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(71) Applicant: MODERNATX, INC. [US/US]; 200 Technology Square, Cambridge, Massachusetts 02139 (US).

(72) Inventors: QUINN, Michael Vincent; 42 Tiffany Drive, East Hanover, New Jersey 07936 (US). CRONEN-

BERG, Richard A.; 108 Kohout Drive, Mahwah, New Jersey 07430 (US).

(74) Agent: DODENHOFF, Amy K. et al.; Cooley LLP, 1299 Pennsylvania Avenue, NW, Suite 700, Washington, District of Columbia 20004-2400 (US).

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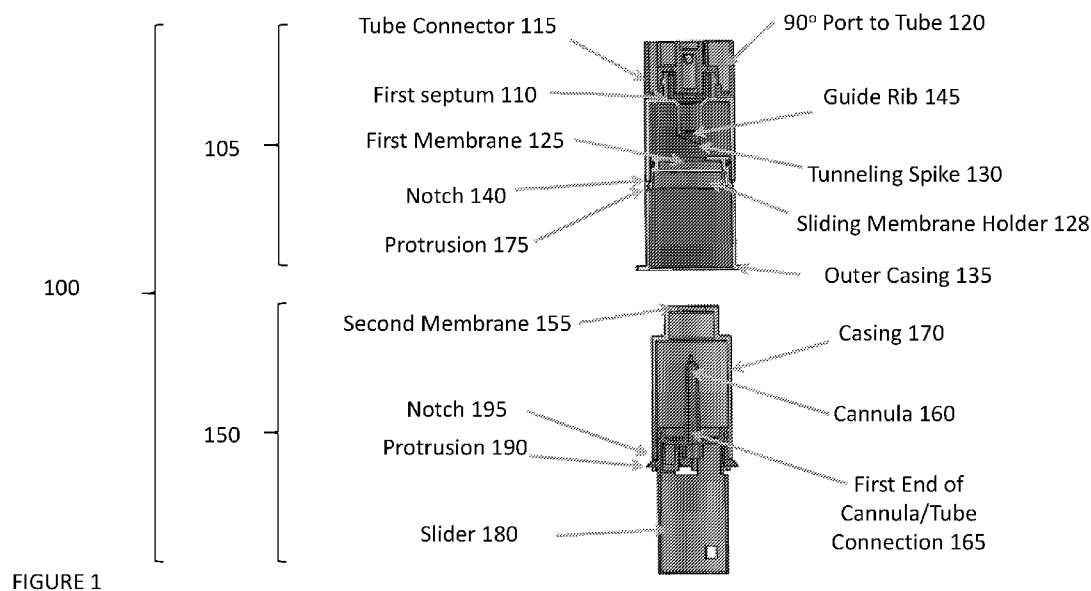


FIGURE 1

(57) Abstract: An aseptic connector comprises a first portion having a first septum and first membrane, a tunneling spike between the first septum and first membrane, and an outer casing around at least the first membrane and the tunneling spike, and a second portion having a second membrane, a cannula, and a casing around the cannula. The second membrane forms at least part of an outer edge of the casing, and the casing comprises at least one first protrusion. The second portion fits within the first portion outer casing, such that when an edge of the outer casing is in contact with the at least one first protrusion of the second portion casing, the first and second membranes are in contact. When pressure is applied, the outer casing moves past the at least one first protrusion, and the tunneling spike punctures at least the first and second membranes to create an opening.

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ASEPTIC CONNECTOR FOR FLUIDIC CONNECTIONS

CROSS-REFERENCE TO RELATED APPLICATIONS

[0001] This application claims benefit of and priority to US Provisional Patent Application No. 62/544,480, filed August 11, 2017, and entitled “Aseptic Connector for Fluidic Connections.” Each of the aforementioned applications is herein expressly incorporated by reference in its entirety.

FIELD OF THE DISCLOSURE

[0002] The present disclosure relates to apparatuses, methods, systems, and assemblies for aseptic connectors which can be used in fluidic connections.

