time to allow the medications to diffuse into the tissues of the eye of a patient to achieve superior mydriasis than would be obtained by eye drops, topical gel, or intracameral application. The reservoir may be fashioned as a single piece, or split into multiple parts each with a specific chemical content.

[0026] Iontophoresis is a non-invasive technique in which an electric current is applied to enhance ionized drug penetration into tissue. The drug is applied with an electrode carrying a similar electric charge type (e.g., positive or negative charge) as the drug, and the ground electrode, which is of an opposite charge, is placed elsewhere on the body to complete the circuit. Once in place, the device is electrically charged by a controller for a period of time using a voltage and current. Electrodes may be positioned within the device having one or more electrical polarities. The electrical waveforms may be continuous over the treatment period, or may alternate, or have ramp-up, and/or ramp-down characteristics to best suit the application. The voltage and current induce a charge to propel the medication into the tissues of the eye of a patient to achieve superior mydriasis than would be obtained by topical or intracameral application. Examples of topical and intracameral methods are described by G. Morgado, et al., "Comparative study of mydriasis in cataract surgery: topical versus Mydriasert versus intracameral mydriasis in cataract surgery," Eur J Ophthalmol, 2010; 20 (6), 989-993.

[0027] Magnetic electroporation is a non-invasive technique in which a magnetic field is applied to enhance ionized drug penetration into tissue. The magnetic field pulses do not require the use of contacting electrodes to conduct electric or ionic current. This method improves penetration of pharmaceutical substances without direct contact with tissue, and may be called magnetopermeabilization. Once in place, the magnet is activated by a controller for a period of time. The waveforms may be continuous over the treatment period, or may alternate, or have ramp-up, and/or ramp-down characteristics to best suit the application. The magnetic field propels the medication into the tissues of the eye of a patient to achieve superior mydriasis than would be obtained by topical or intracameral application.

Examples of magnetic electroporation are described by U.S. Patent Application Publications 2010/0249488 and 2009/0326366.

[0028] Ultrasound poration is a non-invasive technique in which high frequency energy is applied to enhance ionized drug penetration into tissue. The ultrasound pulses do not require the use of contacting electrodes to conduct electric or ionic current. This method improves penetration of pharmaceutical substances without direct contact with tissue. Once in place, the ultrasound transducer is activated by a controller for a period of time. The waveforms may be continuous over the treatment period, or may alternate, or have ramp-up, and/or ramp-down characteristics to best suit the application. The ultrasound energy propels the medication into the tissues of the eye of a patient to achieve superior mydriasis than would be obtained by topical or intracameral application.

BRIEF DESCRIPTION OF THE DRAWINGS

[0029] Figure 1A is a perspective view of an embodiment of a direct absorption device with a single chamber as described herein.

[0030] Figure 1B is a perspective view of the direct absorption device of Figure 1A positioned on an eye of a patient.

[0031] Figure 1C is a cross-sectional view of the direct absorption device of Figure 1B.

[0032] Figure 2A is an isometric view of an embodiment of a direct absorption device with a fill port as described herein.

[0033] Figure 2B is a perspective view of the direct absorption device of Figure 2A positioned on an eye of a patient.

[0034] Figure 2C is a cross-sectional view of the direct absorption device of Figure 2B.

[0035] Figure 3A is a perspective view of an embodiment of a direct absorption device with two chambers as described herein.

[0036] Figure 3B is a perspective view of the direct absorption device of Figure 3A positioned on an eye of a patient.

[0037] Figure 3C is a cross-sectional view of the direct absorption device of Figure 3B.

[0038] Figure 4A is a perspective view of an embodiment of an direct absorption device with fill ports on each of the chambers as described herein.

[0039] Figure 4B is a perspective view of the direct absorption device of Figure 4A positioned on an eye of a patient.

[0040] Figure 4C is a cross-sectional view of the direct absorption device of Figure 4B.

[0041] Figure 5A is a perspective view of an embodiment of a direct absorption device with a ring shaped chamber as described herein.

[0042] Figure 5B is a perspective view of the direct absorption device of Figure 5A positioned on an eye of a patient.

[0043] Figure 5C is a cross-sectional view of the direct absorption device of Figure 5B.

[0044] Figure 6A is a perspective view of an embodiment of a direct absorption device with a fill port on a ring shaped chamber as described herein.

[0045] Figure 6B is a perspective view of the direct absorption device of Figure 6A positioned on an eye of a patient.

[0046] Figure 6C is a cross-sectional view of the direct absorption device of Figure 6B.

[0047] Figure 7A is a perspective view of an embodiment of a direct absorption device with two chambers that form a ring shape as described herein.

[0048] Figure 7B is a perspective view of the direct absorption device of Figure 7A positioned on an eye of a patient.

[0049] Figure 7C is a cross-sectional view of the direct absorption device of Figure 7B.

[0050] Figure 8A is a perspective view of an embodiment of a direct absorption device with fill ports on each of the chambers that form a ring shape as described herein.

[0051] Figure 8B is a perspective view of the direct absorption device of Figure 8A positioned on an eye of a patient.

[0052] Figure 8C is a cross-sectional view of the direct absorption device of Figure 8B.

[0053] Figure 9A is a perspective view of an embodiment of a direct absorption device with two ring shaped chambers as described herein.

[0054] Figure 9B is a perspective view of the direct absorption device of Figure 9A positioned on an eye of a patient.

[0055] Figure 9C is a cross-sectional view of the direct absorption device of Figure 9B.

[0056] Figure 10A is a perspective view of an embodiment of a direct absorption device with fill ports on each of the ring shaped chambers as described herein.

[0057] Figure 10B is a perspective view of the direct absorption device of Figure 10A positioned on an eye of a patient.

[0058] Figure 10C is a cross-sectional view of the direct absorption device of Figure 10B.

[0059] Figure 11A is a perspective view of an embodiment of a femtosecond laser attachment as described herein.

[0060] Figure 11B is a perspective view of an embodiment of a direct absorption device configured to receive the femtosecond laser attachment of Figure 11A as described herein.

[0061] Figure 11C is a perspective view of the direct absorption device of Figure 11B coupled with the femtosecond laser attachment of Figure 11A.

[0062] Figure 11D is a cross-sectional view of the direct absorption device and femtosecond laser attachment of Figure 11C.

[0063] Figure 12A is a perspective view of an embodiment of a direct absorption device with two ring shaped chambers and configured to receive a femtosecond laser attachment as described herein.

[0064] Figure 12B is a perspective view of the direct absorption device of Figure 12A coupled with a femtosecond laser attachment.

[0065] Figure 12C is a cross-sectional view of the direct absorption device and femtosecond laser attachment of Figure 12B.

[0066] Figure 13A is a perspective view of an embodiment of a direct absorption device with fill ports on each of the ring shaped chambers and configured to receive a femtosecond laser attachment as described herein.

[0067] Figure 13B is a perspective view of the direct absorption device of Figure 13A coupled with a femtosecond laser attachment.

[0068] Figure 13C is a cross-sectional view of the direct absorption device and femtosecond laser attachment of Figure 13B.

[0069] Figure 14A is a perspective view of an embodiment of a 2-lead electric charge controller as described herein.

[0070] Figure 14B is a perspective view of an embodiment of a 3-lead electric charge controller as described herein.

[0071] Figure 15 is a perspective view of an embodiment of a syringe configured to dispense a medication as described herein.

[0072] Figure 16 is a cross-sectional view of an embodiment of a scleral contact lens as described herein.

[0073] Figure 17 is a cross-sectional view of an embodiment of a corneal contact lens as described herein.

[0074] Figure 18 is a cross-sectional view of an embodiment of a vaulted chamber as described herein.

[0075] Figure 19 is a cross-sectional view of an embodiment of a scleral contact lens with bulb as described herein.

[0076] Figure 20 is a cross-sectional view of an embodiment of a vaulted chamber with bulb as described herein.

[0077] Figure 21 is a cross-sectional view of a chamber similar to that of Figure 18 and an embodiment of a magnet positioned over the eye of a patient as described herein.

[0078] Figure 22 is a cross-sectional view of a chamber similar to that of Figure 18 and an embodiment of an ultrasound transducer positioned over the eye of a patient as described herein.

[0079] Figure 23 is a cross-sectional view of a chamber similar to that of Figure 18 and an embodiment of a lamp positioned over the eye of a patient as described herein.

DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENT

[0080] In the field of eye care, it is often desirable to dilate the pupil of a patient. By relaxing the iris, the opening at the center of the iris can be made to enlarge, providing pupil dilation (mydriasis).

[0081] In certain current procedures, mydriasis is generally accomplished by the instillation of dilating drops or gels. The speed and efficacy of these drugs to dilate the pupil is limited by a number of factors, including low penetration through the cornea and/or sclera.

[0082] Sometimes dilating drops and gels are ineffective and it is necessary to follow with intracameral injection of mydriatic agents or viscoelastics to further enhance mydriasis. Intracameral injections may be incompatable with certain types of cataract surgery, such as femtosecond-laser assisted cataract extraction where the globe must remain without perforation and tolerant of the application of pressure from the laser interface device being applied to the eye. In addition, poor pupil dilation may preclude femtosecond laser cataract extractions because the poorly dilated iris covers much of the anterior surface of the lens, blocking the laser light from making incisions of adequate diameter into the cataractous lens.

[0083] In many patients, normal pupil dilation is impeded by the prevalent use of alpha 1a inhibitors. Alpha 1a inhibitors are used to enhance urinary flow in patients with prostate hypertrophy and for other purposes. This class of drugs, typified by tamsulosin (Flomax), binds irreversibly to the iris and results in miosis and a "floppy iris syndrome." This floppy iris syndrome is shown to significantly increase the rate of complications during cataract surgery. Other drugs of this kind shown to cause floppy iris syndrome include terazoson, doxazosin, alfuzosin, minipress, alphavase, hypovas and prazosin.

[0084] Many anterior and posterior segment ocular surgeries, including cataract, benefit from wide mydriasis. The advantages of wide mydriasis include (1) faster surgical time, (2) fewer complications, (3) compatibility with femtosecond-laser assisted cataract and anterior and posterior segment surgery.

[0085] Cataract surgery with intraocular lens placement is the most frequently performed surgical procedure in the world and estimated to effect over 17% of the population over age 40. Also, there are surgical procedures being developed to treat the crystalline lens to restore accommodation.

[0086] These surgical procedures and others yet to be developed would benefit from more reliable equipment and methods for rapidly and effectively achieving wide mydriasis while minimizing systemic absorption of the drugs leading to unwanted side effects sometimes seen with dilating eyedrops. Also, a less invasive device and procedure is desirable in order to avoid use of injections and their associated risks, such as intraocular infection.

[0087] Certain devices described herein utilize direct absorption to deliver mydriatic medications transclerally or transcorneally into the eye in order to enlarge the pupil. The drug is applied with a reservoir that provides a seal with the eye while maintaining contact between at least a portion of the drug and the surface of the eye.

[0088] Figure 16 illustrates an embodiment of a direct absorption device 1600 with a chamber 1602 (e.g., reservoir). The chamber 1602 includes an opening extending from a first surface 1603 of the chamber 1602 to a cavity 1601 configured to receive at least one medication. Furthermore, the chamber 1602 can be configured with an outer annular portion to maintain a seal with the sclera of an eye 1606 of a patient while a central vaulted portion maintains a quantity of drug in contact with the cornea.

[0089] Figure 17 illustrates a further embodiment of direct absorption device 1700 with a chamber 1702 (e.g., reservoir). The chamber 1702 includes an opening extending from a first surface 1703 of the chamber 1702 to a cavity 1701 configured to receive at least one medication. The chamber 1702 can be configured with an outer annular portion to maintain a seal with the sclera while maintaining a quantity of drug in contact with the sclera. The chamber 1702 can be configured to at least partially surround at least a portion of a cornea of an eye 1706. For example, the chamber 1702 can be configured to avoid contact with the cornea of the eye 1706. Instead, the chamber 1702 can be configured to cover a portion of a sclera of the eye. In certain embodiments, the chamber 1702 is at least a partial annulus. For example, the at least one opening and the first surface 1703 of the chamber 1702 can be configured as at least a partial annulus. In further embodiments, the chamber 1702 and/or the at least one opening and the first surface 1703 of the chamber is an annulus. The annulus may have an inner diameter greater than about 12 mm to avoid contact with the cornea.

[0090] Figure 18 illustrates an embodiment of direct absorption device 1800 with a chamber 1802 (e.g., reservoir). The chamber 1802 includes an opening extending from a first surface 1803 of the chamber 1802 to a cavity 1801 configured to receive at least one medication. The chamber 1802 can be configured with an outer perimeter to maintain a seal with the sclera while maintaining a quantity of drug in contact with both the cornea and the sclera (e.g., corneal and scleral coverage with perimeter seal).

[0091] The chambers described herein can have a variety of configures such as those described herein. For example, the chamber can have a single reservoir or can be split with a plurality of reservoirs such as concentric reservoirs.

[0092] Figure 19 illustrates an embodiment of a direct absorption device 1900 similar to the direct absorption device 1600 of Figure 16. The chamber 1902 (e.g., reservoir) can be configured with an outer annular portion to maintain a seal with the sclera while a central vaulted portion maintains a quantity of drug in contact with the cornea. A negative pressure device 1930 can be fluidly coupled to the chamber 1902 and configured to be able to create a vacuum in the chamber 1902 while in contact with the eye 1906. For example, the negative pressure device 1930 can be a squeeze bulb configured to provide a vacuum for holding the device in place against the eye.

[0093] Figure 20 illustrates an embodiment of a direct absorption device 2000 similar to the direct absorption device 1700 of Figure 17. The chamber 2002 (e.g., reservoir) can be configured with an outer perimeter to maintain a seal with the sclera while maintaining a quantity of drug in contact with both the cornea and the sclera. A negative pressure device 2030 can be fluidly coupled to the chamber 2002 similar to that of the negative pressure device 1930 of Figure 19 such as a squeeze bulb configured to provide a vacuum for holding the device in place against the eye.

[0094] Negative pressure can be applied to selected regions of the eye. For example, scleral suction can be used with a vaulted cornea reservoir or corneal suction can be used with a sclera reservoir. Other attachment means beyond suction are also possible. For example, relatively thin devices can be secured by weight, surface tension, suction, speculum, and/or eyelid blinking.

[0095] Figure 21 illustrates an embodiment of a magnet 2140 positioned over the eye 2106 of a patient and configured to assist with the penetration of drug through the tissue

surface and absorption of the drug into the underlying cells. A direct absorption device 2100 similar to those described above can be used with the magnet 2140.

[0096] Figure 22 illustrates an embodiment of an ultrasound transducer 2240 positioned over the eye 2206 of a patient configured to assist the penetration of drug through the tissue surface and absorption of the drug into the underlying cells. A direct absorption device 2200 similar to those described above can be used with the ultrasound transducer 2240.

[0097] Figure 23 illustrates an embodiment of light source 2340 (e.g., lamp) positioned over the eye 2306 of a patient configured to assist the penetration of drug through the tissue surface and absorption of the drug into the underlying cells. A direct absorption device 2300 similar to those described above can be used with the light 2340.

[0098] Certain devices described herein utilize coulomb controlled iontophoresis to deliver mydriatic medications transclerally or transcorneally into the eye via electrorepulsion in order to enlarge the pupil. Iontophoresis is a non-invasive technique in which an electric current is applied to enhance ionized drug penetration into tissue. The drug is applied with an electrode carrying a similar electric charge type (e.g., positive or negative charge) as the drug, and the ground electrode, which is of an opposite charge, is placed elsewhere on the body to complete the circuit. The drug serves as a conductor of the current through the tissue.

[0099] Like the skin, the sclera and cornea support a net negative charge under physiological pH conditions and has an isoelectric point (pI) between 3.5 and 4. Equally, the principles of transscleral and transcorneal iontophoretic transport of low molecular weight compounds are consistent with those observed for skin.

[0100] Transcorneal iontophoresis delivers a high concentration of drug to the anterior segment of the eye (e.g., cornea, aqueous humor, ciliary body, iris and lens) with the potential of treating anterior segment diseases, such as: keratitis, glaucoma, dry eyes, corneal ulcers and ocular inflammations. However, this procedure can produce complications, including epithelial edema, decrease in endothelial cells, inflammatory infiltration and burns. Such damage is reliant upon the site of application, the current density and the iontophoretic duration.

[0101] Any damage to the cornea surface immediately affects the vision and comfort of the patient which is less pronounced when applied to the sclera. The clarity of the cornea is essential for interaction with light while the sclera is not relevant for light interaction. The cornea is an avascular and highly innervated tissue, thus sensitive to pain and hypoxia. Transcorneal iontophoresis can affect the light gathering portion of the eye, while transscleral iontophoresis can affect the retina underneath the application site, which is essential for visual image formation.

[0102] The electric current can be programmed for controlled delivery of drugs by adjusting the current, as the flux of drug into the system is in proportion to the current. This technique may overcome certain biological variables such as variable electrical resistance.

[0103] The electric current can be either positive or negative, depending on the characteristics of the drug. Iontophoresis thus uses an electrode of same polarity as the charge on the drug to drive ionic (charged) drugs into the body by electrostatic repulsion. Simply stated, the mechanism of iontophoresis is based on the physical phenomenon that "like charges repel and opposite charges attract". The drugs are forced into the tissue by simple electronic repulsion of similar charges. Thus, anionic drugs can enter the tissue by using a negatively charged working electrode. Similarly, cationic drugs enter the tissue more successfully when a positively charged electrode is used. While delivering a negatively charged drug across a biological membrane, the drug is placed between the negative electrode (e.g., cathode) and the membrane. The drug ion is then attracted through the membrane towards the positive electrode (e.g., anode) by the electromotive force provided by the cell. In the case of positively charged drugs, the electrode polarities are opposite. Once the drug has passed through the outer barrier layer of tissue, it reaches its site of action. The electric circuit is completed by the movement of endogenous counter ions from within the tissue.

[0104] Although normal iontophoresis is done with the help of continuous DC current, pulsed waveform of DC has also been used, which has been able to produce significant and rapid delivery of drugs. Moreover, this has been found to be less damaging to the tissue.

[0105] A number of factors can affect the iontophoretic process. Variables affecting the iontophoresis process include: the drug concentration, drug salt form, pH of the drug micro environment, the current intensity and duration, competing ions in the electrode solution/matrix, stability of the drug during the iontophoresis process, the type of matrix containing the drug and current density. Additionally, patient anatomical factors and the presence and extent of inflammation can influence the depth of drug penetration.

[0106] **Drug Concentration**: Increased uptake by the eye tissue during and after iontophoresis generally increases with higher drug concentration until a plateau level is reached at which no further increase in flux may be observed.

[0107] **Drug Salt Form**: Different salt forms have different specific conductivities that affect the general suitability of a drug for iontophoresis. The salt form of drugs along with the pH of the solution influence the amount of drug in the ionized state.

[0108] **pH of the Drug Micro environment**: The pH of a solution influences the amount of drug present in the ionized state. For optimum iontophoresis, it can be desired to have a relatively large proportion of the drug in the ionized state. However, this may need to be counterbalanced with delivery of a drug at a pH that is tolerable and safe for the patient.

[0109] **Current Intensity and Duration**: In an electrolytic solution, the transported quantity of electricity depends on the strength of the current and the duration of its passage. This would suggest that the same number of ions can be transported at different strengths of current if the time for current flow is inversely related to their strengths. However, in some cases, higher current may deliver more drug than lower current, which is possibly due to induced changes in tissue permeability by the higher current, resulting in a greater flow of drugs. The strength of the current used may be limited by the sensitivity and tolerance of patient or other factors.

[0110] **Competing Ions in the Electrodes**: Electrical current is carried by positive and negative ions in solution. There is no major distinction between ions of the same charge even though they are composed of different chemical elements. Therefore, in certain embodiments, solutions for iontophoresis should be as pure as practical and generally contain as few extraneous substances as possible. Drug solutions can be prepared with purified water (e.g., deionized, distilled, reverse osmosis). It is has been shown that the presence of excipients in dosage forms, e.g., preservatives in injections as well as compounds

used as external buffers, may alter the amount of drug delivered. In vitro, the total current will be carried by drug ions along with the same charges as drug ions in the donor cell plus the counter ions present in the receptor cell. Therefore, the competing ions in the donor cell and the counter ions in the receptor cell can be affecting the actual current carried by the drug moiety. During iontophoresis, there can be a shift in pH due to hydrolysis of water which may result in a loss of efficiency of drug transfer due to competing ions. Buffers may be built into the electrode to minimize this effect. The buffer materials can be bound, or immobile, and configured to not be released for iontophoresis transport, as they would then compete with the active drug.

