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(54) **CONTROLLABLE RELEASE NASAL SYSTEM**

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See application file for complete search history.

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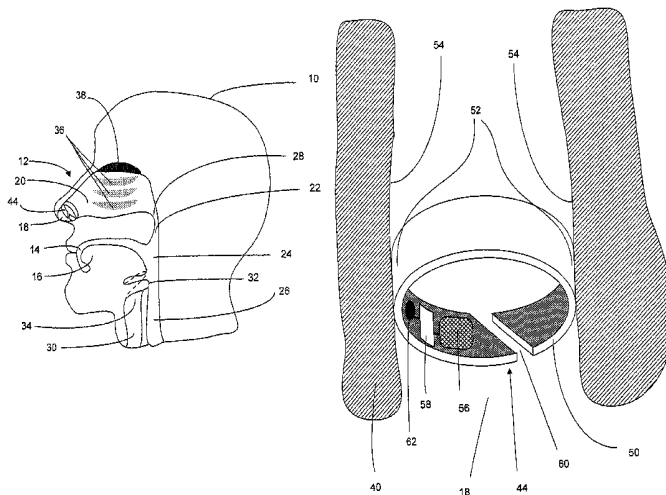
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(57) **ABSTRACT**
Embodiments of devices and system for controllable nasal delivery of materials are described. Methods of use of such devices and system and software for controlling the operation of such devices and systems are also disclosed.

25 Claims, 37 Drawing Sheets



Related U.S. Application Data

continuation-in-part of application No. 10/827,576, filed on Apr. 19, 2004, now Pat. No. 8,337,482, and a continuation-in-part of application No. 10/827,578, filed on Apr. 19, 2004, and a continuation-in-part of application No. 10/827,572, filed on Apr. 19, 2004, now Pat. No. 7,850,676, and a continuation-in-part of application No. 10/827,390, filed on Apr. 19, 2004, now Pat. No. 8,361,013, and a continuation-in-part of application No. 11/403,230, filed on Apr. 12, 2006, now Pat. No. 9,011,329.

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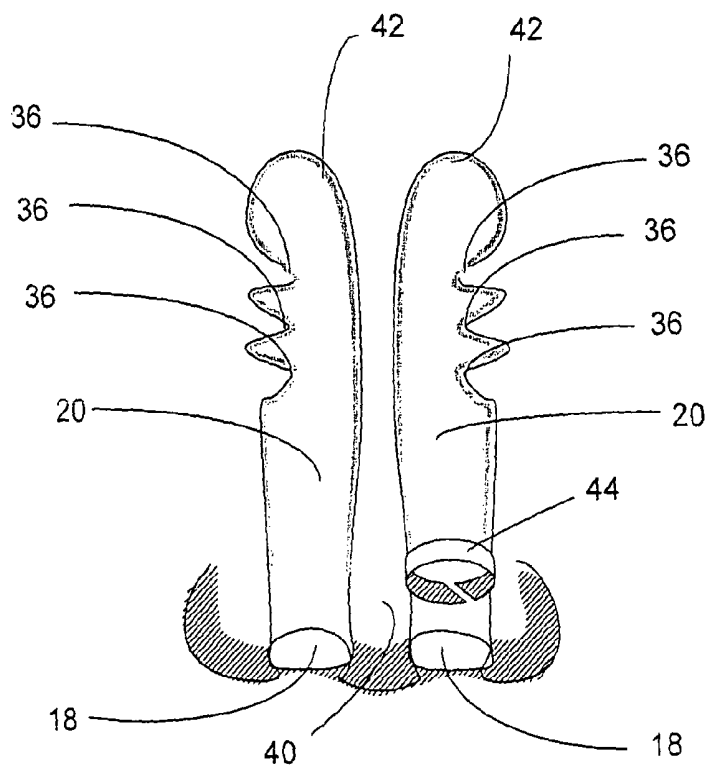
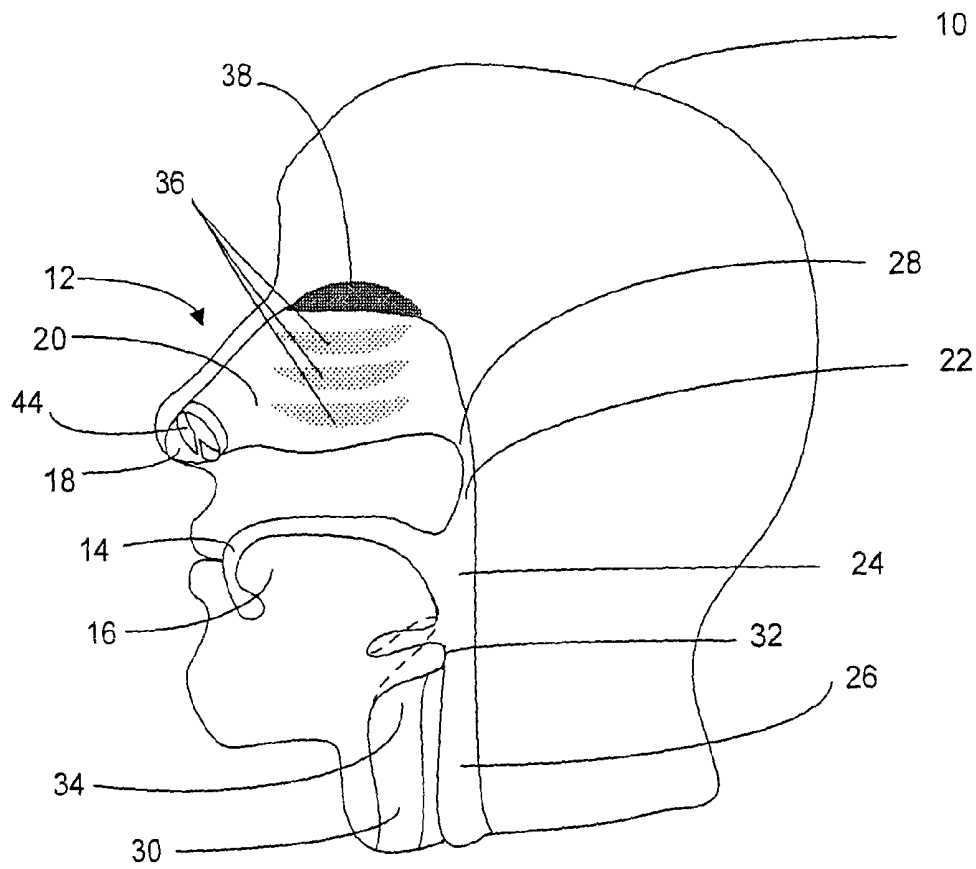
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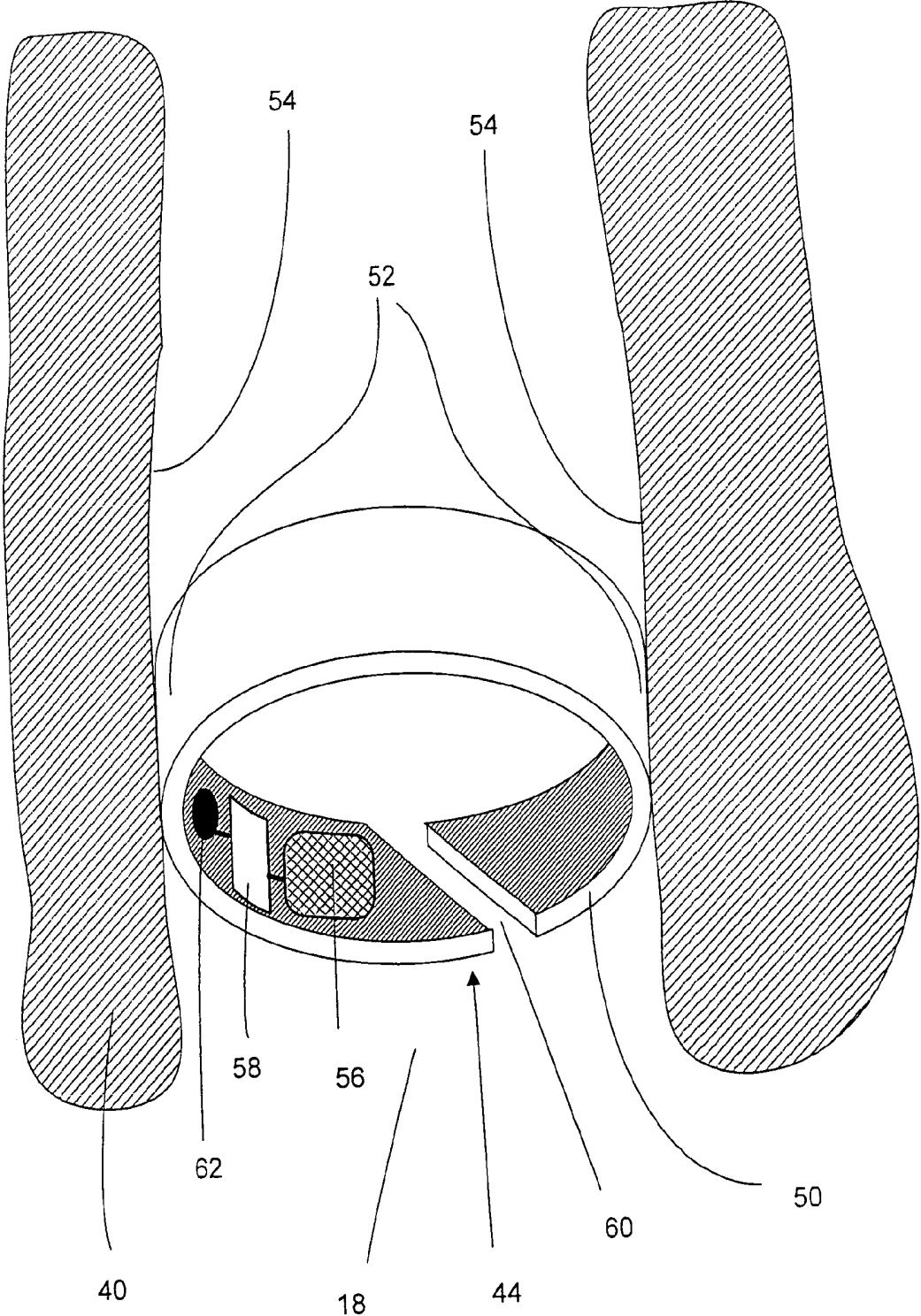


FIG. 3

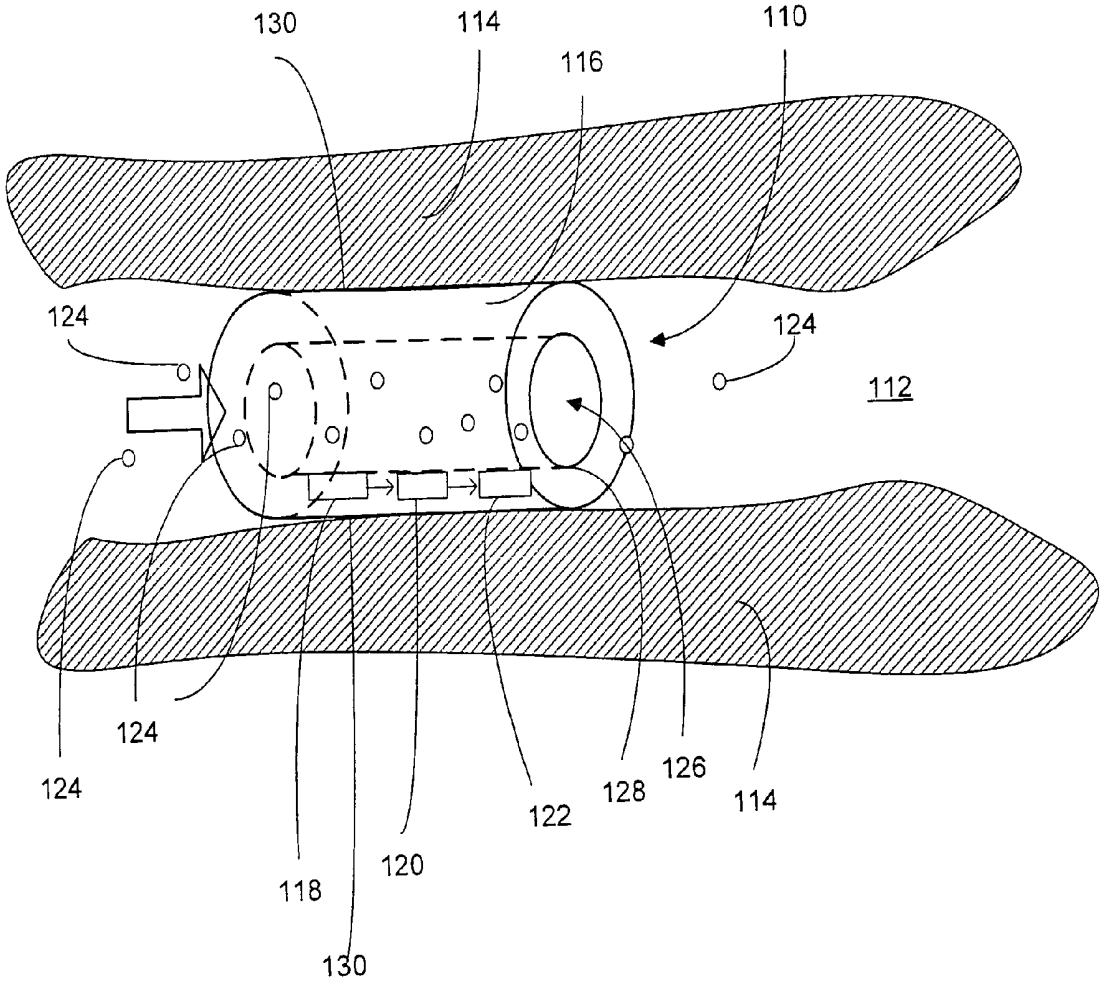


FIG. 4

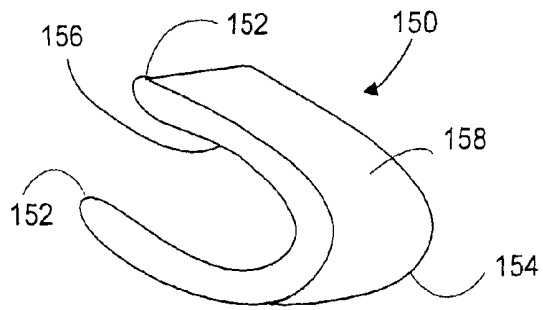


FIG. 5

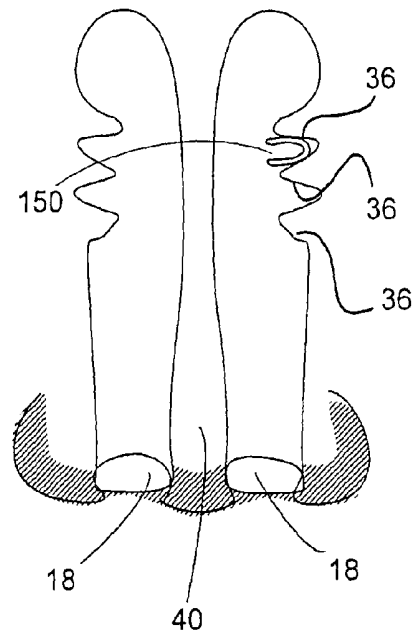


FIG. 6

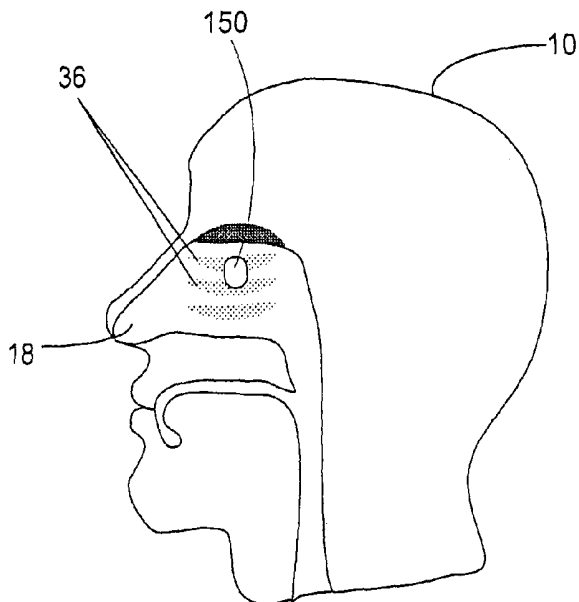


FIG. 7

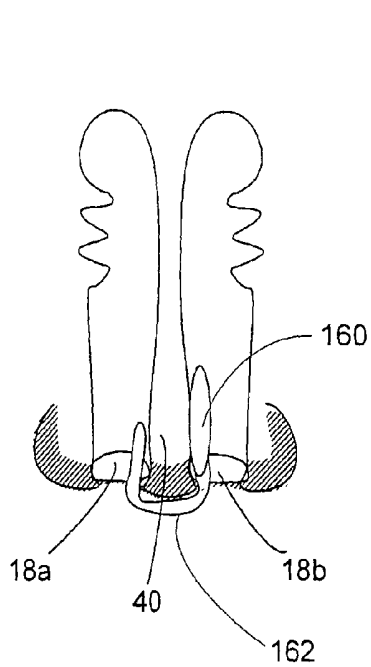


FIG. 8

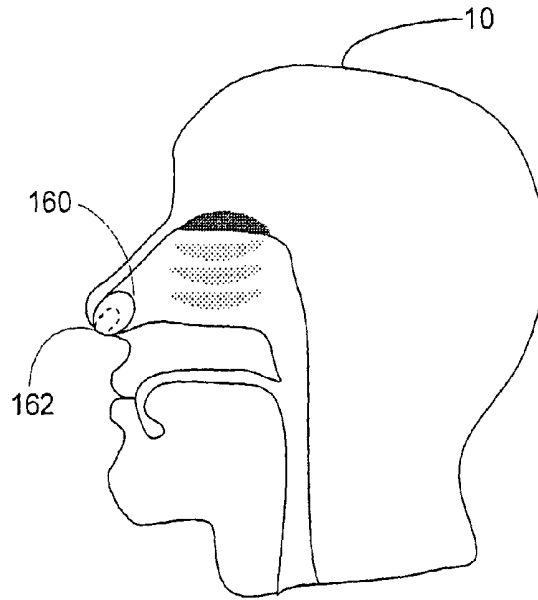


FIG. 9

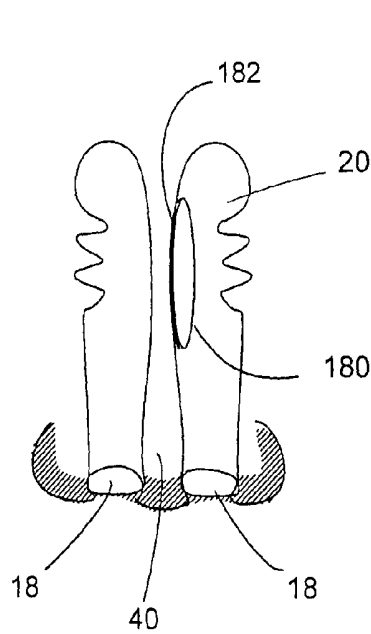
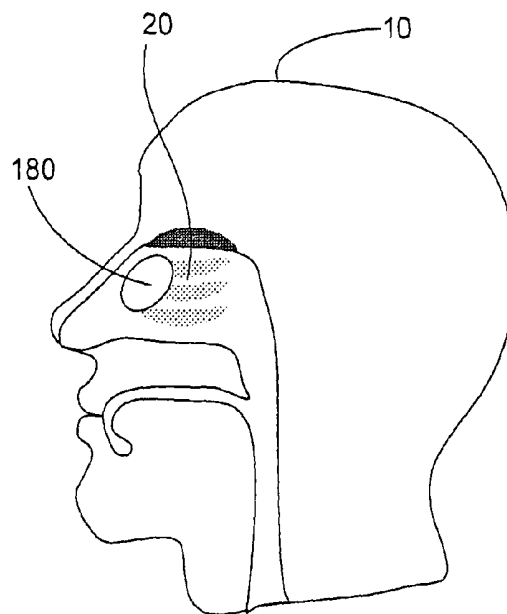