BACKGROUND

[0003] Pharmaceutical/medical machines often are expensive to manufacture and therefore are often used to create treatments for (or treat) many different patients. Nonetheless, cross-contamination between patients may result in catastrophic results, such as death or transferring disease from one patient to the next. As a result, the larger and more expensive portions of a machine may be used to create treatments for (or treat) many patients, while a disposable fluid pathway may be specific to a single patient. This way, any fluids that are circulated through and/or transferred in and out of a patient are maintained within the fluid pathway, while the main machine stays dry. The fluid pathway may include many tubes, which are connected using aseptic connectors. The pathway may also be connected to medicine vials, medicine bags, etc., which are also connected to the pathway via aseptic connectors. Thus, connections throughout the pathway are made from dry-to-dry, wet-to-dry, and dry-to-wet.

[0004] The aseptic connectors currently on the market are only capable of connecting dry-to-dry. This means that there cannot be fluid on either side of the connector in order to ensure that the connection is not contaminated. As a result, the connectors often have valves on both sides or

at least on the wet side of the connector so that the connector does not get wet until the connection is made. In order to make this connection, most of the connectors on the market use a double peel method such that each side of the connector has a piece of laminated paper, plastic, or foil, and once the connector is assembled, the paper, plastic, or foil is removed, thereby opening the flow path. These foils need to be manually pulled out, and therefore the process cannot be automated.

SUMMARY OF SOME OF THE EMBODIMENTS

[0005] Some embodiments of this disclosure present apparatuses, methods, systems, and assemblies for aseptic connectors which can be used in fluidic connections.

[0006] In some embodiments, an aseptic connector assembly is provided. The connector assembly comprises a first portion having a first septum, a second septum, a tunneling spike configured between the first and second septum, and an outer casing configured around at least the second septum and the tunneling spike. The connector also comprises a second portion having a membrane, a cannula, and a casing configured around the cannula. The membrane forms at least part of an outer edge of the casing, and the casing comprises at least one first protrusion. The second portion is configured to fit within the first portion outer casing, such that when an edge of the outer casing is in contact with the at least one first protrusion of the second portion casing, the membrane and the second septum are in contact with one another. The outer casing is configured to move past the at least one first protrusion when pressure is applied, and when said pressure is applied, the tunneling spike punctures at least the second septum and the membrane to create an opening.

[0007] The tip of the tunneling spike may be configured to push the membrane and the second septum away from the opening when the tunneling spike punctures the second septum and the membrane. The first septum may be an elastomeric material, such as rubber. The second septum and the membrane may be an easily frangible sterile barrier, such as foil.

[0008] An interior area of the first portion may be sterile, and an interior area of the second portion may be sterile. In some embodiments, when the tunneling spike punctures the second septum and the membrane to create the opening, the interior area of the tunneling spike, the cannula, and the first septum remain sterile.

[0009] The casing may comprise at least one second protrusion such that when further pressure is applied, the outer casing is configured to move past the at least one second protrusion, and the cannula travels through the opening and the tunneling spike to penetrate the first septum.

[0010] The outer casing may be configured with at least a second protrusion extending towards the interior of the outer casing, such that when further pressure is applied, the inner casing is configured to move past the at least one second protrusion, and the cannula travels through the opening and the tunneling spike to penetrate the first septum.

[0011] In any of the embodiments, the cannula may be sterile.

[0012] The first septum may form a boundary between a liquid container and the connector assembly.

[0013] The cannula may contain two distinct channels. One channel may be connected to a vent line, and the other may be a fluid path. These channels may be concentric, or the channels may be side-by-side.

[0014] In other embodiments, an aseptic connector assembly is disclosed. The assembly comprises a first portion having a first septum, a second septum, and an outer casing configured around at least the second septum and the first septum. The assembly comprises a second portion having a membrane, a tunneling spike, a cannula positioned within the tunneling spike, and a casing configured around the tunneling spike and the cannula, wherein the membrane forms at least part of an outer edge of the casing, and the casing comprises at least one first protrusion. The second portion is configured to fit within the first portion outer casing, such that when an edge of the outer casing is in contact with the at least one first protrusion of the second portion casing, the membrane and the second septum are in contact with one another. The outer casing is configured to move past the at least one first protrusion when pressure is applied, and when said pressure is applied, the tunneling spike punctures at least the second septum and the membrane to create an opening.