[0111] Electrodes may use an immobilized buffer to maintain a safe solution pH (for example, between 4 and 8) during treatment. Buffers include ions or charged molecules. These buffer ions may compete with the target ions for iontophoretic delivery if they are not immobilized. Electrodes may incorporate a layered design that separates the buffering layer from the ionic solution reservoir. In this design, the granular buffer is intentionally placed next to the conductor in the electrode to neutralize the acid or base molecules as soon as they are generated. The ions targeted for delivery are concentrated in the layer nearest the tissue.

[0112] **Drug Stability**: In certain embodiments, the drug undergoing iontophoresis is stable in the solution environment before and during the iontophoretic process. Oxidation or reduction of a drug not only decreases the total drug available, but the degradation compounds, if they possess the same charge as the drug ion, may compete with the drug ion and reduce the overall rate of administration.

[0113] **Gel vs. Solution**: The migration of the drug under the influence of the electrical current may be different as the matrices are different. This can be related to differences in viscosities, material electrical charge, and porosities. The progress of molecules through a more viscous substance is slower than its progress through a less viscous substance. Viscosity enhancing agents (e.g., thickeners) may be used to improve the uniformity of delivery, but may decrease the delivery rate.

[0114] **Current density**: Higher current density may result in higher rates of drug delivery. However, current density may be limited for various considerations. For example, the current may be limited to not produce harmful effects to the tissue or affect electrochemical stability of the drug.

[0115] A few relationships that can be important in iontophoresis are described below.

[0116] **Ohm's Law** states that V = IR, where V is electromotive force in volts, I is current in amps and R is resistance in ohms. The importance of this relationship is that at constant voltage, any change in resistance results in a change in current level. Often the resistance decreases during a procedure; as a result, the current (e.g., in milliamps) may increase. However, it the current device is programmed to deliver a constant current, then the voltage can vary to compensate for changes in resistance.

[0117] **Coulombs Law** states that Q = IT, where Q is the quantity of electricity, I is current in amps and T is time in minutes. Thus, "mA-min" can be used to describe the "current dosage" used during iontophoresis. In certain embodiments, iontophoresis of any similar charged drugs is applied for less than about 4 minutes. In some embodiments, the electrical current is no greater than about 7 mA. In further embodiments, the current dosage is from about 1.5 mA-min to about 20 mA-min. The current can be monitored in the controller device using a milliampmeter and adjusted by a rheostat to remain constant throughout the iontophoresis. In addition, the controller device can have a safety cutoff so that it will discontinue treatment when a set mAmp-minute of drug has been delivered.

[0118] Thus, the amount of drug delivered is given by an equation of the form: D = IT/VC, where D is the amount of drug delivered (in gm-equivalents), I is current in mAmps, T is time in minutes, V is valance of the drug and C is Faraday's constant (e.g., the electrical charge carried by 1 gram equivalent of the drug). From this relationship, the more electricity delivered (e.g., by increasing current or time), the more drug delivered. However, due to the complexity of the factors involved during the process of iontophoresis, theoretical predictions based on a formula are difficult.

[0119] **Medications:** Certain devices and methods described herein utilize one or more of the following medications alone or in combination. The mydriatic agents may be neutral, negatively charged, or positively charged depending on the nature of the drug delivery to be provided by the composition. As the iontophoretic device is dependent on utilizing drugs that are cationic or anionic, neutrally charged molecules may be modified to increase their valence.

[0120] In some embodiments, the device is configured with an inert electrode which electrolyzes water to produce hydroxide or hydronium ions. These ions propel charged drug molecules. Iontophoresis of cationic drugs at physiologic pH utilizes anodic electrolysis, generating hydronium ions that promote the movement of the cation into ocular tissues and fluids. To avoid too much lowering of pH, the drug solution (or hydrogel) may include buffers and the electrode can be kept a distance away from the portion of the gel or liquid opposing the ocular surface. The iontophoretic delivery of an anionic drug at physiologic pH utilizes cathodic electrolysis, producing hydroxide ions that promote movement of the anionic drug into ocular tissues and fluids, while raising the pH of the drug solution. Again, the use of buffers and distal placement of the electrode away from the portion facing the ocular surface can mitigate large changes in pH.

[0121] Agents that are considered cationic may be administered using anodic iontophoresis with the return electrode on the patient's forehead or other part of the body.

[0122] Cationic mydriatic drugs include:

atropine hyperduric,
atropine methylbromide,
atropine methylnitrate,
atropine N-oxide,
atropine sulfate,
cyclopentolate hydrochloride,
epinephrine,
epinine,
hydroxyamphetamine iodide,
hydroxyamphetamine iodide,
hydroxyamphetamine hydrobromide,
homatropine hydrobromide,
homatropine hydrochloride,
homatropine methylbromide,
ibopamine,
lidocaine,
phenylephrine hydrochloride,

scopolamine hydrobromide,
scopolamine hydrochloride,
scopolamine methyibromide,
scopolamine methylnitrate,
scopolamine N-oxide,
tropicamide,
tropicamide hydrobromide, and
tropine hydrochloride.

[0123] Agents that are considered anionic may be administered using cathodic iontophoresis. Cathodic iontophoresis includes a negatively charged chamber acting as a cathode, and a neutral return electrode on the patient's forehead or other part of the body.

[0124] Anionic medications include:

bromfenac,
diclofenac,
ketorolac,
amfenac, and
nepafanac
(nepafanac, the prodrug of amfenac, is neutral at physiological pH and may require some modification to be used for iontophoresis).

[0125] The iontophoresis of lidocaine alone or in combination with the aforementioned drugs may also result in analgesia for ocular surgery, in addition to further enhancing mydriasis. Furthermore, certain drugs can be grouped into classifications such as 1) lidocaine which provides mydriasis and analgesia, 2) epinephrine (or possibly phenylephrine) which is a sympathomimetic amine which stimulates both alpha and beta receptors and creates mydriasis as an agonist of the iris dilator muscle, and 3) tropicamide (a muscarinic antagonist) which creates mydriasis by relaxation of the iris sphincter muscle. Furthermore, drugs in the epinephrine classification, such as bromfenac, can be a non-steroidal anti-inflammatory, which helps create and prolong mydriasis and also reduces inflammation and cystoid macular edema.

[0126] The iontophoresis of non-steroidal drugs may further enhance mydriasis, in addition to reducing postoperative inflammation and cystoid macular edema. Furthermore, iontophoresing a steroid can reduce postoperative inflammation or cystoid macular edema. Iontophoresis of a fluoroquinolone (e.g., moxifloxacin, which is a cation) or of a glycopeptide antibiotic such as vancomycin (which is positively charged at physiological pH) can be used for prophylaxis of endophthalmitis. Although a steroid may not create mydriasis, it can be iontophoresed preoperatively as an anti-inflammatory and to prevent cystoid macular edema. Additional examples of using iontophoresis of a corticosteroid to treat postoperative intraocular inflammation are described in U.S. Patent Publication No. 2009/0206579, and additional examples of iontophoresis of ocular drugs are described by E. Eljarrat-Binstock, et al., "Iontophoresis: A non-invasive ocular drug delivery," Journal of Controlled Release, 110 (2006), 479-489, the entirety of each of which is hereby incorporated by reference.

[0127] Mydriatic medications are normally dissolved in non-saline water and the active agents adjusted by pH to have a valency of equal to or greater than 1.

[0128] The mydriatic medications described herein can be delivered in the form of a liquid, gel, foam, hydrogel, paste, film, contact lens, microsphere or mucoadherent formulation. In the gel or foam form, the agent can placed into a chamber, and the chamber is inverted and placed onto the eye of a patient after application of topical anesthetic drops, such as proparacaine. If used in a liquid form, the chamber is first placed onto the eye of a patient after administration of a topical anesthetic drop, then agent may be introduced into the chamber through a fill tube.

[0129] Most drugs are generally weak acids or bases. For acids, they have at least one site that can reversibly dissociate a proton (e.g., hydronium ion) and create an anion. For bases, they reversibly associate a proton and form a cation. The fractionated protonated and unprotonated species of the drug can be shifted by the pH of the media. The ease of proton dissociation is called the pKa (dissociation constant), which equals the pH + log (protonated/unprotonated drug). Some find it easier to think of pKa as the pH at which there are equal amounts of protonated and unprotonated species.

[0130] Drugs that are anions including steroids, such as dexamethasone phosphate and many Non Steroidal Anti Inflammatory Drugs (NSAIDS), can use cathodic

iontophoresis. Cathodic iontophoresis induces produced negatively charged hydroxide anions to repel the drug into the tissue.

[0131] For cationic drugs, like lidocaine, tropicamide, epinephrine or phenylephrine, anodic iontophoresis can be used, since this will create positive charge hydronium ions from the electrolysis of water and these will repel the drug. Other interesting positively charged ocular drugs are moxifloxacin and vancomycin, which could be used for prophylactic treatment against endophthalmitis prior to cataract surgery.

[0132] Since the iontophoresis process will change the pH of the medium, the medium may also contain supplemental agents, such as electrolytes, pH regulating buffers, preservatives, stability additives PEGylating agents and other additives that may increase the half life and/or availability of the drugs.

[0133] The list of possible NSAIDS includes 2-acetoxybenzoic acid, indomethacin, tolmetin, ibuprofen, flurbiprofen, ketoprofen, naproxen, axoprozin, pranoprofen, suprofen, piroxicam, and amide derivatives of amfenac, bromfenac, diclofenac, ketorolac, flurbiprofen and suprofen.

[0134] Some embodiments may use a corticosteroid for anti-inflammatory effect. Inflammation after cataract surgery can lead to pain/discomfort, photophobia, corneal edema and cystoid macular edema (CME) (The stress of ocular surgery can produce prostaglandins (including PGE2) and other mediators that break the blood-ocular-barrier, increases perifoveal capillary permeability and intraretinal fluid. This can lead to cystoid macular edema (CME) in 4 to 6 weeks. According to Schmeir JK in Retina 2007; 27:621-8, his review of 139,759 cataract surgeries, CME was the leading cause of decreased vision in uncomplicated cataract surgery, affecting 1.95%.

[0135] An embodiment may use a cocktail of cationic drugs (lidocaine, tropicamide, phenylephrine or epinephrine), possibly adding an antibiotic such as moxifloxacin. Embodiments of these drugs may deliver them alone or in combination. The anionic drugs (e.g., the NSAID and possibly the corticosteroid) may need to be mixed separately from the cationic, and could be delivered alone or in combination. While the NSAID has effects on dilation, the corticosteroid should affect only inflammation, pain, photophobia and development of CME.

[0136] If only mydriasis is used, then the chemistry may be limited to lidocaine, tropicamide, epinephrine (or phenylephrine) and the NSAID separately.

Construction:

[0137] There are a number of approaches for drug retaining in the iontophoretic device. One approach is to fill an eye cup with the drug solution, while an electrode extended from the controller contacts the solution. The eye cup with an internal diameter of 5–10 mm is placed over the eye and the drug solution is continuously infused into the cup during the treatment period.

[0138] In one embodiment, the eye cup may have two ports. One port delivers the drug solution. The other aspirates air bubbles that may disrupt the current supply. In some embodiments, inflow and outflow pressures may be adjusted to maintain a slightly negative pressure to hold the applicator in place.

[0139] The ground electrode is attached to the patient and attached as close as possible to the former electrode to obtain minimal resistance. In some embodiments, the electrode may be placed on the forehead. In other embodiments, the electrode may be clipped to the ear.

[0140] In some embodiments, a drug saturated gel is configured as the delivery probe. The gel may be configured to make a direct contact with the eye. In some embodiments, a hydrogel comprising polyacetal sponge may be used.

[0141] In some embodiments, the drug applicator includes a small silicone shell that contains a conductive element, a hydrogel pad to absorb the drug formulation, and a small, flexible wire to connect the conductive element to the dose controller. At the time of administration, the dry hydrogel matrix is hydrated with the drug solution and placed against the conjunctiva overlying the sclera in the lower cul-de-sac of the eye. The return electrode can be positioned anywhere on the body to complete the electrical circuit.

[0142] In other embodiments, the device may be configured with a selective membrane which increases drug transport by excluding the transport of non-drug ions, thus making drug-ions the primary carrier of electrical current through scleral tissue. A polyacrylic-porous hydrogel saturated with gentamicin or dexamethasone solutions may be configured for transcorneal and transscleral iontophoresis.

[0143] In some configurations, the device may be configured as a probe. In this configuration, hydrogel is inserted into a well at the tip of the electrode, and the probe placed onto the eye. The use of a hydrogel probe applicator may have fewer current interruptions and be less harmful to the eye surface compared with the eye cup approach.

[0144] Different reservoir shapes may be used. In some embodiments, the reservoir is configured as a cup and placed over the cornea and a portion of the sclera. In other embodiments, the reservoir may be configured as annular shape with an opening to avoid contact with the cornea. In some embodiments, the opening may be in the range of about 13 mm.

[0145] In some embodiments, the material may be a pliable elastomer, such as silicone. In other embodiments, the reservoir may be metallic.

[0146] Described below are examples of direct absorption devices. Although they may be described in the context of being an iontophoresis device, the devices can be used in other configurations. For example, the iontophoresis devices described below can also be used as a chamber for direct absorption without electrorepulsion (e.g., without electrodes).

[0147] Figures 1A-C illustrate an embodiment of an iontophoresis device 100 with a chamber 102 (e.g., reservoir) having a cup shape. The chamber 102 includes an opening extending from a first surface 103 of the chamber 102 to a cavity 101 configured to receive at least one medication. As illustrated in Figures 1B and 1C, the at least one opening and/or the first surface 103 can be configured to be placed in contact with an eye 106 of a patient. The iontophoresis device 100 can also include an electrode 104 (e.g., anode or cathode) configured to be in electrical communication with the at least one medication when the at least one medication is within the cavity 101 of the chamber 102. For example, the electrode 104 can be in electrical communication with the chamber 102, and the chamber 102 can be in electrical communication with the at least one medication. The at least one medication can include at least one active ingredient, and the at least one active ingredient can be configured to enter tissue of the eye 306 through a process of iontophoresis.

[0148] Figures 2A-C illustrate another embodiment of an iontophoresis device 200 that is similar to the iontophoresis device 100 in Figures 1A-C. As discussed above, the chamber 202 includes an opening extending from a first surface 203 of the chamber 202 to a

cavity 201 configured to receive at least one medication. The at least one opening and/or the first surface 203 can be configured to be placed in contact with an eye 206 of a patient. The iontophoresis device 200 can also include an electrode 204 configured to be in electrical communication with the at least one medication when the at least one medication is within the cavity 201 of the chamber 202. Furthermore, the iontophoresis device 200 includes at least one fill tube 208 extending from the cavity 201 to a second surface 205 of the chamber 202 and configured to receive the at least one medication such that the cavity 201 can receive the at least one medication while the chamber 202 is in contact with the eye 206.

[0149] Figures 3A-C illustrate a further embodiment of an iontophoresis device 300 that includes a first chamber 302a and a second chamber 302b. The first chamber 302a includes at least one opening extending from a first surface 303a of the first chamber 302a to a cavity 301a configured to receive at least one first medication. The at least one opening and/or the first surface 303a can be configured to be placed in contact with an eye 306 of a patient. A first electrode 304a can be configured to be in electrical communication with the at least one first medication when the at least one first medication is within the cavity 301a of the first chamber 302a. The at least one first medication can include at least one active ingredient, and the at least one active ingredient can be configured to enter tissue of the eye 306 through a process of iontophoresis.

[0150] The second chamber 302b includes at least one opening extending from a first surface 303b of the second chamber 302b to a cavity 301b configured to receive at least one second medication. The at least one opening of the second chamber 302b also configured to be placed in contact with an eye of a patient. A second electrode 304b can be configured to be in electrical communication with the at least one second medication when the at least one second medication is within the cavity 301b of the second chamber 302b. The at least one second medication can include at least one active ingredient, and the at least one active ingredient can be configured to enter tissue of an eye through a process of iontophoresis. Furthermore, the iontophoresis device 300 can include a coupling device 310 configured to couple together the first chamber 302a and the second chamber 302b while maintaining electrical isolation between the first chamber 302a and the second chamber 302b. In certain embodiments, a gap is between the first chamber 302a and the second

chamber 302b. Alternatively, an electrically insulative material can be between or sandwiched between the first chamber 302a and the second chamber 302b.

[0151] In certain embodiments, the cavity 301a of the first chamber 302a is fluidly separate from the cavity 301b of the second chamber 302b. For example, the at least one first medication can be different than the at least one second medication and/or the at least one active ingredient of the at least one first medication can be different than the at least one active ingredient of the at least one second medication. Examples of medications and active ingredients are described above, and each chamber 302a, 302b can include a different medication and/or active ingredient. Furthermore, iontophoresis devices can include more than two chambers.

[0152] Figures 4A-C illustrate a further embodiment of an iontophoresis device 400 that includes a first chamber 402a and a second chamber 402b similar to the iontophoresis device 300 in Figures 3A-C. Each chamber 402a, 402b includes an opening extending from a first surface 403a, 403b to a cavity 401a, 401b configured to receive at least one medication. The at least one opening and/or the first surface 403a, 403b can be configured to be placed in contact with an eye 406 of a patient. Each chamber 402a, 402b can also include an electrode 404a, 404b configured to be in electrical communication with the at least one medication when the at least one medication is within the cavity 401a, 401b of the respective chamber 402a, 402b. The iontophoresis device 400 can include a coupling device 410 as discussed above. Furthermore, the first chamber 402a can includes at least one first fill tube 408a extending from the cavity 401a to a second surface 405a of the first chamber 402a and configured to receive the at least one medication such that the first cavity 401a can receive the at least one medication while the first chamber 402a is in contact with the eye 406. In addition, the second chamber 402b can also include at least one second fill tube 408b extending from the cavity 401b to a second surface 405b of the second chamber 402b and configured to receive the at least one medication such that the second cavity 401b can receive the at least one medication while the second chamber 402b is in contact with the eye 406.

[0153] Another embodiment of an iontophoresis device 500 is illustrated in Figures 5A-C. The chamber 502 is configured to at least partially surround at least a portion of a cornea of an eye 506. For example, the chamber 502 can be configured to avoid contact

with the cornea of the eye. Instead, the chamber 502 can be configured to cover a portion of a sclera of the eye. In certain embodiments, the chamber 502 is at least a partial annulus. For example, the at least one opening and the first surface 503 of the chamber 502 can be configured as at least a partial annulus. In further embodiments, the chamber 502 and/or the at least one opening and the first surface 503 of the chamber is an annulus. The annulus may have an inner diameter greater than about 12 mm to avoid contact with the cornea. The iontophoresis device 500 may further include a support structure 512 coupled to the chamber 502 to, for example, provide a method of holding the iontophoresis device 500. The electrode 504 can be in electrical communication with the support structure 512 which can also be in electrical communication with the chamber 502 and the at least one medication.

[0154] Figures 6A-C illustrate an embodiment of an iontophoresis device 600 similar to the iontophoresis device 500 in Figures 5A-C. The chamber 602 includes an opening extending from a first surface 603 of the chamber 602 to a cavity 601 configured to receive at least one medication. The chamber 602 is configured to at least partially surround at least a portion of a cornea of an eye 606. The iontophoresis device 600 further includes a support structure 612 and an electrode 604. In addition, the iontophoresis device 600 can include one or more fill tubes 608 extending from the cavity 601 to a second surface 605 of the chamber 602 and configured to receive the at least one medication such that the cavity 601 can receive the at least one medication while the chamber 602 is in contact with the eye 606.

[0155] Figures 7A-C illustrate an embodiment of an iontophoresis device 700 similar to the iontophoresis device 500 in Figures 5A-C but with a first chamber 702a and a second chamber 702b similar to the iontophoresis device 300 in Figures 3A-C. Each chamber 702a, 702b includes an opening extending from a first surface 703a, 703b to a cavity 701a, 701b configured to receive at least one medication. The at least one opening and/or the first surface 703a, 703b can be configured to be placed in contact with an eye 706 of a patient. Each chamber 702a, 702b can also include an electrode 704a, 704b configured to be in electrical communication with the at least one medication when the at least one medication is within the cavity 701a, 701b of the respective chamber 702a, 702b. The iontophoresis device 700 can include a coupling device 710 as discussed above. Furthermore, a first support structure 712a can be coupled to the first chamber 702a and a

second support structure 712b can be coupled to the second chamber 702b. In certain embodiments, a gap is between the first support structure 712a and the second support structure 712b. Alternatively, an electrically insulative material can be between or sandwiched between the first support structure 712a and the second support structure 712b.