FIG. 10



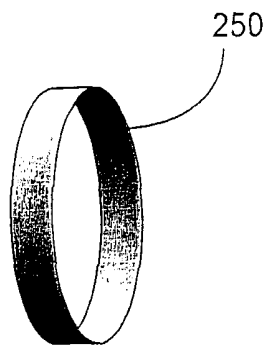


FIG. 12

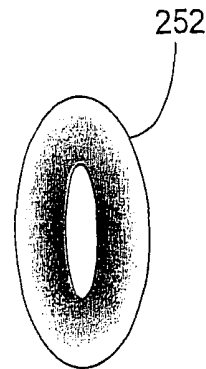


FIG. 13

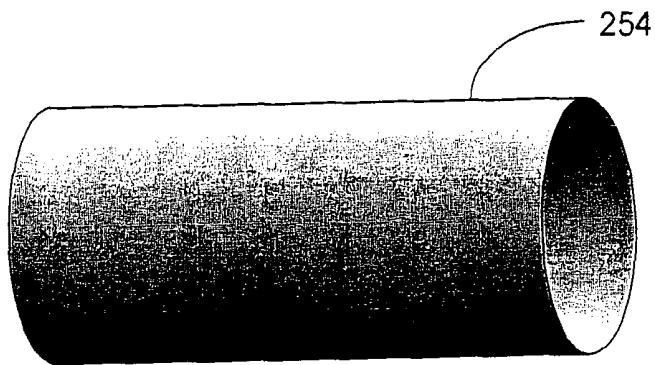


FIG. 14

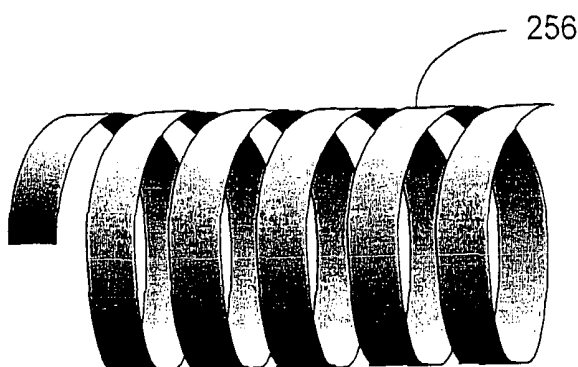


FIG. 15

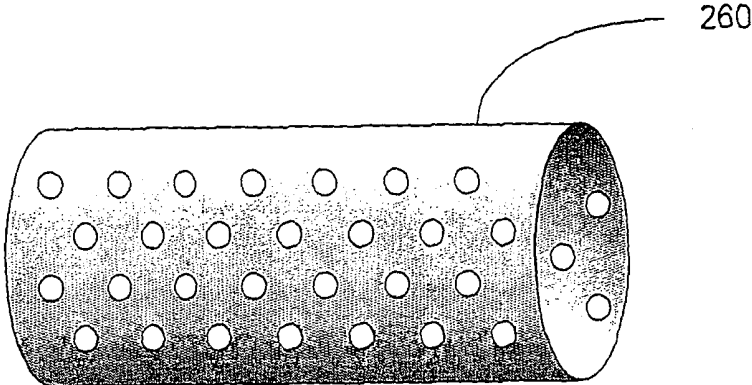


FIG. 16

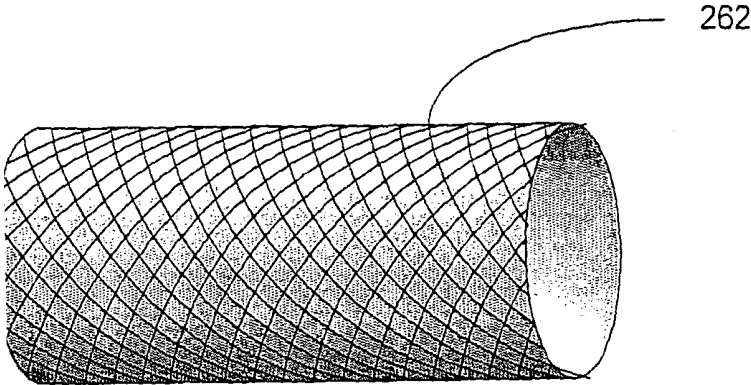


FIG. 17

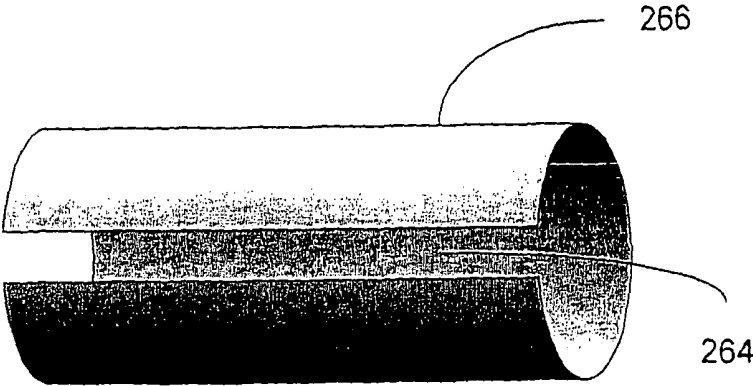


FIG. 18

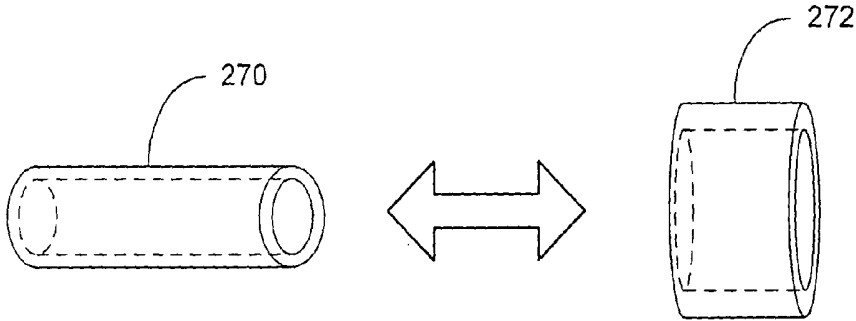


FIG. 19A

FIG. 19B

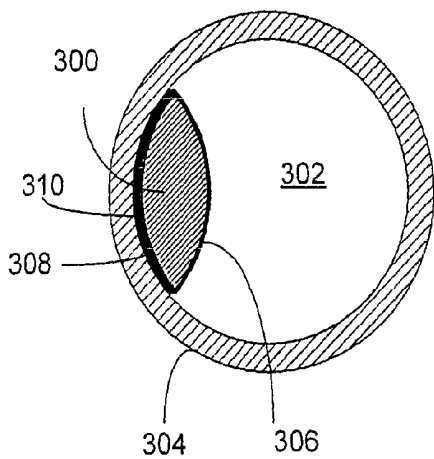


FIG. 20

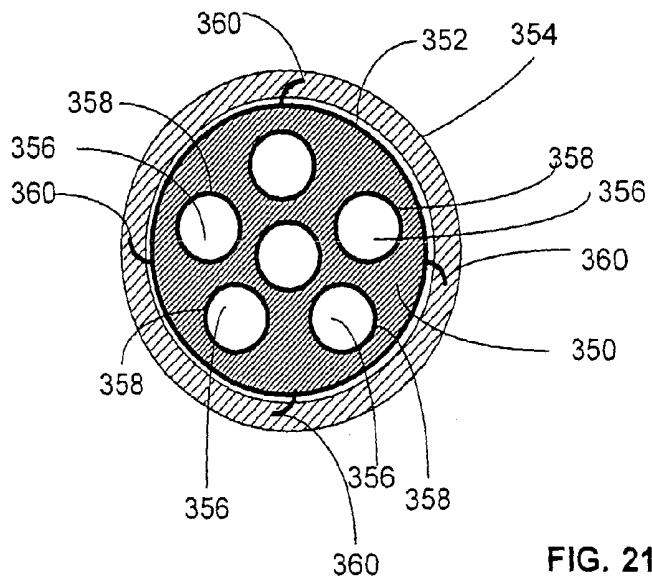


FIG. 21

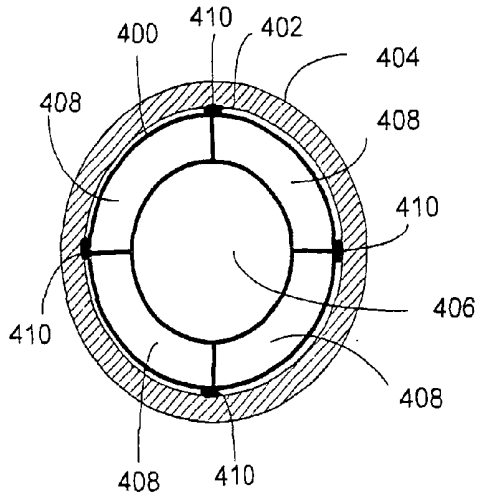


FIG. 22

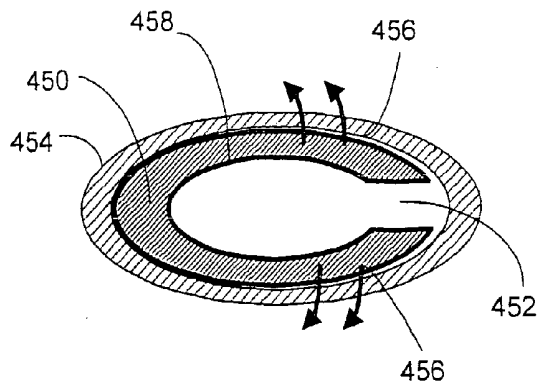


FIG. 23

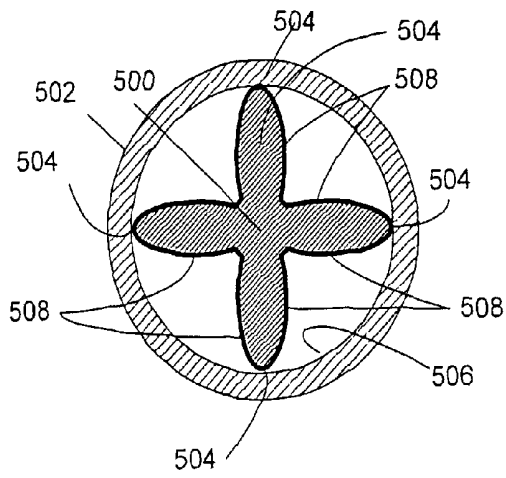


FIG. 24

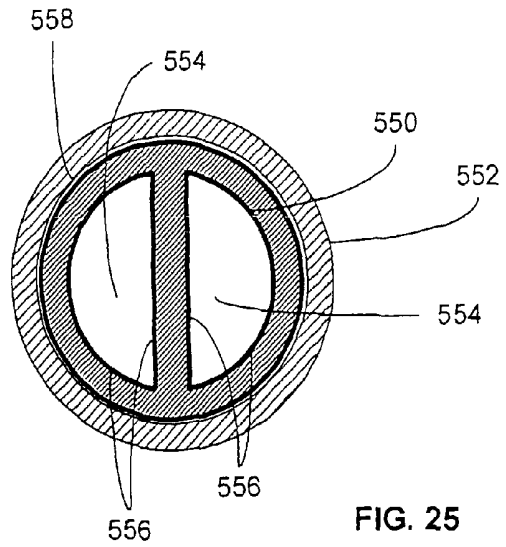


FIG. 25

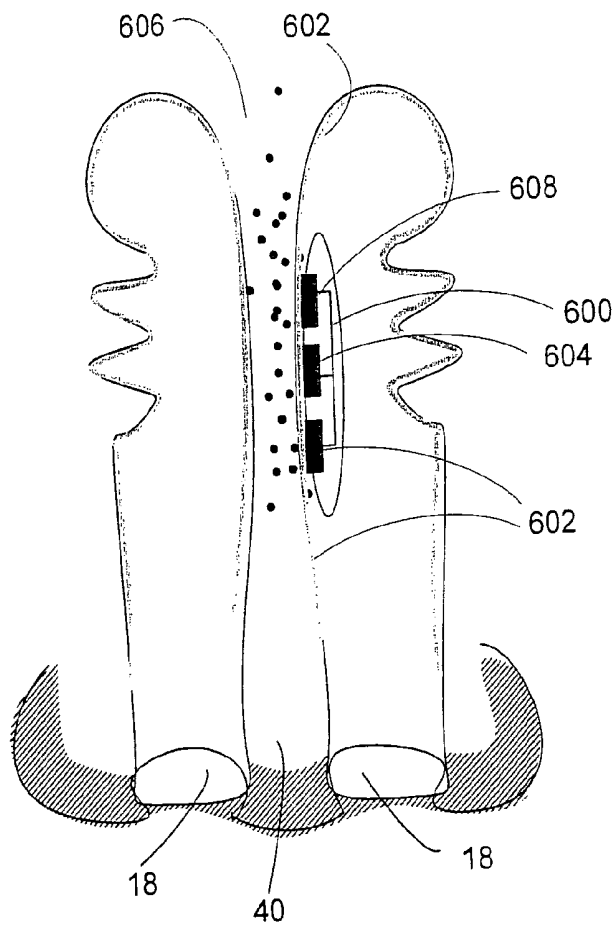


FIG. 26

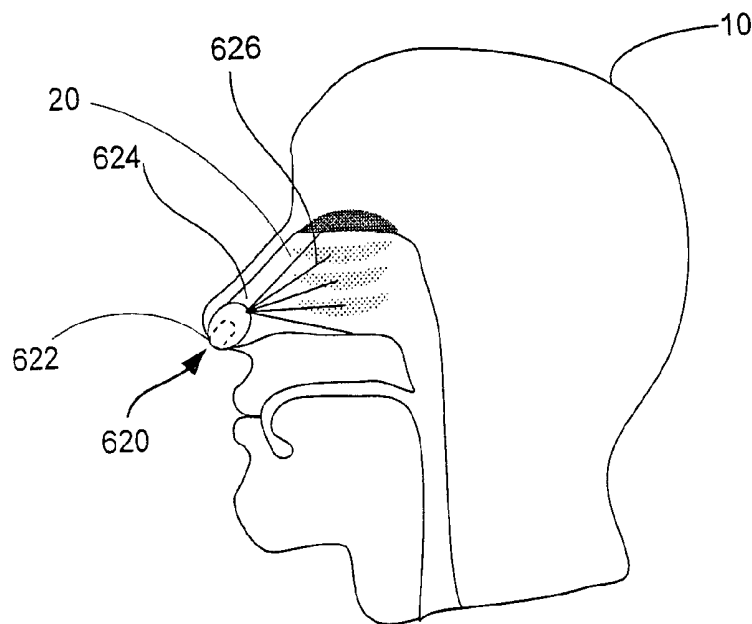
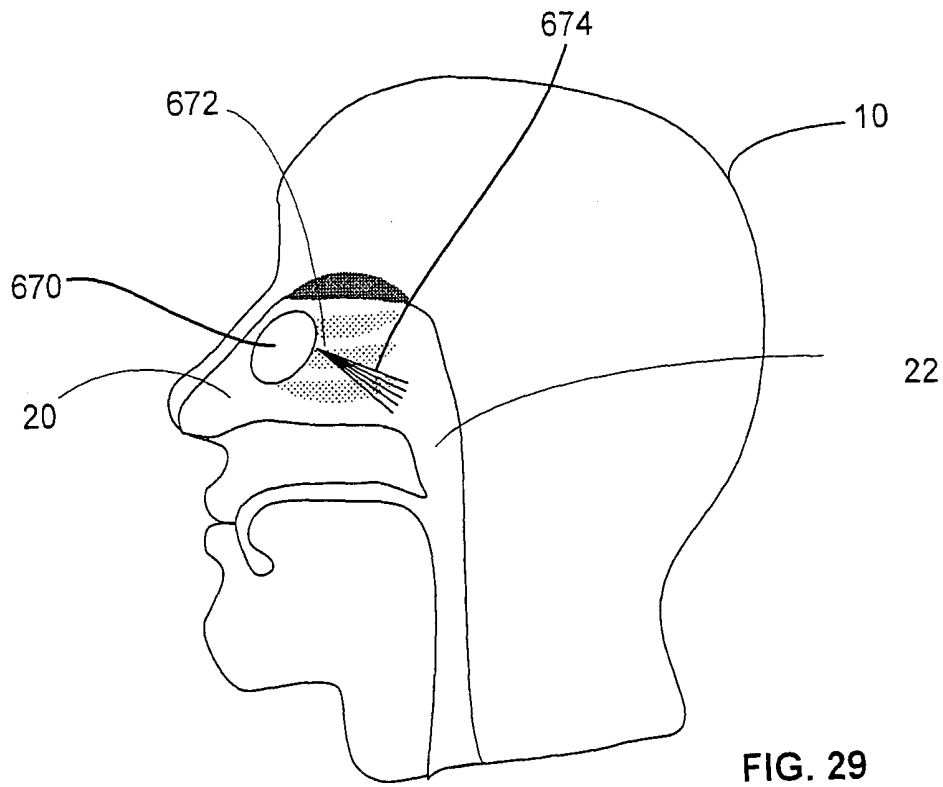
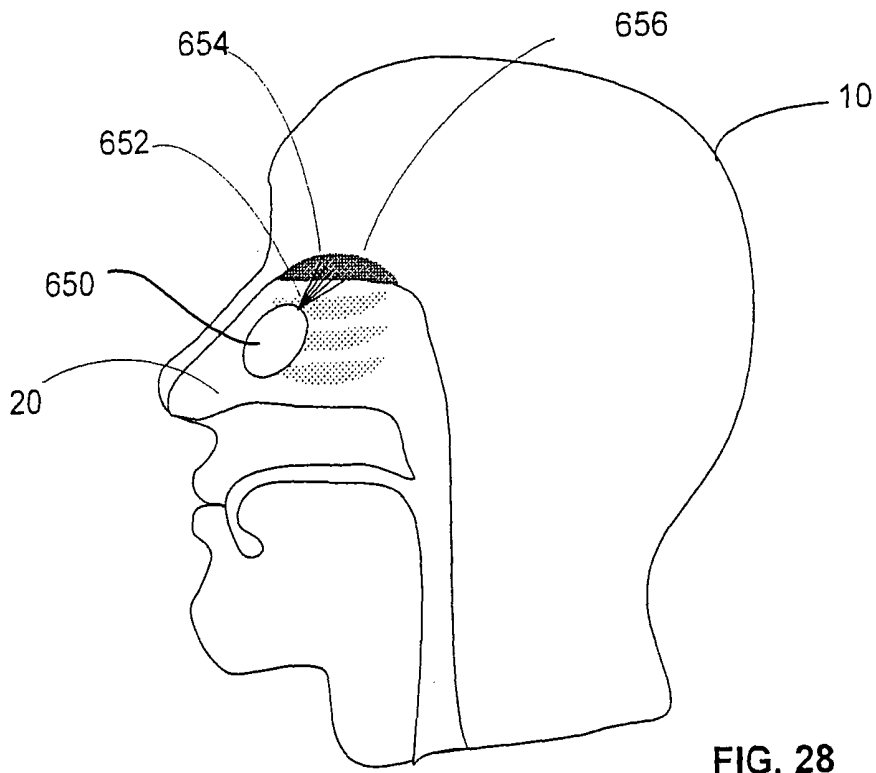