BRIEF DESCRIPTION OF SOME OF THE EMBODIMENTS

[0015] **FIGURE 1** is an illustration depicting two sides of a connector, according to some embodiments.

[0016] **FIGURE 2** is an illustration depicting two sides of a connector as they are brought together, according to some embodiments.

[0017] **FIGURE 3** is an illustration depicting a connector in a partly assembled configuration, according to some embodiments.

[0018] **FIGURE 4** is an illustration depicting a connector, such as that of **FIGURES 1-3**, in a fully assembled configuration, according to some embodiments.

[0019] **FIGURES 5A-5D** show various cross-sectional perspective view of the two sides of the connector, according to some embodiments.

[0020] **FIGURES 6A-6C** show various views of the outside of the two sides of the connector, according to some embodiments.

[0021] **FIGURE 7A** is a top view looking down on the first and second sides of the connector, according to some embodiments.

[0022] **FIGURE 7B** is a bottom view looking up at the second and first sides of the connector, according to some embodiments.

[0023] **FIGURE 8** is an illustration depicting two sides of a connector, according to some embodiments.

[0024] **FIGURE 9** is an illustration depicting two sides of a connector as they are brought together, according to some embodiments.

[0025] **FIGURE 10** is an illustration depicting the connector in a partly assembled configuration, according to some embodiments.

[0026] **FIGURE 11** is an illustration depicting a connector, such as that of **FIGURES 8-10**, in a fully assembled configuration, according to some embodiments.

[0027] **FIGURE 12A** is an illustration depicting a perspective view of a connector, according to some embodiments,

[0028] **FIGURE 12B** is an illustration depicting a perspective view of a keying ring, according to some embodiments.

[0029] **FIGURES 13A-C** are illustrations depicting a first side of a connector and a first side keying ring, according to some embodiments.

[0030] **FIGURES 14A-B** are illustrations depicting a first side of a connector and a first side keying ring, according to some embodiments.

[0031] **FIGURES 15A-B** are illustrations depicting a second side of a connector and a second side keying ring, according to some embodiments.

[0032] **FIGURES 16A-B** are illustrations depicting a second side of a connector and a second side keying ring, according to some embodiments.

[0033] **FIGURE 17** is an illustration depicting first and second sides of a connector, according to some embodiments.

[0034] **FIGURE 18** is an illustration depicting first and second sides of a connector as they are brought together, according to some embodiments.

[0035] **FIGURE 19** is an illustration depicting first and second sides of a connector as they are brought together, according to some embodiments.

[0036] **FIGURE 20** is an illustration depicting a connector in a fully assembled configuration, according to some embodiments.

[0037] **FIGURE 21A** is an illustration depicting a connector, according to some embodiments.

[0038] **FIGURES 21B-C** are illustrations depicting a connector as viewed from axis A, marked on **FIGURE 21A**, according to some embodiments.

[0039] **FIGURE 22** is an illustration depicting two sides of a connector, at least one of which is configured for attachment to a bottle or vial, according to some embodiments.

[0040] **FIGURE 23** is an illustration depicting two sides of a connector, at least one of which is configured for attachment to a bottle or vial, according to some embodiments.

[0041] **FIGURE 24** is an illustration depicting two sides of a connector as they are brought together, according to some embodiments.

[0042] **FIGURE 25** is an illustration depicting a connector in a partly assembled configuration, according to some embodiments.

[0043] **FIGURE 26** is an illustration depicting a connector, such as that of **FIGURES 22-25**, in a fully assembled configuration, according to some embodiments.