[0156] Figures 8A-C illustrate an embodiment of an iontophoresis device 800 similar to the iontophoresis device 700 in Figures 7A-C. Each chamber 802a, 802b includes an opening extending from a first surface 803a, 803b to a cavity 801a, 801b configured to receive at least one medication. The at least one opening and/or the first surface 803a, 803b can be configured to be placed in contact with an eye 806 of a patient. Each chamber 802a, 802b can also include an electrode 804a, 804b. The iontophoresis device 800 can include a coupling device 810, a first support structure 812a, and a second support structure 712b, as discussed above. Furthermore, similar to the iontophoresis device 400 in Figures 4A-C, the first chamber 802a can includes at least one first fill tube 808a and the second chamber 802b can also include at least one second fill tube 808b.

[0157] Figures 9A-C illustrate an embodiment of an iontophoresis device 900 similar to the iontophoresis device 700 in Figures 7A-C. The first chamber 902a and the second chamber 902b have an annular shaped with the second chamber 902b being inside the first chamber 902a (e.g., concentric rings). For example, the chambers 902a, 902b are configured to at least partially surround at least a portion of a cornea of an eye 906, and the second chamber 902b is between the first chamber 902a and the cornea. In certain embodiments, the second chamber 902b has an inner diameter greater than a diameter of the cornea (e.g., greater than about 12 mm) and the first chamber 902a has an inner diameter greater than an outer diameter of the second chamber 902b. For example, the first chamber 902a may have an inner diameter of about 14 mm and the second chamber 902b may have an inner diameter of about 13 mm. As discussed above, each chamber 902a, 902b includes an opening extending from a first surface 903a, 903b to a cavity 901a, 901b configured to receive at least one medication. The at least one opening and/or the first surface 903a, 903b can be configured to be placed in contact with an eye 906 of a patient. The iontophoresis device 900 can include other features as discussed above such as electrodes 904a, 904b, a coupling device 910, and support structures 912a, 912b.

[0158] Figures 10A-C illustrate an embodiment of an iontophoresis device 1000 similar to the iontophoresis device 900 in Figures 9A-C. Each chamber 1002a, 1002b includes an opening extending from a first surface 1003a, 1003b to a cavity 1001a, 1001b configured to receive at least one medication. The at least one opening and/or the first surface 1003a, 1003b can be configured to be placed in contact with an eye 1006 of a patient. The iontophoresis device 1000 can include other features as discussed above such as electrodes 1004a, 1004b, a coupling device 1010, and support structures 1012a, 912b. Furthermore, the iontophoresis device 1000 can include fill tubes 1008a, 1008b as previously discussed.

[0159] Figure 11A illustrates a femtosecond laser attachment 1120 configured to receive a femtosecond laser for treating an eye of a patient. Figure 11B illustrates an iontophoresis device 1100 configured to receive the femtosecond laser attachment 1120 in Figure 11A. The iontophoresis device 1100 is similar to the iontophoresis device 800 in Figures 8A-C. However, the support structures 1112a and 1112b provide a larger opening between them to accommodate the femtosecond laser attachment 1120. Figure 11C illustrates the femtosecond laser attachment 1120 coupled with the iontophoresis device 1100. In certain embodiments, iontophoresis device 1100 and the femtosecond laser attachment 1120 are configured to be removably coupled. In certain embodiments, the iontophoresis device 1100 includes a gasket 1113 (e.g., o-ring) along an inside perimeter of the support structures 1112a and 1112b, as illustrated in Figure 11D. The gasket 1113 can help to provide a snug fit between the iontophoresis device 1100 and the femtosecond laser attachment 1120.

[0160] Figures 12A-C illustrate an iontophoresis device 1200 configured to receive a femtosecond laser attachment 1220 similar to iontophoresis device 1100 and femtosecond laser attachment 1120 in Figures 11A-D. Furthermore, the iontophoresis device 1200 is similar to the iontophoresis device 900 in Figures 9A-C; however, the support structures 1212a and 1212b provide a larger opening between them to accommodate the femtosecond laser attachment 1220.

[0161] Figures 13A-C illustrate another iontophoresis device 1300 configured to receive a femtosecond laser attachment 1320 similar to iontophoresis device 1200 and femtosecond laser attachment 1220 in Figures 12A-D. However, the iontophoresis device

1300 further includes fill tubes 1308a, 1308b coupled to the respective chambers 1302a, 1302b similar to the iontophoresis device 1000 in Figures 10A-C.

[0162] The iontophoresis device can also be configured to receive other devices. For example, the iontophoresis device can be configured to surround an Intralase cone or replace an Intralase suction device.

[0163] Furthermore, iontophoresis devices can include a controller in electrical communication with the electrodes and a portion of the patient. If the iontophoresis device includes a single chamber such as those illustrated in Figures 1A-C, 2A-C, 5A-C, and 6A-C, a 2-lead controller 1430 can be used, as illustrated in Figure 14A. The controller 1430 can include a first lead 1434 configured to be in electrical communication with an electrode of the iontophoresis device and a second lead 1436 configured to be in electrical communication with a portion of the patient. The controller 1430 can further include an interface 1432 to control electrical potential applied to the leads 1434, 1436. If the iontophoresis device includes two chambers such as those illustrated in Figures 3A-C, 4A-C, 7A-C, 8A-C, 9A-C, 10A-C, 11A-C, 12A-C, and 13A-C, a 3-lead controller 1440 can be used, as illustrated in Figure 14B. Similar to the controller 1430 in Figure 14A, the controller 1440 can include leads 1444, 1446, 1448 and an interface 1442. A first lead 1444 can be configured to be in electrical communication with a first electrode of the iontophoresis device, a second lead 1446 can be configured to be in electrical communication with a second electrode of the iontophoresis device, and a third lead 1448 can be configured to be in electrical communication with a portion of the patient. If the iontophoresis device includes more than two chambers, the controller can also include additional leads.

[0164] **Method of Use:** In use, the device is applied to the eye, and a current is applied for a treatment period. The iontophoresis devices described herein can be used in a number of methods to deliver medications into an eye of a patient including delivering mydriatic medications in order to enlarge a pupil of the eye. In certain embodiments, a method includes contacting a first surface of a first chamber with the eye. The first chamber includes at least one opening extending from the first surface to a cavity. The method can further include filling the cavity of the first chamber with at least one first medication and applying an electrical potential between the first chamber and the patient to cause at least one active ingredient of the at least one first medication to enter the eye.

[0165] As described herein, the iontophoresis device can include two or more chambers. In some embodiments, the method further includes contacting a first surface of a second chamber with the eye. The second chamber includes at least one opening extending from the first surface to a cavity. The method may further include filling the cavity of the second chamber with at least one second medication and applying an electrical potential between the second chamber and the patient to cause at least one active ingredient of the at least one second medication to enter the eye.

[0166] The at least one first medication can be different than the at least one second medication. Furthermore, the first medication and the second medication may be administered serially (e.g., one medication at a time) or in parallel (e.g., both medications at the same time). Furthermore, the cavity of the first chamber may be fluidly separate from the cavity of the second chamber. In addition, the first chamber and the second chamber may be coupled together while maintaining electrical isolation between the first chamber and the second chamber.

[0167] In one embodiment, the device is configured as a double chamber sclera cup with fill ports. In use, the device is placed onto the eye of a patient, then the chambers are each filled using syringes (such as the syringe 1500 illustrated in Figure 15) or other means. Next, the chambers are electrically activated for a period of time using a 3-lead controller. If the mydriatic agent in one of the chambers is a cationic medication, the controller applies a positive voltage to that chamber. If the mydriatic agent in one of the chambers is an anionic medication, the controller applies a negative voltage to that chamber. One or more return lines are attached to the forehead or other body part of the patient to complete the circuits.

[0168] In an alternate embodiment, the device is configured as a double chamber sclera cup without fill ports. In use, the chambers are filled with gels, then the device is placed onto the eye of a patient. The chambers are then electrically activated for a period of time using a 3-lead controller. If the mydriatic agent in one of the chambers is a cationic medication, the controller applies a positive voltage to that chamber. If the mydriatic agent in one of the chambers is an anionic medication, the controller applies a negative voltage to that chamber. One or more return lines are attached to the forehead or other body part of the patient to complete the circuits.

[0169] In an alternate embodiment, the device is configured as a single chamber sclera cup with fill ports. In use, the device is placed onto the eye of a patient, then the chamber is filled using a syringe or other means. Next, the chamber is electrically activated for a period of time using a 2-lead controller. If the mydriatic agent is a cationic medication, the controller applies a positive voltage to the chamber. If the mydriatic agent is an anionic medication, the controller applies a negative voltage to the chamber. A return line is attached to the forehead or other body part of the patient to complete the circuit.

[0170] In an alternate embodiment, the device is configured as a single chamber sclera cup without fill ports. In use, the device is filled with gel, and then placed onto the eye of a patient. The chamber is then electrically activated for a period of time using a 2-lead controller. If the mydriatic agent is a cationic medication, the controller applies a positive voltage to the chamber. If the mydriatic agent is an anionic medication, the controller applies a negative voltage to the chamber. A return line is attached to the forehead or other body part of the patient to complete the circuit.

[0171] In an alternate embodiment, the device is configured as a double chamber eye cup with fill ports. In use, the device is placed onto the eye of a patient, and then the chambers are filled using syringes or other means. Next, the chambers are electrically activated for a period of time using a 3-lead controller. If the mydriatic agent in one of the chambers is a cationic medication, the controller applies a positive voltage to that chamber. If the mydriatic agent in one of the chambers is an anionic medication, the controller applies a negative voltage to that chamber. One or more return lines are attached to the forehead or other body part of the patient to complete the circuits.

[0172] In an alternate embodiment, the device is configured as a double chamber eye cup without fill ports. In use, the device is filled with gels, and then placed onto the eye of a patient. The chambers are then electrically activated for a period of time using a 3-lead controller. If the mydriatic agent in one of the chambers is a cationic medication, the controller applies a positive voltage to that chamber. If the mydriatic agent in one of the chambers is an anionic medication, the controller applies a negative voltage to that chamber. One or more return lines are attached to the forehead or other body part of the patient to complete the circuits.

[0173] In an alternate embodiment, the device is configured as a single chamber eye cup with fill ports. In use, the device is placed onto the eye of a patient, then the chamber is filled using a syringe or other means. Next, the chamber is electrically activated for a period of time using a 2-lead controller. If the mydriatic agent is a cationic medication, the controller applies a positive voltage to the chamber. If the mydriatic agent is an anionic medication, the controller applies a negative voltage to the chamber. A return line is attached to the forehead or other body part of the patient to complete the circuit.

[0174] In an alternate embodiment, the device is configured as a single chamber eye cup without fill ports. In use, the device is filled with gel and then placed onto the eye of a patient. The chamber is then electrically activated for a period of time using a 2-lead controller. If the mydriatic agent is a cationic medication, the controller applies a positive voltage to the chamber. If the mydriatic agent is an anionic medication, the controller applies a negative voltage to the chamber. A return line is attached to the forehead or other body part of the patient to complete the circuit.

[0175] The iontophoresis device can be stand alone or incorporated into the interface of a femtosecond laser used for cataract surgery.

[0176] In some embodiments, the diameter of the sclera ring is configured to fit around the circumference of the patient interface. In this embodiment, the sclera cup is attached to the femtosecond laser patient interface, and the two functions are handled as a unit. Once the patient interface is positioned onto the eye of a patient, the chambers of the iontophoresis device are filled, and the electrical connections are made as previously described. The iontophoresis process of mydriatic medications takes place before, during, or after the operation of the femtosecond laser.

[0177] In one embodiment, an O-Ring is configured to be retained by the device, with a portion thereof protruding within an inner diameter of the device. In use, a portion of the O-Ring is configured to interface with a portion of the femtosecond laser patient interface causing retention there between.

[0178] In one embodiment, the electrode (either inert or active) is far away from the surface applied to the eye, since most of the pH changes occur near the electrode and the electrode may create thermal effects. For example, the electrode may be about 6 millimeters away from the surface of the eye. In some embodiments, the electrophoresis is just done

serially with the various drugs. In further embodiments, a NSAID can be used and could be strong enough that it could obviate the need for the steroid. For example, if iontophoresing bromfenac is used. Some embodiments may add a hydrophilic foam to the drugs in the device.

[0179] Various embodiments have been described above. Although the invention has been described with reference to these specific embodiments, the descriptions are intended to be illustrative and are not intended to be limiting. Various modifications and applications may occur to those skilled in the art without departing from the true spirit and scope of the invention as defined in the appended claims.

WHAT IS CLAIMED IS:

1. A device to deliver medications into an eye of a patient in order to enlarge the pupil comprising:

a chamber, the chamber comprising at least a partial opening along a surface, the open surface configured to be brought into contact with the eye of a patient;

wherein the chamber is configured be at least partially filled with medication, the medication comprising at least one active ingredient, and the at least one active ingredient capable of entering the tissue of the eye.

2. The device of Claim 1, wherein the at least one active ingredient capable of entering the tissue of the eye through a process of iontophoresis.

3. The device of Claim 2, wherein said iontophoresis is accomplished via electrorepulsion between said chamber and said medication.

4. The device of Claim 3, wherein said chamber is positively charged acting as an anode and said medication comprises active ingredients consisting of positively charged cations.

5. The device of Claim 3, wherein said chamber is negatively charged acting as a cathode and said medication comprises active ingredients consisting of negatively charged anions.

6. The device of Claim 1, wherein the chamber comprises at least one cavity comprising a circular ring, the ring configured for covering a portion of the sclera of the eye of a patient.

7. The device of Claim 1, wherein the chamber comprises multiple cavities comprising segments of a ring, the segments of the ring configured to cover a portion of a sclera of the eye of a patient.

8. The device of Claims 6 or 7, wherein the chamber is configured to deliver the medication transclerally.

9. The device of Claim 1, wherein the chamber comprises at least one cavity, the chamber configured to cover a cornea and a portion of a sclera of the eye of a patient.

10. The device of Claim 1, wherein the chamber comprises multiple chambers configured to cover a cornea and a portion of a sclera of the eye of a patient.

11. The device of Claims 9 or 10, wherein the chamber is configured to deliver the medication transcorneally.

12. The device of Claim 1, wherein the chamber is configured to receive the medication comprising a gel.

13. The device of Claim 12, wherein the chamber is configured as a cavity to receive the gel prior to placing the chamber in contact with the eye of a patient.

14. The device of Claim 1, wherein the chamber is configure to receive the medication comprising a liquid.

15. The device of Claim 14, wherein the chamber is configured to receive the liquid after placing the chamber in contact with the eye of a patient.

16. The device of Claim 15, wherein the chamber comprises a fill tube through the liquid medication may be introduced after the chamber is placed into contact with the eye of a patient.

17. The device of Claim 1, wherein the chamber comprises a retention means for maintaining contact between the chamber and the eye of a patient.

18. The device of Claim 17, wherein the retention means comprises an eye speculum configured to maintain said contact between the eye and the chamber.

19. The device of Claim 17, wherein the retention means comprises a weight sufficient to maintain said contact between the eye and the chamber.

20. The device of Claim 17, wherein the retention means comprises viscous adhesion to maintain said contact between the eye and the chamber.

21. The device of Claim 1, wherein the chamber is circumferentially disposed about a central axis of sufficient clearance diameter to allow passage of a portion of a femtosecond laser patient attachment to reside therein.

22. The device of Claim 21, wherein a portion of the device is configured to be fastened to a portion of the femtosecond laser patient attachment.

23. The device of Claim 22, wherein said portion comprises a friction fit.

24. The device of Claim 23, wherein said friction fit is by interference with a compressible element.

25. The device of Claim 24, wherein said compressible element is an elastomeric O-ring.

26. A method to deliver medications into the eye of a patient in order to enlarge the pupil comprising

bringing an open surface of a chamber into contact with the eye of the patient;

filling the chamber at least partially with a medication having at least one active ingredient; and

propeling the at least one active ingredient into tissue of the eye.

27. The method of Claim 26, further comprising attaching electrodes; and activating a transmitter to propel the at least one active ingredient into the tissue of the eye through a process of iontophoresis.

28. An iontophoresis device comprising:

a first chamber comprising at least one opening extending from a first surface of the first chamber to a cavity configured to receive at least one first medication, the at least one opening configured to be placed in contact with an eye of a patient; and

a first electrode configured to be in electrical communication with the at least one first medication when the at least one first medication is within the cavity of the first chamber;

wherein the at least one first medication comprises at least one active ingredient, the at least one active ingredient configured to enter tissue of an eye through a process of iontophoresis.

29. The iontophoresis device of Claim 28, wherein the at least one first medication comprises a mydriatic medication.

30. The iontophoresis device of Claim 29, wherein the at least one first medication further comprises a second drug different from the mydriatic medication.

31. The iontophoresis device of Claim 30, wherein the second drug comprises a steroidal.

32. The iontophoresis device of Claim 30, wherein the second drug comprises a nonsteroidal.

33. The iontophoresis device of Claim 30, wherein the second drug comprises an antibiotic medication.

34. The iontophoresis device of Claim 30, wherein the second drug comprises an anti-inflammatory.

35. The iontophoresis device of Claim 30, further comprising at least one fill tube extending from the cavity to a second surface of the first chamber and configured to receive the at least one first medication such that the cavity can receive the at least one first medication while the first chamber is in contact with the eye.

36. The iontophoresis device of Claim 28, further comprising:

a second chamber comprising at least one opening extending from a first surface of the second chamber to a cavity configured to receive at least one second medication, the at least one opening configured to be placed in contact with an eye of a patient; and

a second electrode configured to be in electrical communication with the at least one second medication when the at least one second medication is within the cavity of the second chamber;

wherein the at least one second medication comprises at least one active ingredient, the at least one active ingredient configured to enter tissue of an eye through a process of iontophoresis.

37. The iontophoresis device of Claim 36, wherein the cavity of the first chamber is fluidly separate from the cavity of the second chamber.

38. The iontophoresis device of Claim 37, further comprising a coupling device configured to couple together the first chamber and the second chamber while maintaining electrical isolation between the first chamber and the second chamber.

39. The iontophoresis device of Claim 36, further comprising at least one fill tube extending from the cavity of the second chamber to a second surface of the second chamber and configured to receive the at least one second medication such that the cavity can receive the at least one medication while the second chamber is in contact with the eye.

40. The iontophoresis device of Claim 36, wherein the at least one first medication is different than the at least one second medication.

41. The iontophoresis device of Claim 28, wherein the first chamber is configured to at least partially surround at least a portion of a cornea of the eye.

42. The iontophoresis device of Claim 41, wherein the first chamber is configured to avoid contact with the cornea of the eye.

43. The iontophoresis device of Claim 41, wherein the first chamber is configured to cover a portion of a sclera of the eye.

44. The iontophoresis device of Claim 41, wherein the at least one opening and the first surface of the first chamber is configured as at least a partial annulus.

45. The iontophoresis device of Claim 41, wherein the at least one opening and the first surface of the first chamber is an annulus.

46. The iontophoresis device of Claim 41, further comprising a first support structure coupled to the first chamber.

47. The iontophoresis device of Claim 36, wherein the second chamber is configured to at least partially surround at least a portion of the cornea of the eye.

48. The iontophoresis device of Claim 47, wherein the second chamber is configured to avoid contact with the cornea of the eye.

49. The iontophoresis device of Claim 47, wherein the second chamber is configured to cover a portion of the sclera of the eye.

50. The iontophoresis device of Claim 47, wherein the at least one opening and the first surface of the second chamber is configured as at least a partial annulus.

51. The iontophoresis device of Claim 47, wherein the at least one opening and the first surface of the second chamber is an annulus.

52. The iontophoresis device of Claim 47, further comprising a second support structure coupled to the second chamber.

53. The iontophoresis device of Claim 47, wherein the second chamber is between the first chamber and the cornea.

54. The iontophoresis device of Claim 46, further comprising a femtosecond laser attachment configured to be coupled with a first support structure.

55. The iontophoresis device of Claim 52, further comprising a femtosecond laser attachment configured to be coupled with second support structure.

56. The iontophoresis device of Claim 28, further comprising a controller in electrical communication with the first electrode.

57. The iontophoresis device of Claim 36, further comprising a controller in electrical communication with the first electrode and the second electrode.

58. The iontophoresis device of Claim 40, wherein the at least one second medication comprises a steroidal.

59. The iontophoresis device of Claim 40, wherein the at least one second medication comprises a nonsteroidal.

60. The iontophoresis device of Claim 40, wherein the at least one second medication comprises an antibiotic medication.

61. The iontophoresis device of Claim 40, wherein the at least one second medication comprises an anti-inflammatory.

62. A method of delivering mydriatic medications into an eye of a patient in order to enlarge a pupil of the eye comprising:

contacting a first surface of a first chamber with the eye, the first chamber comprising at least one opening extending from the first surface to a cavity; and

filling the cavity of the first chamber with at least one first medication.

63. The method of Claim 62, further comprising applying an electrical potential between the first chamber and the patient to cause at least one active ingredient of the at least one first medication to enter the eye.