FIG. 27



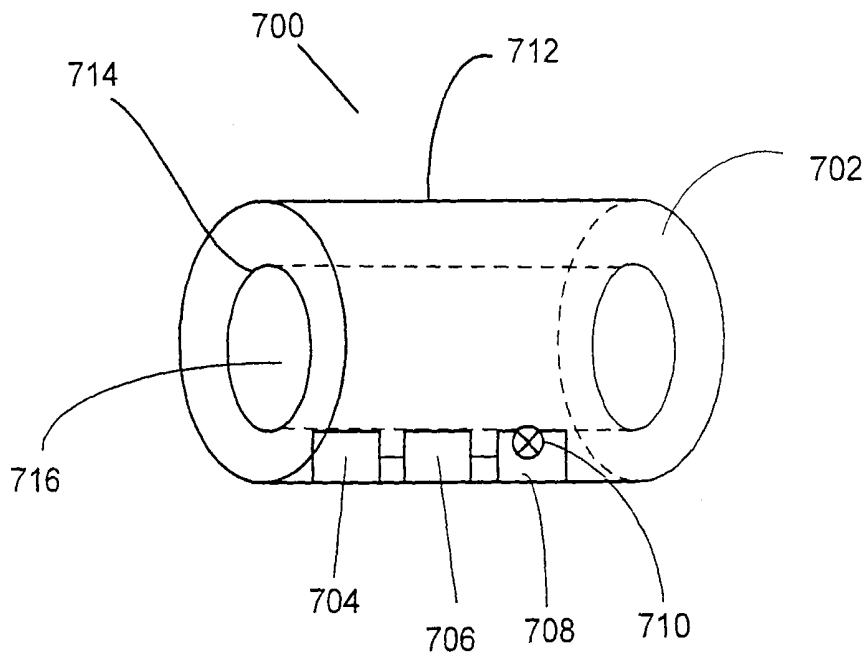


FIG. 30

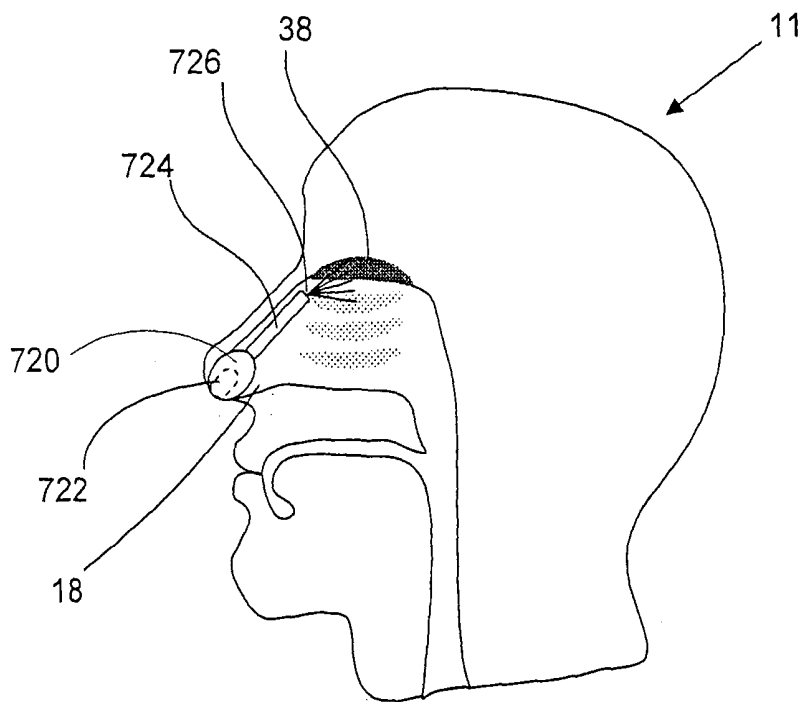


FIG. 31

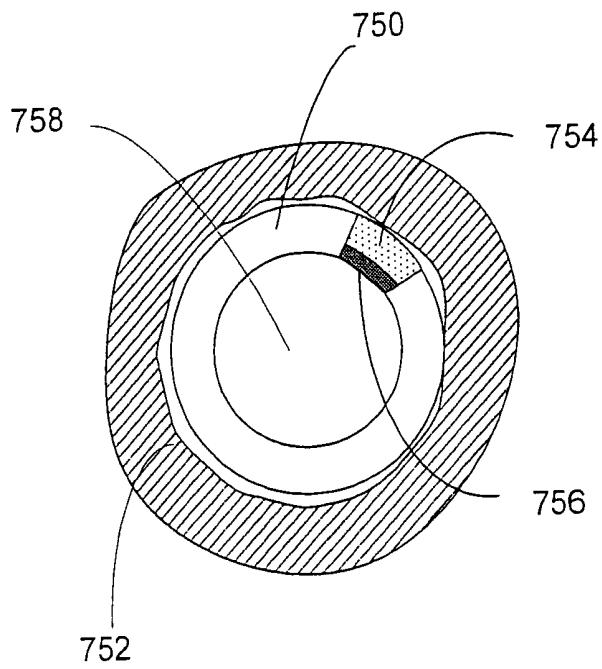


FIG. 32

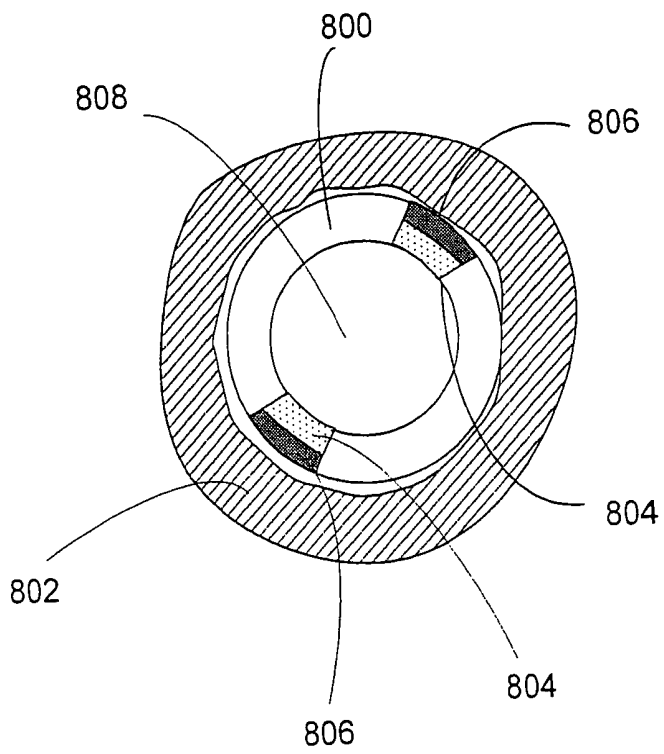


FIG. 33

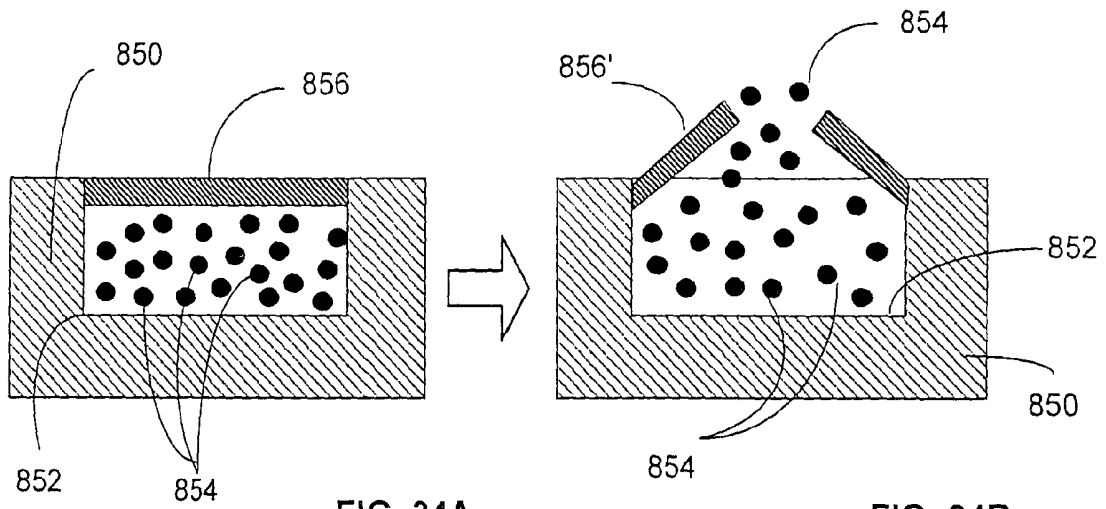


FIG. 34A

FIG. 34B

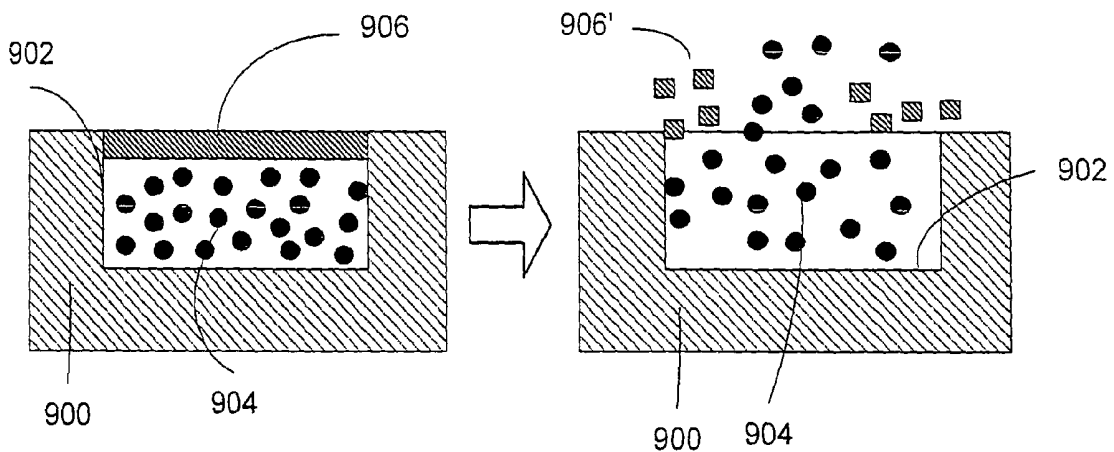


FIG. 35A

FIG. 35B

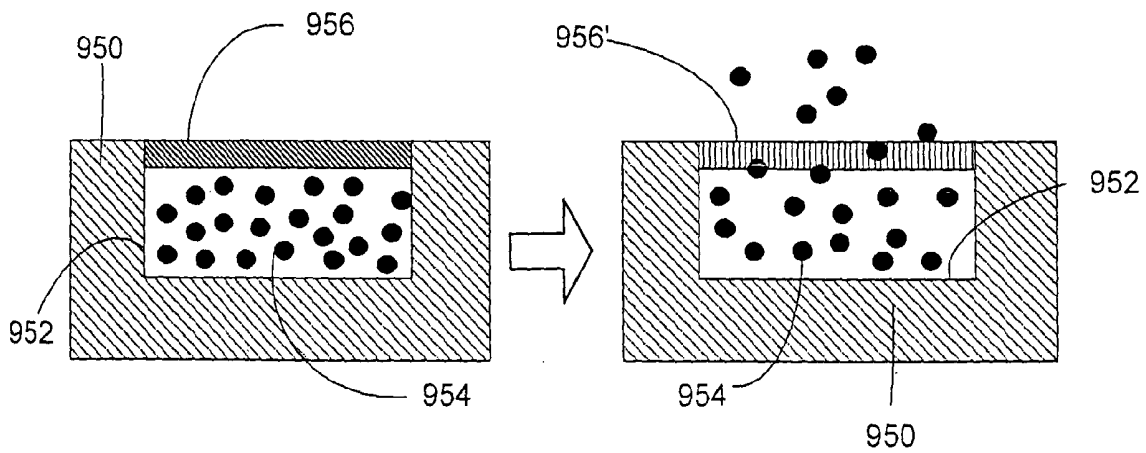


FIG. 36A

FIG. 36B

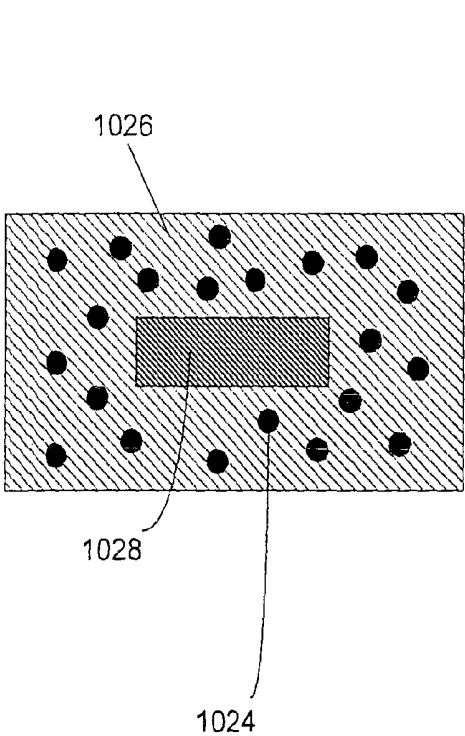


FIG. 37A

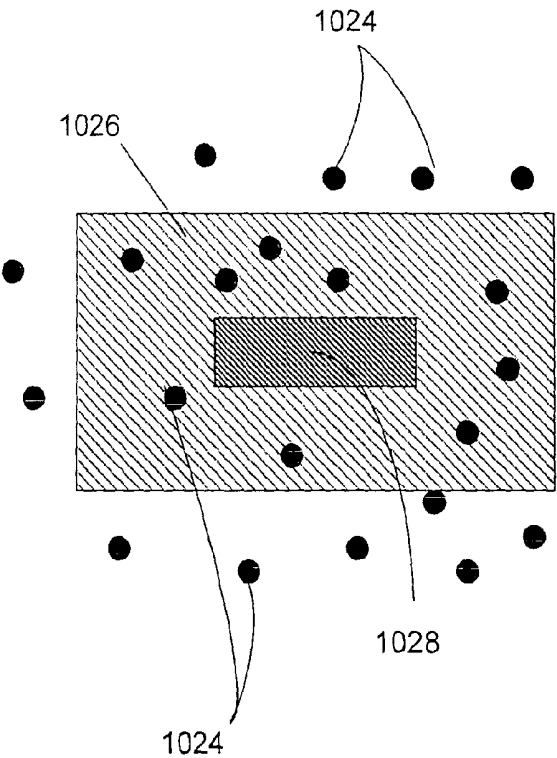


FIG. 37B

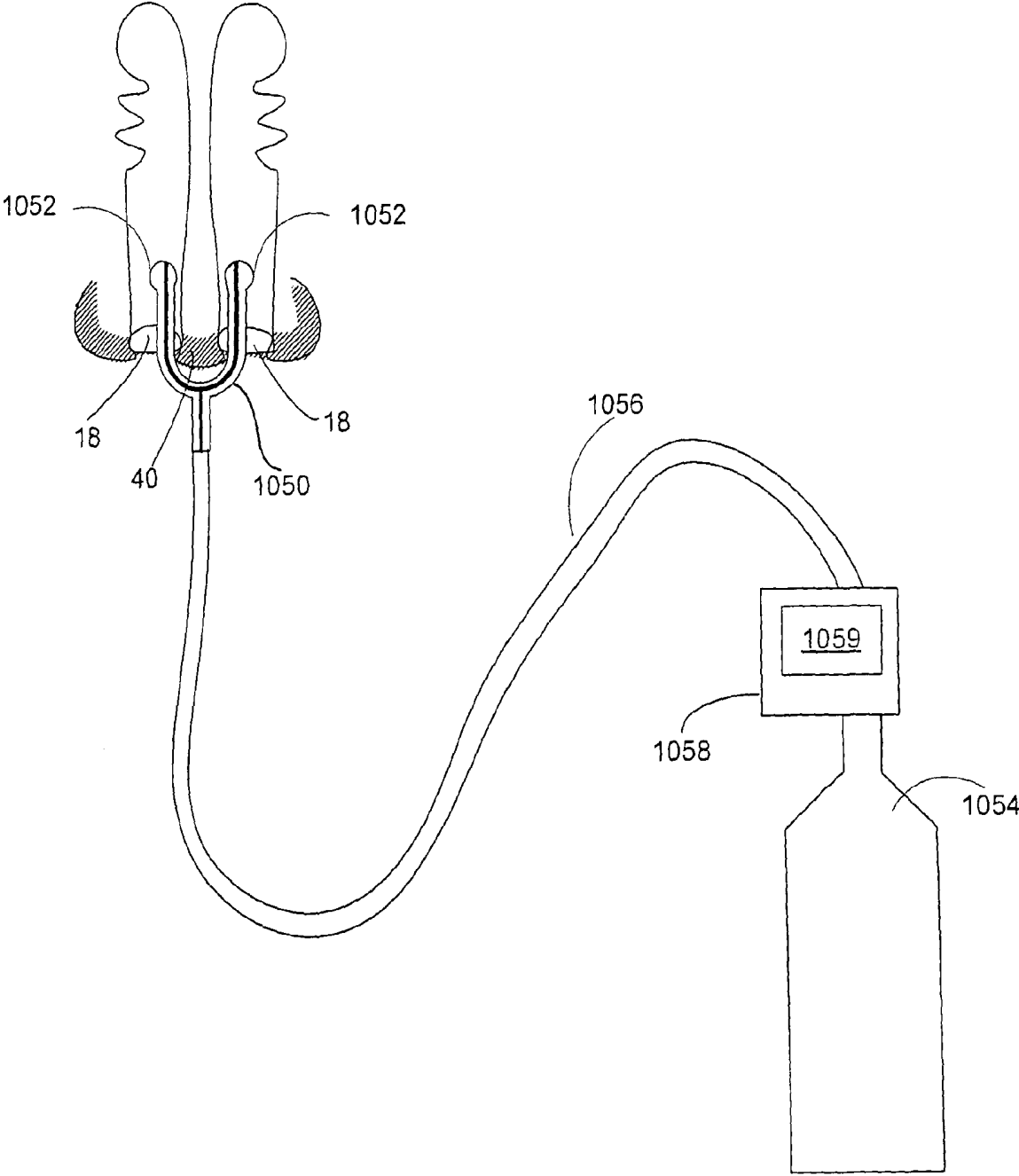


FIG. 38

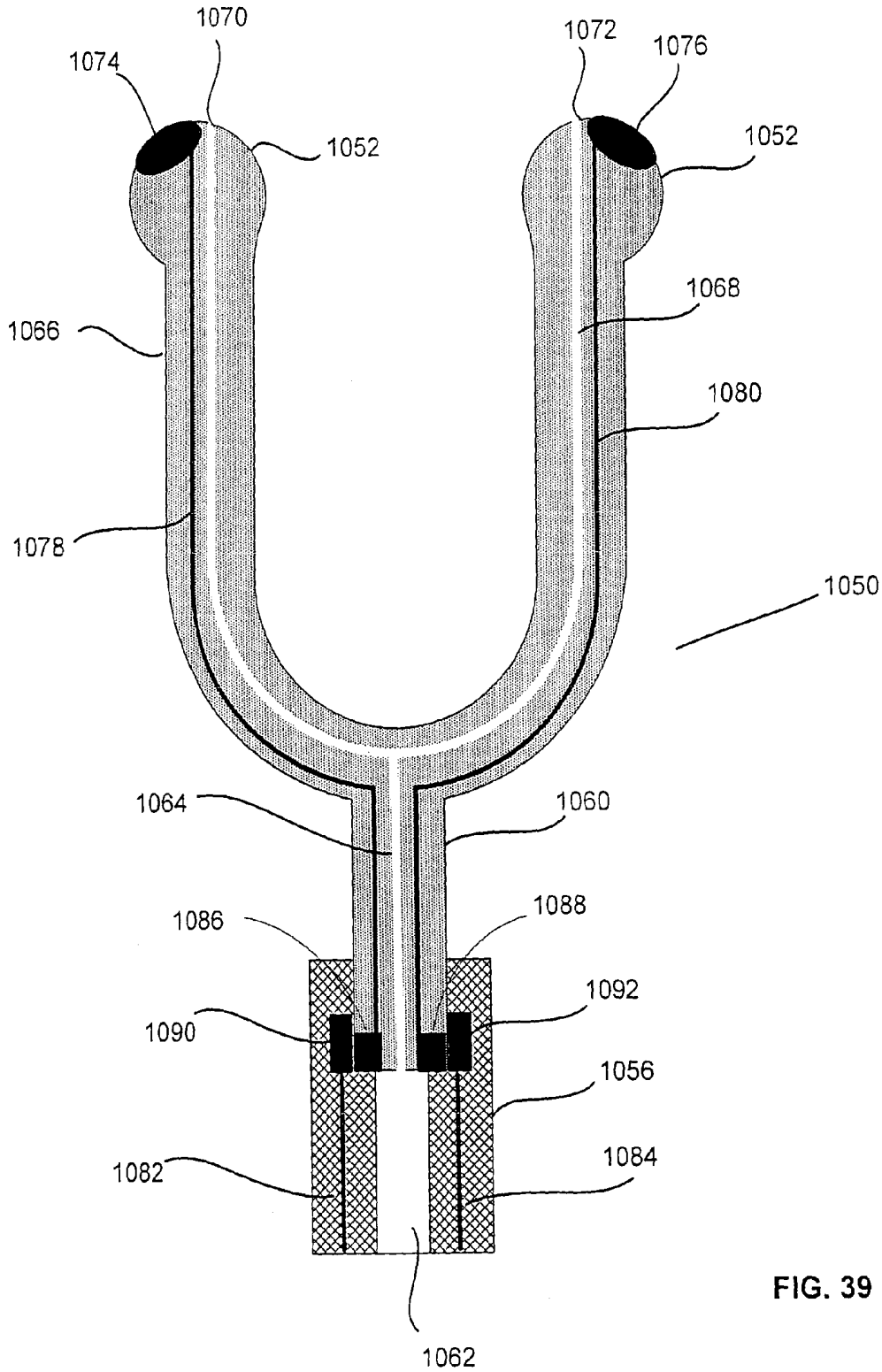


FIG. 39

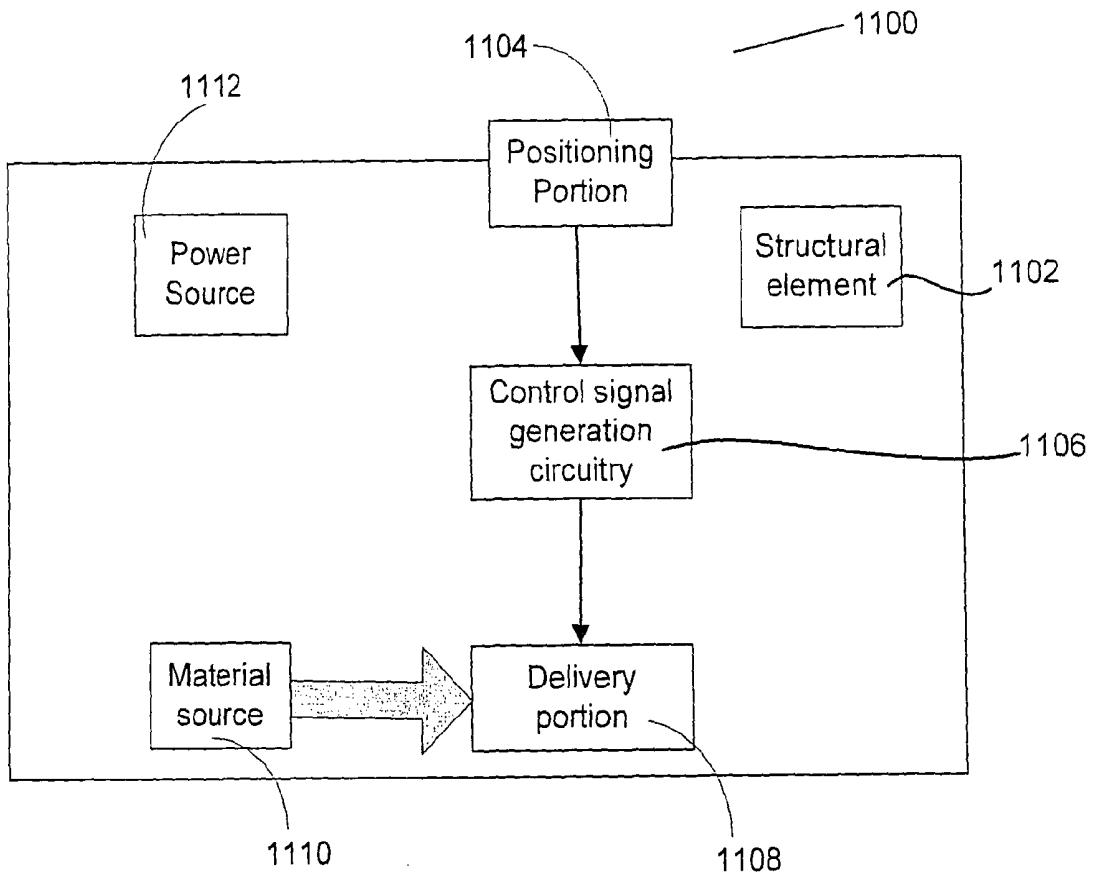


FIG. 40

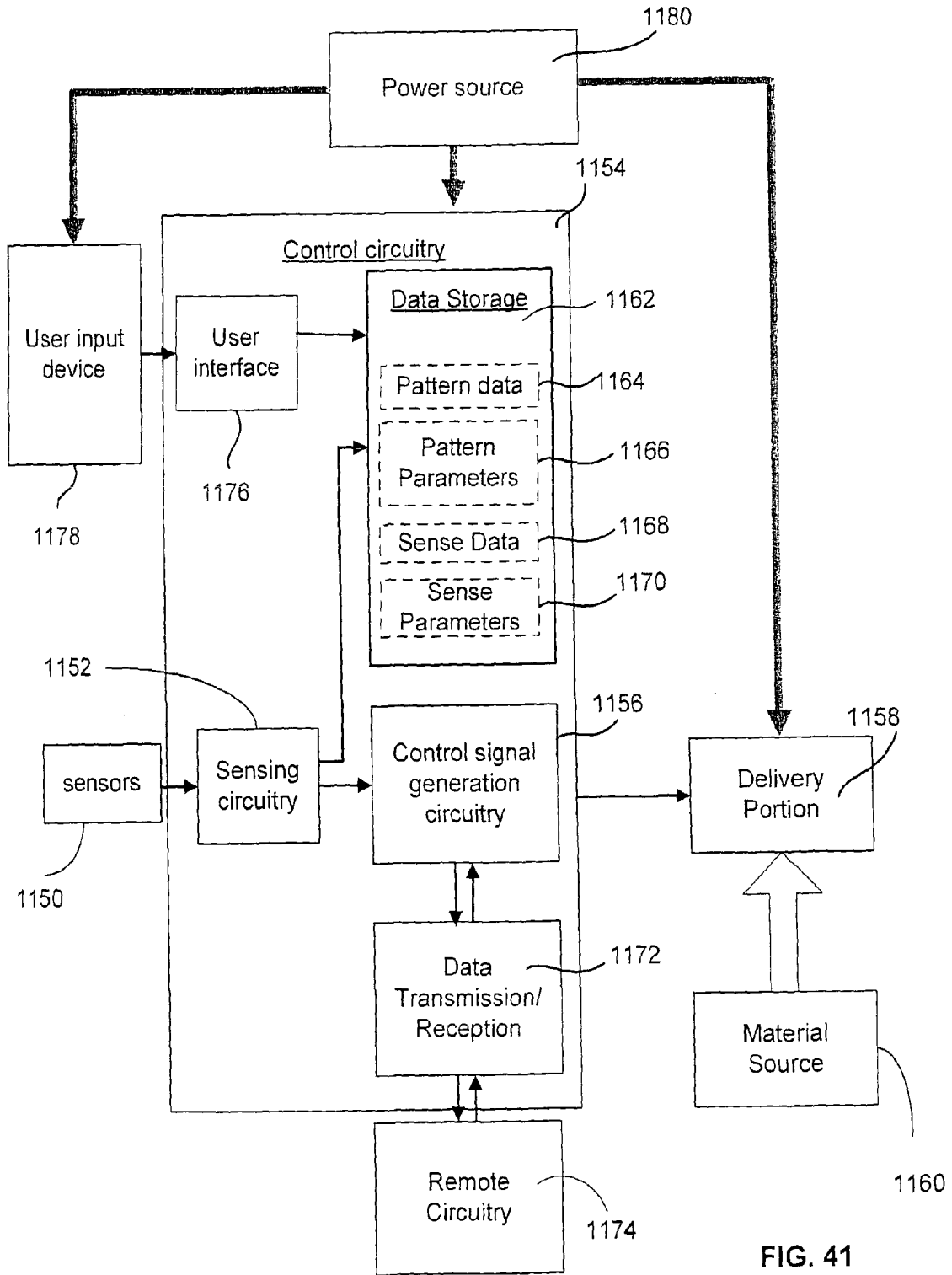


FIG. 41

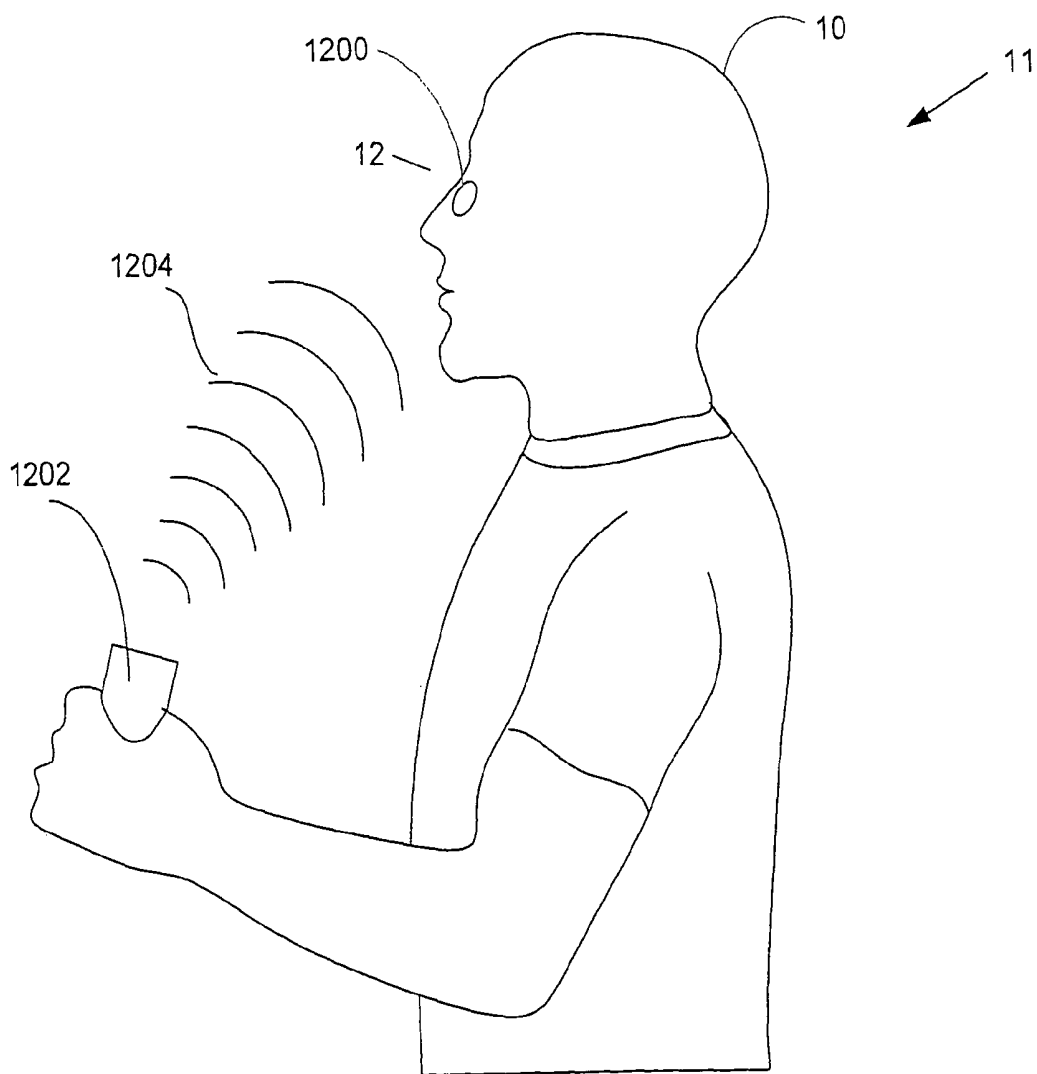


FIG. 42

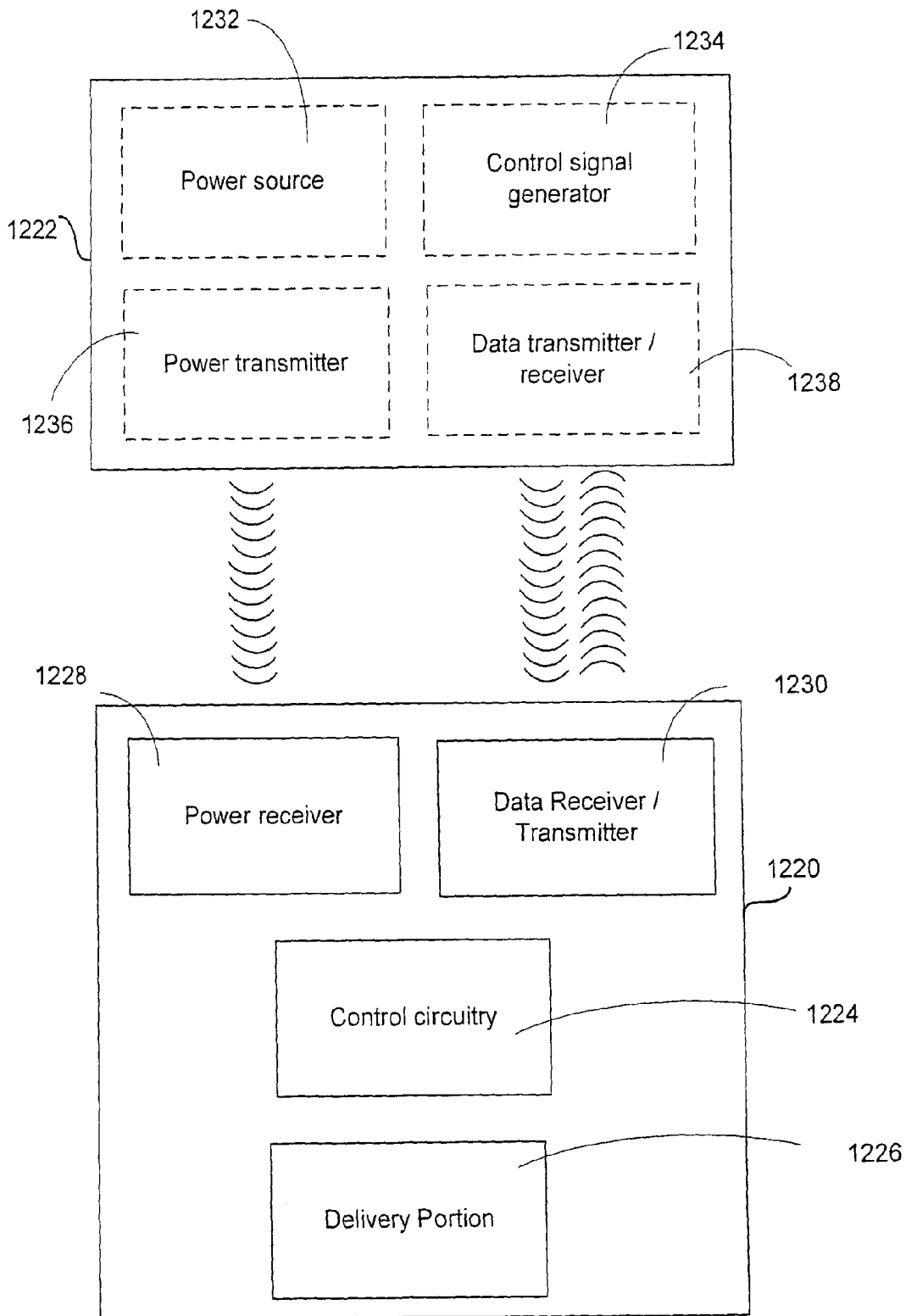


FIG. 43

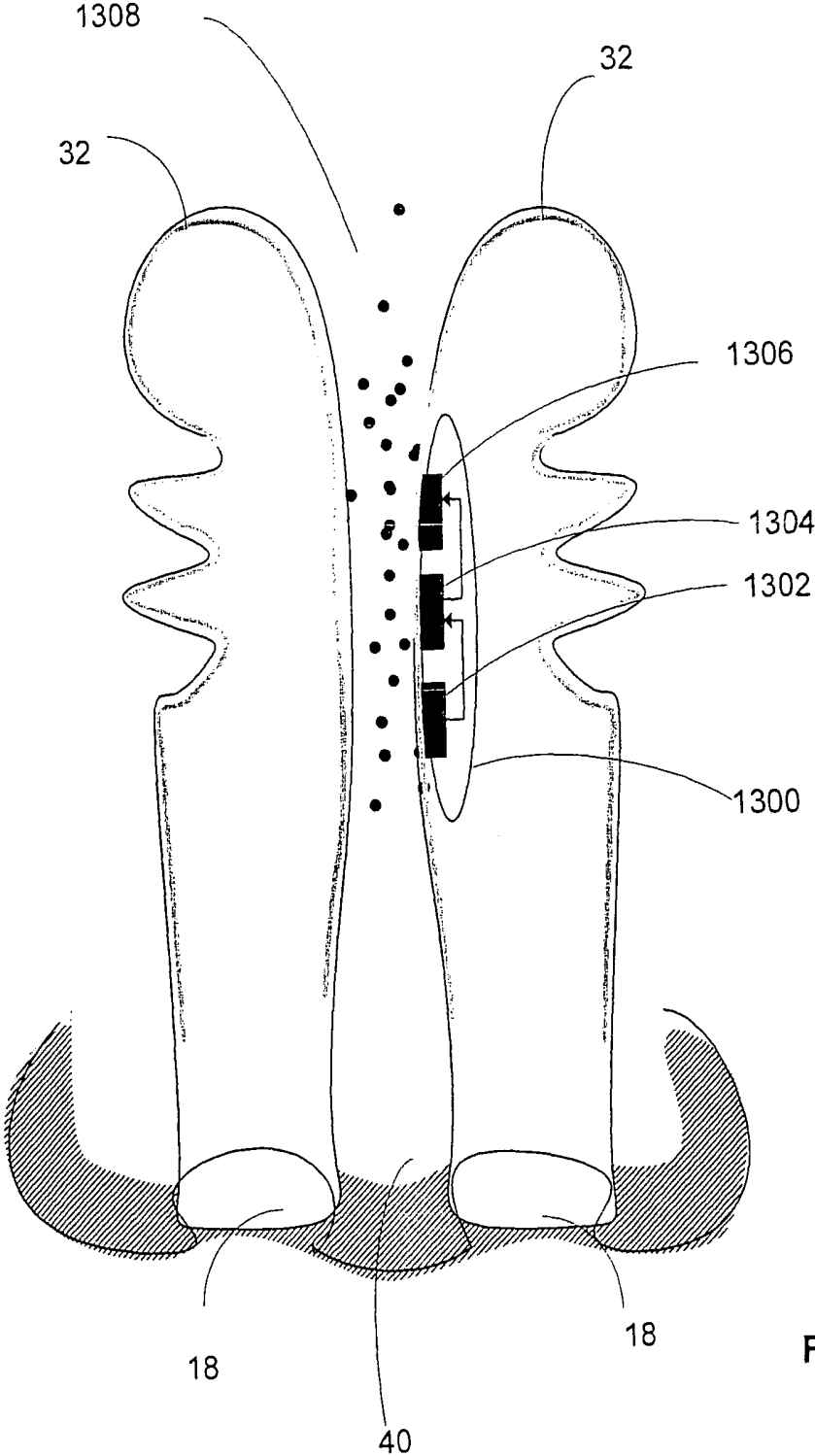


FIG. 44

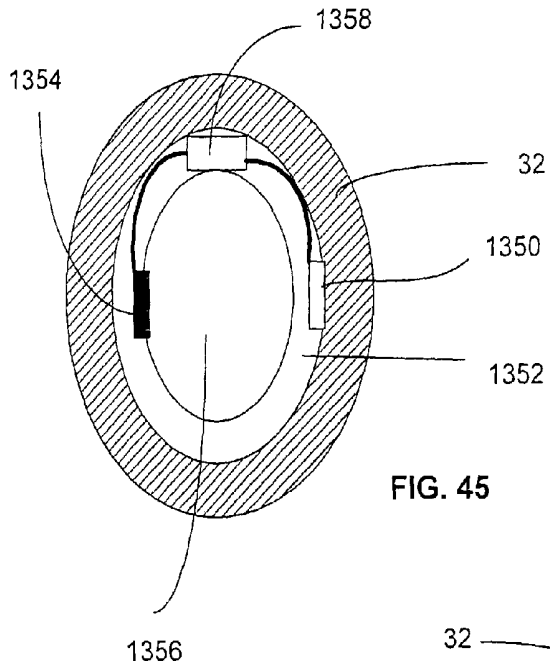


FIG. 45

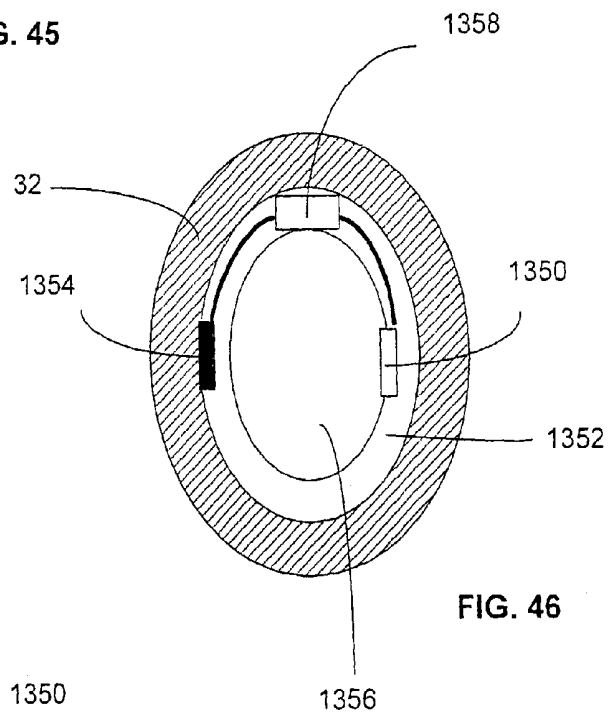


FIG. 46

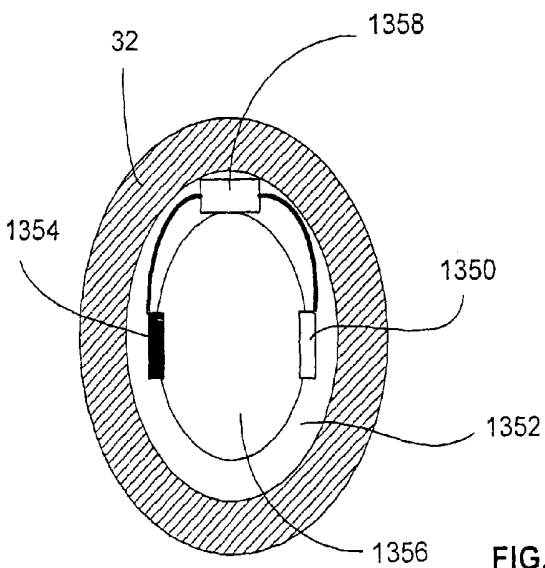


FIG. 47

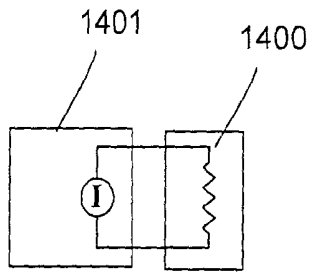


FIG. 48

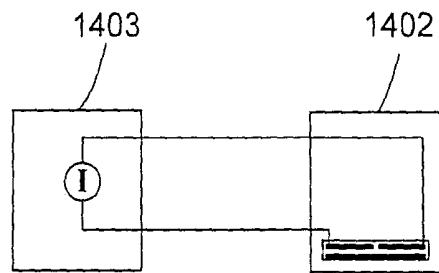


FIG. 49

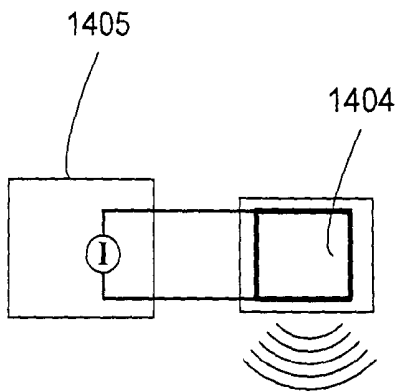


FIG. 50

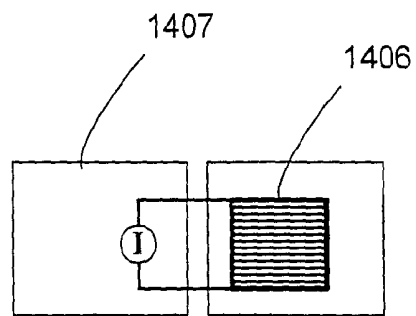


FIG. 51

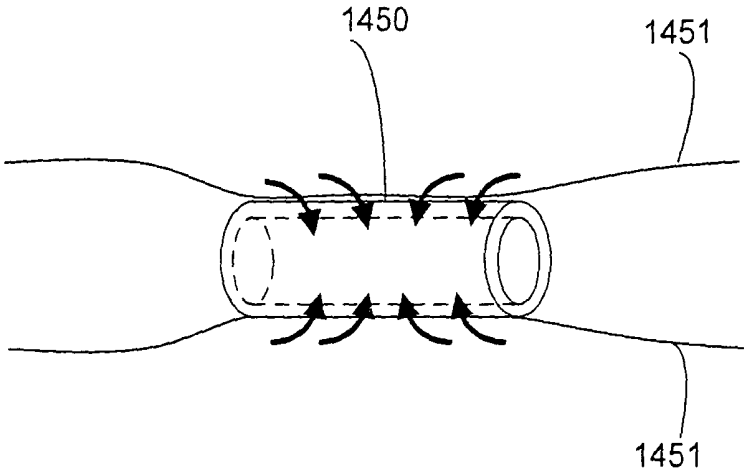


FIG. 52

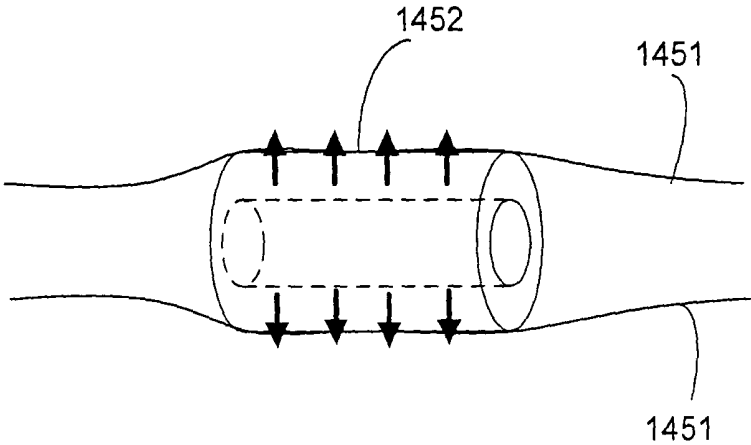


FIG. 53

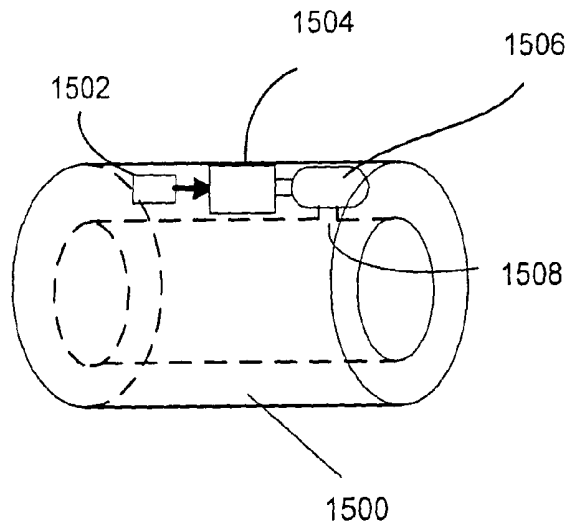


FIG. 54

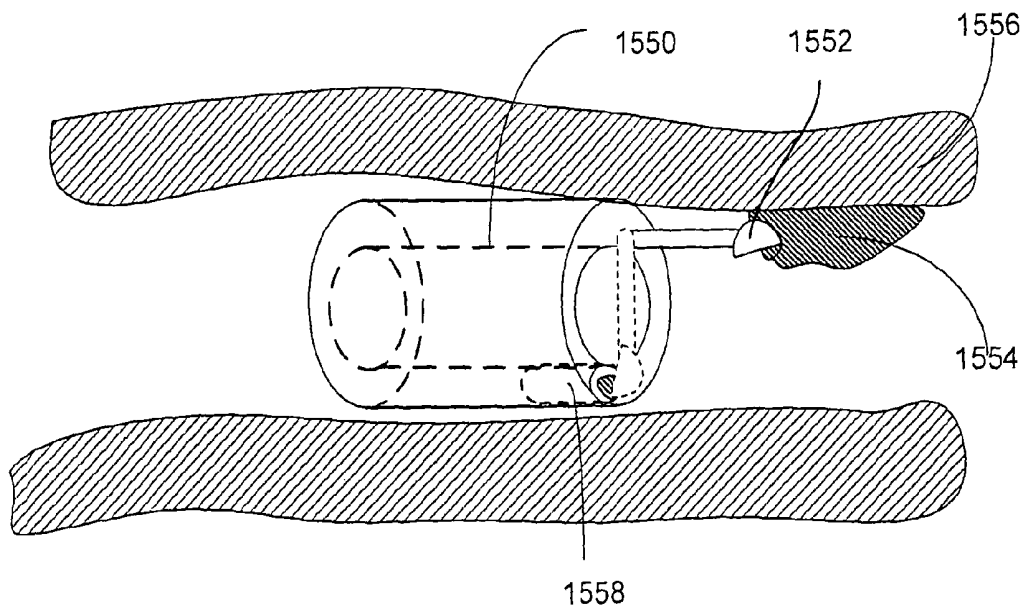


FIG. 55

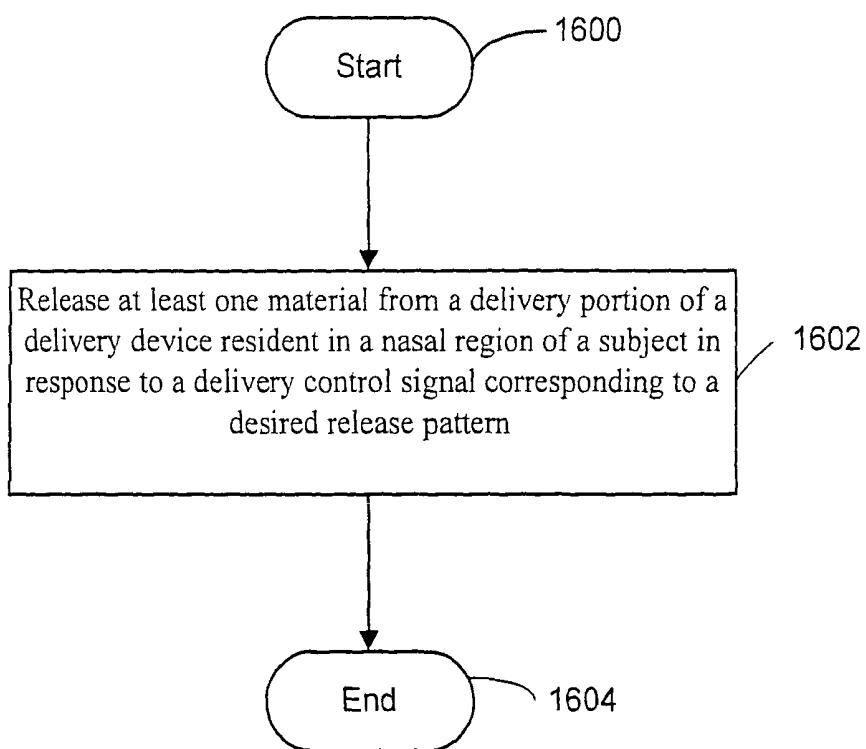


FIG. 56

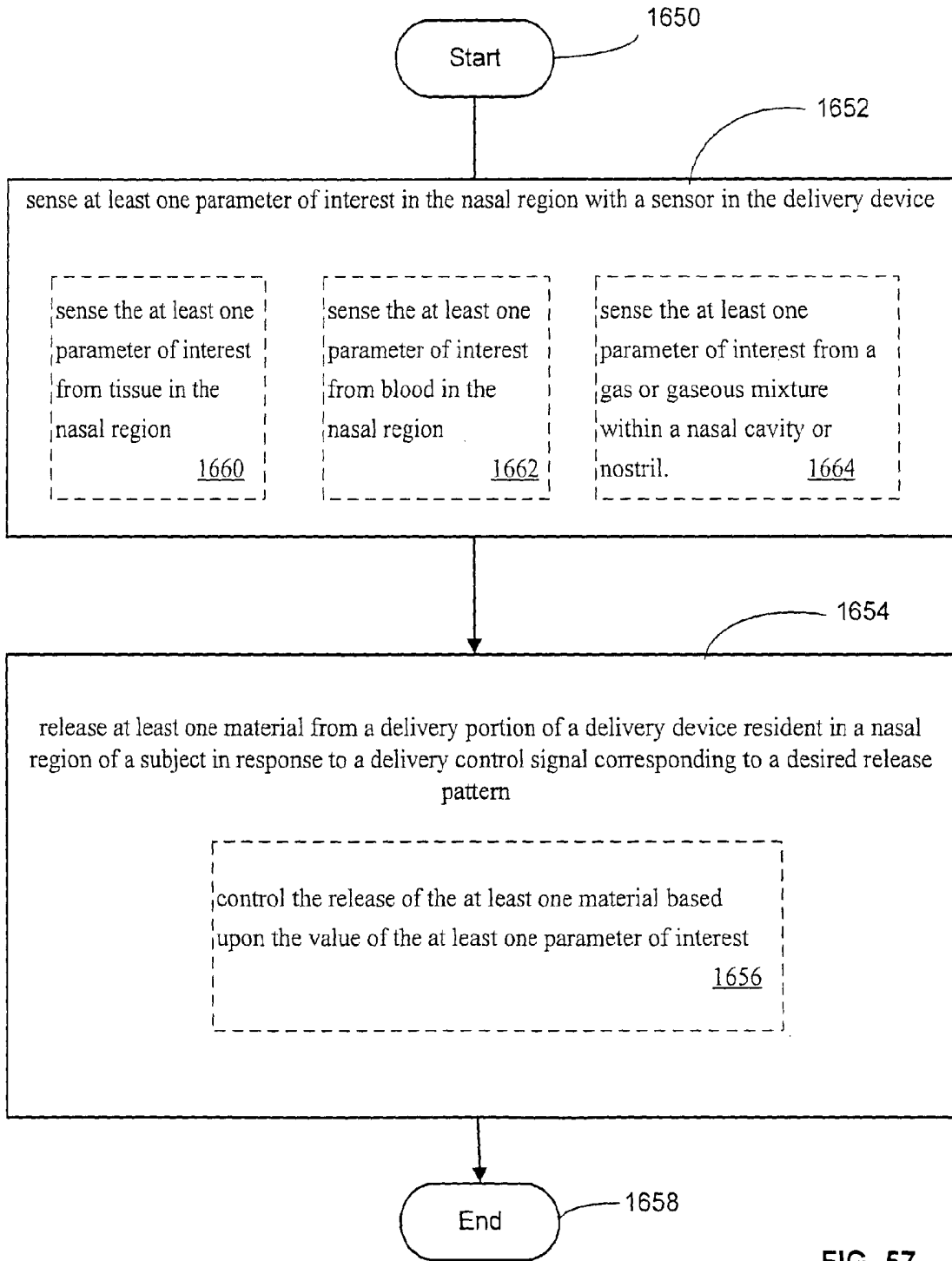


FIG. 57

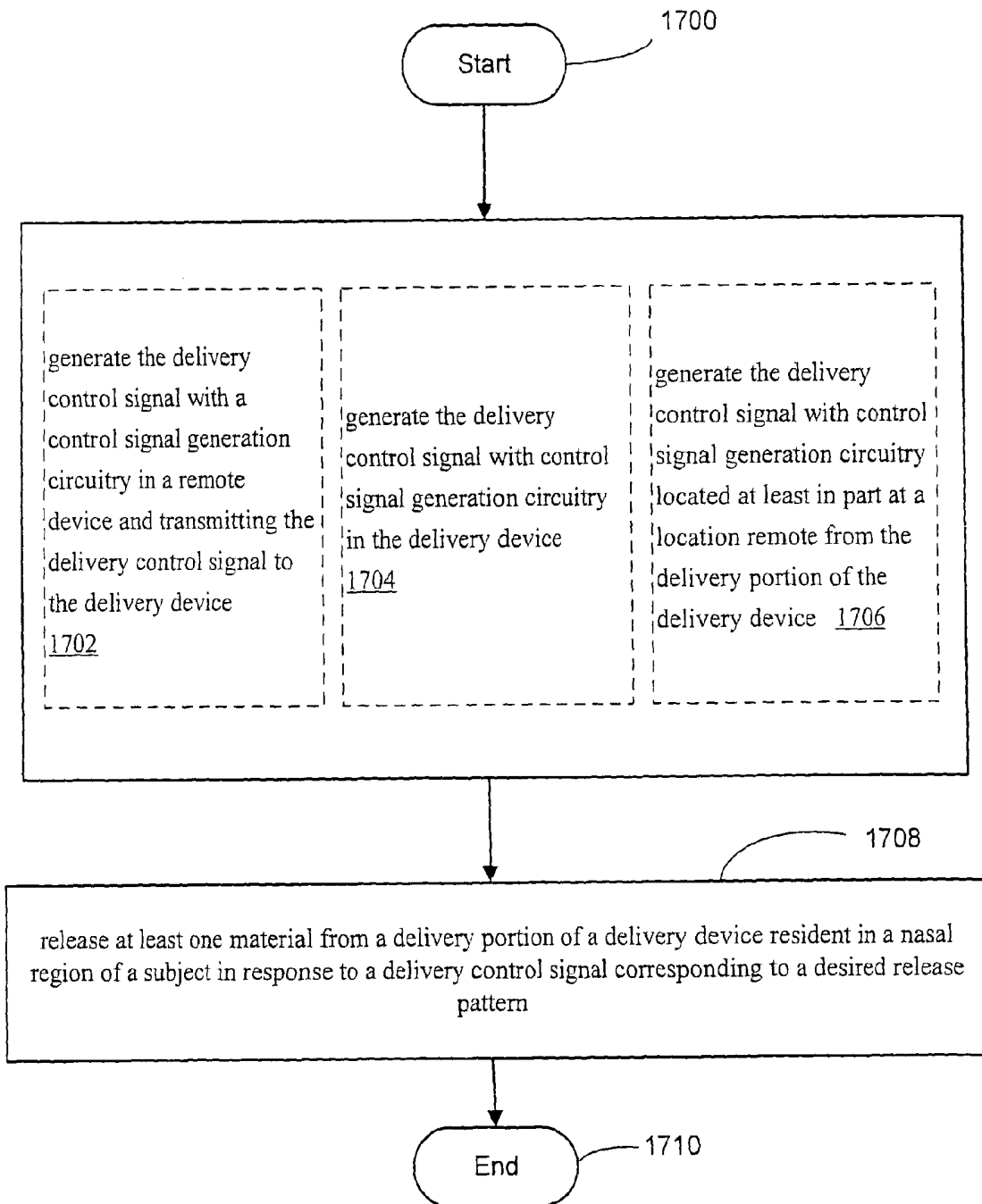


FIG. 58

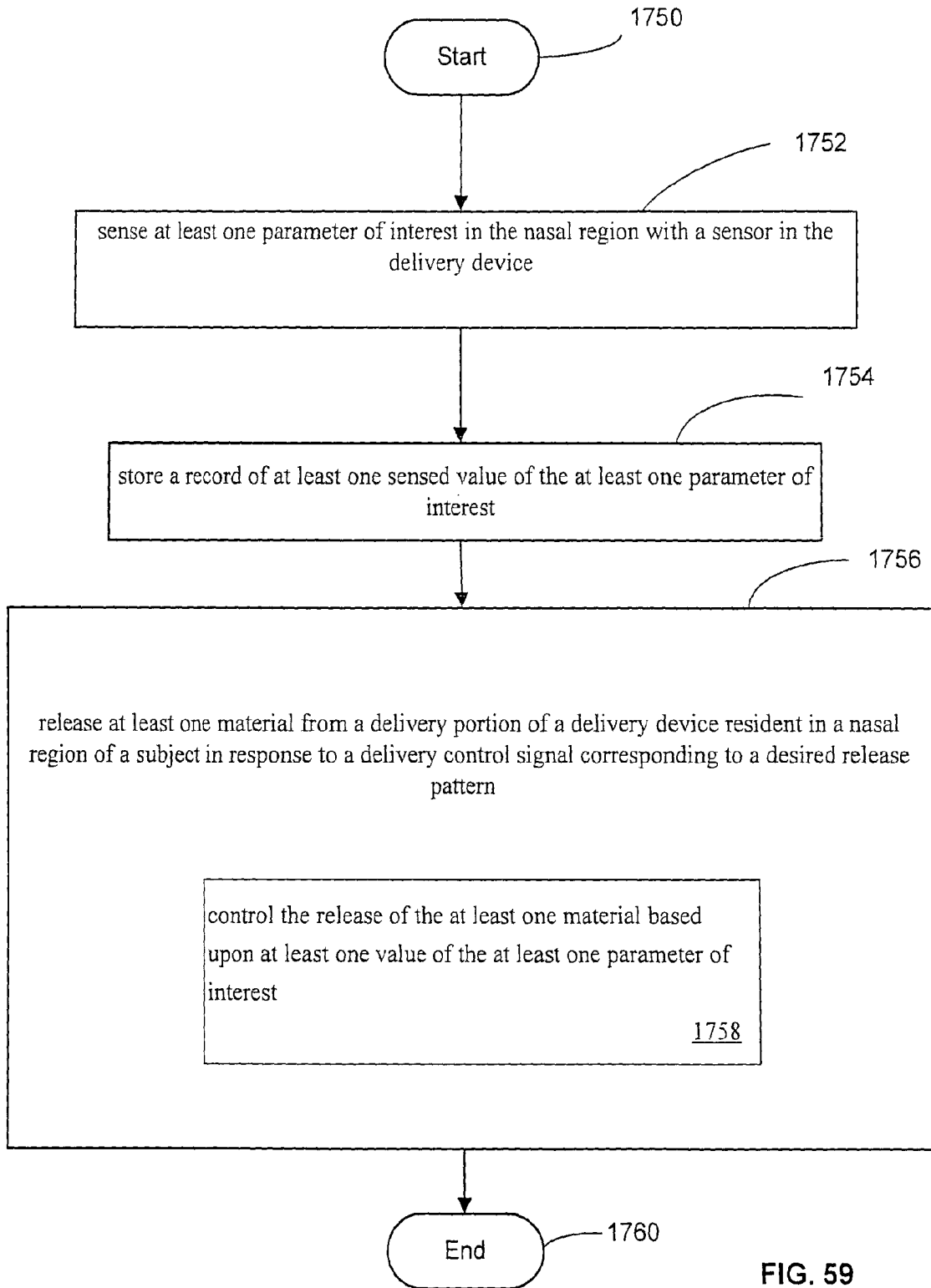


FIG. 59

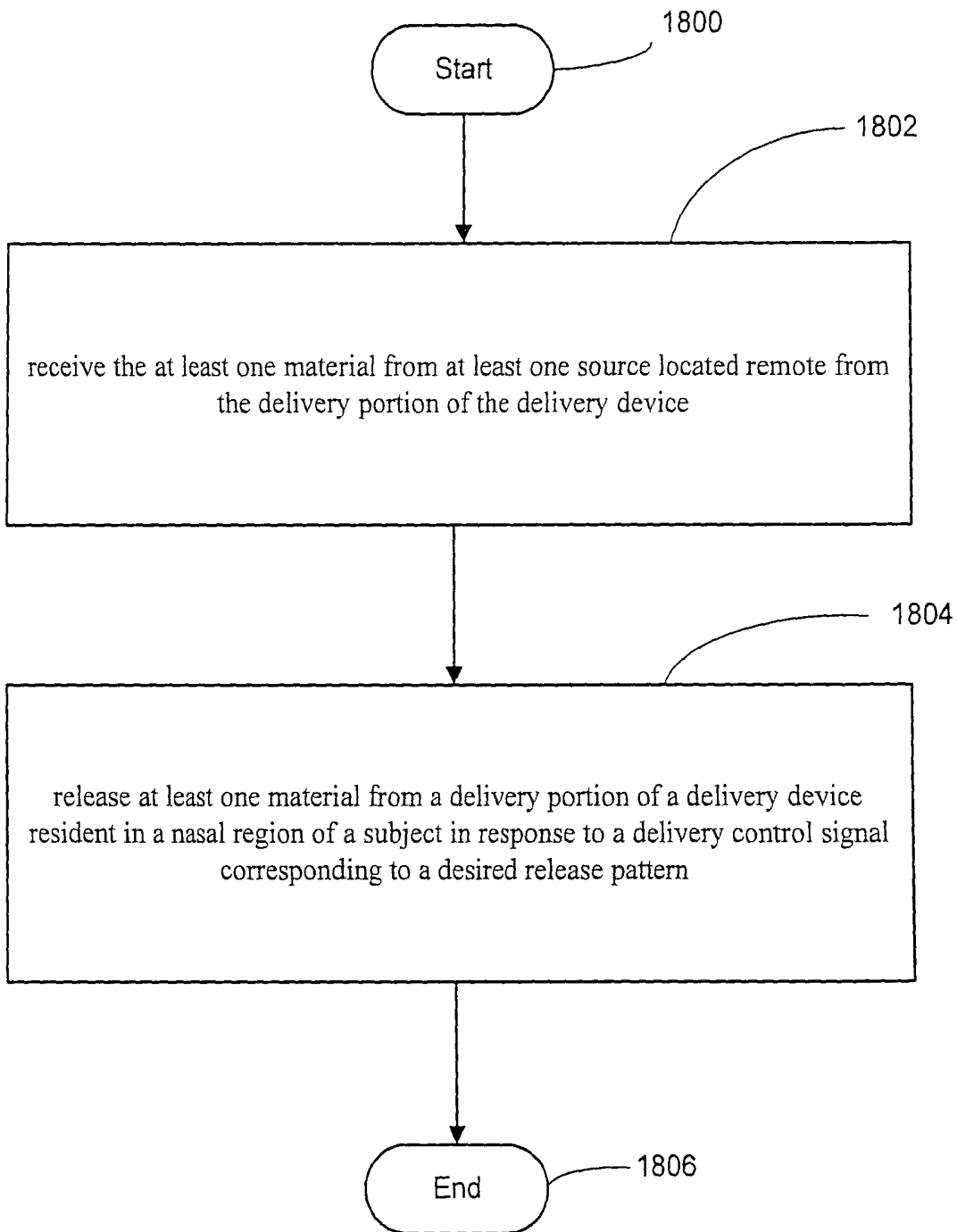


FIG. 60

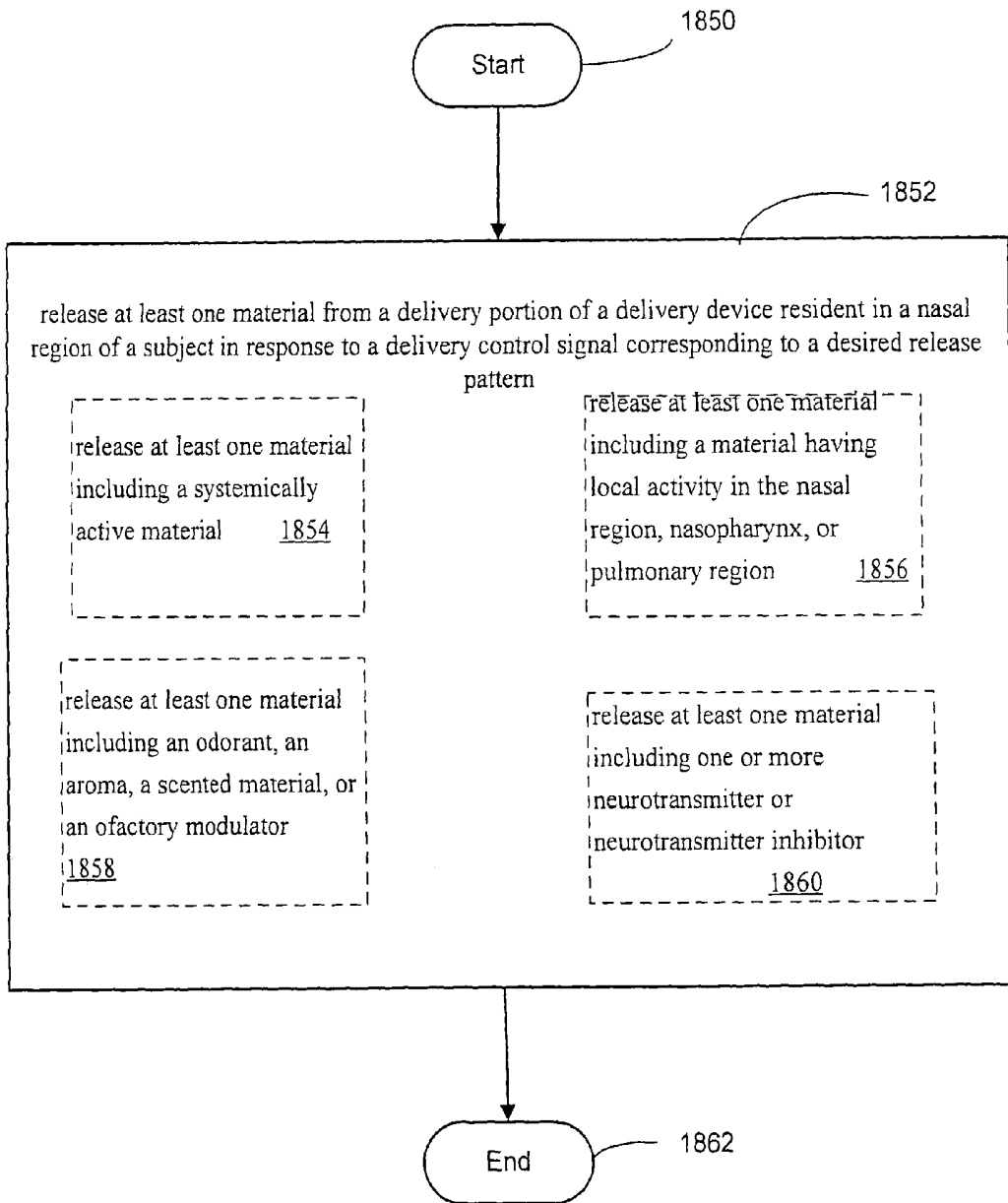


FIG. 61

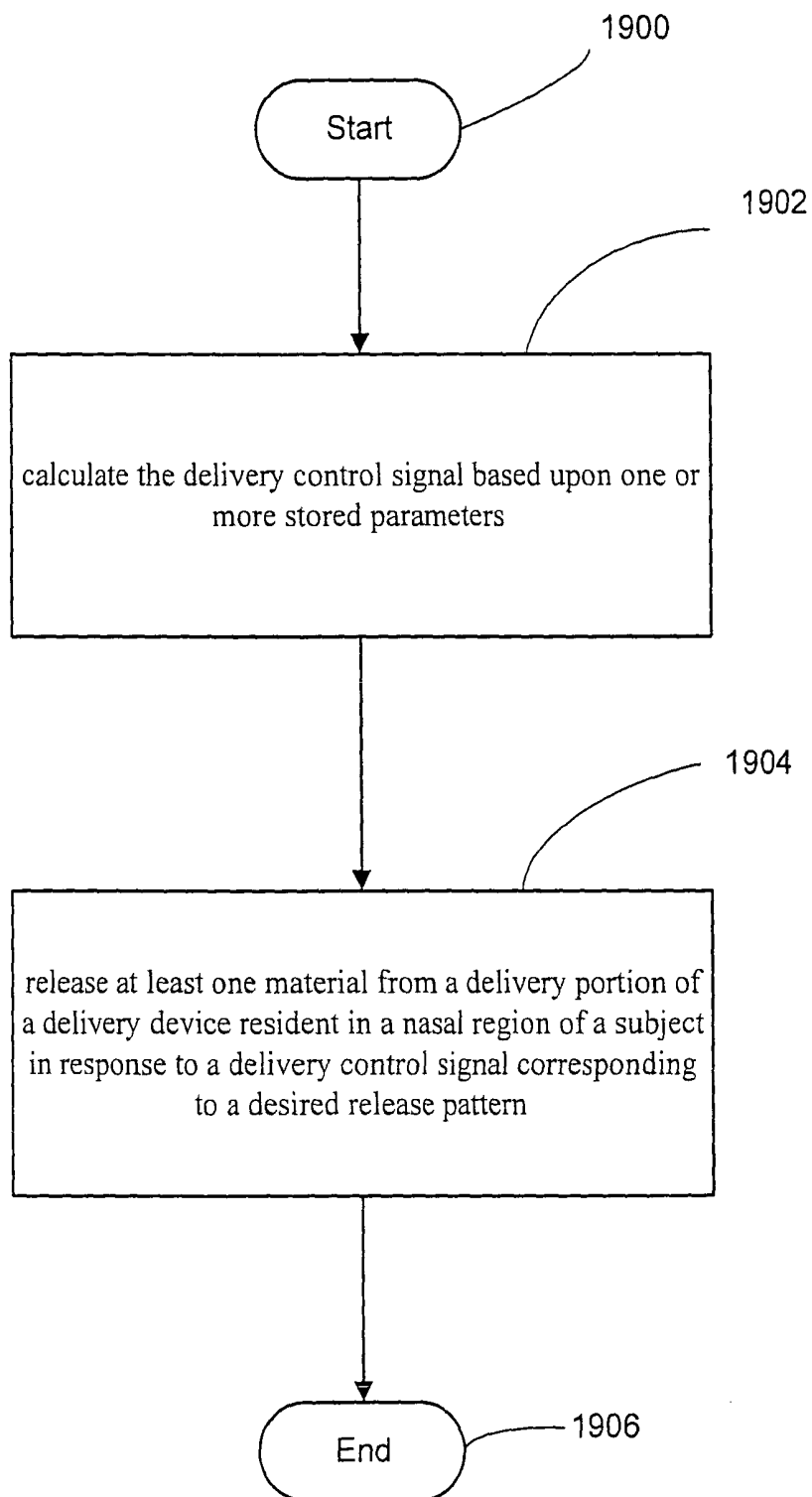


FIG. 62

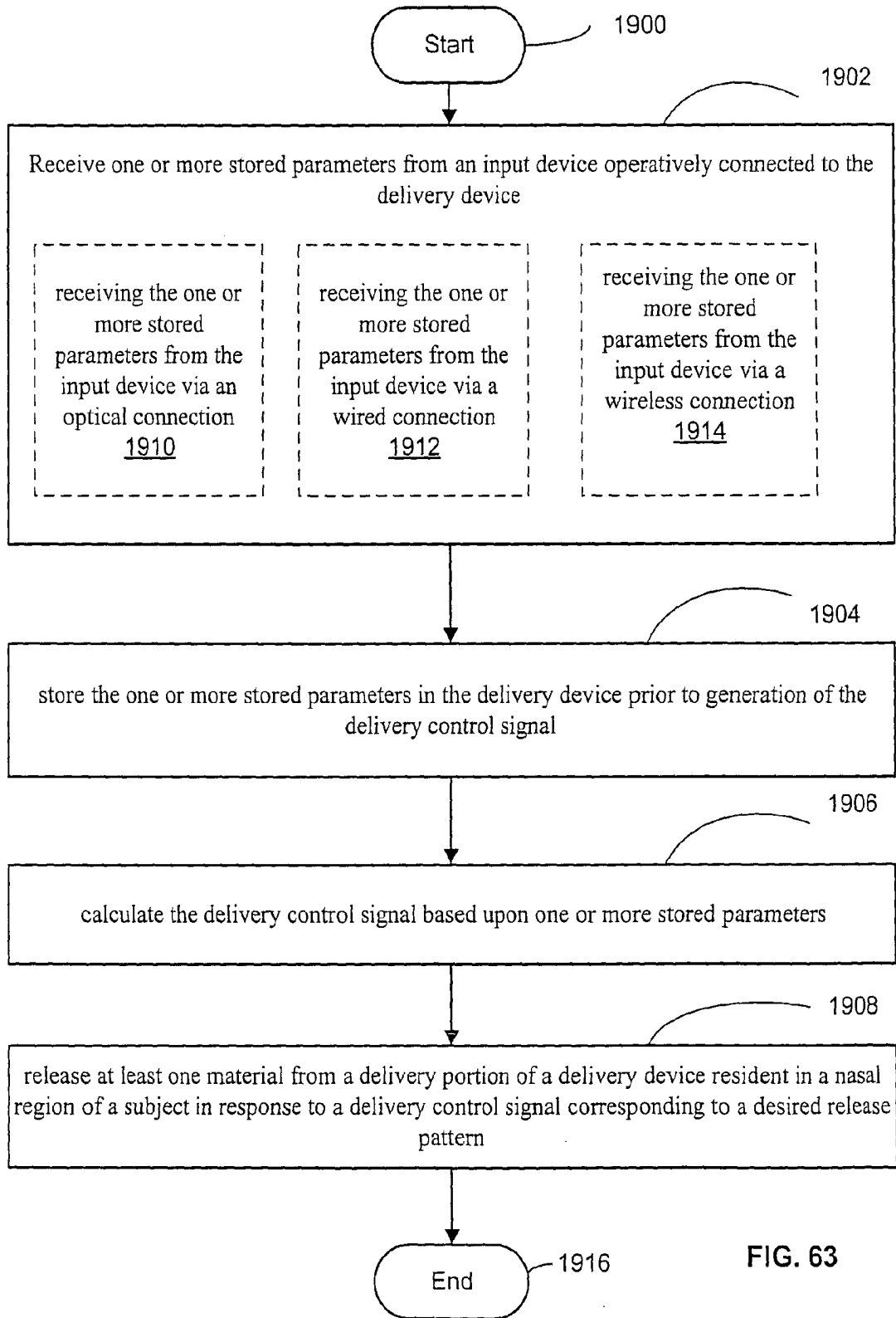


FIG. 63

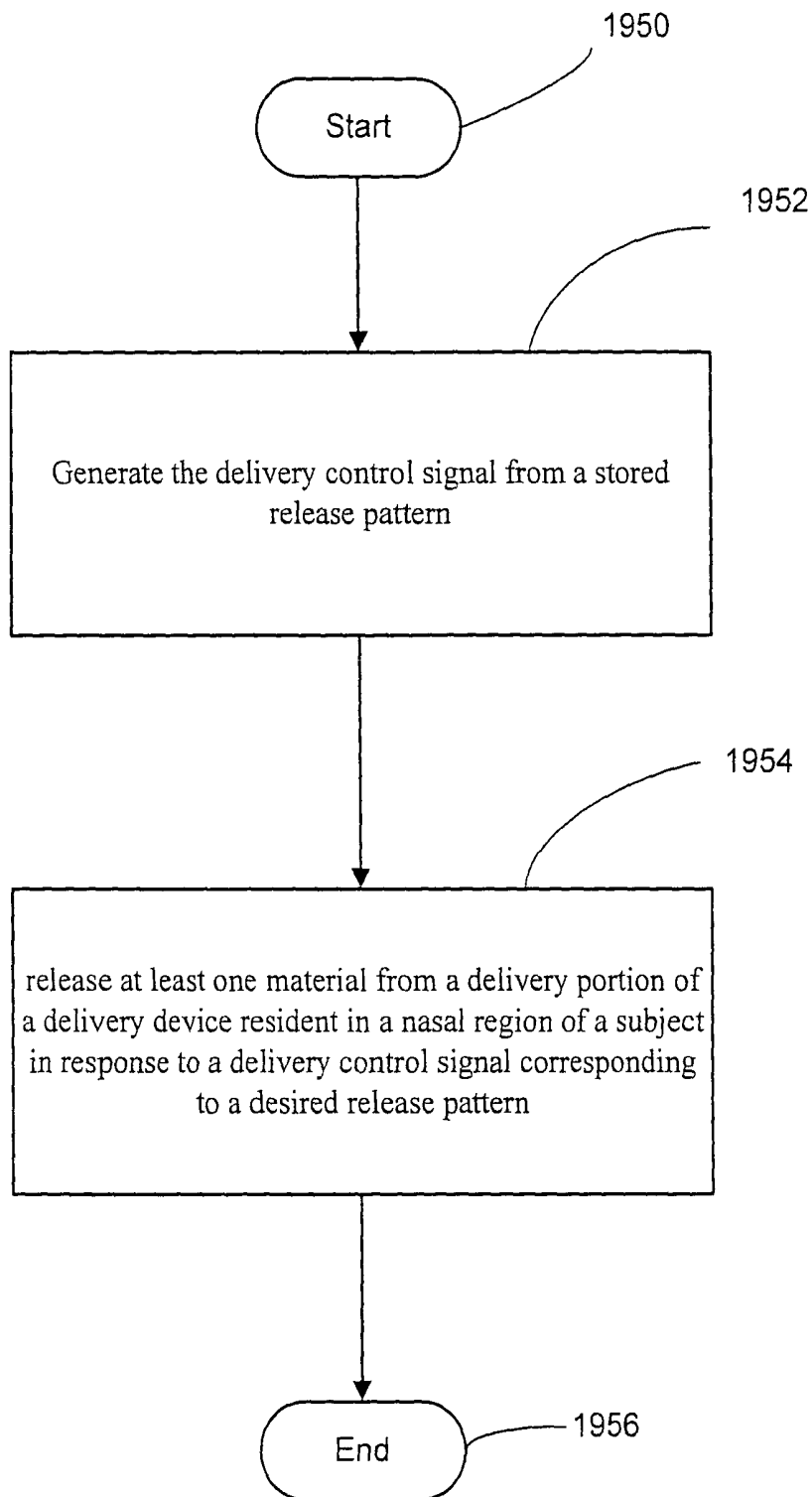


FIG. 64

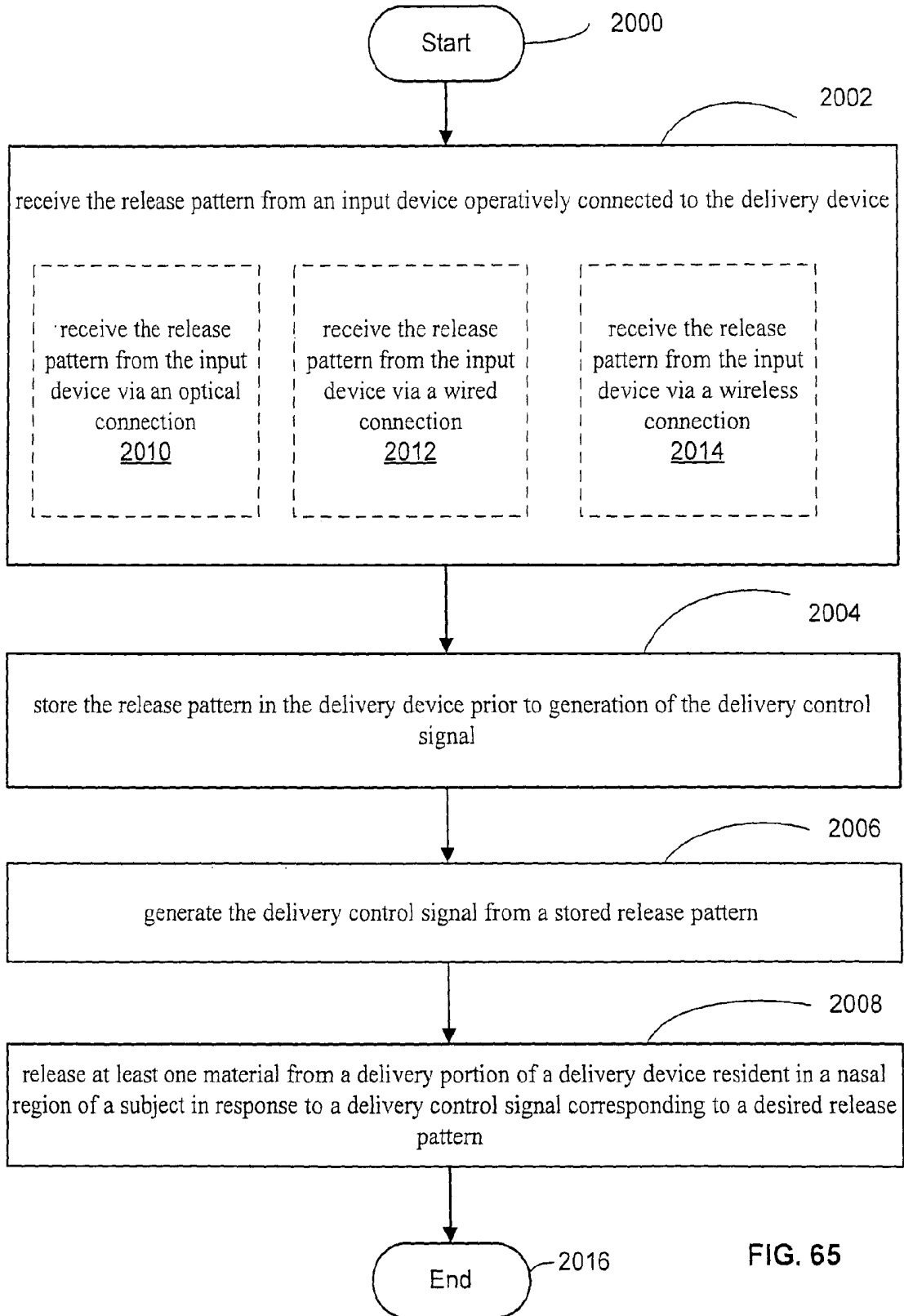


FIG. 65

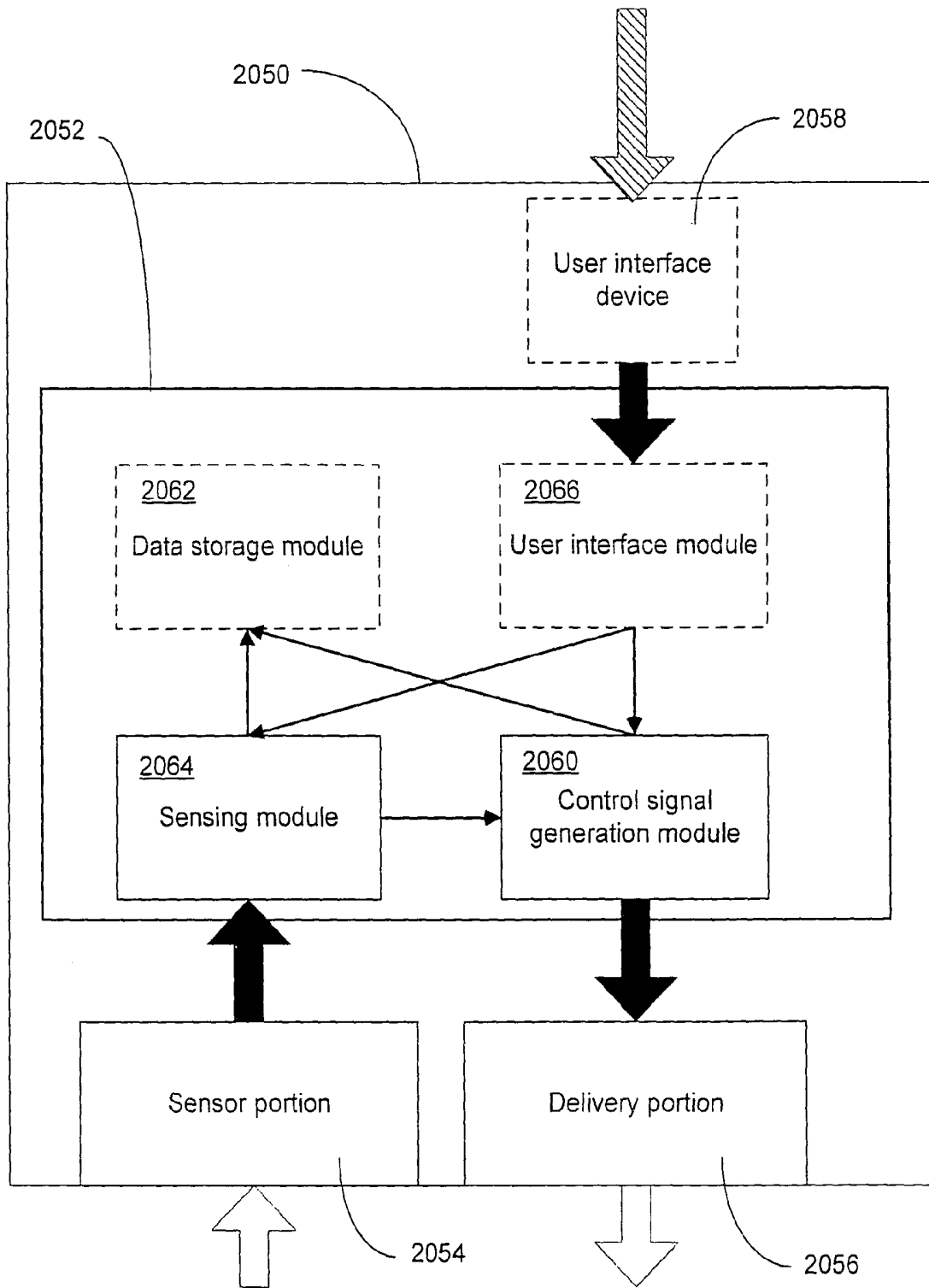


FIG. 66

CONTROLLABLE RELEASE NASAL SYSTEM**CROSS-REFERENCE TO RELATED APPLICATIONS**

The present application is related to and claims the benefit of the earliest available effective filing date(s) from the following listed application(s) (the "Related Applications") (e.g., claims earliest available priority dates for other than provisional patent applications or claims benefits under 35 USC §119(e) for provisional patent applications, for any and all parent, grandparent, great-grandparent, etc. applications of the Related Application(s)).

RELATED APPLICATIONS

For purposes of the USPTO extra-statutory requirements, the present application constitutes a continuation-in-part of U.S. patent application Ser. No. 10/949,186, entitled A CILIATED STENT-LIKE SYSTEM, naming Richa Wilson, Victoria Y. H. Wood, W. Daniel Hillis, Clarence T. Tegreene, Muriel Y. Ishikawa, and Lowell L. Wood, Jr. as inventors, filed 24 Sep. 2004, which is currently co-pending, or is an application of which a currently co-pending application is entitled to the benefit of the filing date.

For purposes of the USPTO extra-statutory requirements, the present application constitutes a continuation-in-part of U.S. patent application Ser. No. 10/827,576, entitled A SYSTEM FOR PERFUSION MANAGEMENT, naming Lowell L. Wood, Jr. as inventor, filed 19 Apr. 2004, which is currently co-pending, or is an application of which a currently co-pending application is entitled to the benefit of the filing date.