DETAILED DESCRIPTION OF SOME OF THE EMBODIMENTS

[0044] An aseptic connector may use double puncture technology in order to create a sterile bore (or tunnel) through which fluid may pass. A first side of the connector may be attached to a first tube and a second side of the connector may be attached to a second tube. The end of each side of the connector may have a septum or membrane which are configured to contact one another in order for the connection to be made. A spike may be configured within one of the sides, and when the sides are pushed together, the spike punctures the septum/membrane and pushes at least a portion of the septum/membrane aside. The septum/membrane may be displaced into a dirty area of the connector, however the area within the spike creates a clean tunnel that remains sterile. This way, a cannula can pass through the sterile tunnel and puncture a secondary membrane/septum that is in one or both of the first and second sides of the connector. The secondary membrane may be an elastomeric material (such as rubber), and may form a boundary between a wet area (such as a medicine bag, medicine vial, fluid line, etc.,) and the connector. Thus, when the cannula punctures the secondary membrane/septum, a sterile flow path is created through the cannula from the puncture of the secondary membrane/septum to a tube connected to the other side of the connector. Additionally, by using an elastomeric material, the secondary septum/membrane can reseal itself once the cannula is removed and/or the connector is separated. Furthermore, because the connection may be created by pushing the two sides together, the connection is made via a linear motion, meaning that the process of making the connection can be automated and/or performed using a machine. Moreover, the connection need not be assembled in a sterile environment, because the displacement of the septum/membrane by the spike creates a sterile tunnel within which the connection is made.

[0045] **FIGURE 1** shows the two parts of the connector 100 before the connection is made. A first side (also referred to herein as “first portion”) 105 of the connector 100 may have a first septum 110. The first septum 110 may be an elastomeric material, such as rubber. The first septum 110 may form a boundary between a portion of the flow path and the area within the connector 100. The portion of the flow path may comprise a tube, a medicine vial, a medicine bag, and/or

the like, and as such, the portion of the flow path may be wet or dry. Above the boundary, the connector 100 may have a mechanism to attach to a tube and/or a port to the tube. For example, as shown in **FIGURE 1**, tube connector 115 has a 90° port to a tube 120. The port to a tube may be 90°, may be straight, and/or may be collapsible. The port may also be at any other angle. In some embodiments, the connector 100 may be attached to a tube which can be attached directly to a medicine vial, medicine bag, and/or the like. Alternatively, the connector 100 may be attached directly to a medicine vial, medicine bag, etc.

[0046] The first portion 105 may also comprise a first membrane 125 which is held by a sliding membrane holder 128. The first membrane 125 may be an easily frangible sterile barrier, such as foil, laminated paper, plastic, Tyvek, thin polypropylene, and/or the like. A tunneling spike 130 may be configured between the first septum 110 and first membrane 125. The tunneling spike 130 may have a specialized tip (i.e., a tip that has a particular shape), as explained in further detail below.

[0047] An outer casing 135 may encapsulate at least part of the first portion 105. In some embodiments, the outer casing 135 may be configured around the tunneling spike 130 and the first membrane 125. The outer casing 135 may also extend over the first septum 110. In some embodiments, the outer casing 135 may extend over the first septum 110, the tunneling spike 130, and the first membrane 125, and may further extend past the first membrane 125 in the direction away from the first septum 110. Within the casing 135, an interior area of the first portion is sterile. The sterile area of the first portion includes at least the tunneling spike 130 and the first septum 110.

[0048] Additionally, in some embodiments, the outer casing 135 may have a notch 140. The notch 140 may be an indentation around the inside of the outer casing 135. The outer casing 135 may have a single notch 140, such as a single notch that goes around the entire inner perimeter of the casing 135. Alternatively, the outer casing 135 may have more than one notch 140 through or around the perimeter of the outer casing 135. The notch 140 may be configured to hold protrusion 175. Protrusion 175 may be attached to sliding membrane holder 128, and may prevent the first membrane 125 from contacting the tunneling spike 130 prematurely – i.e., before the first portion 105 and second portion 150 are connected.

[0049] In some embodiments, the outer casing 135 may have a second notch and/or second set of notches around the inner perimeter of the outer casing 135. The second notch(es) may be arranged further towards the first septum 110 than the first notch(es). Alternatively, the outer casing 135 may have a protrusion and/or set of protrusions around the perimeter of the outer casing 135, where the protrusion(s) are configured further towards the first septum 110 than the first notch(es).