64. The method of Claim 62, wherein the at least one first medication comprises a mydriatic medication.

65. The method of Claim 64, wherein the at least one first medication further comprises a second drug different from the mydriatic medication.

66. The method of Claim 65, wherein the second drug comprises a steroidal.

67. The method of Claim 65, wherein the second drug comprises a nonsteroidal anti-inflammatory.

68. The method of Claim 65, wherein the second drug comprises an antibiotic medication.

69. The method of Claim 65, wherein the second drug comprises an anti-inflammatory.

70. The method of Claim 62, further comprising:

contacting a first surface of a second chamber with the eye, the second chamber comprising at least one opening extending from the first surface to a cavity; and

filling the cavity of the second chamber with at least one second medication.

71. The method of Claim 70, applying an electrical potential between the second chamber and the patient to cause at least one active ingredient of the at least one second medication to enter the eye.

72. The method of Claim 70, wherein the at least one first medication is different than the at least one second medication.

73. The method of Claim 72, wherein the at least one second medication comprises a steroidal.

74. The method of Claim 72, wherein the at least one second medication comprises a nonsteroidal anti-inflammatory.

75. The method of Claim 72, wherein the at least one second medication comprises an antibiotic medication.

76. The method of Claim 72, wherein the at least one second medication comprises an anti-inflammatory.

77. The method of Claim 72, wherein the cavity of the first chamber is fluidly separate from the cavity of the second chamber.

78. The method of Claim 70, wherein the first chamber and the second chamber are coupled together while maintaining electrical isolation between the first chamber and the second chamber.

79. The method of Claim 62, wherein the first chamber at least partially surrounds at least a portion of a cornea of the eye.

80. The method of Claim 79, wherein the first chamber does not contact with the cornea of the eye.

81. The method of Claim 77, wherein the first chamber covers a portion of a sclera of the eye.

82. The method of Claim 70, wherein the second chamber at least partially surrounds at least a portion of the cornea of the eye.

83. The method of Claim 82, wherein the second chamber does not contact the cornea of the eye.

84. The method of Claim 82, wherein the second chamber covers a portion of the sclera of the eye.

85. The method of Claim 82, wherein the second chamber is between the first chamber and the cornea.

86. The method of Claim 62, further comprising applying photons to the eye with the femtosecond laser.

87. The method of Claim 62, further comprising coupling the femtosecond laser to the first chamber.

88. The method of Claim 62, further comprising coupling the femtosecond laser attachment to the second chamber.

89. The method of Claim 62, further comprising applying a magnetic field to the at least one first medication to cause at least one active ingredient of the at least one first medication to enter the eye.

90. The method of Claim 62, further comprising applying ultrasound waves to the at least one first medication to cause at least one active ingredient of the at least one first medication to enter the eye.

91. The method of Claim 62, further comprising applying light to the at least one first medication to cause at least one active ingredient of the at least one first medication to enter the eye.

92. The method of Claim 62, further comprising creating a negative pressure between the first chamber and the eye.

93. The device of Claim 1, further comprising a magnetic field generator configured to assist the at least one active ingredient to enter the tissue of the eye.

94. The device of Claim 1, further comprising an ultrasound transducer configured to assist the at least one active ingredient to enter the tissue of the eye.

95. The device of Claim 1, further comprising a light source configured to assist the at least one active ingredient to enter the tissue of the eye.

96. The device of Claim 1, further comprising negative pressure device configured to create negative pressure between the chamber and the eye.

97. The device of Claim 96, wherein the negative pressure device comprises a suction bulb.

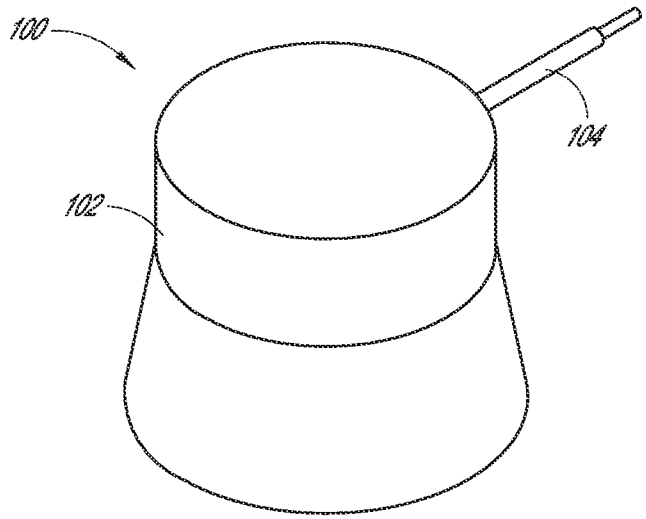


FIG. 1A

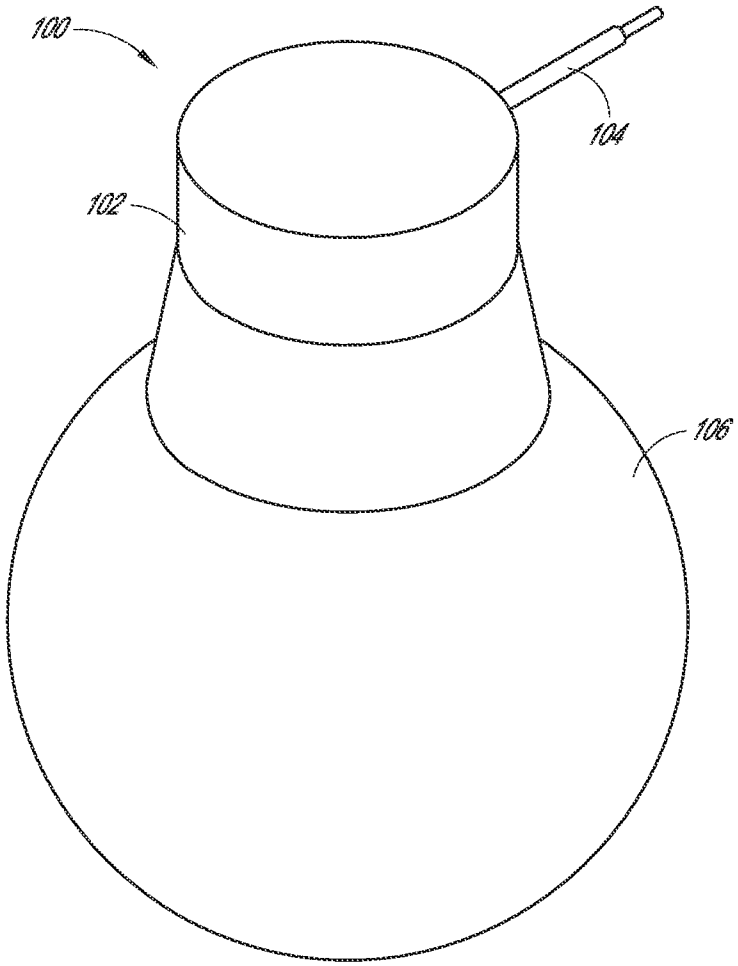


FIG. 1B

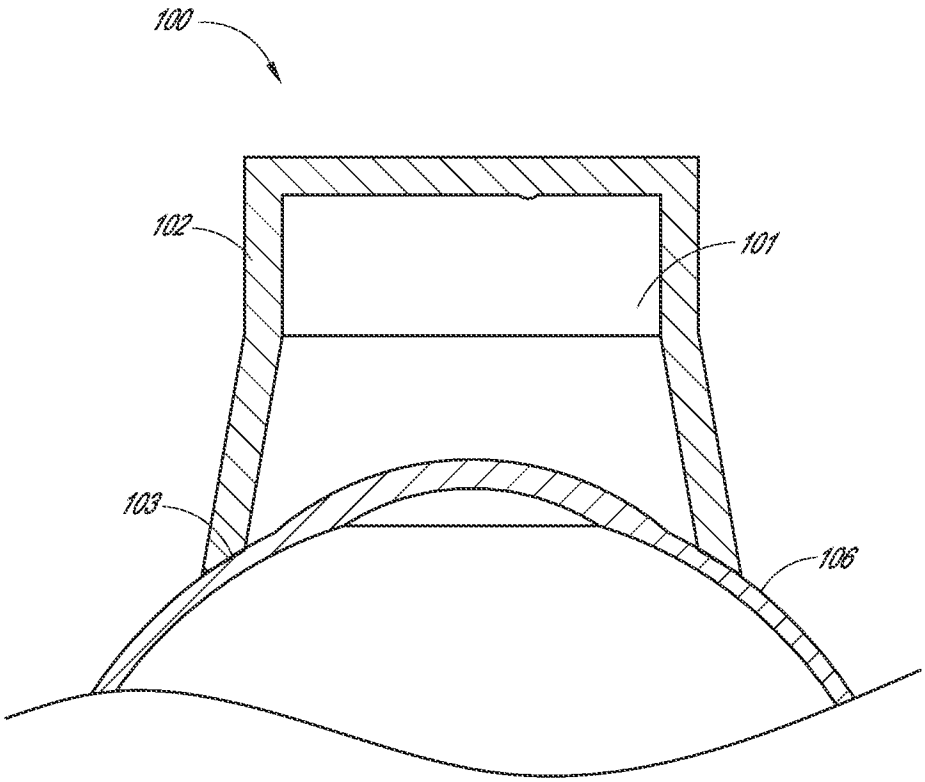


FIG. 1C

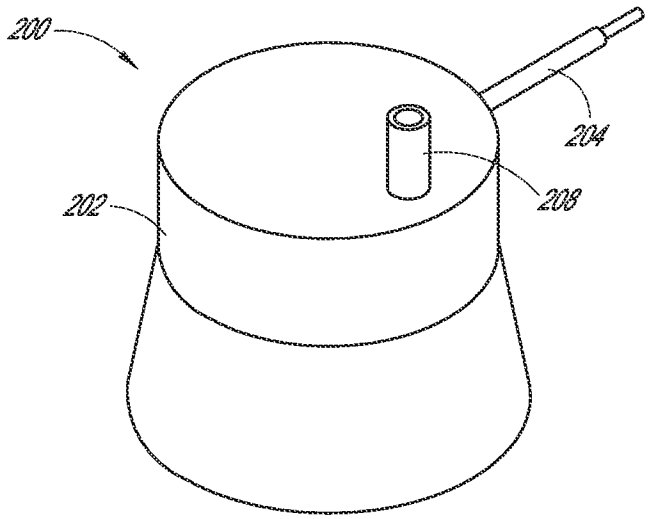


FIG. 2A

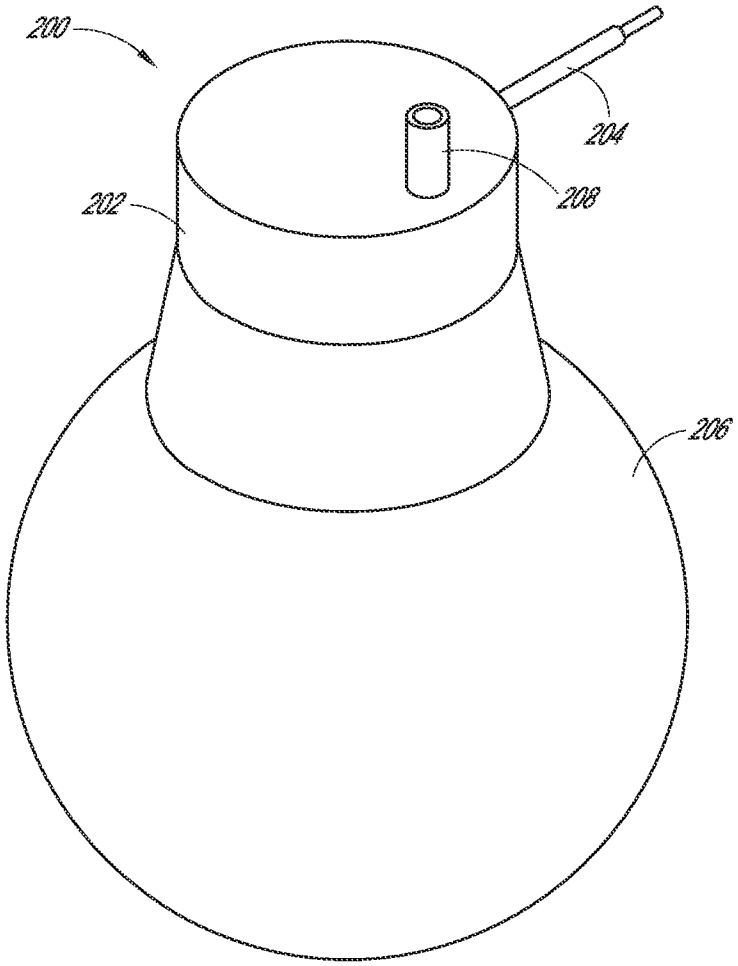


FIG. 2B

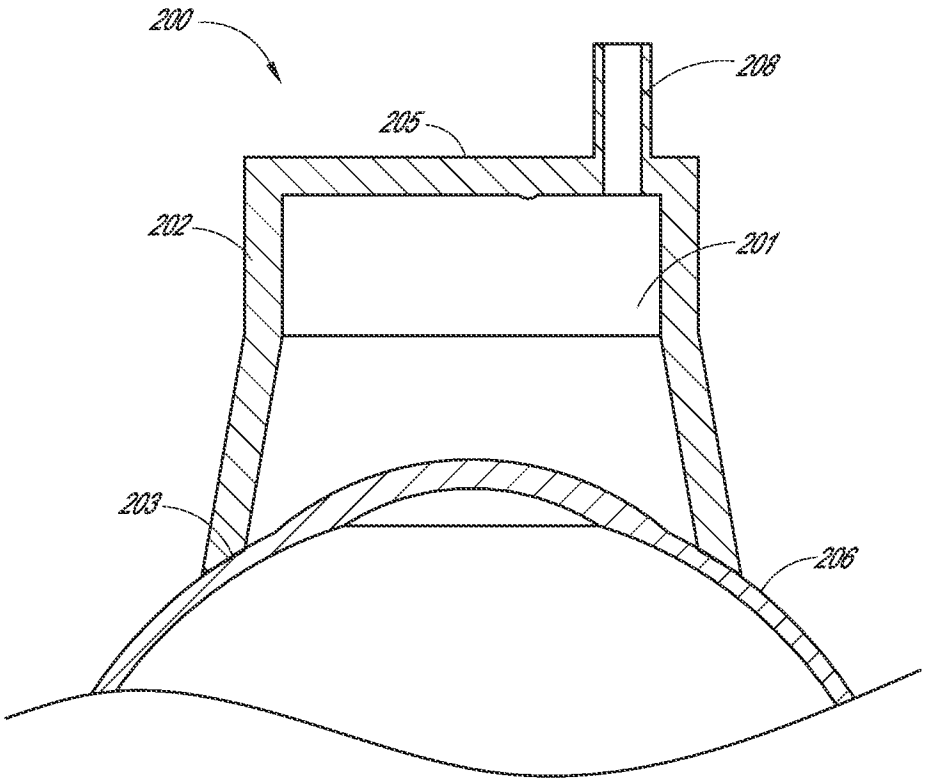


FIG. 2C

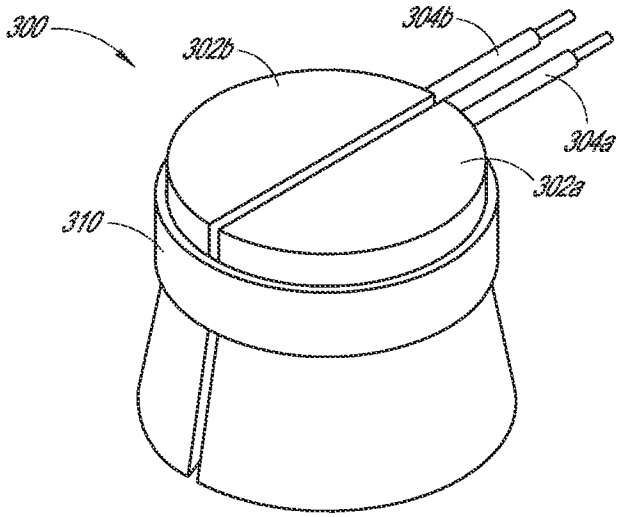


FIG. 3A

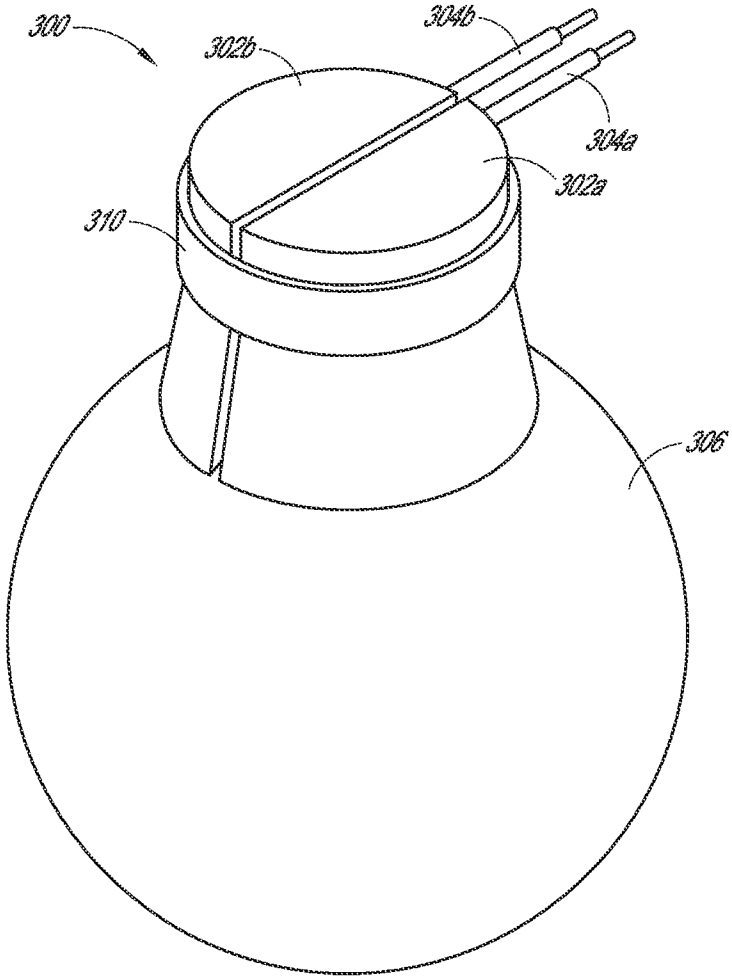


FIG. 3B

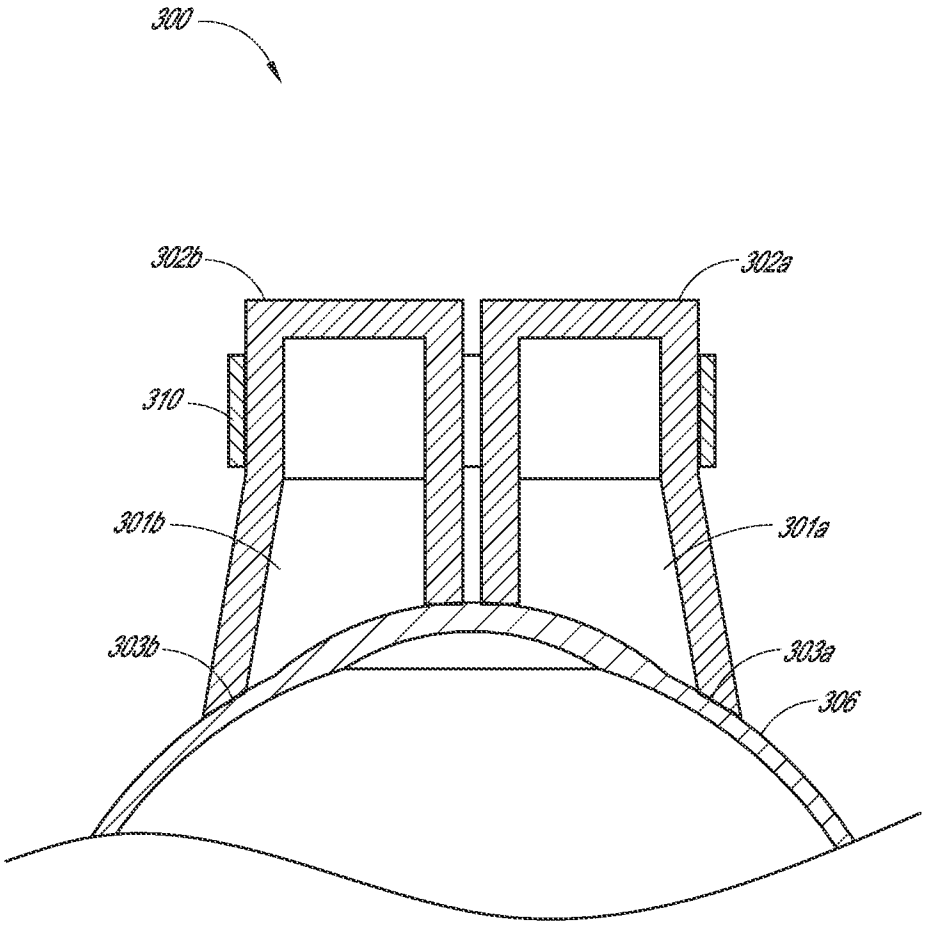
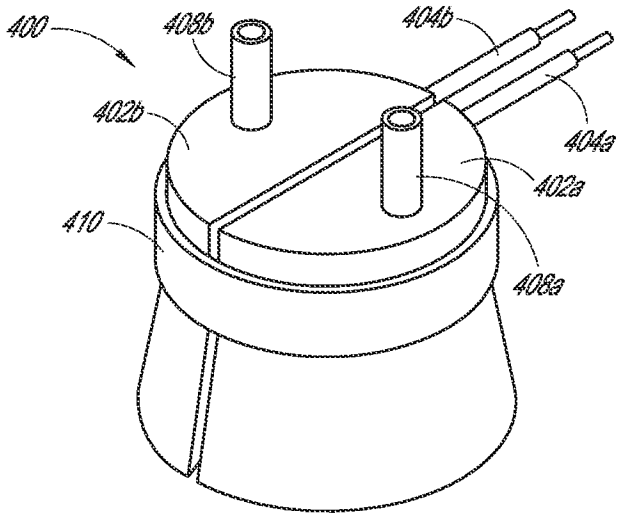