For purposes of the USPTO extra-statutory requirements, the present application constitutes a continuation-in-part of U.S. patent application Ser. No. 10/827,578, entitled A SYSTEM WITH A SENSOR FOR PERFUSION MANAGEMENT, naming Lowell L. Wood, Jr. as inventor, filed 19 Apr. 2004, which is currently co-pending, or is an application of which a currently co-pending application is entitled to the benefit of the filing date. For purposes of the USPTO extra-statutory requirements, the present application constitutes a continuation-in-part of United U.S. patent application Ser. No. 10/827,572, entitled A SYSTEM WITH A RESERVOIR FOR PERFUSION MANAGEMENT, naming Lowell L. Wood, Jr. as inventor, filed 19 Apr. 2004, which is currently co-pending, or is an application of which a currently co-pending application is entitled to the benefit of the filing date.

For purposes of the USPTO extra-statutory requirements, the present application constitutes a continuation-in-part of U.S. patent application Ser. No. 10/827,390, entitled A TELESCOPING PERFUSION MANAGEMENT SYSTEM, naming Lowell L. Wood, Jr. as inventor, filed 19 Apr. 2004, which is currently co-pending, Or is an application of which a currently co-pending application is entitled to the benefit of the filing date.

For purposes of the USPTO extra-statutory requirements, the present application constitutes a continuation-in-part of U.S. patent application Ser. No. 11/403,230, entitled LUMENALLY-ACTIVE DEVICE, naming Bran Ferren, W. Daniel Hillis, Roderick A. Hyde, Muriel Y. Ishikawa, Edward K. Y. Jung, Nathan P. Myhrvold, Elizabeth A. Sweeney, Clarence T. Tegreene, Richa Wilson, Lowell L. Wood, Jr. and Victoria Y. H. Wood as

inventors, filed 12 Apr. 2006, which is currently co-pending, or is an application of which a currently co-pending application is entitled to the benefit of the filing date.

For purposes of the USPTO extra-statutory requirements, the present application constitutes a continuation-in-part of U.S. patent application Ser. No. 11/417,898, entitled CONTROLLABLE RELEASE NASAL SYSTEM, naming W. Daniel Hillis, Roderick A. Hyde, Muriel Y. Ishikawa, Elizabeth A. Sweeney, Clarence T. Tegreene, Richa Wilson, Lowell L. Wood, Jr. and Victoria Y.H. Wood as inventors, filed 4 May 2006, which is currently co-pending, or is an application of which a currently co-pending application is entitled to the benefit of the filing date.

The United States Patent Office (USPTO) has published a notice to the effect that the USPTO's computer programs require that patent applicants reference both a serial number and indicate whether an application is a continuation or continuation-in-part. Stephen G. Kunin, *Benefit of Prior-Filed Application*, USPTO Official Gazette Mar. 18, 2003, available at <http://www.uspto.gov/web/offices/com/sol/og/2003/week11/pathbene.htm>. The present applicant entity has provided above a specific reference to the application(s) from which priority is being claimed as recited by statute. Applicant entity understands that the statute is unambiguous in its specific reference language and does not require either a serial number or any characterization, such as "continuation" or "continuation-in-part," for claiming priority to U.S. patent applications. Notwithstanding the foregoing, applicant entity understands that the USPTO's computer programs have certain data entry requirements, and hence applicant entity is designating the present application as a continuation-in-part of its parent applications as set forth above, but expressly points out that such designations are not to be construed in any way as any type of commentary and/or admission as to whether or not the present application contains any new matter in addition to the matter of its parent application(s).