[0050] A second side (also referred to herein as “second portion”) 150 of the connector 100 may have a second membrane 155. The second membrane 155 may be an easily frangible sterile barrier, such as foil, laminated paper, plastic, Tyvek, thin polypropylene, and/or the like. The second membrane 155 may be configured at an end of the second portion 150. Additionally, the second portion 150 may comprise a cannula 160. The cannula 160 may be a spike or a needle. In some embodiments, the cannula 160 may connect to tubing and/or a flow path at a first end 165, while the other end may be a free end. The cannula 160 may be oriented such that the free end of the cannula 160 points towards the second membrane 155 and the first end 165 is oriented away from the second membrane 155.

[0051] A casing 170 may be configured around the cannula 160. The second membrane 155 may form at least part of the casing 170, such as part of an end of the casing 170. An area within casing 170 is sterile, including at least the cannula 160, which is sterile.

[0052] Additionally, the casing 170 may have at least one notch 195 that is configured to receive a protrusion 190. In some embodiments, the casing 170 may have a single notch, such as a single notch that goes around the entire outer perimeter of the casing. Alternatively, the casing 170 may have more than one notch 195 around the perimeter of the casing 170. In some embodiments, the casing 170 may have a second notch or a second set of notches. The second notch(es) may be configured further away from second membrane 155 than the first notch(es).

[0053] The second portion of the connector may have a slider 180 that is configured to push the cannula 160 towards the side of the second side 150 having the second membrane 155. The slider 180 may fit within the casing 170. In some embodiments, at least a portion of an outer diameter of the slider 180 may be substantially the same as an inner diameter of the casing 170 so as to ensure that an area between the end of the slider 180 oriented towards the second membrane 155 and the second membrane 155, including the cannula 160, remains sterile.

[0054] The slider 180 may be configured with a protrusion 190 that is configured to fit within notch 195. When the protrusion 190 is within notch 195, the slider 180 is prevented from moving freely, thereby ensuring that the cannula 160 does not puncture the second membrane 155 before the connector 100 is connected. In some embodiments, the force required to remove the protrusion 190 from the notch 195 is greater than the force required to remove protrusion 175 from notch 140. In other implementations, the protrusion 190 may be locked into or otherwise prevented from moving out of notch 195 until protrusion 175 is removed from notch 140.

[0055] When attaching the two sides of the connector 100, the end of the second side 150 with second membrane 155 is inserted into an end of outer casing 135 of the first portion 105 such that the second membrane 155 and the first membrane 125 contact one another. This forms the configuration shown in **FIGURE 2**. Here, the second membrane 155 and first membrane 125 are touching, and part of casing 170 is within outer casing 135. Also, the protrusions 175, 190 are still within their respective notches 140, 195.

[0056] Tunneling spike 130 is poised above the first membrane 125 and second membrane 155, such that when the two sides are pushed further together, as shown in **FIGURE 3**, the tunneling spike 130 breaks through the first membrane 125 and second membrane 155. In order for this to occur, the first side 105 and second side 150 are pushed together with enough force that protrusion 175 slides out of notch 140, thereby allowing the tunneling spike 130 to pierce the first membrane 125 and second membrane 155.

[0057] The tunneling spike 130 may have a specialized tip so that when it breaks through the first membrane 125 and second membrane 155, it pushes the broken portions of the first membrane 125 and second membrane 155 aside, thereby creating an opening that forms a sterile pathway between the first and second portions of the connector. In particular, at least the interior area of the tunneling spike 130, the first septum 110, and the cannula 160 are sterile.

[0058] As the two sides are pushed together, the protrusion(s) 190 of the second portion 150 may provide resistance to and/or stop the slider 180 from moving until the tunneling spike 130 has pierced the first membrane 125 and second membrane 155. As shown in **FIGURE 3**, the tunneling spike 130 has pierced through the first membrane 125 and second membrane 155. Once this occurs, the first portion 105 and second portion 150 have moved together such that the bottom of the outer casing 135 reaches protrusion(s) 190. The bottom edge of the outer casing 135 pushes

against and causes inward bending of protrusion(s) 190 such that the protrusion(s) begin to dislodge from the notch(es) 195. Once the protrusion(s) 190 are at least partly dislodged from the notch(es) 195, the slider 180 can be pushed such that cannula 160 can be moved towards the opening in the first membrane 125 and second membrane 155 that has been created by the tunneling spike 130.