FIG. 3C


400
408b
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404a
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408a

FIG. 4A

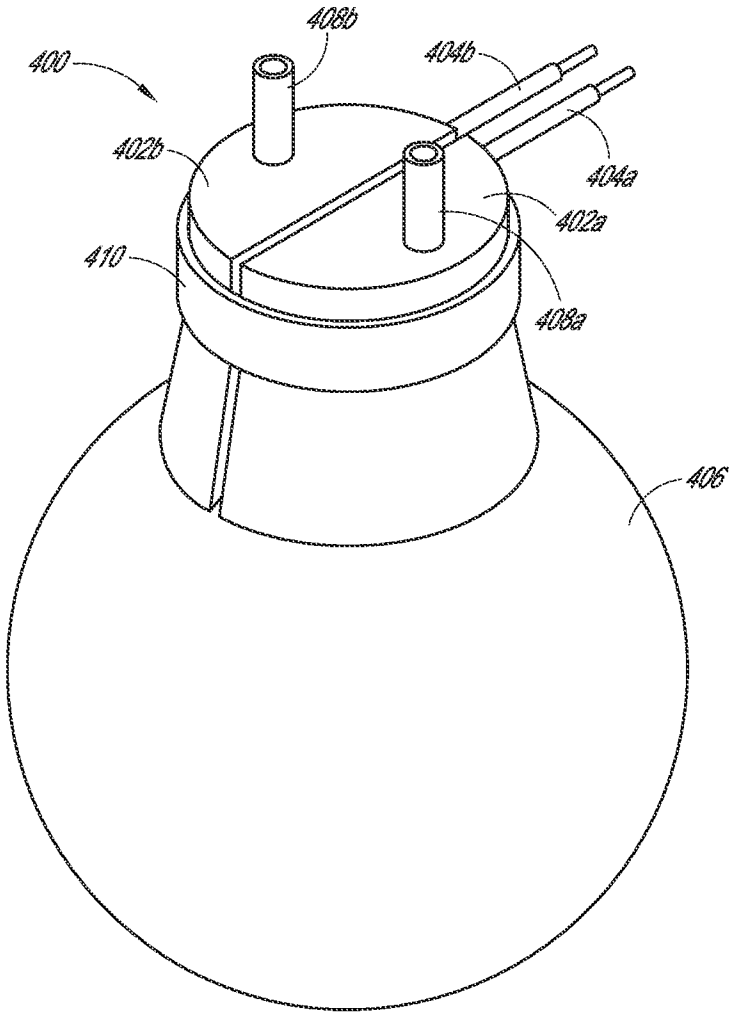
408b
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FIG. 4B

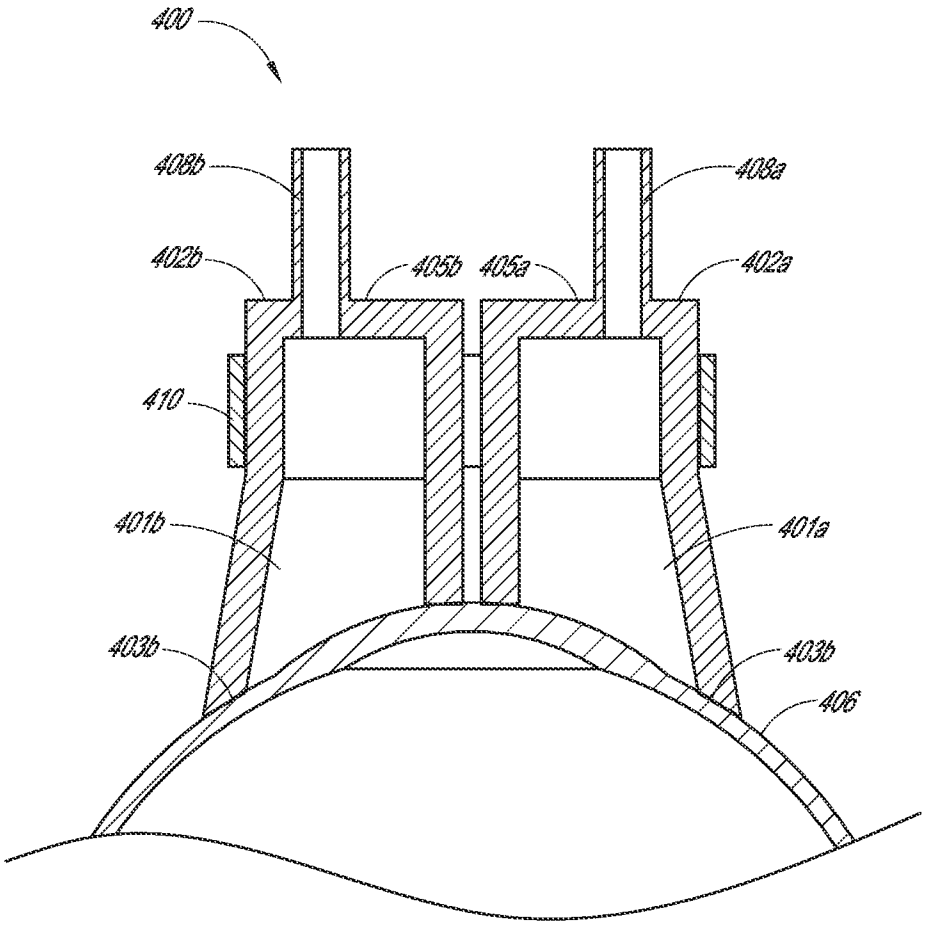


FIG. 4C

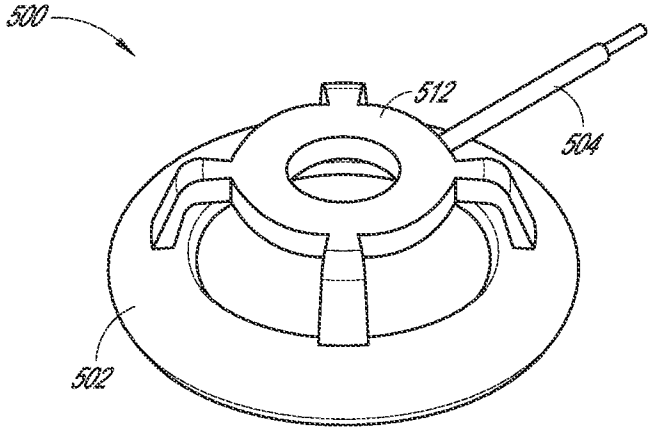


FIG. 5A

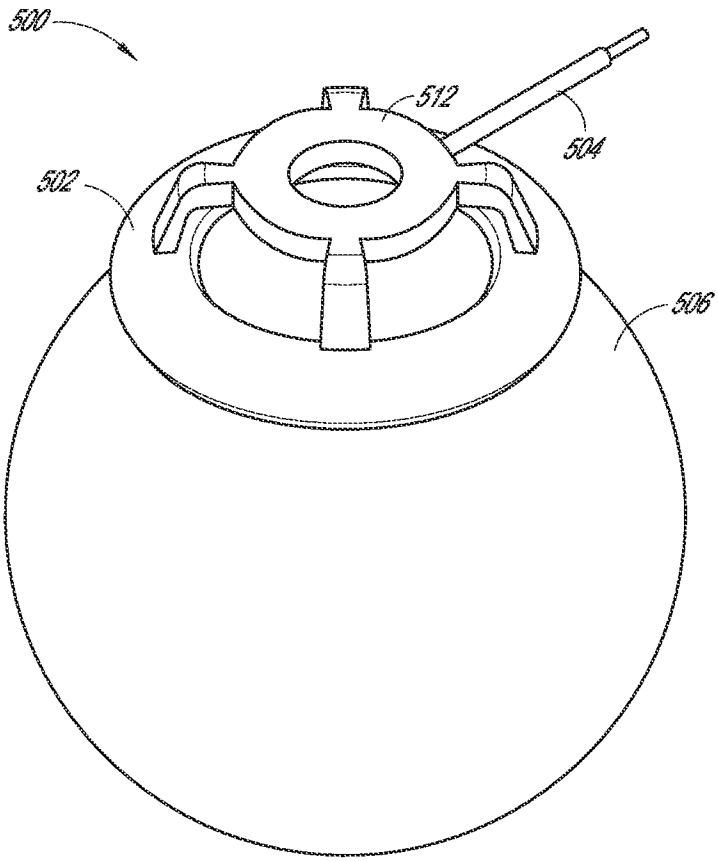


FIG. 5B

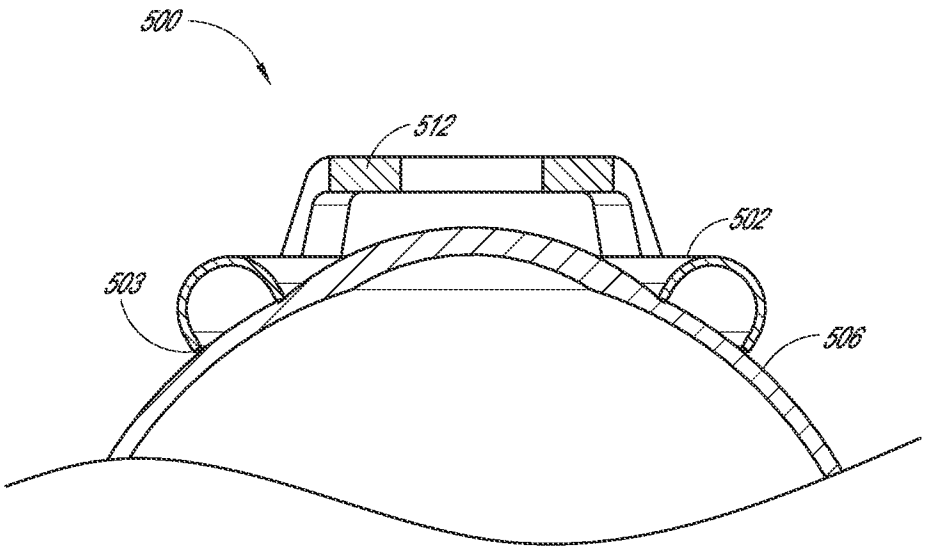


FIG. 5C

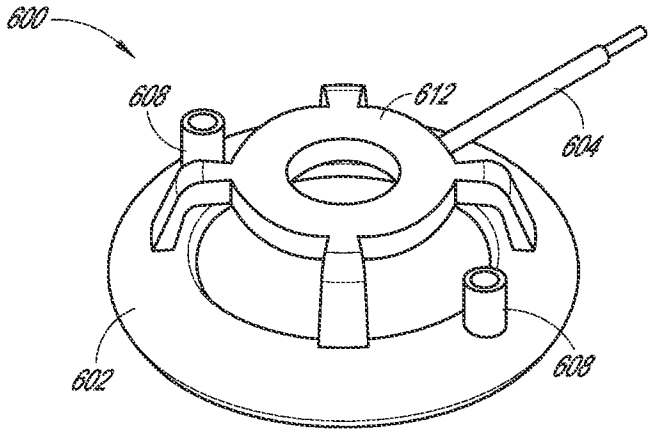


FIG. 6A

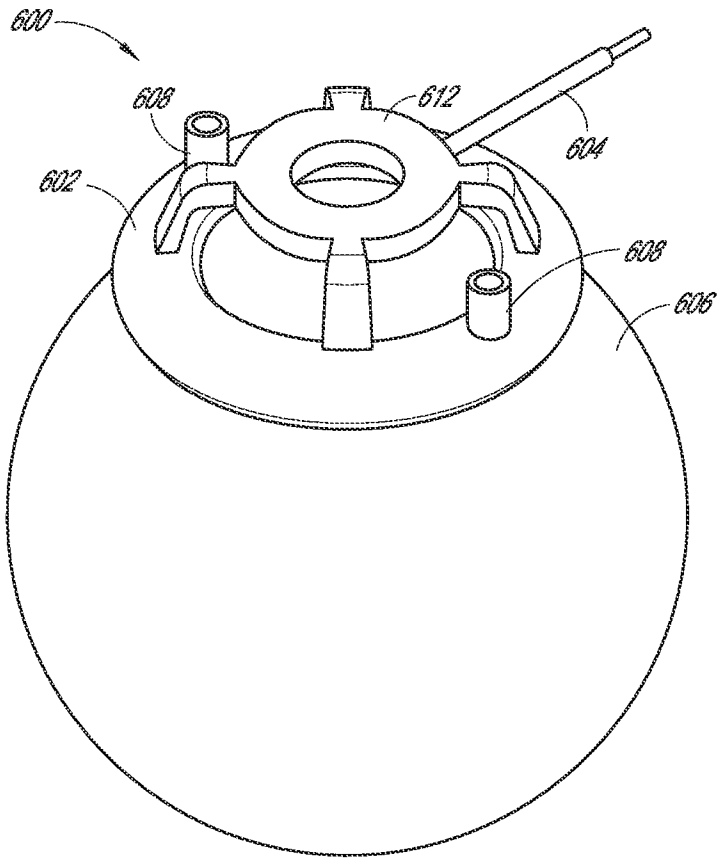


FIG. 6B

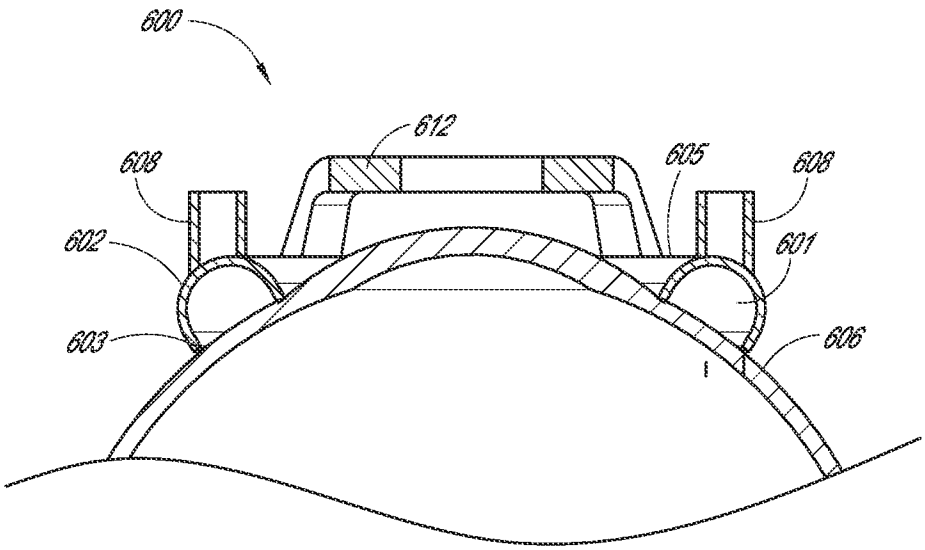


FIG. 6C

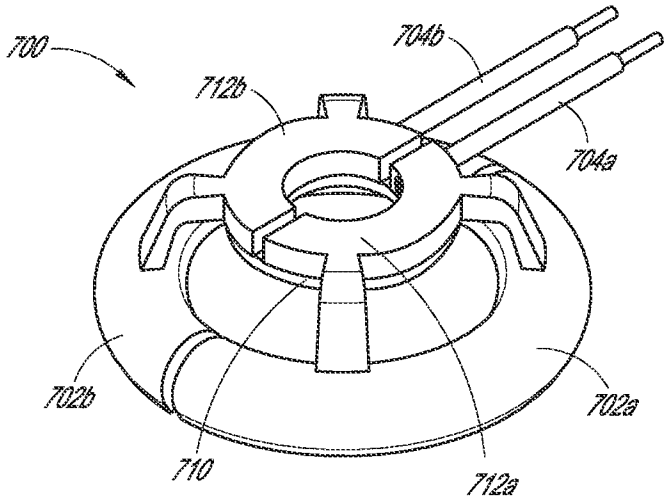
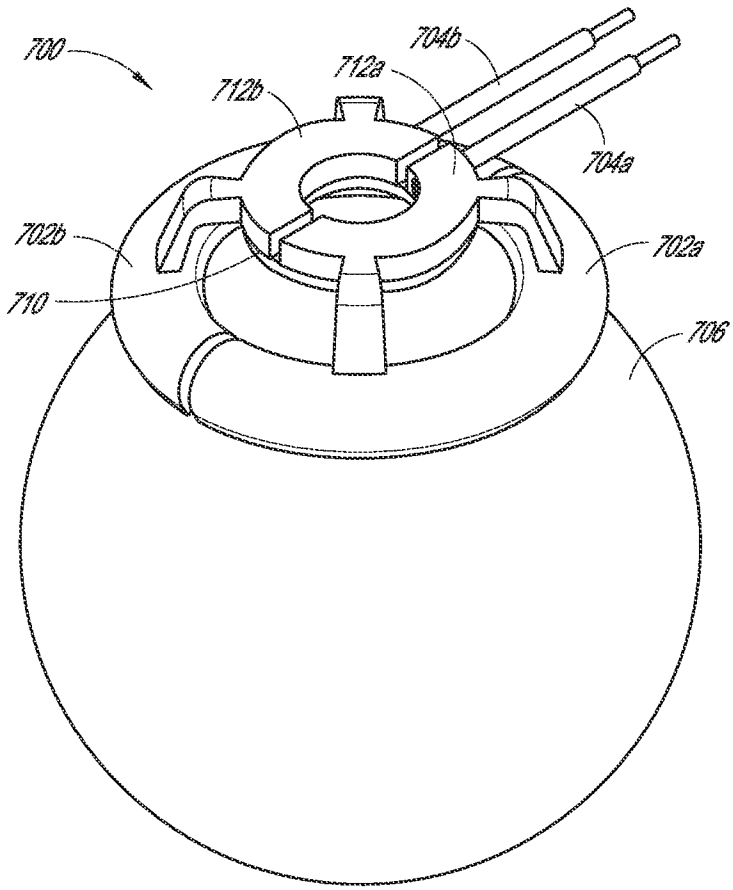

700
704b
712b
704a
702b
702a
710
712a

FIG. 7A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702b
702a
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706