All subject matter of the Related Applications and of any and all parent, grandparent, great-grandparent, etc. applications of the Related Applications is incorporated herein by reference to the extent such subject matter is not inconsistent herewith.

BACKGROUND

Devices and systems have been developed for use in various body lumens, particularly in the cardiovascular system, digestive, and urogenital tract. Catheters are used for performing a variety of sensing and material delivery tasks. Stents are implanted in blood vessels for the purpose of preventing stenosis or restenosis of blood vessels. Capsules containing sensing and imaging instrumentation, that may be swallowed by a subject and which travel passively through the digestive tract have also been developed. Robotic devices intended to move through the lower portion of the digestive tract under their own power are also under development.

SUMMARY

The present application describes devices, systems, and related methods for delivery of a material to a nasal region of a subject. Embodiments of delivery devices and systems for placement within a nasal region are disclosed. In one aspect, a system includes but is not limited to a structural element including a positioning portion configured for contacting an interior surface of a nasal region and mounting the structure

element within the nasal region of a subject, a delivery portion mounted relative to the structural element and configured to release at least one material responsive to a delivery control signal, and control signal generation circuitry configured to generate a delivery control signal corresponding to a desired pattern of release of the at least one material into the nasal region. In addition to the foregoing, other system aspects are described in the claims, drawings, and text forming a part of the present disclosure.

In one aspect, a method includes but is not limited to releasing at least one material from a delivery portion of a delivery device mounted within a nasal region of a subject in response to a delivery control signal corresponding to a desired release pattern. The method may include sensing a parameter of interest in the nasal region with a sensor in the delivery device and controlling the release of the at least one material based upon the value of the parameter of interest. In some aspects, the method may include generating the delivery control signal. In addition to the foregoing, other method aspects are described in the claims, drawings, and text forming a part of the present disclosure.

Various aspects of the operation of such delivery devices may be performed under the control of hardware, software, firmware, or a combination thereof. In one or more various aspects, related systems include but are not limited to circuitry and/or programming for effecting the herein-referenced method aspects; the circuitry and/or programming can be virtually any combination of hardware, software, and/or firmware configured to effect the herein referenced method aspects depending upon the design choices of the system designer. Software for operating a delivery device according to various embodiments is also described.

The foregoing summary is illustrative only and is not intended to be in any way limiting. In addition to the illustrative aspects, embodiments, and features described above, further aspects, embodiments, and features will become apparent by reference to the drawings and the following detailed description.