[0059] As such, once the sterile pathway/tunnel has been formed, the slider 180 may be pushed up into the second portion 150, thereby moving the cannula 160 through the opening and the tunneling spike 130. In some implementations, the tunneling spike 130 may have a guide rib 145 that helps to guide the cannula through the center of the tunneling spike 130 towards first septum 110.

[0060] As shown in **FIGURE 4**, the cannula 160 pierces the first septum 110. The motion of the slider 180 may be stopped by the second protrusion(s) and/or notch(es) configured on the first and/or second sides. As discussed above, the first septum 110 may be an elastomeric material, such as rubber, and the first septum 110 may form a boundary between a liquid container and the connector 100. Thus, when the cannula 160 pierces the first septum 110, the elastomeric material seals around the cannula 160. As a result, any liquid on the other side of the first septum 110 does not leak into the connector 100. The liquid can, however, be drawn through the cannula 160, thereby connecting the flow path tubing, medicine vial, medicine bag, and/or the like that are on each side of the connector 100. Furthermore, because, in some embodiment, the first septum 110 is rubber, liquid on the other side of the septum may be under pressure and the rubber will hold the pressurized liquid until the cannula 160 pierces the first septum 110.

[0061] In some implementations, the cannula 160 may comprise two channels; one channel draws fluid and is connected to the fluid path, while the other channel is (or is connected to) a vent line. These channels may be concentric or may be side-by-side within the cannula 160. Alternatively, the second portion 150 may have a second cannula next to cannula 160, where the second cannula serves as or is connected to a vent line. This is of particular importance in implementations where the flow path is connected, via the connector 100, to a medicine vial. When the connector is connected to a medicine bag, the bag deflates when the fluid is drawn through the flow path, and when the connector is connected to tubing, the fluid moves, via the connector, through the tubing. When connected to a vial, however, the vial is preferably vented

so that the fluid is better able to flow freely through the cannula 160 and connector 100 to the rest of the flow path.

[0062] Additionally, the connector 100 may be detached. Because the first septum 110 is formed from an elastomeric material, the first septum 110 will reseal if the connector is detached. For example, slider 180 may be pulled out in order to pull cannula 160 back through the first septum 110. Additionally and/or alternatively, the casing 170 may be pulled out of outer casing 135. In some embodiments, however, latches may be added such that the connector 100 cannot be separated. In other implementations, the two sides of the connector 100 may only be separated after twisting the two sides.

[0063] In another embodiment, as shown in **FIGURES 8-11**, the connector 200 may be largely configured as discussed above, but tunneling spike 230 may be configured within the second portion 250 instead of the first portion 205. Thus, in this embodiment, the first portion 205 may have a septum 210, a first membrane 225, and an outer casing 235 configured around at least the septum 210 and the first membrane 225. The second portion 250 may have a second membrane 255, a tunneling spike 230, a cannula 260 configured radially inwards and/or within the tunneling spike 230, and a casing 270 configured around the tunneling spike 230 and the cannula 260. The second membrane 255 may form at least part of an outer edge of the casing 270, and the casing 270 may have at least one protrusion 290 and at least one notch 295 that prevent the slider 280 from moving the cannula 260 until the tunneling spike 230 has pierced the first membrane 225 and second membrane 255. Thus, with the exception of the tunneling spike 230 being configured in the second portion 250 instead of the first portion 205, the connector is configured and operates much in the same way as discussed above.

[0064] **FIGURE 8** shows the first portion 205 and second portion 250 before the connection is made. In **FIGURE 9**, the second portion 250 has slid into first portion 205 such that the first membrane 225 and second membrane 255 are touching. The tunneling spike 230 is poised below the first membrane 225 and second membrane 255, but the tunneling spike 230 has not yet pierced either the first membrane 225 or second membrane 255. Protrusion 290 is within notch 295, thereby preventing the slider 280 from moving the cannula 260. As shown, the first membrane 225 and second membrane 255 are touching, but have not yet been pierced by the tunneling spike

230, and the bottom edge of the outer casing 235 has not yet started applying inwards pressure on the protrusion(s) 290 to push them out of the notch(es) 295.