FIG. 7B

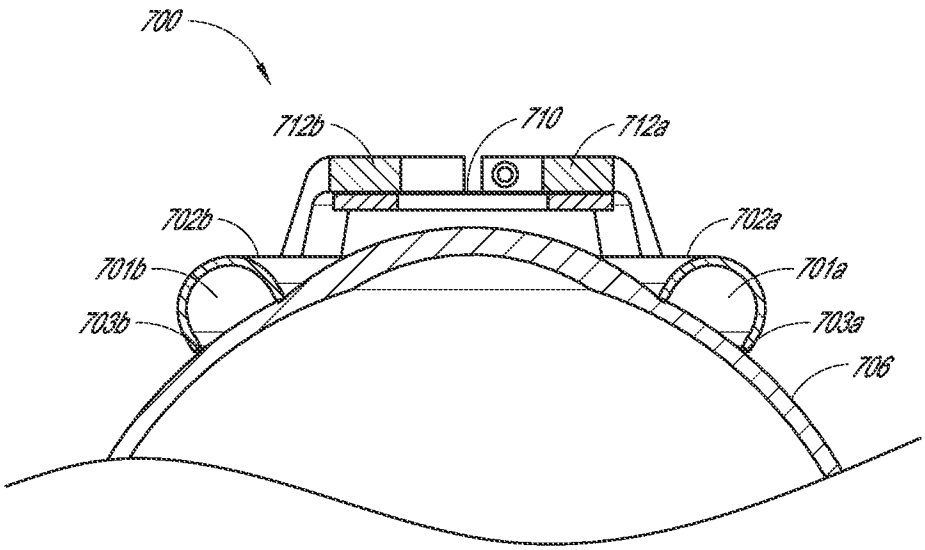
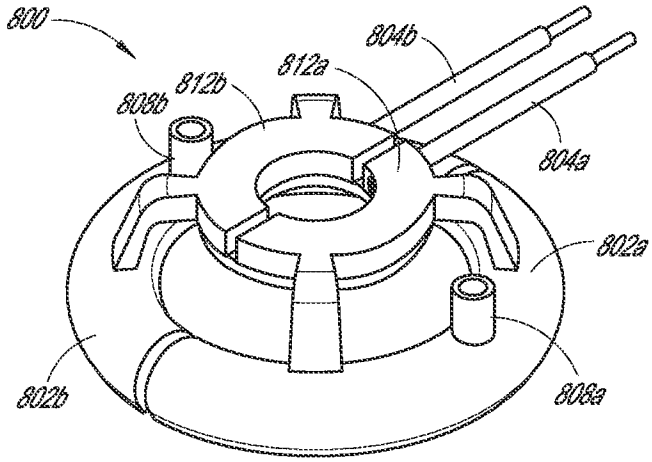


FIG. 7C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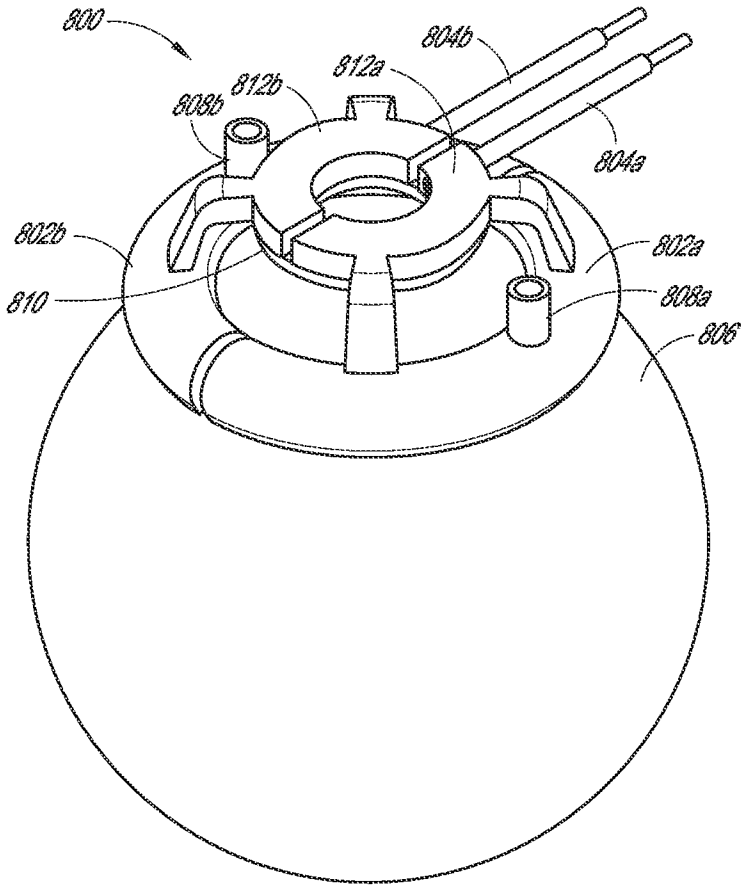
808a

FIG. 8A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808b
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810
808a
806

FIG. 8B

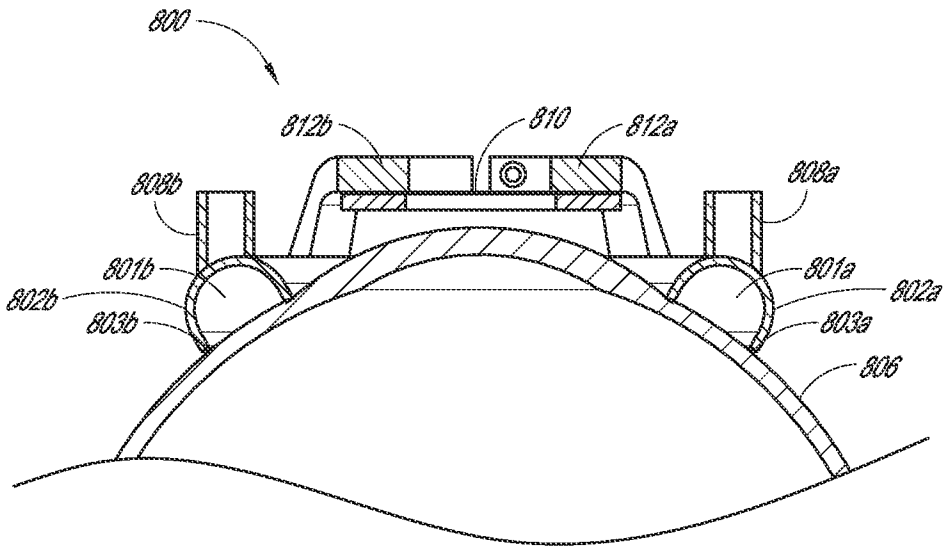
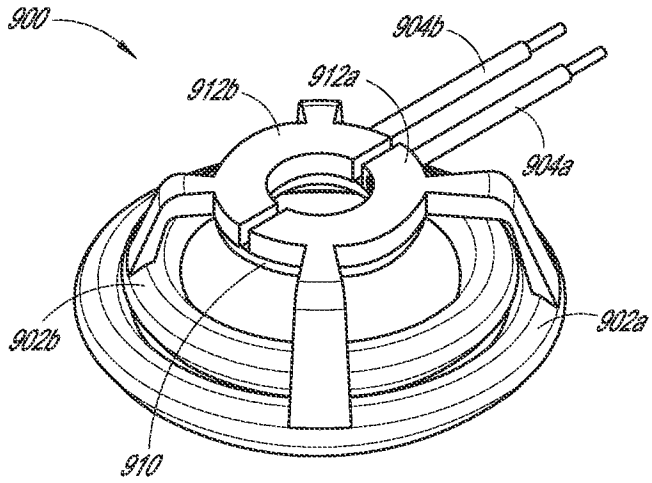


FIG. 8C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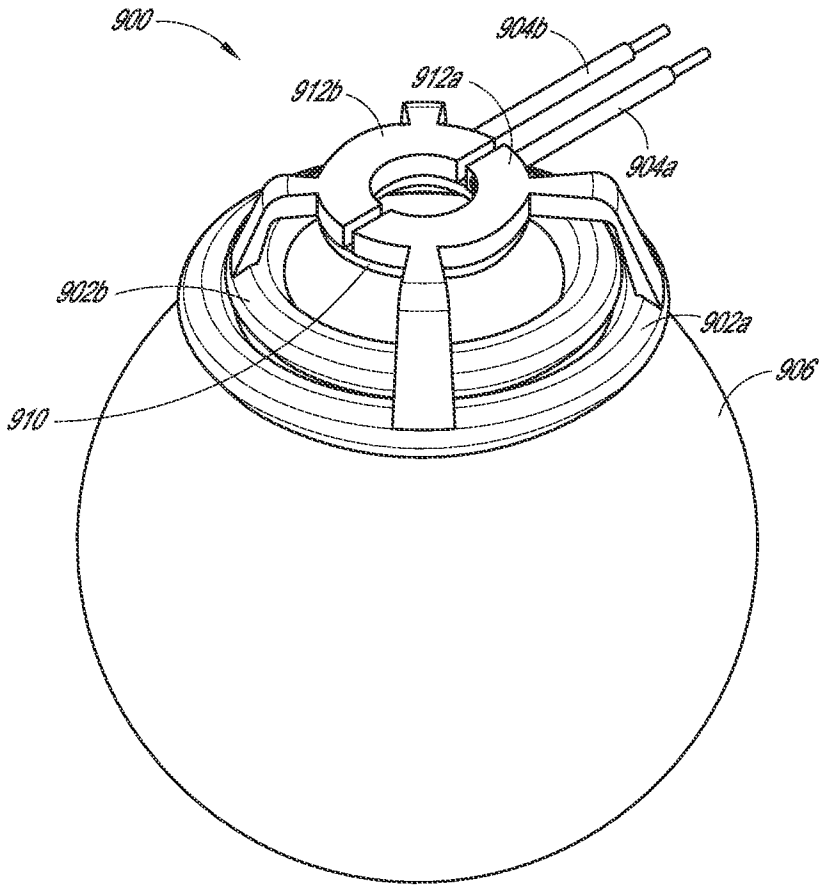
904b
912b
912a
904a
902b
902a
910

FIG. 9A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904b
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906
910

FIG. 9B

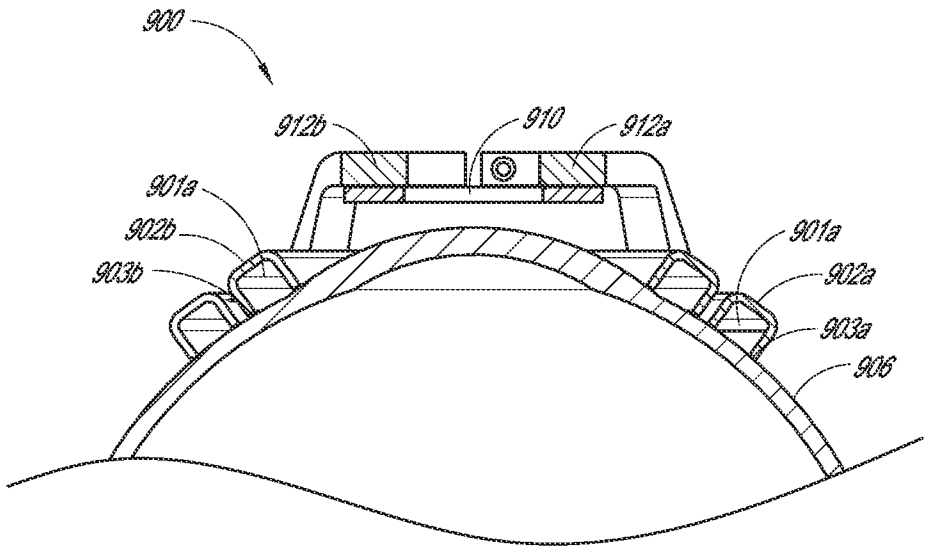


FIG. 9C

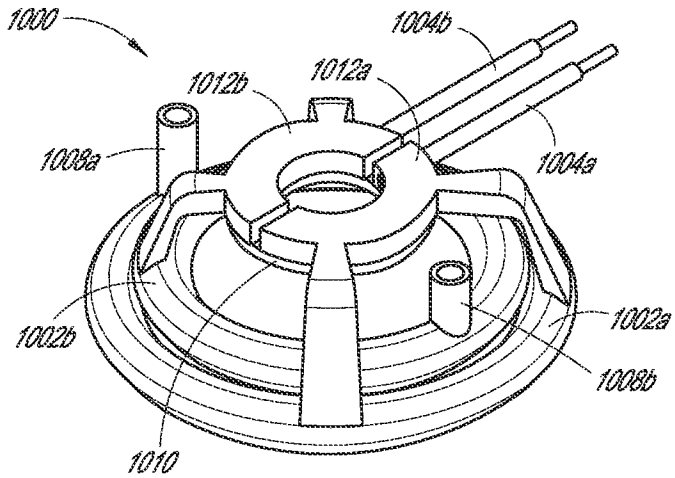


FIG. 10A

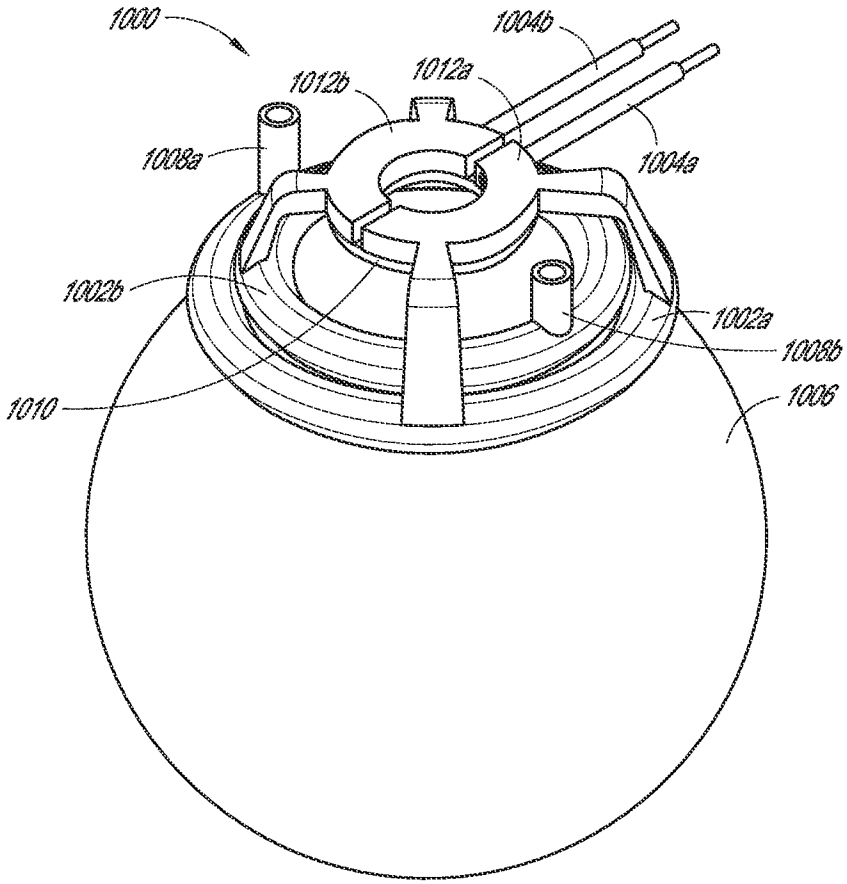
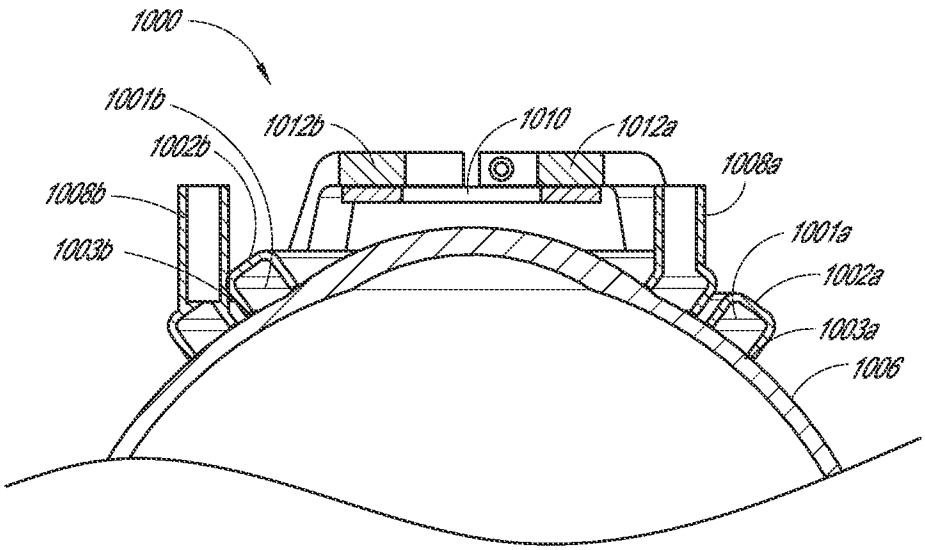


FIG. 10B


1000
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1010
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1006b
1001a
1003b
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1003a
1006