BRIEF DESCRIPTION OF THE FIGURES

FIG. 1 is a side cross-sectional view of an embodiment of controllable release nasal device emplaced in a nostril;

FIG. 2 is a front cross-sectional illustration of the controllable release nasal device depicted in FIG. 1;

FIG. 3 is a detailed view of the controllable release nasal device shown in FIGS. 1 and 2;

FIG. 4 is an illustration of a lumenally active device;

FIG. 5 is an illustration of another embodiment of a controllable release nasal device;

FIG. 6 is a front cross-section view of the device of FIG. 5;

FIG. 7 is a further depiction of the device of FIG. 6;

FIG. 8 is a front cross-sectional view of an embodiment of a controllable release nasal device including a clip;

FIG. 9 is a side cross-sectional view of the embodiment of FIG. 8;

FIG. 10 is a front cross-sectional view of another embodiment of a controllable release nasal device;

FIG. 11 is a side cross-sectional view of the embodiment of FIG. 10;

FIG. 12 is an illustration of an embodiment of a structural element;

FIG. 13 is an illustration of another embodiment of a structural element;

FIG. 14 is an illustration of another embodiment of a structural element;

FIG. 15 is an illustration of another embodiment of a structural element;

FIG. 16 is an illustration of a further embodiment of a structural element;

FIG. 17 is an illustration of another embodiment of a structural element;

FIG. 18 is an illustration of another embodiment of a structural element;

FIG. 19A and 19B depicted changes in dimension of an embodiment;

FIG. 20 is a cross-sectional view of an embodiment of a structural element;

FIG. 21 is a cross-sectional view of another embodiment of a structural element;

FIG. 22 is a cross-sectional view of another embodiment of a structural element;

FIG. 23 is a cross-sectional view of another embodiment of a structural element;

FIG. 24 is a cross-sectional view of another embodiment of a structural element;

FIG. 25 is a cross-sectional view of yet another embodiment of a structural element;

FIG. 26 is a front cross-sectional depiction of release of material from a controllable release nasal device;

FIG. 27 is a side cross-sectional view of delivery of material to the nasal mucosa from a controllable release nasal device;

FIG. 28 is a side cross-sectional view of delivery of material to the olfactory region from a controllable release nasal device;

FIG. 29 is a side cross-sectional view of delivery of material toward the nasopharynx from a controllable release nasal device;

FIG. 30 is an illustration of a device including stored deliverable material;

FIG. 31 is an illustration a delivery device including an extension;

FIG. 32 is a cross-sectional view of an embodiment of a device including a stored deliverable material and a barrier release mechanism;

FIG. 33 is a cross-sectional view of another embodiment of a device including a stored deliverable material and a barrier release mechanism;

FIGS. 34A and 34B are depictions of the release of a stored deliverable material from a reservoir via a rupturable barrier;

FIGS. 35A and 35B are depictions of the release of a stored deliverable material from a reservoir via a degradable barrier;

FIGS. 36A and 36B are depictions of the release of a stored deliverable material from a reservoir via a barrier having controllable permeability;

FIGS. 37A and 37B are depictions of the release of a stored deliverable material from a carrier material;

FIG. 38 is an illustration of an embodiment of a controllable release nasal system including an external material source;

FIG. 39 is a close-up illustration of the nasal device portion of the system of FIG. 38;

FIG. 40 is a block diagram of a controllable release nasal system;

FIG. 41 is a schematic diagram illustrating components of control circuitry of a controllable release nasal system;

FIG. 42 is an illustration of a controllable release nasal system including an external control portion;

FIG. 43 is a block diagram of a controllable release nasal system including an external control portion;

FIG. 44 is a front cross-sectional view of an embodiment of a controllable release nasal device;

FIG. 45 is an illustration of an embodiment of a controllable release nasal device including a delivery portion and a sensor;

FIG. 46 is an illustration of another embodiment of a controllable release nasal device including a delivery portion and a sensor;

FIG. 47 is an illustration of another embodiment of a controllable release nasal device including a delivery portion and a sensor;

FIG. 48 depicts an embodiment of an active portion including a heating element;

FIG. 49 depicts an embodiment of an active portion including a cooling element;

FIG. 50 depicts an embodiment of an active portion including an electromagnetic radiation source;

FIG. 51 depicts an embodiment of an active portion including an acoustic signal source;

FIG. 52 depicts an embodiment of an active portion including a negative pressure source;

FIG. 53 depicts an embodiment of an active portion including a positive pressure source;

FIG. 54 is an illustration of another embodiment of a controllable release nasal device;

FIG. 55 is a depiction of an embodiment of a controllable release nasal device including a material collection structure;

FIG. 56 is a flow diagram of a method of delivering a material to a nasal region of a subject;

FIG. 57 is a flow diagram of a method of delivering a material to a nasal region of a subject;

FIG. 58 is a flow diagram of a method of delivering a material to a nasal region of a subject;

FIG. 59 is a flow diagram of a method of delivering a material to a nasal region of a subject;

FIG. 60 is a flow diagram of a method of delivering a material to a nasal region of a subject;

FIG. 61 is a flow diagram showing further aspects of a method of delivering a material to a nasal region of a subject;

FIG. 62 is a flow diagram showing further aspects of a method of delivering a material to a nasal region of a subject;

FIG. 63 is a flow diagram showing further aspects of a method of delivering a material to a nasal region of a subject;

FIG. 64 is a flow diagram showing further aspects of a method of delivering a material to a nasal region of a subject;

FIG. 65 is a flow diagram showing further aspects of a method of delivering a material to a nasal region of a subject; and

FIG. 66 is a schematic diagram of software for controlling release of a material from device mounted within a nasal region of a subject.

DETAILED DESCRIPTION

In the following detailed description, reference is made to the accompanying drawings, which form a part hereof. In the drawings, similar symbols typically identify similar components, unless context dictates otherwise. The illustrative embodiments described in the detailed description, drawings, and claims are not meant to be limiting. Other embodiments may be utilized, and other changes may be made, without departing from the spirit or scope of the subject matter presented here.

FIG. 1 is a cross-sectional illustration of a head 10 of a person, showing the basic anatomy of nasal region 12. The mouth 14 and tongue 16 are also indicated in FIG. 1. Nasal region 12 includes nostril 18 and nasal cavity 20. Nasopharynx 22 is the uppermost portion of the pharynx (throat) 24, which connects to esophagus 26. Nasopharynx 22 connects to nasal cavity 20 via internal naris 28. Trachea (windpipe) 30

lies anterior to esophagus 26. Epiglottis 32 closes off the opening of larynx 34 leading to trachea 30 (shown with a solid line) during eating and drinking, and opens (shown with a dashed line) to permit the flow of air between pharynx 24 and trachea 30 during breathing. Nasal conchae 36 form shelf-like projections which may be seen more clearly in the front cross-sectional view of FIG. 2. The olfactory region 38 is located in the uppermost portion of nasal cavity 20. The nasal cavity 20 is divided into right side and left sides by nasal septum 40, as shown in FIG. 2. Nasal mucosa 42 lines the interior of the nasal cavity 20, as shown by a gray line in FIG. 2. (The nasal mucosa will not be indicated in other figures, but may be expected to be present within the nasal cavity under normal circumstances.)

In the example depicted in FIGS. 1 and 2, a delivery device 44 forming at least a portion of a controllable release nasal system is positioned within nostril 18 of nasal region 12. Delivery device 44 may be a self-expanding device that may be positioned within the nostril, for example by a care provider or by the person using the delivery device, and then may expand intrinsically or be made to expand under control to provide a snug fit sufficient to retain delivery device 44 within the nostril for as long as is desired.

FIG. 3 illustrates further aspects of delivery device 44. As shown in FIG. 3, in one aspect, an embodiment of a controllable release nasal system may include a structural element 50 including at least one positioning portion 52 configured for contacting an interior surface 54 of a nasal region (in this example, nostril 18) and mounting the structural element 50 within the nasal region of a subject; a delivery portion 56 mounted relative to the structural element 50 and configured to release at least one material responsive to a delivery control signal; and control signal generation circuitry 58 configured to generate a delivery control signal corresponding to a desired pattern of release of the at least one material into the nasal region. In the example of FIG. 3, positioning portion 52 is the exterior surface of structural element 50, which mounts structural element 50 within the nasal region (i.e., nostril 18 in this example) by a pressure and/or frictional fit. In other embodiments, other types of positioning portions may be used, as will be discussed herein. Delivery device 44 may include one or more sensor 62, which may be capable of detecting a physiological or environmental condition. Control signal generation circuitry 58 may receive as input a signal from sensor 62, which may be used in the calculation of the control signal for controlling the release of material from delivery portion 56.

A delivery portion of a controllable release nasal system (for example, delivery portion 56 of delivery device 44 in FIG. 3) may be designed to release material into different portions of the nasal region depending on various considerations, including the specific material being delivered, the intended effect of the material, sensed ambient physiological and/or environmental conditions, and, in some applications, the mechanism of absorption or uptake of the material by the body. In some embodiments, the material may be released directly into the nasal mucosa for absorption by local tissue. Or by blood circulating through local fine capillaries, while in other embodiments, the material may be released into the nasal cavity in the form of a liquid, a gas, finely dispersed particles or droplets, or mixtures thereof, which may be carried by ambient airflow to more distant portions of the nasal mucosa or other portions of the respiratory tract, which may be exhaled along with exhaled gases, or which may be inhaled to various depths of the bronchial tree or within or into the gas-exchange portions of the lung, for example. In some

embodiments, the finely dispersed particles or droplets may be controlled to be within the diameter-range of 0.01 to 0.00001 cm, for example.

Materials delivered to the nasal regions may have a number of effects or uses. In some cases, materials such as odorants or neurotransmitters may stimulate the olfactory region to produce a sensory effect, for example for an esthetic, recreational, or medical purpose (e.g., aromatherapy; blockade, modification or enhancement of the flavors of foods, drinks, or orally delivered medications; one-or-more scents or olfactory modulators delivered according to a pattern or script in order to provide an olfactory analog to a soundtrack of a motion picture; amplified delivery of scents or odorants or olfactory modulators to supplement deficiencies or enhance to supra-normal levels the innate sense of smell, etc.). In some embodiments, materials may be released for delivery to the nasal mucosa and/or to sites elsewhere in the respiratory tract for absorption into the blood to effect systemic delivery of the materials, which may be, for example, various types of drugs, medications, contraceptives, hormones, vaccines, tolerance-inducing allergens, or therapeutic compounds. In some embodiments, materials may be delivered to the nasal mucosa or elsewhere in the respiratory tract to produce a local effect (e.g., to reduce inflammation or swelling of tissues, or for anti-pathogenic action) or inhaled into the lungs either to produce a local effect or for systemic uptake. In some embodiments, the material may form a functional coating on the surface of the nasal region, respiratory tract portion or lung, rather than be absorbed, e.g. to function as a surfactant, a protective layer, or a barrier. In some embodiments, one or more materials delivered into the nasal region may act on exhaled gases to act on or in cooperation with substances in the exhaled gases, for example to remove undesired materials from the exhaled gases, or to enhance, amplify or modify the effect of substances of interest in the exhaled gases.

Some embodiments of controllable release nasal systems may be considered to be lumenally active devices. Lumenally active devices in general are described in commonly owned U.S. patent application Ser. No. 11/403,230, entitled "Lumenally Active Device" and filed Apr. 12, 2006, which is incorporated herein by reference.

In some aspects, as described herein, controllable release nasal systems may release materials into a body lumen (e.g., a nasal cavity or nostril), while in other aspects, controllable release nasal systems may release materials into tissue surrounding the lumen and not into the lumen per se. The "Lumenally Active Device" patent application describes a lumenally active device which may include a structural element configured to fit within at least a portion of a body lumen, the structural element including a lumen-wall-engaging portion and a fluid-contacting portion configured to contact fluid within the body lumen; a sensor capable of detecting a condition of interest in the fluid; response initiation circuitry operatively connected to the sensor and configured to generate a response initiation signal upon detection of the condition of interest in the fluid by the sensor; and an active portion operatively connected to the response initiation circuitry and capable of producing a response upon receipt of the response initiation signal. Such a system is depicted in FIG. 4, which shows a delivery device 110 positioned in a body lumen 112. Body lumen 112 is defined by wall portions 114, which may be the walls of lumen-containing structure within the body of an organism, e.g., a nasal region or, in other embodiments and applications, a blood vessel or other lumen containing structure. Delivery device 110 includes structural element 116, sensor 118, response initiation circuitry 120, and active portion 122. A fluid may flow through lumen 112. The term fluid,

as used herein, may refer to liquids, gases, and other compositions, mixtures, or materials exhibiting fluid behavior. The fluid within the body lumen may include a liquid, or a gas or gaseous mixtures. As used herein, the term fluid may encompass liquids, gases, or mixtures thereof that also include solid particles in a fluid carrier. Liquids may include mixtures of two or more different liquids, solutions, slurries, or suspensions. Examples of liquids present within body lumens include blood, lymph, serum, urine, semen, digestive fluids, tears, saliva, mucus, cerebro-spinal fluid, intestinal contents, bile, epithelial exudate, or esophageal contents. Liquids present within body lumens may include synthetic or introduced liquids, such as blood substitutes or drug, nutrient, or (possibly buffered) saline or electrolyte solutions. Fluids may include liquids containing dissolved gases or gas bubbles, or gases containing fine liquid droplets or solid particles. Gases or gaseous mixtures found within body lumens may include inhaled and exhaled air, e.g. in the nasal or respiratory tract, or intestinal gases. According to this definition, fluids within the nasal region will typically include gases and mixtures of gases. Fluid may flow through the central openings 126 of structural element 116, with the interior surface of structural element 116 forming fluid-contacting surface 128. In the embodiment of FIG. 4, sensor 118 and active portion 122 may be located at a fluid-contacting surface 128. Outer surface 130 of structural element 116 may function as a lumen-wall engaging portion, providing a frictional fit with wall portions 114. In other embodiments of delivery devices, other structures and methods for engaging the lumen wall may be employed. Structural elements may include two or more openings or lumens passing through the structural element, rather than a single central opening as depicted in FIG. 4, and the lumen-wall-engaging portion of the structural element is not limited to embodiments having a substantially smooth outer surface that conforms to the interior cross-section of a nasal lumen, but may have a variety of surface shapes, textures, and contours, some of which may conform or contact only a portion or portions of the interior cross section of a nasal lumen.

Embodiments of the lumenally-active system may be configured for use in various different body lumens of an organism including, for example, a nostril or nasal cavity, one or more portions of the respiratory tract, the cardiovascular system (e.g., a blood vessel), the lymphatic system, the biliary tract, the urogenital tract, the oral cavity, the digestive tract, the tear ducts, a glandular system, a reproductive tract or portion thereof, the cerebral ventricles, spinal canal, and other fluid-containing structure of the nervous system of an organism. Other fluid-containing lumens within the body may be found in the auditory or visual systems, or in interconnections thereof, e.g., the Eustachian tubes.

Wherever a controllable release nasal system is to be used, the dimensions and mechanical properties (e.g., rigidity) of the delivery device, and particularly of the structural element of the delivery device, may be selected for compatibility with the location of use, in order to provide for reliable positioning of the device and to prevent damage to the lumen-containing structure.

The structural element may include a self-expanding structure configured to expand to mount the structural element within the nasal region of the subject. For example, structural element 50 of the delivery device depicted in FIGS. 1 through 3 is a generally spring-like structure that may be formed of a loop of resilient, springy, or self-expanding material which may be compressed slightly by virtue of slit 60, as shown in FIG. 3, to permit insertion into the nostril and which may then expand sufficiently to cause the structural element to be

retained within the nostril until it is to be removed. In such embodiments, the resilient, springy or self-expanding portion of the structural element may function as the positioning portion of the delivery device.

FIGS. 5 through 7 depict a further spring-like structural element which may be placed between the nasal conchae and which may expand slightly to secure it in place. FIG. 5 depicts structural element 150. Structural element 150 includes end regions 152, curved portion 154, inner surface 156 and outer surface 158. Structural element 150 may also include a delivery portion and control signal generation circuitry (not shown). Structural element 150 may be compressed by pressing together end regions 152. As shown in FIG. 6, structural element 150 may be inserted between two nasal conchae 36, and allowed to expand to hold it in place. The position of structural element 150 relative to nostrils 18, nasal septum 40, and nasal conchae 36, can be seen in both FIG. 6 and FIG. 7.

The self-expanding structure may permit the structural element to be placed within a nasal region (e.g., a nostril, or a portion of a nasal cavity) while in a first, contracted, state and then transformed into a second, expanded, state of a nature such that the structural element contacts opposing interior walls of a portion of the nasal region in order to satisfactorily position and mount the structural element at least temporarily within the nasal region.

In some embodiments, as depicted in FIGS. 8 and 9, a structural element 160 may include a clip structure 162, at least a portion of which is configured to extend outside the nasal region of the subject. In FIG. 8, clip structure 162 clamps onto nasal septum 40, with a portion projecting into a first nostril 18a, with structural element 160 residing within second nostril 18b. Construction of clip structures of this general type may be as described, for example, in U.S. Pat. No. 5,947,119, which is incorporated herein by reference. In the embodiment shown in FIG. 8, a single structural element 160 is shown. In other embodiments (not shown), a clip structure may have associated with it two or more structural elements, with one residing in each nostril. In still other embodiments, two or more structural elements may reside in an individual nostril, or in both nostrils. FIG. 9 is a side view of structural element 160 with clip structure 162.

In some embodiments, a controllable release nasal system may be configured to reside entirely within the nasal region of the subject. In other embodiments of a controllable release nasal system, a first portion of the controllable release nasal system may be configured to reside within the nasal region of the subject and a second portion of the controllable release nasal system may be configured to reside external to the nasal region of the subject. The second portion may be simply structural, like the extra-nasal portion depicted in FIG. 8. However, in some embodiments, the second portion of the controllable release nasal system may include components such as the control signal generation circuitry or a source of the material delivered by the device (or a component thereof).

FIGS. 10 and 11 depict an embodiment of a structural element 180 in which the positioning portion may include an adhesive 182. As shown in the front sectional view of FIG. 10, structural element 180 is located in nasal cavity 20 and positioned against nasal septum 40 with a layer of adhesive 182. The side sectional view of FIG. 11 illustrates the position of structural element 180 within nasal cavity 20. In other embodiments, the positioning portion may include a remotely guidable section and/or a means for facilitating extraction when it is desired to remove the structural element or device from the nasal region. In some embodiments, the positioning portion may include other structures for mounting or positioning the structural element within at least a part of a nasal

region. The positioning portion may include one or more barb-like structures (e.g., as depicted in FIG. 21), at least one vacuum-generating device capable of mounting the structural element within a nasal region by producing sufficient vacuum (or suction) to cause the structural element to stick to at least a portion of the nasal region, or at least one hair-engaging structure (which may be, for example, a clip, clasp, grip or coil-like structure capable of reversibly engaging one or more hairs within the nasal region to mount the structural element within the nasal region).

In the various embodiments disclosed herein, the positioning portion may be used to mount the structural element of the delivery device within a nasal region for a use period that may be brief (e.g. on the order of minutes) or extended (weeks, months, or longer). Following placement of the structural element in the desired location for use, which may be done manually or with the use of an insertion device, the delivery device may be held in place without further intervention. The positioning portion may include any fastening structure or mechanism that is capable of mounting (securing, retaining and/or supporting) the structural element within the nasal region for the duration of its use without the need for the person using the device (or another party) to hold or otherwise maintain the structural element in place.

As shown variously in FIGS. 1 through 11, in some embodiments, at least a part of the structural element may be configured for mounting within a nostril of the subject, and in some embodiments at least a part of the structural element may be configured for mounting within a nasal cavity of the subject.

FIGS. 12 through 15 depict a number of possible configurations for structural elements of delivery devices for use in body lumens. Structural elements may have the form of a short cylinder 250, as shown in FIG. 12; an annulus 252, as shown in FIG. 13; a cylinder 254, as shown in FIG. 14; or a spiral 256, as shown in FIG. 15. Elongated forms such as cylinder 254 or spiral 256 may be suitable for use in generally tubular portions of lumen-containing structures such as the nostrils, possibly with a significant taper over their length (not shown in FIGS. 14-15). Structural elements may be formed from various materials, including metals, polymers, fabrics, and various composite materials, including ones of either inorganic or organic character, the latter including materials of both biologic and abiologic origin, selected to provide suitable biocompatibility and mechanical properties.

As shown in FIGS. 16-18, the basic form of a structural element may be subject to different variations, e.g., by perforations, as shown in structural element 260 in FIG. 16; a mesh structure, as shown in structural element 262 in FIG. 16; or the inclusion of one or more slots 264 in structural element 266 in FIG. 18. Slot 264 runs along the entire length of structural element 266; in other embodiments, one or more slots (or mesh or perforations) may be present in only a portion of the structural element. By using spiral, mesh, or slotted structural elements (as in FIGS. 15, 17, and 18) formed from resilient, elastic, springy or self-expanding/self-contracting materials or substrates, suitable structural elements may be formed. Spiral, mesh, or slotted elements need not be elongated tubular structures as depicted in FIGS. 15, 17, and 18, but may be shorter, generally ring-like structures similar in profile to the structural element shown in FIGS. 1 through 3, which is essentially a spring having only a single loop.

A self-expanding or contracting structural element may facilitate positioning or secure emplacement of the structural element within a body lumen of an organism, such as a nasal structure. In some embodiments, flexible material having

adjustable diameter, taper, and length properties may be used. For example, some materials may change from a longer, narrower configuration 270 as shown in FIG. 19A, to a shorter, wider configuration 272 as shown in FIG. 19B, or may taper over their length. Structural elements that may exhibit this type of expansion/contraction property may include mesh structures formed of various metals or plastics, and some polymeric materials, for example.

The exemplary embodiments depicted in FIGS. 1-4 and 12-19B either are substantially cylindrical, and hollow and tubular in configuration, or ring-like, with a single central opening. Thus, the exterior of the cylindrical or ring-like structural element may contact and engage the wall of the body lumen, and the interior of the structural element (within the single central opening) may form a fluid-contacting portion of the structural element. Structural elements are not limited to cylindrical or ring-like structural elements having a single central opening, however.

FIGS. 20 through 25 depict a variety of cross-sectional configurations for structural elements of delivery devices. Note that the illustrated cross-sectional configurations are suitable to be fit into a lumen having a roughly circular cross-section, as would be the case, for example, with a nostril viewed from above or below. Analogous structures may be designed to fit within lumens having non-circular cross-sections. In FIG. 20, a delivery device 300 is positioned in lumen 302 of lumen-containing structure 304. In this embodiment, fluid-contacting portion 306 may be the surface of structural element 300 that faces lumen 302, while the lumen-wall engaging portion 308 may be a layer of tissue adhesive on surface 310 of structural element 300. An example of a device having a cross-section similar to that shown in FIG. 20, is the embodiment shown in FIGS. 10 and 11.

FIG. 21 depicts in cross-section a further embodiment of a structural element 350 in lumen 352 of lumen-containing structure 354. Structural element 350 includes multiple openings 356, each of which includes an interior surface 358 that forms a fluid-contacting portion. Structural element 350 may include one or more barb-like structures 360 that serve as lumen-wall engaging portions that maintain structural element 350 in position with respect to lumen-containing structure 354. Barb like structures may be fixed in some embodiments, or retractable or moveable in other embodiments.

FIG. 22 depicts in cross-section an embodiment of a structural element 400 in lumen 402 of lumen-containing structure 404. Structural element 400 includes a large central opening 406 and multiple surrounding openings 408. The interior surface of each opening 406 or 408 serves as a fluid-contacting portion, while projections 410 function as lumen-wall engaging portions, which may engage frictionally or may project slightly into the interior of the wall of lumen-containing structure 404.

FIG. 23 depicts a further embodiment in which structural element 450 has a substantially oval cross-section and includes a slot 452. Lumen-containing structure 454 may be generally oval in cross section, or may be flexible enough to be deformed to the shape of structural element 450. Structural element 450 may be a compressed spring-like structure that produces outward forces as indicated by the black arrows, so that end portions 456 of structural element 450 thus press against and engage the lumen wall. Interior surface 458 of structural element 450 serves as the fluid-contacting portion of structural element 450.

FIG. 24 is a cross-sectional view of a structural element 500 in a lumen-containing structure 502. Structural element 500 includes multiple projecting arms 504 which contact lumen wall 506 of lumen-containing structure 502, and func-

tion as lumen-wall engaging portions. Inner surfaces 508 of arms 504 function as fluid-contacting portions of structural element 500.

FIG. 25 depicts (in cross-section) another example of a structural element 550 positioned within a lumen-containing structure 552. Structural element 550 includes two openings 554. The interior surfaces 556 of openings 554 function as fluid-contacting portions, while the outer surface 558 of structural element 550 serves as a lumen-wall engaging portion.

The structural elements depicted in FIGS. 1-25 are intended to serve as examples, and are in no way limiting. The choice of structural element size and configuration appropriate for a particular body lumen may be selected by a person of skill in the art. Structural elements may be constructed by a variety of manufacturing methods, from a variety of materials. Appropriate materials may include metals, ceramics, polymers, and composite materials having suitable biocompatibility, sterilizability, mechanical, and physical properties, as will be known to those of skill in the art. Examples of materials and selection criteria are described, for example, in *The Biomedical Engineering Handbook*, Second Edition, Volume I, J. D. Bronzino, Ed., Copyright 2000, CRC Press LLC, pp. IV-1-43-31. Manufacturing techniques may include injection molding, extrusion, die-cutting, rapid-prototyping, or self-assembly, for example, and will depend on the choice of material and device size and configuration. Sensing and active portions of the delivery device as well as associated electrical circuitry may be fabricated on the structural element using various microfabrication and/or MEMS techniques, or may be constructed separately and subsequently assembled to the structural element, as one or more distinct components.

In a controllable release nasal device or system, a fluid contacting portion typically contacts inspired or expired air/gases moving through the nasal region, while a lumen wall engaging portion may contact the tissue lining the wall of the nostril or the nasal cavity. In some embodiments, the lumen wall-engaging portion may closely contact the nasal mucosa, and/or may be in proximity to capillary beds in the nasal mucosa. In some embodiments of a controllable release nasal device or system, a lumen wall engaging portion may be in proximity to neural tissue in the olfactory region. Contact with or proximity to mucosa, capillaries, and/or neural tissue by the lumen wall engaging portion of a controllable release nasal device or system may facilitate the release or transfer of material to some or all of these tissues by a delivery portion located on the lumen wall engaging portion, or the sensing of various parameters regarding or pertinent to these tissues by a sensing portion. Similarly, contact or proximity of a fluid-contacting portion of a controllable release nasal device or system to a fluid mixture (i.e., gases, fine particles, liquid droplets, etc.) within the nostrils or nasal cavity may facilitate the release of materials into the fluid mixture by a delivery portion located on the fluid-contacting portion, or the sensing of various parameters pertinent to the fluid mixture by a sensing function.

The delivery portion may be configured to release the at least one material directly into the nasal mucosa for absorption in some embodiment, as illustrated in FIG. 26. Structural element 600, which is similar to that depicted in FIGS. 10 and 11, may be positioned against nasal mucosa 602 on the surface of nasal septum 40, so that delivery portion 604 is positioned adjacent to nasal mucosa 602. Material 606 released from delivery portion 604 may then be absorbed into nasal mucosa 602. Control signal generation circuitry 608 on structural element 600 may generate a control signal that stimu-

lates release of material **606** from delivery portion **604**. In some such embodiments, the delivery portion may include a permeation enhancer (that may be released in association with the material being delivered, for example) that is capable of increasing the permeation of the at least one material into the nasal mucosa. Permeation enhancers may include chemical permeation enhancers such as isopropyl myristate, bile salts, surfactants, fatty acids and derivatives, chelators, cyclodextrins or chitosan, as described in Murthy, S. N. Hiremath, S. R. R. "Physical and Chemical Permeation Enhancers in Transdermal Delivery of Terbutaline Sulphate," AAPS PharmSciTech., 2001, 2(1) or Senel, S. Hincal, A. A. "Drug permeation enhancement via buccal route: possibilities and limitations," J. Control Release, 2001 May 14, 72(1-3):133-44, both of which are incorporated herein by reference. Permeation may also be enhanced by including a magnetic component, as described in Murthy, S. N., Hiremath, S. R. R. "Physical and Chemical Permeation Enhancers in Transdermal Delivery of Terbutaline Sulphate," AAPS PharmSciTech., 2001, 2(1), or by the use of microprotrusions of the type described in U.S. Pat. No. 6,953,589, or other microneedles or microfine lances. The foregoing references are incorporated herein by reference. Other technologies that may be used for enhancing permeability of materials include, but are not limited to, iontophoresis, microdialysis, ultrafiltration, electromagnetic, osmotic, electroosmosis, sonophoresis, microdialysis, suction, electroporation, thermal poration, microporation, microfine cannulas, skin permeabilization, or a laser.

As illustrated in FIG. 27, in other embodiments, the delivery portion may be configured to release the at least one material into the nasal cavity in the form of a spray or similar aero-suspension of finely dispersed particles, powders or droplets. In FIG. 27, delivery device **620** includes structural element **622** similar to structural element **160** in FIGS. 8 and 9. Delivery portion **624** of delivery device **620** is configured to direct the release of the at least one material **626** toward the nasal mucosa, e.g. in the interior of nasal cavity **20**. In other embodiments, as shown in FIG. 28, delivery device **650** may include delivery portion **652** configured to direct the release of the at least one material **654** toward the olfactory portion **656** of the nasal mucosa. In still other embodiments, as shown in FIG. 29, a delivery device **670** may include a delivery portion **672** configured to direct the release of the at least one material **674** toward the nasopharynx **22**. Material directed toward nasopharynx may subsequently be inhaled into the other portions of the respiratory tract, including the lungs, of the person in which delivery device **670** is emplaced, and it may be configured for preferential delivery to or deposition onto one or more surfaces of particular portions thereof.