FIG. 10C

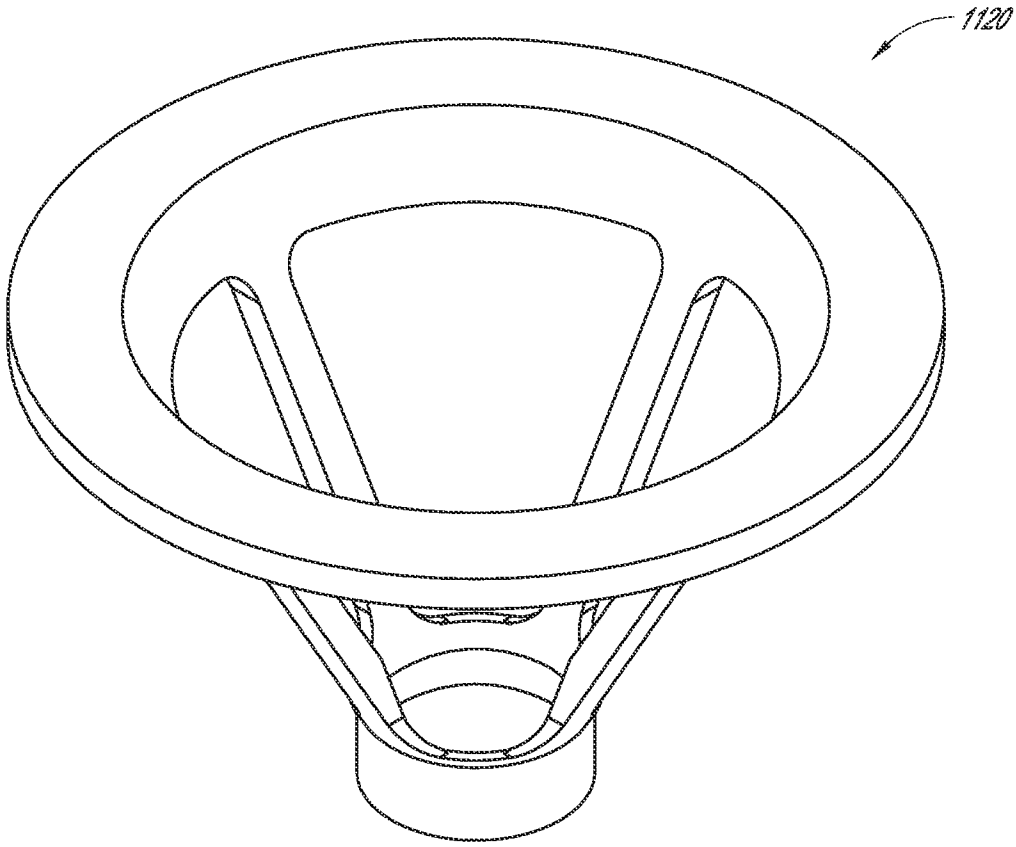


FIG. 11A

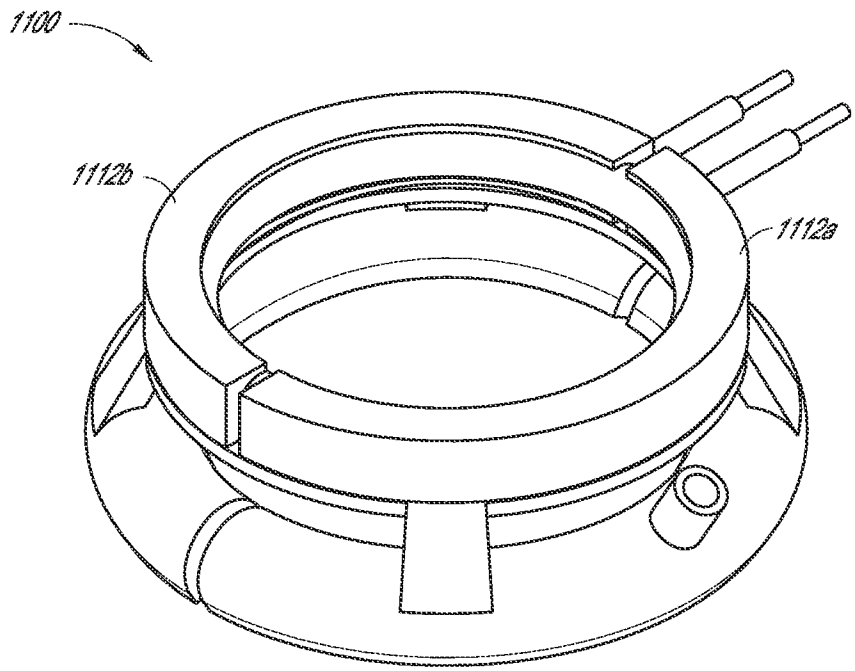


FIG. 11B

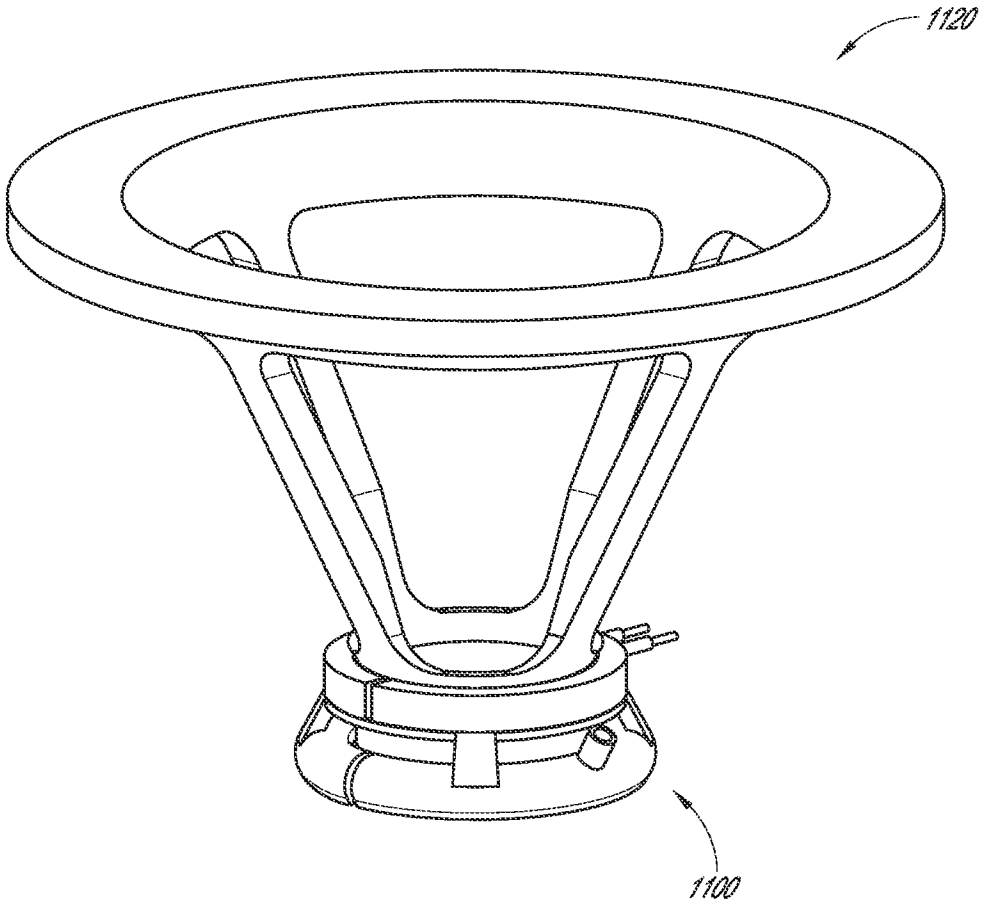


FIG. 11C

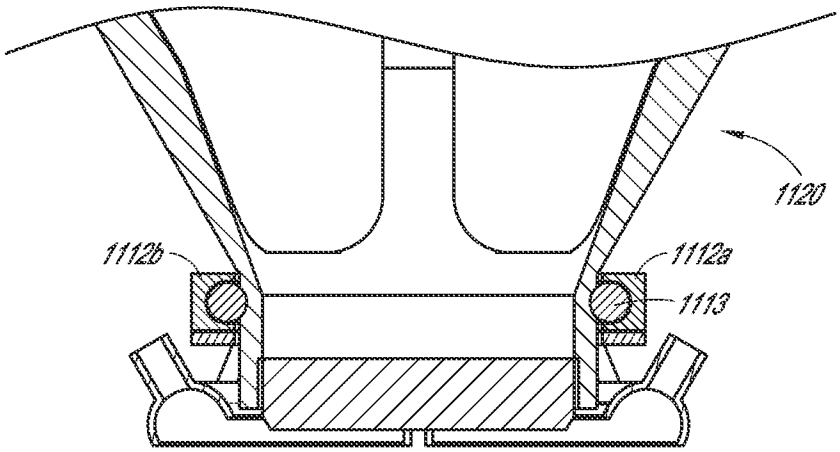


FIG. 11D

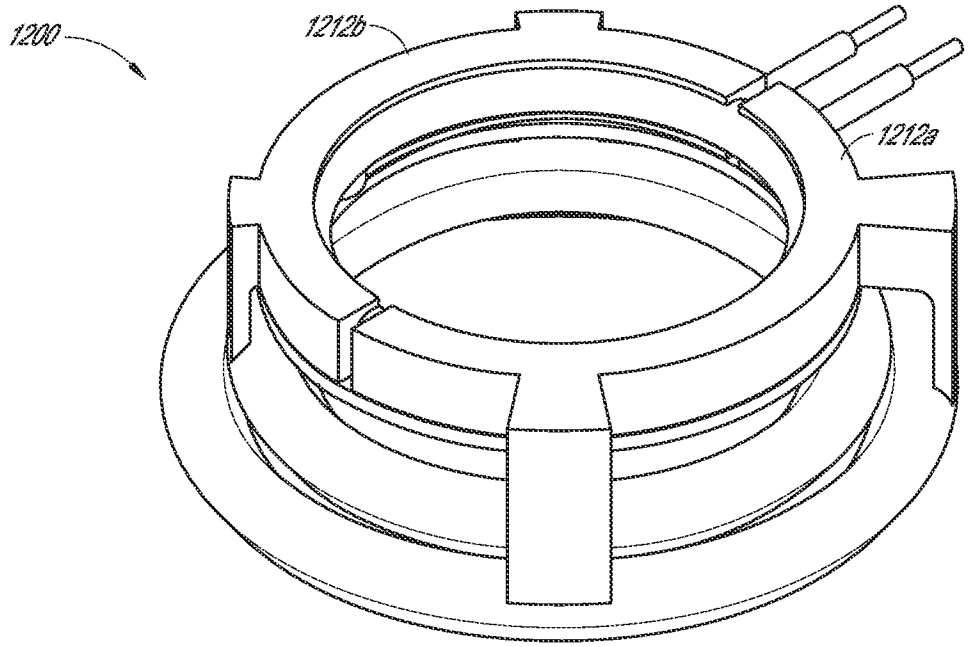


FIG. 12A

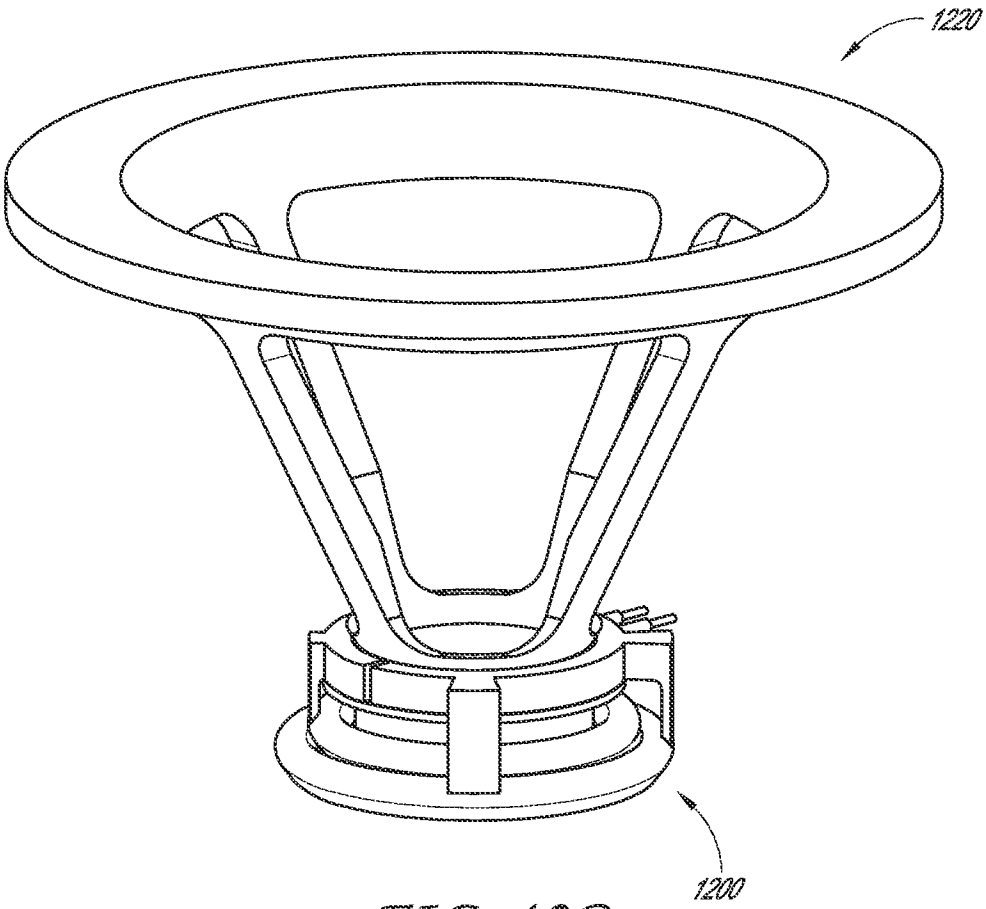


FIG. 12B

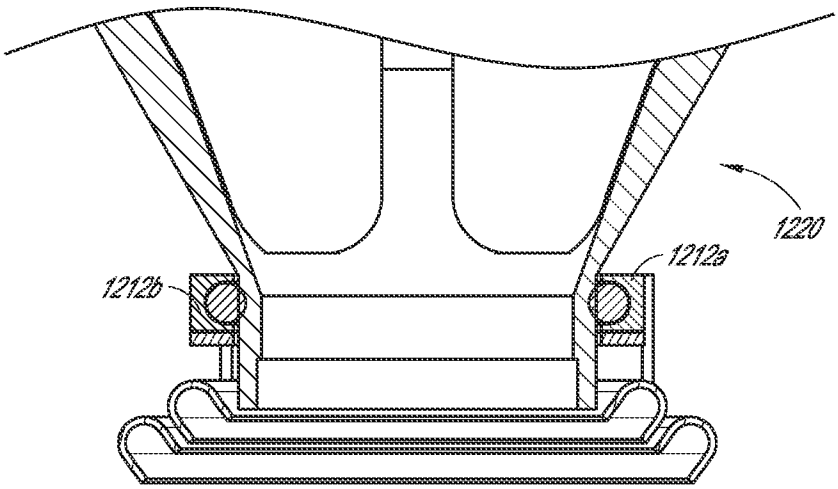


FIG. 12C

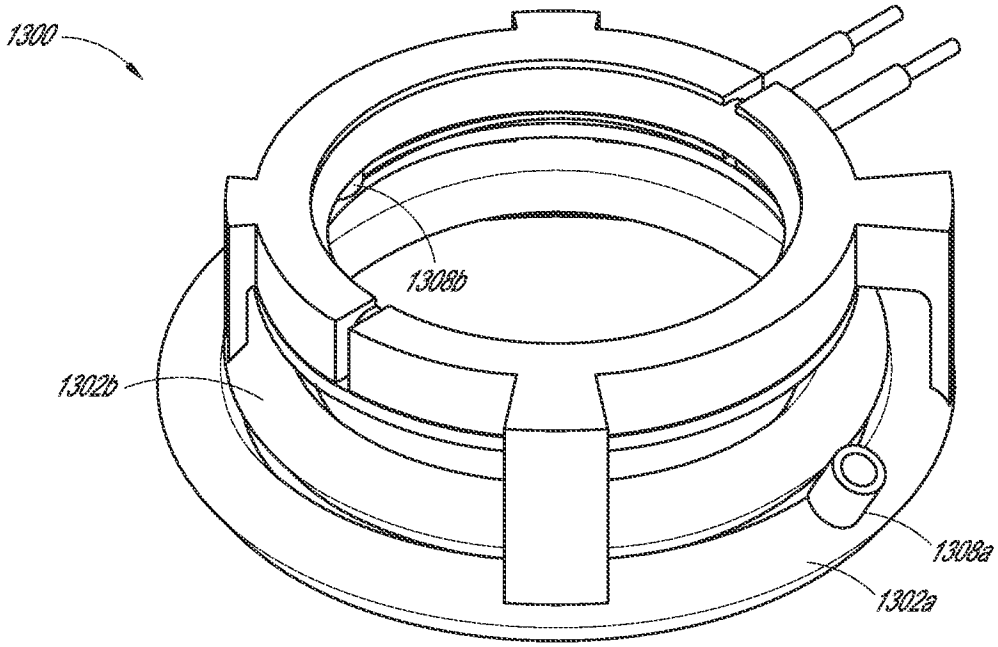


FIG. 13A

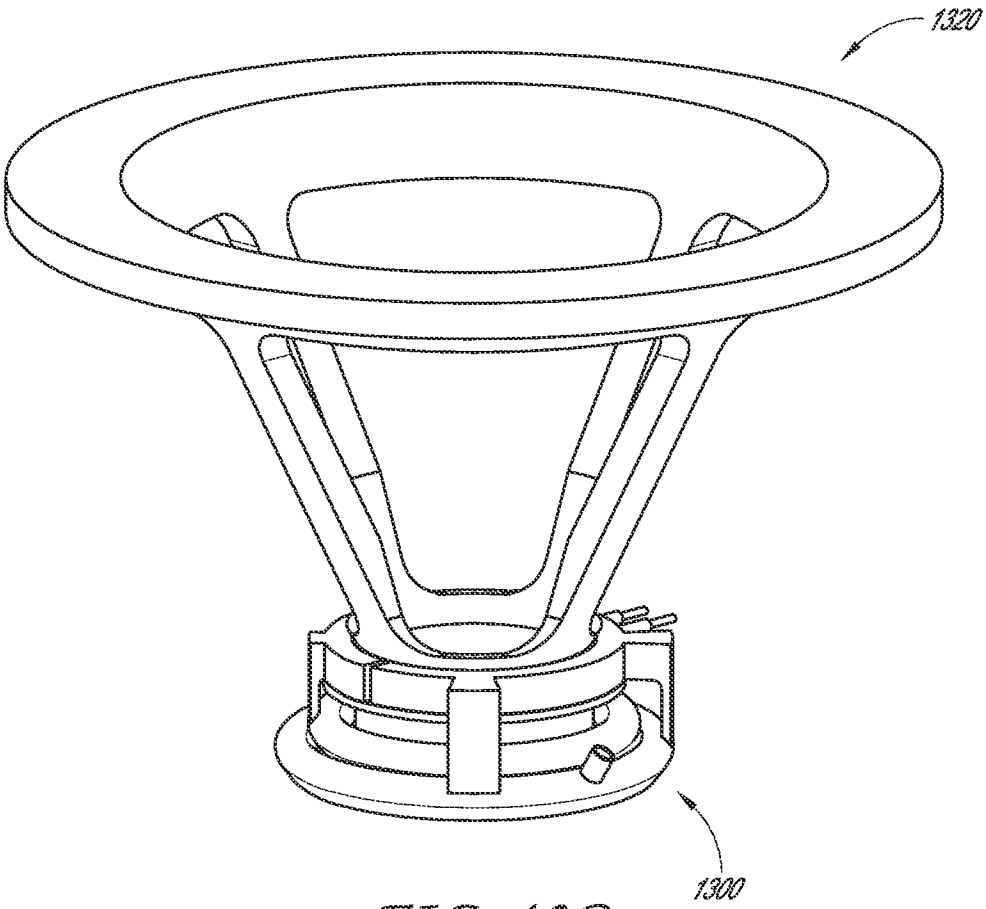


FIG. 13B

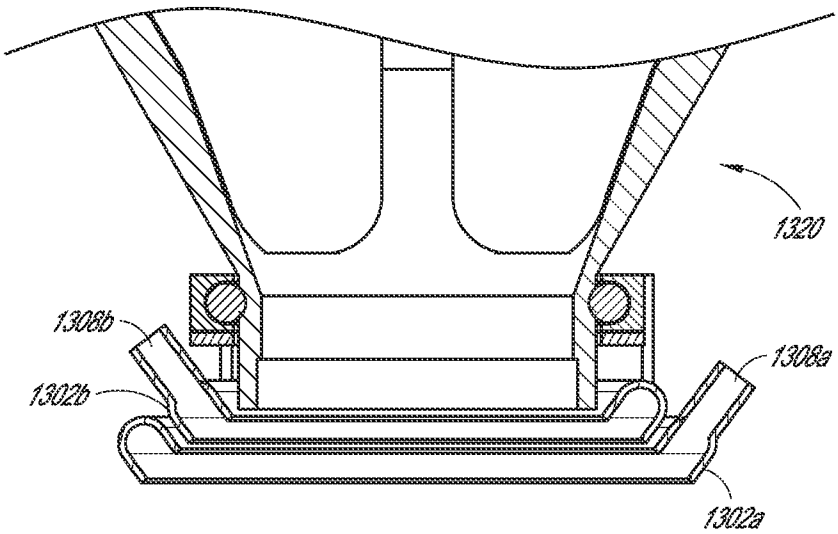


FIG. 13C

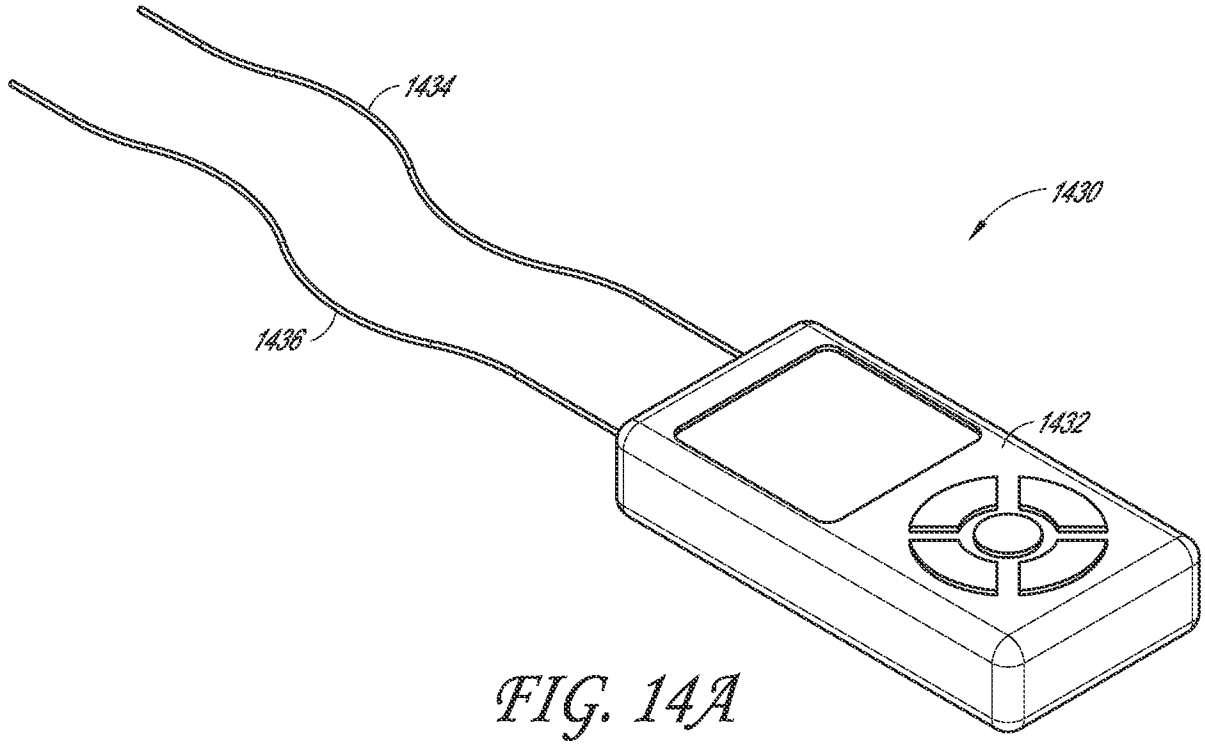


FIG. 14A

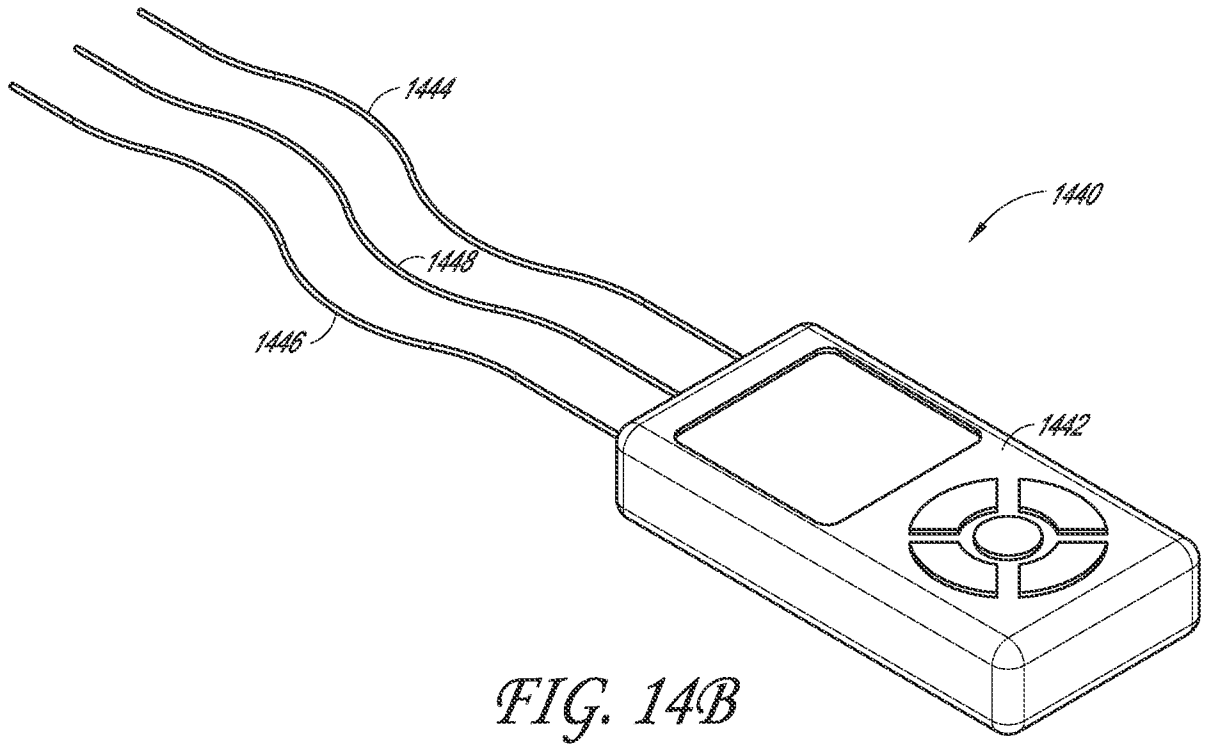


FIG. 14B

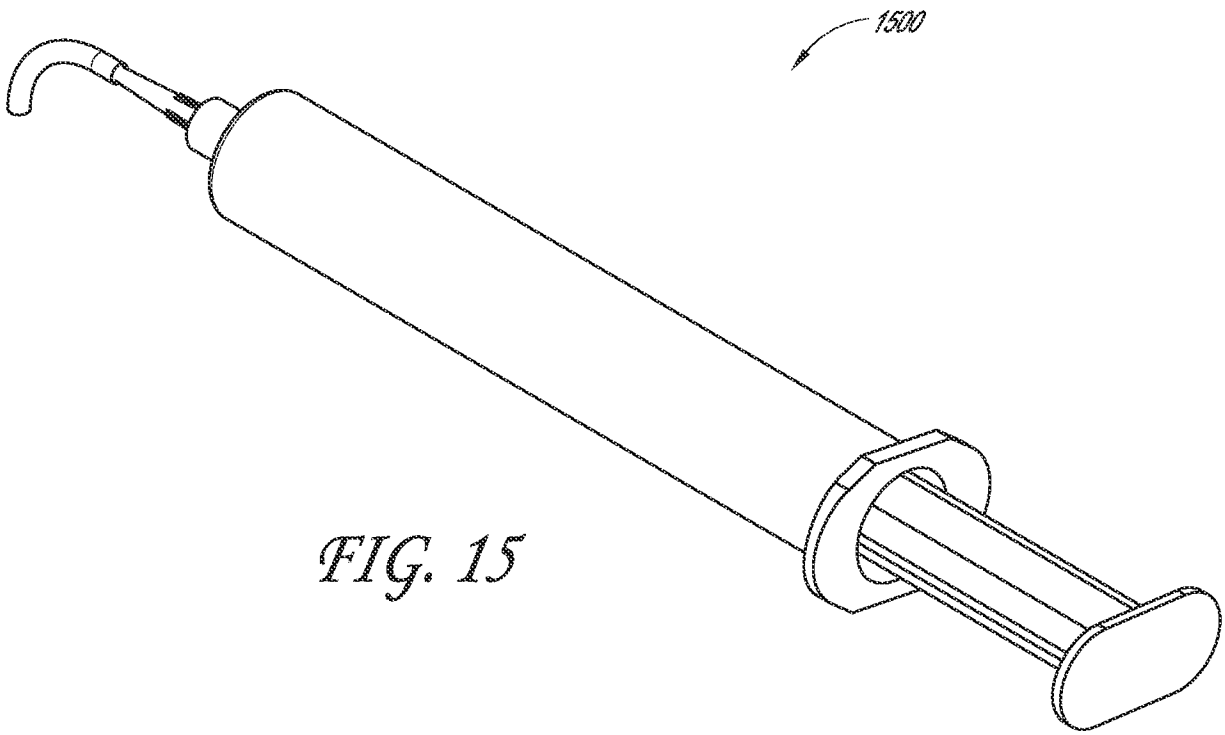


FIG. 15

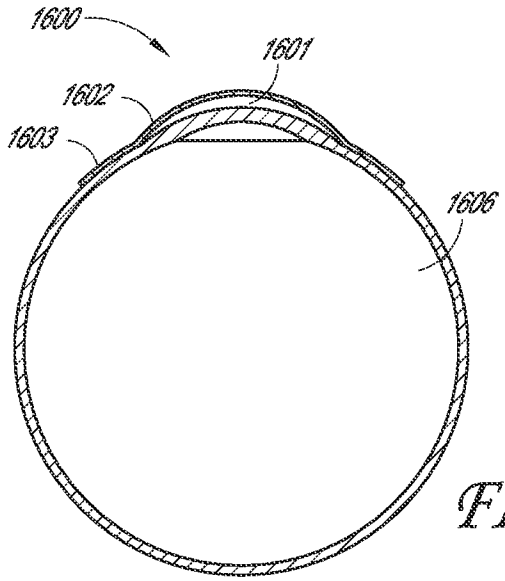


FIG. 16

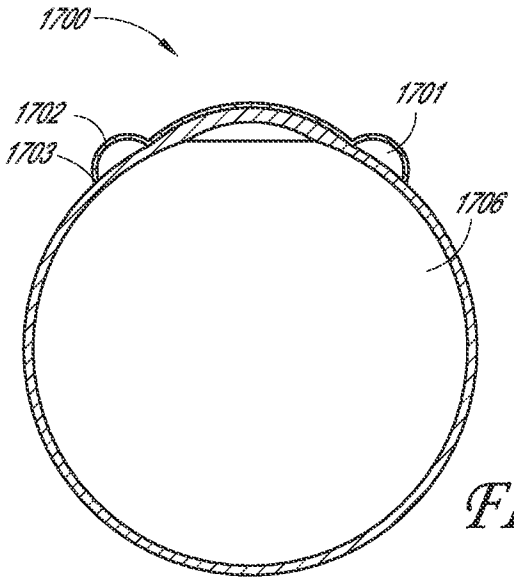


FIG. 17

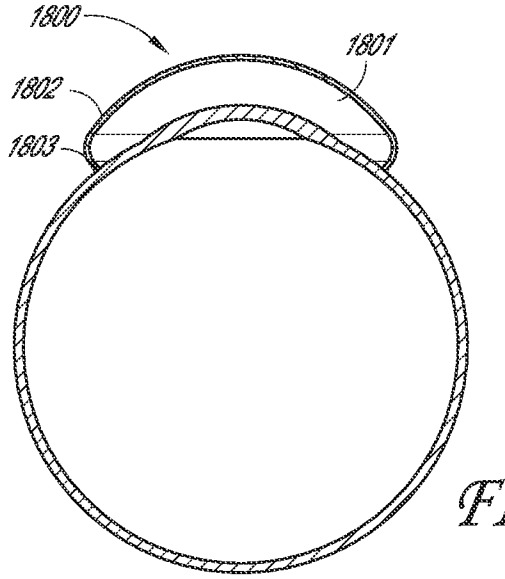


FIG. 18

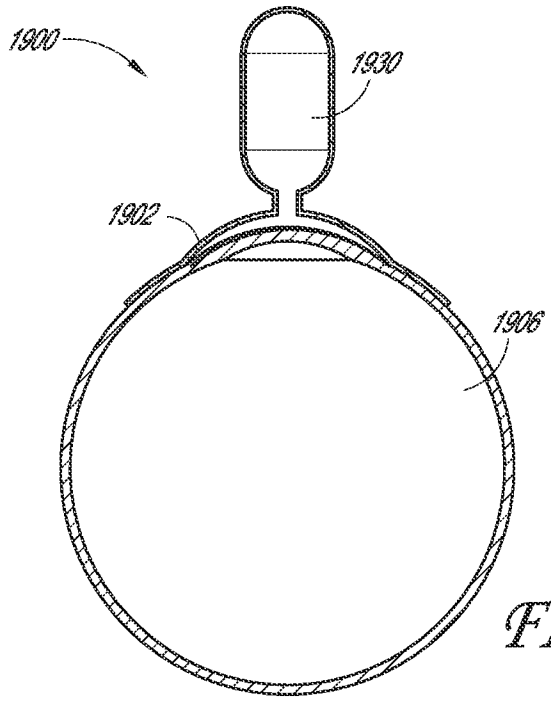


FIG. 19

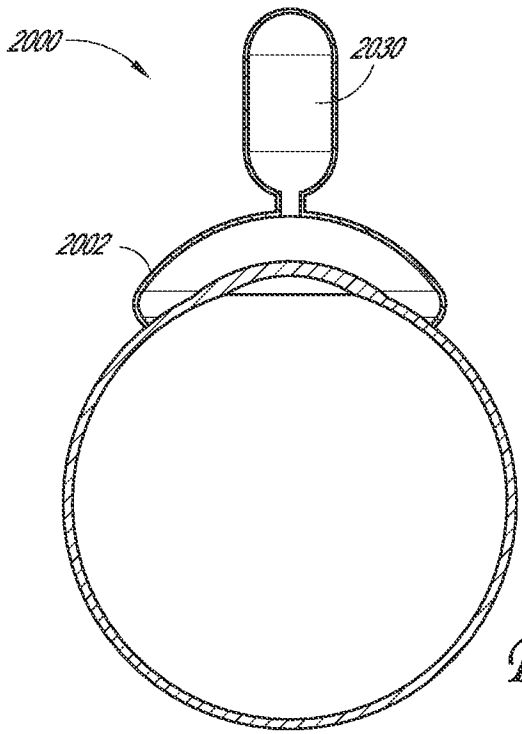


FIG. 20

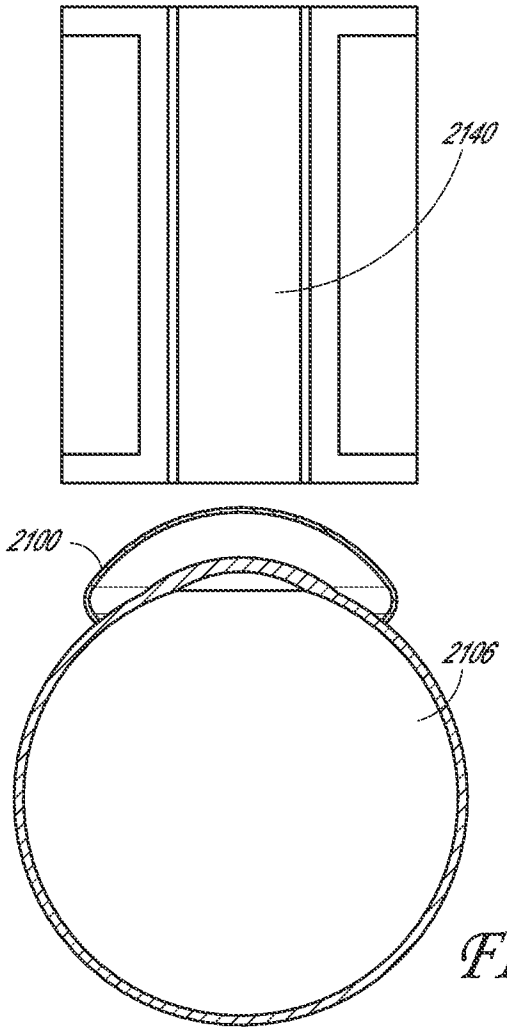


FIG. 21

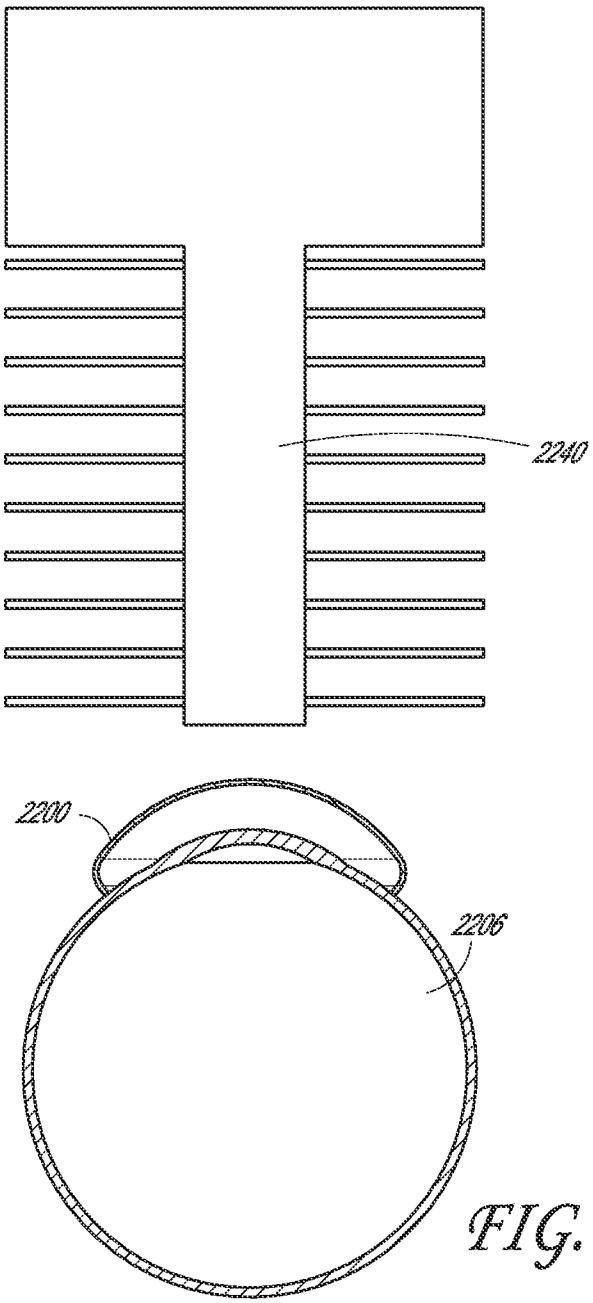
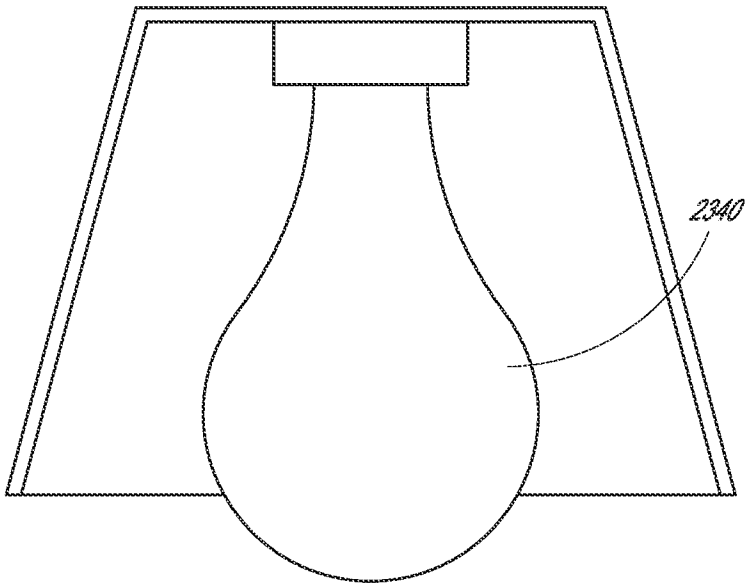


FIG. 22



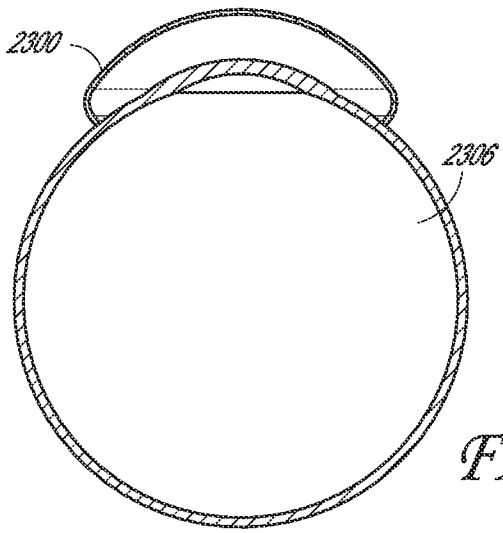


FIG. 23

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 12/39267

A. CLASSIFICATION OF SUBJECT MATTER
IPC(8) - A61M 35/00 (2012.01)
USPC - 604/20
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 604/20

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
IPC(8): A61M 35/00 (2012.01)
USPC: 604/19, 20, 289, 294, 295, 300, 30

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
PubWEST and Google: eyem ocular, opthalmic, mydriatic, mydriasis, pupil, dilate, drug, medicine, delivery, absorb, absorption, fill, chamber, reservoir, cavity, iontophoresis, iontophoretic, electrorepulsive, electromigration, laser, femtosecond, anode, cathode, electrode, negative, positive, sclera, cornea, couple, fasten, attach, o-ring, frictio

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X --- Y	US 6,154,671 A (Parel et al) 28 November 2000 (28.11.2000), entire document, especially col 1, ln 7-8; col 2, ln 5-8; col 3, ln 1-6; col 5, ln 16-64; Fig. 1, 2a-c and 3a-c	1-2, 6-8, 12-20, 26-28, 36-52, 56-57, 62-63, 70-72 and 77-84 --- 3-5, 9-11, 21-25, 29-35, 53-55, 58-61, 64-69, 73-76 and 85-97
Y	US 2009/0088721 A1 (de Bizemont et al) 02 April 2009 (02.04.2009), entire document, especially para [0183]	3-5
Y	US 6,101,411 A (Newsome) 08 August 2000 (08.08.2000), entire document, especially col 2, ln 28-38; col 3, ln 26-32; col 4, ln 23-37	9-11, 29-35, 59-61, 64-69 and 74-76
Y	US 2002/0107508 A1 (Burnett) 08 August 2002 (08.08.2002), entire document, especially para [0022]-[0023]; Fig. 1 and 2A	21-25, 54-55, 86-88, 91 and 95
Y	US 2011/0077582 A1 (Tuitupou et al) 31 March 2011 (31.03.2011), entire document, especially para [0071]-[0072] and [0089]	53, 85, 92, 96 and 97
Y	US 2009/0306579 A1 (Jaffe et al) 10 December 2009 (10.12.2009), entire document, especially para [0051]	31, 58, 66 and 73
Y	US 2007/0282405 A1 (Wong, Jr. et al) 06 December 2007 (06.12.2007), entire document, especially para [0013]	89 and 93

☒ 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	Date of mailing of the international search report
15 August 2012 (15.08.2012)	06 SEP 2012
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/US 12/39267

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 7,758,561 B2 (Eppstein) 20 July 2010 (20.07.2010), entire document, especially col 3, ln 33 -48; col 41, ln 3-25	90 and 94
Y	US 6,697,668 B2 (Parkinson et al) 24 February 2004 (24.02.2004), entire document, especially col 3, ln 56 to col 4, ln 22	4-5
Y	US 6,315,727 B1 (Coleman et al) 13 November 2001 (13.11.2001), entire document, especially col 3, ln 37-57; col 4, ln 6-17; Fig. 2	22-25
A	US 2007/0123814 A1 (Roy) 31 May 2007 (31.05.2007), entire document, especially para [0039]-[0082]; Fig. 2 and 4-6	1-97
A	US 6,267,752 B1 (Svetliza) 31 July 2001 (31.07.2001), entire document, especially col 5, ln 25-35; Fig. 2	1-97
A	US 2005/0245856 A1 (Roy) 03 November 2005 (03.11.2005), entire document, especially para [0043]-[0083]; Fig. 2	1-97
A	US 2002/0035345 A1 (Beck) 21 March 2002 (21.03.2002), entire document, especially para [0046]-[0098]; Fig. 2-6	1-97
A	US 6,190,691 B1 (Mak) 20 February 2001 (20.02.2001), entire document, especially col 3, ln 8 to col 4, ln 23	1-97