In other embodiments, the active portion of a delivery device may include a material release structure operatively coupled to the response initiation circuitry and configured to release a material in response to detection of a condition of interest. A condition of interest may be detected by a sensor, which may be located in or on the release delivery device.

FIG. 30 depicts a delivery device **700** including a structural element **702**, sensor **704**, control signal generation circuitry **706**, and release structure **708** including release mechanism **710**. Structural element **702** includes external surface **712**, configured to fit within a body lumen, and internal surface **714** defining central opening **716**, through which a fluid may flow. Upon sensing of a condition of interest in the fluid by sensor **704**, control signal generation circuitry **706** may cause release of material from material release structure **708** by activating release mechanism **710**. Release mechanism **710** may include a variety of different types of release mecha-

nisms, including, for example a controllable valve as depicted in FIG.30. Various types of valves and microvalves are known to those of skill in the art, and may be used to regulate the release of material from material release structure **708** in response to a control signal from control signal generation circuitry **706**. Control signal generation circuitry **706** may activate release mechanism **710** by supplying a delivery control signal, which may be an electrical signal, for example. In some embodiments, other types of delivery control signals, including magnetic signals, optical signals, acoustic signals, or other types of signals may be used. Combinations of several types of signals may be used in some embodiments. In some embodiments, control signal generation circuitry **706** may cause release of material from material release structure in response to passage of a certain amount of time, as monitored, for example, by a timekeeping device. In some embodiments, material release structure **708** may include a pressurized reservoir of material. In still other embodiments, the material (or materials) to be released may be generated within the material release structure. In other embodiments, the material(s) may diffuse away from the release structure along a concentration gradient.

In some embodiments, the system may include an extension connected to the structural element, wherein the structural element is mounted with a first portion of the nasal region of the subject, and wherein the extension extends from the structural element to a second portion of the nasal region to deliver the at least one material to the second portion of the nasal region. FIG. 31 illustrates an embodiment of a delivery device including a structural element **720** mounted in a nostril **18** of a person **11** by means of clip **722**. Structural element **720** also includes extension **724** that project toward a more internal portion of the nasal region, which in this example is olfactory mucosa **38**, where it releases material from end portion **726**. End portion **726** may be the opening of a tubular structure connected to a material source in structural element **720**, or end portion **726** may be a release location for a material source located at end portion **726**. Other embodiments of delivery devices may include extensions configured to deliver material(s) to other portions of the nasal region, while the main part of the delivery device resides in a relatively accessible location, for example, the nostril.

FIG. 32 illustrates, in cross sectional view, a structural element **750** of a delivery device positioned in a lumen-containing structure **752**. A reservoir **754** contains stored deliverable material. Barrier **756** is a controllable barrier that controls the release of the stored deliverable material into central opening **758**, and thus into a fluid that fills and/or flows through lumen-containing structure **752**. Various types of barriers may be used to control the release of material from the delivery portion of the controllable release nasal system. For example, the delivery portion may include a rupturable barrier, a barrier having a controllable permeability, a stimulus-responsive gel or polymer, or a pressurized fluid source.

FIG. 33 illustrates an embodiment including a structural element **800** of a delivery device positioned in a lumen-containing structure **802**. Two reservoirs **804** contain stored deliverable material(s). Each reservoir **804** includes a controllable barrier **806** that controls release of the at least one stored deliverable material. In the embodiment of FIG. 33, activation of barrier **806** causes release of the at least one stored deliverable material toward the lumen wall of lumen-containing structure **802**, rather than into central opening **808**. FIG. 33 also illustrates that delivery devices may include more than one reservoir.

FIGS. 34A, 34B, 35A, 35B, 36A and 36B, illustrate several alternative embodiments of material release structures that

include controllable barriers. In FIGS. 34A and 34B, release structure 850 includes reservoir 852 containing stored deliverable material 854. As shown in FIG. 34A, while rupturable barrier 856 is intact, stored deliverable material 854 is contained within reservoir 852. As shown in FIG. 34B, when rupturable barrier 856 has been ruptured (as indicated by reference number 856'), deliverable material 854 may be released from reservoir 852. Rupturable barrier 856 may be ruptured by an increase of pressure in reservoir 852 caused by heating, for example, which may be controlled by response initiation circuitry. In another alternative shown in FIGS. 35A and 35B, release structure 900 includes reservoir 902 containing stored deliverable material 904. As shown in FIG. 35A, while degradable barrier 906 is intact, stored deliverable material 904 is contained within reservoir 902. As shown in FIG. 35B, degradation of degradable barrier 906 to degraded form 906' causes stored deliverable material 904 to be released from reservoir 902. FIGS. 36A and 36B depict release structure 950 including reservoir 952 containing stored deliverable material 954. FIG. 36A, shows barrier 956, which has a controllable permeability, in a first, impermeable state, while FIG. 36B shows barrier 956 in a second, permeable state (indicated by reference number 956'). Stored deliverable material 954 passes through barrier 956', when it is in its permeable state, and is released. Rupturable barriers as described above may be formed from a variety of materials, including, but not limited to, metals, polymers, crystalline materials, glasses, ceramics, semiconductors, etc. Release of materials through rupture or degradation of a barrier is also described in U.S. Pat. No. 6,773,429, which is incorporated herein by reference. Semipermeable barriers having variable permeability are described, for example, in U.S. Pat. No. 6,669,683, which is incorporated herein by reference. Those of skill in the art will appreciate that barriers can be formed and operated reversibly through multiple release cycles, in addition to the single-release functionality available from a rupturable barrier.

In some embodiments, a delivery device may include one or more stored deliverable materials dispersed in a carrier material. Stored deliverable material may be released from the carrier material by a release mechanism upon activation of the release mechanism. The released deliverable material may be released into a central opening of a delivery device and/or into the body lumen. FIGS. 37A and 37B depict in greater detail the release of stored deliverable material from the carrier material. In FIG. 37A, deliverable material 1024 is stored in carrier material 1026. Carrier material 1026 may be, for example, a polymeric material such as a hydrogel, and deliverable material is dispersed or dissolved within carrier material 1026. Release mechanism 1028 may be a heating element, for example a resistive element connected directly to response initiation circuitry, or an electrically or magnetically responsive material that may be caused to move, vibrate, heat, by an externally applied electromagnetic field, which in turn causes release of deliverable material 1024 from carrier material 1026, as shown in FIG. 29B. See, for example, U.S. Pat. Nos. 5,019,372 and 5,830,207, which are incorporated herein by reference. In some embodiments, an electrically or magnetically active component may be heatable by an electromagnetic signal, and heating of the electrically or magnetically active component may cause the polymer to undergo a change in configuration. An example of a magnetically responsive polymer is described, for example, in Neto, et al, "Optical, Magnetic and Dielectric Properties of Non-Liquid Crystalline Elastomers Doped with Magnetic Colloids"; Brazilian Journal of Physics; bearing a date of Mar. 2005; pp. 184-189; Volume 35, Number 1, which is incorpo-

rated herein by reference. Other exemplary materials and structures are described in Agarwal et al., "Magnetically-driven temperature-controlled microfluidic actuators"; pp. 1-5; located at: http://www.unl.im.dendai.ac.jp/INSS2004/INSS2004_papers/OralPresentations/C2.pdf or U.S. Pat. No. 6,607,553, each of which is incorporated herein by reference. Other examples of stimulus-responsive gels or polymers are substance-responsive gels or polymers that swell, change shape, etc. in response to a change in pH, glucose, or other substance (as selected by embedded antibodies, for example). Examples of stimulus responsive gels or polymers are described in Langer, R. & Peppas, N., "Advances in Biomaterials, Drug Delivery, and Bionanotechnology," AICHE Journal, December. 2003, Vol. 49, No. 12, pp. 2990-3006, which is incorporated herein by reference.

The controllable release nasal system may include a source of the material located in or on the structural element, as depicted generally in FIGS. 30-36B (e.g., either as a reservoir containing the material as shown in FIGS. 34A-36B, or as a portion of carrier material containing a dispersed or dissolved material, as shown in FIGS. 37A and 37B). Alternatively, a controllable release nasal system may include a source of material located external to the nasal region of the subject and connected to the delivery portion via a delivery tube that enters the nasal region of the subject via a nostril of the subject, as shown in FIG. 38

In FIG. 38, structural element 1050 includes a clip-like structure that fits onto nasal septum 40, with end regions 1052 projecting into at least one nostril 18, which end-regions may include at-least-one sensor (not shown). Material to be delivered may be supplied from supply reservoir 1054 via supply tube 1056. A control device 1058 including control signal generation circuitry 1059 may control the flow of material (e.g., a gas or gaseous mixture, possibly carrying fluid droplets or fine solid particles) from supply reservoir 1054 to supply tube 1056 and thence into nostrils 18. Supply reservoir 1054 may be a tank capable of containing the material in liquid or gaseous form, or it may contain a solid source which releases material upon heating, change in pressure, or a chemical reaction, for example. In some embodiments, a carrier gas or liquid may be stored in supply reservoir 1054, and one or more active component of the material may be added from a secondary source that may be regulated by control device 1058, for example.

FIG. 39 is a detailed cross-sectional view of structural element 1050 of the embodiment shown in FIG. 38. Supply tube 1056 fits over stem portion 1060 of structural element 1050. Channel 1062 in supply tube 1056 aligns with channel 1064 in structural element 1050. Channel 1064 connects to branch channels 1066 and 1068, which lead to openings 1070 and 1072, respectively. Material may be delivered to the one-or-both nostrils via openings 1070 and 1072. Structural element 1050 also includes sensors 1074 and 1076, which are connected to leads 1078 and 1080, respectively. Leads 1078 and 1080 are connected to leads 1082 and 1084, respectively in supply tube 1056 via contacts 1086 and 1088 in structural element 1050 and corresponding contacts 1090 and 1092 in supply tube 1056. Leads 1082 and 1084 connect sensors 1074 and 1076 to control signal generation circuitry (e.g., control signal generation circuitry 1059 as shown in FIG. 38), where they may serve to provide feedback signals which may be used in the determination of a delivery control signal for controlling the delivery of the material. Sensors 1074 and 1076 may be any of various types of sensors, as are known to those of skill in the art, for example, gas sensors, temperature sensors, flow sensors, pressure sensors, moisture sensors, strain sensors, acoustic sensors, chemical-composition or -con-

centration sensors, or other types of sensors as described elsewhere herein. Sensors 1074 and 1076 may be positioned on structural element 1050 in such a manner that they contact the nasal wall or septum, to sense a parameter of the nasal tissue, or they may be positioned on structural element 1050 in such a way that they sense a parameter from a fluid (gas and/or liquid) within the nostril or nasal cavity.

The delivery portion of the controllable release nasal device or system may deliver a material to a nasal region or a portion thereof by diffusion or low-speed dispersion of the material from the delivery portion (e.g., as depicted in FIG. 26) or it may deliver the material in a spray or jet, as depicted in FIGS. 27 through 29. In some embodiments, the system may rely upon fluid (air/liquid) movement or pressure changes associated with breathing activity to move or distribute the delivered material to the intended destination(s). FIG. 26 provides an example of an embodiment that relies upon diffusion or dispersion of the material into tissue. FIGS. 27 through 29 and 38 depict examples of embodiments in which the material may be delivered under pressure. For example, supply reservoir 1054 may be a pressurized tank. In other embodiments, the material may not be stored under pressure, but may have its pressure or speed-of-movement increased at the time of delivery by heating, for example.

FIG. 40 is a schematic diagram of a controllable release nasal system 1100 as described generally herein. Controllable release nasal system 1100 may include some or all of structural element 1102, positioning portion 1104, control signal generation circuitry 1106, delivery portion 1108, material source 1110, and power source 1112, as well as a sensing function (not shown explicitly).

FIG. 41 is a block diagram illustrating in greater detail various circuitry components of a controllable release nasal system. Circuitry components may include electrical circuitry components, or, alternatively or in addition, fluid circuitry, optical circuitry, biological or chemical circuitry, chemo-mechanical circuitry, and/or other types of circuitry in which information is carried, transmitted, and/or manipulated by non-electronic means. The controllable release nasal system may include one or more sensors 1150 for measuring or detecting a condition of interest. Sensing circuitry 1152 may be associated with sensors 1150. The controllable release nasal system may include various control circuitry 1154, including control signal generation circuitry 1156. Control signal generation circuitry 1156 provides a delivery control signal to delivery portion 1158. Delivery portion may receive a material to be delivered from material source 1160. Control circuitry 1154 may also include data storage portion 1162, which may, for example, be used to store pattern data 1164 or pattern parameters 1166. Data storage portion 1162 may also be used to store sense data 1168 and/or sense parameters 1170, which may be derived from a sense signal, e.g. by sensing circuitry 1152. Control electronics may include data transmission/reception circuitry 1172, which provides for the transmission and reception of data and/or power signals between the delivery device and remote circuitry 1174. User interface circuitry 1176 may receive input signals from user input device 1178. User input device 1178 may provide for the input of user instruction, parameter, etc. to control circuitry 1154. Finally, one or more power sources 180 may provide power to circuitry and other components of the controllable release nasal system.

The control signal generation circuitry, and control circuitry in general, may include a microprocessor and/or at least one of hardware, software, and firmware. The control signal generation circuitry may be configured to generate a delivery control signal based upon a pre-determined delivery

pattern, in which case the system may also include a memory location for storing the pre-determined delivery pattern (e.g., pattern data 1164 stored in data storage portion 1162). In some embodiments, the control signal generation circuitry may be configured to calculate a delivery control signal based upon one or more stored parameters. Again, the system may include a memory location for storing the one or more parameters (e.g., pattern parameters 1166 or sense parameters 1170 stored in data storage portion 1162). For example, the control signal generation circuitry may be configured to generate a delivery control signal corresponding to a pattern of delivery of the at least one material expected to produce a therapeutic effect or a sensory effect. In some embodiments, the control signal generation circuitry may be configured to generate a delivery control signal corresponding to a pattern of delivery of the at least one material expected to produce a therapeutic effect tailored specifically to the subject. For example, the control signal generation circuitry may be configured to generate a delivery control signal taking into account parameters such as the size, weight, gender, age, as well as specifics relating to the subject's preferences, medical condition or other parameters.

Circuitry components as discussed in connection with FIG. 41 may be located entirely on the structural element of a delivery device portion of a controllable release nasal system, or may be distributed between the delivery device and a remote portion as depicted in FIG. 42. In FIG. 42, a delivery device 1200 is positioned in nasal region 12 of head 10 of a person 11. Remote portion 1102 may be held by person 11, or otherwise positioned nearby person 11. For example, remote portion 1202 may be carried or attached to a wristband or necklace. Remote portion 1102 may transmit signal 1204 to delivery device 1200. Signal 1204 may be a one- or two-way signal, containing control, data, or power signals. In some embodiments, remote portion 1202 may permit person 11 to provide user input to specify delivery of material to nasal region 12 with delivery device 1200.

Alternatively, in some embodiments, control signal generation circuitry may be located remote from the structural element and associated with a transmitting structure capable of transmitting the delivery control signal to the structural element, and wherein the delivery portion is associated with a receiving structure capable of receiving the delivery control signal. FIG. 43 is a block diagram of a controllable release nasal system including a delivery device 1220 and remote portion 1222. Delivery device 1220 may include various components as depicted in FIG. 41, including (but not limited to) control circuitry 1224, delivery portion 1226, and one or both of a power receiver 1228 and data receiver/transmitter 1230. In some embodiments, data receiver/transmitter 1230 may only receive data signals, while in other embodiments it may only transmit data signals, and in still other embodiments it may both transmit and receive data signals. Power receiver 1228 may receive power signals transmitted from remote portion 1222. Remote portion 1222 may include one or both of power source 1232 and control signal generator 1234. Power transmitter 1236 may be used in connection with power source 1232 in order to transmit power to power receiver 1228 in delivery device 1220. Data transmitter/receiver 1238 may transmit a delivery control signal from control signal generator 1234 to delivery device 1220, or receive sense or parameter data signals transmitted from delivery device 1220 by data receiver/transmitter 1230. In some embodiments of the system, the control signal generation circuitry may be a part of the delivery device, located in or on the structural element.

In some embodiments of delivery devices or systems, a delivery device may be a self-contained device that may be positioned in a body lumen and that includes all functionalities necessary for operation of the device. In other embodiments, as shown in FIGS. 42 and 43, a controllable release nasal system may include a delivery device that may be placed in a nasal region, and a remote portion that includes a portion of the functionalities of the controllable release nasal system. In some embodiments, all functionalities essential for the operation of the delivery device may be located on the delivery device, but certain auxiliary functions may be located in the remote portion. For example, the remote portion may provide for monitoring of the operation of the delivery device or data collection or analysis. The remote portion may be located within the body of the subject at a distance from the delivery device, or outside the body of the subject, as depicted in FIG. 42, either proximate to or distant from it. Data and/or power signals may be transmitted between delivery device and remote portion with the use of electromagnetic or acoustic signals, or, in some embodiments, may be carried over electrical or optical links. In general, the remote portion may be placed in a location where there is more space available than within the body lumen, that is more readily accessible, and so forth. It is contemplated that a portion of the circuitry portion of the controllable release nasal system (which may include hardware, firmware, software, or any combination thereof) may be located in a remote portion. Methods of distributing functionalities of a system between hardware, firmware, and software located at two or more sites are well known to those of skill in the art. The control circuitry portion of the controllable release nasal system may include, but is not limited to, electrical circuitry associated with the sensor, response initiation circuitry, and electronics associated with the active portion.

In various embodiments, the system may include a power source such as a battery. A power source may also be considered to include a power receiver capable of receiving inductively coupled power from an external power source, e.g., as depicted in FIG. 43. Delivery devices and systems according to various embodiments as described herein may include a power source, such as one or more batteries located on the delivery device, possibly a microbattery like those available from Quallion LLC (<http://www.quallion.com>) or designed as a film (U.S. Pat. Nos. 5,338,625 and 5,705,293), which are incorporated herein by reference. Batteries may include primary or secondary batteries, including various types of electrochemical energy storage devices. In some embodiments, the power source may be one or more fuel cell such as an enzymatic, microbial, or photosynthetic fuel cell or other biofuel cell (US20030152823A1; WO03106966A2, and "A Miniature Biofuel cell"; Chen, T. et al., J. Am. Chem. Soc., Vol. 123, pp. 8630-8631, 2001, all of which are incorporated herein by reference), and could be of any size, including the micro- or nano-scale. In some embodiments, the power source may be a nuclear battery. The power source may be any of various mechanical energy storage devices, including but not limited to pressurized bladders or reservoirs, wind-up and spring-loaded devices. The power source may be an energy-scavenging device such as a pressure-rectifying mechanism that utilizes pulsatile changes in blood pressure, for example, or an acceleration-rectifying mechanism as used in self-winding watches; it may derive energy from the cyclic flow of gas through the upper airway. In some embodiments, the power source may be an electrical power source located remote from the structural element and connected to the structural element by a wire, or an optical power source located remote from the structural element and connected to the structural element by

a fiber-optic line or cable. In some embodiments, the power source may be a power receiver capable of receiving power from an external source, acoustic energy from an external source, a power receiver capable of receiving electromagnetic energy (e.g., microwave, infrared or optical electromagnetic energy) from an external source.

The control signal generation circuitry may include at least one of hardware, software, and firmware; in some embodiments the control signal generation circuitry may include a microprocessor or a (programmable) logic array. The control signal generation circuitry may be located in or on the structural element in some embodiments, while in other embodiments the response initiation circuitry may be at a location remote from the structural element.

FIG. 44 depicts a controllable release nasal device 1300 including a sensor 1302 capable of detecting a parameter of interest in the nasal region of the subject. Controllable release nasal device 1300, may include sensor 1302, control signal generation circuitry 1304, and delivery portion 1306. The control signal generation circuitry may be configured to modulate generation of the delivery control signal based upon at least one parameter of interest sensed by the sensor. Controllable release nasal device may be positioned on nasal septum 40, with delivery portion 1306 located against the nasal mucosa 32. Sensor 1302 may sense a parameter from the tissue (for example, a chemical parameter such as a glucose concentration, a heart rate or blood pressure parameter, or a temperature, among others). Control signal generation circuitry 1304 may generate a delivery control signal based upon a sense signal received from sensor 1302. The delivery control signal may be provided to delivery portion 1306, to drive delivery of material 1308.

In the controllable release nasal device depicted in FIG. 44, both sensor 1302 and delivery portion 1306 are positioned adjacent to nasal mucosa 32. FIGS. 45, 46 and 47 depict other possible configurations for sensors and delivery portions of controllable release nasal devices. FIGS. 45 through 47 are cross-sectional views of a controllable release nasal device in a nostril. In FIG. 45, sensor 1350 is positioned on structural element 1352 so as to be positioned adjacent to the nasal mucosa 32 when structural element 1352 is mounted within the nasal region of the subject. Delivery portion 1354 is positioned adjacent lumen 1356 of structural element 1352, away from nasal mucosa 32. Control signal generation circuitry 1358 is also indicated. Alternatively, as shown in FIG. 46, sensor 1350 may be positioned on structural element 1352 so as to be positioned adjacent to lumen 1356 when structural element 1352 is mounted within the nasal region of the subject. In still other embodiments, as illustrated in FIG. 47, both sensor 1350 and delivery portion 1354 may be positioned adjacent to lumen 1356 when structural element 1352 is mounted within the nasal region of the subject.

Sensors used in the various embodiments described herein (e.g., sensors 1074 and 1076 in FIG. 39, sensor 1302 in FIG. 44, or sensor 1350 in FIGS. 45-47) may be of various types, including, for example pressure sensors, temperature sensors, flow sensors, or chemical sensors, for example. Sensors may be used to detect a condition of interest in the fluid (e.g. gas and/or liquid droplets or small solid particles) within a lumen of the nasal cavity (or lumen of a delivery device continuous therewith), or in tissue surrounding the lumen, which may include, for example, detecting pressure, temperature, fluid flow, presence of a cell of interest, or concentration of a chemical or chemical species (including ionic species) of interest. A sensor may sense a wide variety of physical or chemical properties. In some embodiments, detecting a condition of interest may include detecting the presence (or

absence) of a material or structure of interest in the fluid. A sensor may include one or more of an optical sensor, an imaging device, an acoustic sensor, a pressure sensor, a temperature sensor, a flow sensor, a viscosity sensor, or a shear sensor for measuring the effective shear modulus of the fluid at a frequency or strain-rate, a chemical sensor for determining the concentration of a chemical compound or species, a biosensor, or an electrical sensor, for example. An optical sensor may be configured to measure the absorption, emission, fluorescence, or phosphorescence of at least a portion of the fluid, for example. Such optical properties may be inherent optical properties of all or a portion of the fluid, or may be optical properties of materials added or introduced to the fluid, such as tags or markers for materials of interest within the fluid. A biosensor may detect materials including, but not limited to, a biological marker, an antibody, an antigen, a peptide, a polypeptide, a protein, a complex, a nucleic acid, a cell or cell fragment (and, in some cases, a cell of a particular type, e.g. by methods used in flow cytometry), a cellular component, an organelle, a pathogen, a lipid, a lipoprotein, an alcohol, an acid, an ion, an immunomodulator, a sterol, a carbohydrate, a polysaccharide, a glycoprotein, a metal, an electrolyte, a metabolite, an organic compound, an organophosphate, a drug, a therapeutic, a gas, a pollutant, or a tag. A biosensor may include an antibody or other reasonably specific binding molecule such as a receptor or ligand. A sensor may include a single sensor or an array of sensors, and is not limited to a particular number or type of sensors. A sensor might comprise in part or whole, a gas sensor such as an acoustic wave, chemiresistant, or piezoelectric sensor, or perhaps an "electronic nose". A sensor may be very small, comprising a sensor or array that is a chemical sensor ("Chemical Detection with a Single-Walled Carbon Nanotube Capacitor", E. S. Snow, *Science*, Vol. 307, pp. 1942-1945, 2005.), a gas sensor ("Smart single-chip gas sensor microsystem", Hagleitner, C. et al., *Nature*, Vol. 414 pp. 293-296, 2001.), an electronic nose, a nuclear magnetic resonance imager ("Controlled multiple quantum coherences of nuclear spins in a nanometre-scale device", Go Yusa, *Nature*, Vol. 343: pp. 1001-1005, 2005). Further examples of sensors are provided in *The Biomedical Engineering Handbook*, Second Edition, Volume I, J. D. Bronzino, Ed., Copyright 2000, CRC Press LLC, pp. V-1-51-9, and U.S. Pat. No. 6,802,811, both of which are incorporated herein by reference. A sensor may be configured to measure various parameters, including, but not limited to, the electrical resistivity of the fluid, the density or sound speed of the fluid, the pH, the osmolality, or the index of refraction of the fluid at least one wavelength, as well as its temperature, water content and chemical composition. The selection of a suitable sensor for a particular application or use site is considered to be within the capability of a person having skill in the art. In some applications, detecting a condition of interest in the fluid may include detecting the presence of a material of interest in the fluid (gas and/or liquid) within a nasal lumen. A material of interest in a fluid may include, dust particle, a pollen particle, a pathogen, or parasite, or a cell, cellular component, or collection or aggregation of cells or components thereof.

A controllable release nasal device may include an active portion which may perform an action in the nasal cavity in addition to or instead of the material release function performed by the release portion described herein. A release portion is an exemplar of an active portion. A number of active portions are described, for example, in U.S. patent application Ser. No. 11/403,230, entitled "Lumenally Active Device" and filed Apr. 12, 2006, which is incorporated herein by reference above.

In connection with detection of the presence of a material of interest, for example, an active portion of the controllable release nasal system may be capable of removing, modifying, or destroying the material of interest. Modification or destruction of the material of interest may be accomplished by the release of a suitable material (e.g. an endopeptidase for killing bacteria, or an anti-inflammatory, biomimetic, or biologic to bind to and inactivate an inflammatory mediator such as histamine or an immunoglobulin), by the delivery of suitable energy (e.g., acoustic energy, electromagnetic energy such as light to cause a photoreaction, break bonds in molecule, produce heating, etc., or by delivery of heat or cold or other chemo-physical change (e.g. ambient pressure, pH, osmolality, toxic material introduction/generation) for tissue modification or ablation.

FIGS. 48 through 55 illustrate examples of different active portions which may be included in a controllable release nasal device or system. The active portion may include a heating element 1400 as depicted in FIG. 48, operatively coupled to the response initiation circuitry 1401 and configured to produce heating in response to detection of the condition of interest. The heating element may be a resistive element that produces heat when current is passed through it, or it may be a magnetically active material that produces heat upon exposure to an electromagnetic field. Examples of magnetically active materials include permanently magnetizable materials, ferromagnetic materials such as iron, nickel, cobalt, and alloys thereof, ferrimagnetic materials such as magnetite, ferrous materials, ferric materials, diamagnetic materials such as quartz, paramagnetic materials such as silicate or sulfide, and antiferromagnetic materials such as canted antiferromagnetic materials which behave similarly to ferromagnetic materials; examples of electrically active materials include ferroelectrics, piezoelectrics and dielectrics.

Alternatively, the active portion may include a cooling element 1402 as depicted in FIG. 49, operatively coupled to the response initiation circuitry 1403 and configured to produce cooling in response to detection of the condition of interest. Cooling may be produced by a number of mechanisms and/or structures. For example, cooling may be produced by an endothermic reaction (such as the mixing of ammonium nitrate and water) initiated by opening of a valve or actuation of a container in response to a control signal. Other methods and/or mechanisms of producing cooling may include, but are not limited to, thermoelectric (e.g., Peltier Effect) and liquid-gas-vaporization (e.g., Joule-Thomson) devices.

In some embodiments, the active portion may include an electromagnetic radiation source 1404 as depicted in FIG. 50, operatively coupled to the response initiation circuitry 1405 and configured to emit electromagnetic radiation in response to detection of the condition of interest. Electromagnetic radiation sources may include light sources, for example, such as light emitting diodes and laser diodes, or sources of other frequencies of electromagnetic energy or radiation, radio waves, microwaves, ultraviolet energy, infrared energy, optical energy, terahertz radiation, and the like. In some embodiments, the active portion may include an electric field source or a magnetic field source.

As another alternative, the active portion may include an acoustic energy source 1406 (e.g., a piezoelectric crystal) as depicted in FIG. 51, operatively coupled to the response initiation circuitry 1407 and configured to emit acoustic energy in response to detection of the condition of interest. The active portion may include a pressure source operatively coupled to the response initiation circuitry and configured to apply pres-

sure to a portion of the body lumen in response to detection of the condition of interest. Pressure sources may include materials that expand through absorption of water, or expand or contract due to generation or consumption of gas or conformation change produced by chemical reactions or temperature changes, electrically-engendered Maxwell stresses, osmotic stress-generators, etc. FIG. 52 depicts a negative pressure source 1450 capable of applying negative pressure (in this example, substantially radially-inward force) to lumen walls 1451, while FIG. 53 depicts a positive pressure (expanding or expansion) source 1452, capable of applying positive pressure (in this example, a substantially radially-outward force) to lumen walls 1451.

Alternatively, or in addition, in some embodiments the active portion may include a capture portion operatively coupled to the response initiation circuitry and configured to capture the detected material of interest. FIG. 54 depicts a device 1500 including a fluid capture portion 1506. Delivery device 1500 includes sensor 1502, response initiation circuitry 1504, and fluid capture portion 1506. Fluid enters fluid capture portion 1506 via inlet 1508. Fluid capture portion 1506 may be a reservoir, for example, into which fluid is drawn by capillary action. Alternatively, fluid may be pumped into capture portion 1506. Captured fluid may be treated and released, or simply stored. In some applications, stored fluid may be subjected to analysis.

FIG. 55 depicts delivery device 1550 including a sample collection structure 1552 capable of collecting a solid sample 1554. In the example depicted in FIG. 55, solid sample 1554 is a solid material found upon or immediately under the surface of the lumen-defining wall 1556 (a nasal polyp or inflamed tissue biopsy sample, for example). Solid sample 1554 placed in storage reservoir 1558 by sample collection structure 1552. In a related alternative embodiment, a delivery device may include a filter or selective binding region to remove materials from fluid moving past or through the delivery device.

FIG. 56 is a flow diagram of a method of delivering a material to the nasal region of a subject. As indicated at 1602, the method may include the step of releasing at least one material from a delivery portion of a delivery device mounted within a nasal region of a subject in response to a delivery control signal corresponding to a desired release pattern.

The method may include including transmitting information relating to the operation of the delivery device to a remote location, which may include, for example, information relating to the delivery of material by the delivery device. The method may include transmitting information relating to one or more sensed values of the parameter of interest to a remote location.

As shown in FIG. 57, in addition to releasing at least one material from a delivery portion of a delivery device mounted within a nasal region of a subject in response to a delivery control signal corresponding to a desired release pattern at 1654, the method may include the additional steps of sensing at least one parameter of interest in the nasal region with a sensor in the delivery device at 1652, and controlling the release of the at least one material based upon the value of the at least one parameter of interest at 1656. The method may include sensing the at least one parameter of interest from tissue in the nasal region, as shown at 1660, sensing the at least one parameter of interest from blood in the nasal region, as shown at 1662, or sensing the at least one parameter of interest from a gas or gaseous mixture within a nasal cavity or nostril, as shown at 1664.

As shown in FIG. 58, other method steps may include a number of alternative method steps for generating a delivery

control signal. As shown at step 1702, the method may include generating the delivery control signal with a control signal generation circuitry in a remote device and transmitting the delivery control signal to the delivery device. Alternatively, as shown at step 1704, the method may include generating the delivery control signal with control signal generation circuitry in the delivery device, or generating the delivery control signal with control signal generation circuitry located at least in part at a location remote from the delivery portion of the delivery device, shown at step 1706. Any of steps 1702 through 1706 may be followed by a step of releasing at least one material from a delivery portion of a delivery device mounted within a nasal region of a subject in response to a delivery control signal corresponding to a desired release pattern, as indicated at step 1708.

As shown in FIG. 59, the method may include the steps of sensing at least one parameter of interest in the nasal region with a sensor in the delivery device at 1752, storing a record of at least one sensed value of the at least one parameter of interest at 1754, and releasing at least one material from a delivery portion of a delivery device mounted within a nasal region of a subject in response to a delivery control signal corresponding to a desired release pattern at 1756, including controlling the release of the at least one material based upon the value of the at least one parameter of interest at 1758.

Some embodiments of the method may include generating a delivery control signal at least in part as a function of the individual identity of the subject.

As shown in FIG. 60, the method may include receiving the at least one material from at least one source located remote from the delivery portion of the delivery device at step 1802, and releasing at least one material from a delivery portion of a delivery device mounted within a nasal region of a subject in response to a delivery control signal corresponding to a desired release pattern at 1804.

As shown in FIG. 61, releasing at least one material from a delivery portion of a delivery device mounted within a nasal region of a subject in response to a delivery control signal corresponding to a desired release pattern at 1852 may include releasing at least one material including a systemically active material, as indicated at 1854, releasing at least one material include a material having local activity in the nasal region, nasopharynx, or pulmonary region, as indicated at 1856 releasing at least one material including an odorant, an aroma, an olfactory modulator or a scented material, as indicated at 1858, or releasing at least one material including one or more neurotransmitters or neurotransmitter inhibitors, as indicated at 1860.

In some embodiments, as shown in FIG. 62, the method may include calculating the delivery control signal based upon one or more stored parameters, at 1902, and releasing at least one material from a delivery portion of a delivery device mounted within a nasal region of a subject in response to the delivery control signal corresponding to a desired release pattern at 1904.

In an embodiment as shown in FIG. 63, in addition to the steps of calculating the delivery control signal based upon one or more stored parameters, at 1906, and releasing at least one material from a delivery portion of a delivery device mounted within a nasal region of a subject in response to a delivery control signal corresponding to a desired release pattern at 1908, the method may include storing the one or more stored parameters in the delivery device prior to generation of the delivery control signal, as shown at step 1904. The one or more stored parameters may be received from an input device operatively connected to the delivery device, at step 1902. For example, the method may include receiving the one or more

stored parameters from the input device via an optical connection, as shown at **1910**, receiving the one or more stored parameters from the input device via a wired connection, as shown at **1912**, or receiving the one or more stored parameters from the input device via a wireless connection, as shown at **1914**. In other embodiments, the method may instead (or in addition) include calculating the delivery control signal based upon one or more prior values of the delivery control signal.

As shown in FIG. **64**, one embodiment of the method may include generating the delivery control signal from a stored release pattern, at step **1952**, before releasing at least one material from a delivery portion of a delivery device mounted within a nasal region of a subject in response to a delivery control signal corresponding to a desired release pattern at step **1954**. As shown in FIG. **65**, in addition to generating the delivery control signal from a stored release pattern, at step **2006**, and releasing at least one material from a delivery portion of a delivery device mounted within a nasal region of a subject in response to a delivery control signal corresponding to a desired release pattern at step **2008**, the method may include a step of storing the release pattern in the delivery device prior to generation of the delivery control signal, at step **2004**. The method may also include a step of receiving the release pattern from an input device operatively connected to the delivery device, at **2002**, for example, by receiving the release pattern from the input device via an optical connection, as indicated at **2010**, receiving the release pattern from the input device via a wired connection, as indicated at **2012**, or receiving the release pattern from the input device via a wireless connection, as indicated at **2014**.

Methods of using devices and systems as described herein may include not only the use of the device while it is mounted within the nasal region of a subject, but may also include steps of mounting at least a portion of the delivery device within the nasal region of the subject, and optionally, removing at least a portion of the delivery portion of the delivery device from the nasal region of the subject following a use period. It will be appreciated that for short use periods, a method may include mounting at least a portion of the delivery device within the nasal region of the subject prior to releasing the at least one material from the delivery portion of the delivery device and removing at least the delivery portion of the delivery device from the nasal region of the subject following a use period. On the other hand, in applications where the device is mounted in the nasal region of the subject substantially permanently, the device may be mounted in the nasal region, and no steps taken to remove the device. In some cases, the device may be mounted manually, by the subject, or by someone acting on behalf of the subject, for example a medical care provider. In some cases, the emplacement of the device within the nasal region may be performed with the use of an installation device, such as a tool that will hold the device to allow it to be inserted into portions of the nasal region that would otherwise be inaccessible. Local or general anesthetic may be provided in certain cases, as appropriate to provide for the comfort of the subject.

According to various embodiments, a controllable release nasal system may include software for controlling the release of material from a delivery device mounted within a nasal region of a subject. Such software is illustrated in a block diagram in FIG. **66**. The basic components of the controllable release nasal system **2050** may include software **2052**, at least one sensor **2054**, a delivery portion **2056**, and a user input device **2058**. Non-software components are described elsewhere herein. Software **2052** may include a control signal generation module **2060** capable of generating a delivery control signal corresponding to a desired pattern of delivery

of a material into a nasal region of a subject from a delivery portion of the delivery device mounted within the nasal region of the subject, according to a model of the entire system. Software **2052** may include at least one of a data storage module **2062** capable of storing pattern data or pattern parameters representing the desired pattern of delivery of the material into the nasal region of the subject or a sensing module **2064** capable of receiving and processing a sense signal from a sensor portion of the delivery device, wherein the control signal generation module is configured to generate the delivery control signal based upon at least one of the pattern data, pattern parameters or sense signal, generally proceeding according to a model. In another aspect, the software may include both a data storage module **2062** capable of controlling storage of pattern data or pattern parameters representing the desired pattern of delivery of the material into the nasal region of the subject according to a model and a sensing module **2064** capable of receiving and processing a sense signal from a sensor portion **2054** of the delivery device.

Data storage module **2062** may be capable of storing a sense signal received from the sensing module **2064**. The sense signal may be a processed sense signal from the sensor portion **2054** of the delivery device. The software may include a data storage module **2062** configured to store one or more values from the delivery device.

At least a portion of the one or more values may be sense signal values received from the sensing module **2064**. Alternatively, or in addition, at least a portion of the one or more values are sense parameters received from the sensing module **2064**. In some embodiments, at least a portion of the one or more values may be delivery control signal values from the control signal generation module **2060**.

In another aspect, the software may include a user interface module **2066** configured to receive user input of one or more user-enterable parameters from a user interface device. The software may include a user interface module **2066** configured to receive user input of a desired delivery pattern from a user interface device **2058**. In some embodiments, the user interface module may be configured to receive the desired delivery pattern in the form of a digital data transmission.

The software may include a sensing module **2064** capable of receiving and processing a sense signal from a sensor portion **2054** of the delivery device. The sensing module **2064** may be capable of processing the sense signal by various signal processing methods as are known to those of skill in the art, including, but not limited to filtering, windowing, noise reduction, signal averaging, feature detection, time-domain analysis, frequency domain analysis, feature extraction, comparison of the sense signal with, e.g., a template sense signal, sorting, data reduction, or endpoint determination.

In some embodiments, the control signal generation module **2060** may be capable of generating the delivery control signal by calculating the delivery control signal based upon one or more stored parameters. In some embodiments, at least a portion of the stored parameters may be specific to the subject, relating to size, weight, age, gender, medical or health status, and so forth. The control signal generation module **2060** may be capable of generating the delivery control signal from a stored release pattern. The parameters or release pattern may be stored in a data storage location under the control of data storage module **2062**.

Delivery devices and systems as described herein may be operated under the control of software. Certain components of system **2050** may be primarily hardware-based, e.g., sensor portion **2054**, delivery portion **2056**, and, optionally, user interface device **2058**. Hardware-based devices may include components that are electrical, mechanical, chemical, optical,

electromechanical, electrochemical, electro-optical, and are not limited to the specific examples presented herein. Control signal generation module 2060, data storage module 2062, sensing module 2064, and use interface module 2066 may be all or mostly software-based; however, it will be appreciated that various operations may be performed in hardware, software, firmware, or various combinations thereof.

Those having skill in the art will recognize that the state of the art has progressed to the point where there is little distinction left between hardware and software implementations of aspects of systems; the use of hardware or software is generally (but not always, in that in certain contexts the choice between hardware and software can become significant) a design choice representing cost vs. efficiency tradeoffs. Those having skill in the art will appreciate that there are various vehicles by which processes and/or systems and/or other technologies described herein can be effected (e.g., hardware, software, and/or firmware), and that the preferred vehicle will vary with the context in which the processes and/or systems and/or other technologies are deployed. For example, if an implementer determines that speed and accuracy are paramount, the implementer may opt for a mainly hardware and/or firmware vehicle; alternatively, if flexibility is paramount, the implementer may opt for a mainly software implementation; or, yet again alternatively, the implementer may opt for some combination of hardware, software, and/or firmware. Hence, there are several possible vehicles by which the processes and/or devices and/or other technologies described herein may be effected, none of which is inherently superior to the other in that any vehicle to be utilized is a choice dependent upon the context in which the vehicle will be deployed and the specific concerns (e.g., speed, flexibility, or predictability) of the implementer, any of which may vary. Those skilled in the art will recognize that optical aspects of implementations will typically employ optically-oriented hardware, software, and/or firmware.

The foregoing detailed description has set forth various embodiments of the devices and/or processes via the use of block diagrams, flowcharts, and/or examples.

Insofar as such block diagrams, flowcharts, and/or examples contain one or more functions and/or operations, it will be understood by those within the art that each function and/or operation within such block diagrams, flowcharts, or examples can be implemented, individually and/or collectively, by a wide range of hardware, software, firmware, or virtually any combination thereof. In one embodiment, several portions of the subject matter described herein may be implemented via Application Specific Integrated Circuits (ASICs), Field Programmable Gate Arrays (FPGAs), digital signal processors (DSPs), or other integrated formats. However, those skilled in the art will recognize that some aspects of the embodiments disclosed herein, in whole or in part, can be equivalently implemented in integrated circuits, as one or more computer programs running on one or more computers (e.g., as one or more programs running on one or more computer systems), as one or more programs running on one or more processors (e.g., as one or more programs running on one or more microprocessors), as firmware, or as virtually any combination thereof, and that designing the circuitry and/or writing the code for the software and/or firmware would be well within the skill of one of skill in the art in light of this disclosure. In addition, those skilled in the art will appreciate that the mechanisms of the subject matter described herein are capable of being distributed as a program product in a variety of forms, and that an illustrative embodiment of the subject matter described herein applies regardless of the particular type of signal bearing medium used to actually carry

out the distribution. Examples of a signal bearing medium include, but are not limited to, the following: a recordable type medium such as a floppy disk, a hard disk drive, a Compact Disc (CD), a Digital Video Disk (DVD), a digital tape, a computer memory, etc.; and a transmission type medium such as a digital and/or an analog communication medium (e.g., a fiber optic cable, a waveguide, a wired communications link, a wireless communication link, etc.).

In a general sense, those skilled in the art will recognize that the various embodiments described herein can be implemented, individually and/or collectively, by various types of electromechanical systems having a wide range of electrical components such as hardware, software, firmware, or virtually any combination thereof; and a wide range of components that may impart mechanical force or motion such as rigid bodies, spring or torsional bodies, hydraulics, and electro-magnetically actuated devices, or virtually any combination thereof. Consequently, as used herein "electromechanical system" includes, but is not limited to, electrical circuitry operably coupled with a transducer (e.g., an actuator, a motor, a piezoelectric crystal, etc.), electrical circuitry having at least one discrete electrical circuit, electrical circuitry having at least one integrated circuit, electrical circuitry having at least one application specific integrated circuit, electrical circuitry forming a general purpose computing device configured by a computer program (e.g., a general purpose computer configured by a computer program which at least partially carries out processes and/or devices described herein, or a microprocessor configured by a computer program which at least partially carries out processes and/or devices described herein), electrical circuitry forming a memory device (e.g., forms of random access memory), electrical circuitry forming a communications device (e.g., a modem, communications switch, or optical-electrical equipment), and any non-electrical analog thereto, such as optical or other analogs. Those skilled in the art will recognize that electromechanical as used herein is not necessarily limited to a system that has both electrical and mechanical actuation except as context may dictate otherwise. Non-electrical analogs of electrical circuitry may include fluid circuitry, electromechanical circuitry, mechanical circuitry, and various combinations thereof.

In a general sense, those skilled in the art will recognize that the various aspects described herein which can be implemented, individually and/or collectively, by a wide range of hardware, software, firmware, or any combination thereof can be viewed as being composed of various types of "electrical circuitry." Consequently, as used herein "electrical circuitry" includes, but is not limited to, electrical circuitry having at least one discrete electrical circuit, electrical circuitry having at least one integrated circuit, electrical circuitry having at least one application specific integrated circuit, electrical circuitry forming a general purpose computing device configured by a computer program (e.g., a general purpose computer configured by a computer program which at least partially carries out processes and/or devices described herein, or a microprocessor configured by a computer program which at least partially carries out processes and/or devices described herein), electrical circuitry forming a memory device (e.g., forms of random access memory), and/or electrical circuitry forming a communications device (e.g., a modem, communications switch, or optical-electrical equipment). Those having skill in the art will recognize that the subject matter described herein may be implemented in an analog or digital fashion or some combination thereof.

One skilled in the art will recognize that the herein described components (e.g., steps), devices, and objects and the discussion accompanying them are used as examples for

the sake of conceptual clarity and that various configuration modifications are within the skill of those in the art. Consequently, as used herein, the specific exemplars set forth and the accompanying discussion are intended to be representative of their more general classes. In general, use of any specific exemplar herein is also intended to be representative of its class, and the non-inclusion of such specific components (e.g., steps), devices, and objects herein should not be taken as indicating that limitation is desired.

With respect to the use of substantially any plural and/or singular terms herein, those having skill in the art can translate from the plural to the singular and/or from the singular to the plural as is appropriate to the context and/or application. The various singular/plural permutations are not expressly set forth herein for sake of clarity.

The herein described subject matter sometimes illustrates different components contained within, or connected with, different other components. It is to be understood that such depicted architectures are merely exemplary, and that in fact many other architectures can be implemented which achieve the same functionality. In a conceptual sense, any arrangement of components to achieve the same functionality is effectively "associated" such that the desired functionality is achieved. Hence, any two components herein combined to achieve a particular functionality can be seen as "associated with" each other such that the desired functionality is achieved, irrespective of architectures or intermedial components. Likewise, any two components so associated can also be viewed as being "operably connected", or "operably coupled", to each other to achieve the desired functionality, and any two components capable of being so associated can also be viewed as being "operably couplable", to each other to achieve the desired functionality. Specific examples of operably couplable include but are not limited to physically mateable and/or physically interacting components and/or wirelessly interactable and/or wirelessly interacting components and/or logically interacting and/or logically interactable components.

While particular aspects of the present subject matter described herein have been shown and described, it will be apparent to those skilled in the art that, based upon the teachings herein, changes and modifications may be made without departing from the subject matter described herein and its broader aspects and, therefore, the appended claims are to encompass within their scope all such changes and modifications as are within the true spirit and scope of the subject matter described herein. Furthermore, it is to be understood that the invention is defined by the appended claims. It will be understood by those within the art that, in general, terms used herein, and especially in the appended claims (e.g., bodies of the appended claims) are generally intended as "open" terms (e.g., the term "including" should be interpreted as "including but not limited to," the term "having" should be interpreted as "having at least," the term "includes" should be interpreted as "includes but is not limited to," etc.). It will be further understood by those within the art that if a specific number of an introduced claim recitation is intended, such an intent will be explicitly recited in the claim, and in the absence of such recitation no such intent is present. For example, as an aid to understanding, the following appended claims may contain usage of the introductory phrases "at least one" and "one or more" to introduce claim recitations. However, the use of such phrases should not be construed to imply that the introduction of a claim recitation by the indefinite articles "a" or "an" limits any particular claim containing such introduced claim recitation to inventions containing only one such recitation, even when the same claim includes the introductory

phrases "one or more" or "at least one" and indefinite articles such as "a" or "an" (e.g., "a" and/or "an" should typically be interpreted to mean "at least one" or "one or more"); the same holds true for the use of definite articles used to introduce claim recitations. In addition, even if a specific number of an introduced claim recitation is explicitly recited, those skilled in the art will recognize that such recitation should typically be interpreted to mean at least the recited number (e.g., the bare recitation of "two recitations," without other modifiers, typically means at least two recitations, or two or more recitations). Furthermore, in those instances where a convention analogous to "at least one of A, B, and C, etc." is used, in general such a construction is intended in the sense one having skill in the art would understand the convention (e.g., "a system having at least one of A, B, and C" would include but not be limited to systems that have A alone, B alone, C alone, A and B together, A and C together, B and C together, and/or A, B, and C together, etc.). In those instances where a convention analogous to "at least one of A, B, or C, etc." is used, in general such a construction is intended in the sense one having skill in the art would understand the convention (e.g., "a system having at least one of A, B, or C" would include but not be limited to systems that have A alone, B alone, C alone, A and B together, A and C together, B and C together, and/or A, B, and C together, etc.). It will be further understood by those within the art that virtually any disjunctive word and/or phrase presenting two or more alternative terms, whether in the description, claims, or drawings, should be understood to contemplate the possibilities of including one of the terms, either of the terms, or both terms. For example, the phrase "A or B" will be understood to include the possibilities of "A" or "B" or "A and B."

While various aspects and embodiments have been disclosed herein, other aspects and embodiments will be apparent to those skilled in the art. The various aspects and embodiments disclosed herein are for purposes of illustration and are not intended to be limiting, with the true scope and spirit being indicated by the following claims.

What is claimed is:

1. A controllable release nasal system, comprising:

a structural element including at least one positioning portion to contact an interior surface of a nasal region and to mount the structural element within the nasal region of a subject;

a delivery portion mounted relative to the structural element to release at least one material responsive to a delivery control signal, the delivery portion including a controllable barrier through which the at least one material is released, the controllable barrier including at least one of a rupturable barrier or a barrier having a controllable permeability;

control signal generation circuitry to generate the delivery control signal corresponding to a desired pattern of release of the at least one material into the nasal region; and

a power source for providing power to one or more components of the controllable release nasal system.

2. The system of claim 1, wherein the power source includes at least one of a battery, a microbattery, a power receiver configured for receiving inductively coupled power from an external power source, a fuel cell, a biofuel cell, or a mechanical energy storage structure.

3. The system of claim 1, wherein the control signal generation circuitry is located on the structural element.

4. The system of claim 1, wherein the control signal generation circuitry is located remote from the structural element and is associated with a transmitting structure configured for

transmitting the delivery control signal to the structural element, and wherein the delivery portion is associated with a receiving structure configured for receiving the delivery control signal.

5 5. The system of claim 1, wherein the control signal generation circuitry includes at least one of a microprocessor, hardware, software, or firmware.

6. The system of claim 1, wherein the control signal generation circuitry generates a delivery control signal based upon a pre-determined delivery pattern or calculated from one or more stored parameters.

7. The system of claim 6, including a memory location for storing the pre-determined delivery pattern or the one or more stored parameters.

8. A controllable release nasal system, comprising:

a structural element including at least one positioning portion to contact an interior surface of a nasal region of a subject and to mount the structural element within the nasal region of the subject;

a delivery portion mounted relative to the structural element to release at least one material responsive to a delivery control signal, the delivery portion including a controllable barrier through which the at least one material is released, the controllable barrier including at least one of a rupturable barrier or a barrier having a controllable permeability;

a sensor configured for detecting or measuring a parameter of interest in the nasal region of the subject; and control signal generation circuitry to generate the delivery control signal corresponding to a desired pattern of release of the at least one material into the nasal region.

9. The system of claim 8, wherein the control signal generation circuitry calculates the delivery control signal based at least in part on one or more parameters of interest detected or measured by the sensor.

10. The system of claim 8, wherein the control signal generation circuitry modulates generation of the delivery control signal based upon at least one parameter of interest detected or measured by the sensor.

11. The system of claim 8, wherein the sensor is positioned on the structural element so as to be positioned adjacent to the nasal mucosa when the structural element is mounted within the nasal region of the subject.

12. The system of claim 8, wherein the sensor is positioned on the structural element so as to be positioned adjacent to the lumen of the nasal cavity when the structural element is mounted within the nasal region of the subject.

13. The system of claim 8, wherein the wherein the sensor includes at least one pressure sensor, temperature sensor, moisture sensor, flow sensor, strain sensor, chemical sensor, biosensor, optical sensor, imaging device, or acoustic sensor.

14. A method of delivering a material to the nasal region of a subject, comprising:

sensing at least one parameter of interest in the nasal region of the subject with a sensor in a delivery device mounted within the nasal region;

generating a delivery control signal corresponding to a desired release pattern of at least one material from a delivery portion of the delivery device based upon the value of the parameter of interest; and

releasing the at least one material from the delivery portion of the delivery device, through a controllable barrier

including at least one of a rupturable barrier or a barrier having a controllable permeability, in response to the delivery control signal.

15. The method of claim 14, including transmitting at least one of information relating to the operation of the delivery device, information relating to the delivery of material by the delivery device, or information relating to one or more sensed values of the parameter of interest to a remote location.

16. The method of claim 14, including sensing the at least one parameter of interest from tissue in the nasal region, blood in the nasal region, or a gas or gaseous mixture within a nasal cavity or nostril.

17. The method of claim 14, including generating the delivery control signal with control signal generation circuitry located at least in part at a location remote from the delivery portion of the delivery device.

18. The method of claim 14, including generating the delivery control signal with control signal generation circuitry in the delivery device.

19. The method of claim 14, including storing a record of at least one sensed value of the at least one parameter of interest.

20. The method of claim 14, including calculating the delivery control signal based upon one or more prior values of the delivery control signal, calculating the delivery control signal based upon one or more stored parameters, or generating the delivery control signal from a stored release pattern.

21. The method of claim 20, including storing the one or more stored parameters or the release pattern in the delivery device prior to generation of the delivery control signal.

22. The method of claim 21, including receiving the one or more stored parameters or the release pattern from an input device operatively connected to the delivery device.

23. The method of claim 22, including receiving the one or more stored parameters or the release pattern from the input device via a connection selected from an optical connection, a wired connection, or a wireless connection.

24. A controllable release nasal system, comprising:

a structural element including at least one positioning portion to contact an interior surface of a nasal region and to mount the structural element within the nasal region of a subject;

a delivery portion mounted relative to the structural element to release at least one material responsive to a delivery control signal, the delivery portion including a controllable barrier through which the at least one material is released, the controllable barrier including at least one of a rupturable barrier or a barrier having a controllable permeability;

control signal generation circuitry to generate the delivery control signal corresponding to a desired pattern of release of the at least one material into the nasal region; and

user interface circuitry operably coupled with the control signal generation circuitry to receive a user input via a user input device.

25. The system of claim 1, wherein the controllable barrier includes a rupturable barrier, and wherein the system further includes a heating element configured to increase a pressure of the delivery portion to rupture the rupturable barrier.

UNITED STATES PATENT AND TRADEMARK OFFICE
CERTIFICATE OF CORRECTION

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APPLICATION NO. : 11/485619
DATED : November 3, 2015
INVENTOR(S) : W. Daniel Hillis et al.

Page 1 of 1

It is certified that error appears in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

Claims

Column 31, Lines 34-35, Claim 9 “on one or more parameters of interested detected or measured by the sensor.” should read --on one or more parameters of interest detected or measured by the sensor.--

Column 31, Line 48, Claim 13 “The system of claim 8, wherein the wherein the sensor” should read --The system of claim 8, wherein the sensor--

Signed and Sealed this
Fifth Day of April, 2016



Michelle K. Lee
Director of the United States Patent and Trademark Office

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摘要(译)

描述了用于可控制的鼻腔递送材料的装置和系统的实施例。还公开了使用这种装置的方法以及用于控制这种装置和系统的操作的系统和软件。