[0065] Once pressure is applied to make the connection, tunneling spike 230 pierces the first membrane 225 and second membrane 255, and, simultaneously, the protrusion(s) 290 are pushed inwards, thereby allowing the slider 280 to push the cannula 260 through the opening created by the tunneling spike 230. **FIGURE 10** shows the connector 200 once the tunneling spike 230 has pierced the first membrane 225 and second membrane 255. The bottom of the outer casing 235 has passed the protrusion(s) 290, thereby pushing them inwards and at least partly dislodged the protrusion(s) 290 from the notch(es) 295. Once the protrusion(s) 290 are at least partly dislodged from the notch(es) 295, the slider 280 can be pushed such that the cannula 260 slides through the sterile area created by tunneling spike 230 and first septum 210, as shown in **FIGURE 11**. In some embodiments, the cannula 260 may be guided through a central portion of the tunneling spike 230 by a guide rib 245.

[0066] In some implementations, the embodiments shown in **FIGURES 8-11** may only have a single (set of) notch(es) 295 and single (set of) protrusion(s) 290. The other set of notch(es) 140/protrusion(s) 175 discussed in the embodiments of **FIGURES 1-4** may not be necessary. In the embodiments of **FIGURES 1-4**, the first membrane 125 is connected to a sliding membrane holder 128, which allows the membrane 125 to move towards the tunneling spike 130 when the second portion 150 is slid into first portion 105. The notch 140 and protrusion 175 prevent the sliding membrane holder 128 from moving until the first portion 105 and second portion 150 are assembled and proper force is applied, thereby preventing the tunneling spike 130 from prematurely pierce the first membrane 125. In the embodiments of **FIGURES 8-11**, however, the first membrane 225 may not be attached to a sliding membrane holder. Because the tunneling spike 230 is on the other side of the connector 200 (as compared to connector 100), the first membrane 225 is not at risk of premature piercing. In these embodiments, once the casing 270 slides into outer casing 235, the first membrane 225 and second membrane 255 are touching before tunneling spike 230 can pierce either the first membrane 225 or second membrane 255. This is because the tunneling spike 230 does not move until the outer casing 235 presses on protrusion 290, which occurs when the first membrane 225 and second membrane 255 are touching.

Keying Ring

[0067] In some implementations, multiple connectors may be used, and it may be critical to ensure that the first side of one connector is not connected to the second side of another connector. To help ensure that the first and second sides are a match before the connection is made, a keying ring may be attached to each side of the connector. The keying ring may have at least one set of keys that prevent the first side of one connector from attaching to the second side of a different connector.

[0068] As shown in **FIGURE 12A**, a first side of the connector 305 may be configured with a slot 327 that is configured to receive an elongate protrusion 328 in the second side of the connector 350. When the slot 327 and protrusion 328 are aligned, the first side of the connector 305 and second side of the connector 350 may be pushed together. When the slot 327 and protrusion 328 are not aligned, however, the protrusion 328 will hit the bottom of the outer casing 335 of the first side of the connector 305, thereby not allowing the connector to be fully connected.

[0069] In order to ensure that a first side of a first connector cannot attach to a second side of a second connector, a keying ring may be used. The keying ring helps to ensure that rotating the first side and/or the second side does not simply align a slot 327 from a first side of a first connector and protrusion 328 of the second side of the second connector, thus allowing the mismatched connector to be pushed together.

[0070] Accordingly, a first side of the keying ring 360 may be configured to attach to the first side of the connector 305 and a second side of the keying ring 375 may be configured to attach to the second side of the connector 350. The first side of the keying ring 360 may be configured with a keying ring slot 357, and the second side of the keying ring 375 may be configured with a keying ring protrusion 359. Similar to the slot 327 and protrusion 328 of the first and second sides of the connector, respectively (305, 350), the two sides of the keying ring may only push together when the keying ring slot 357 and keying ring protrusion 359 are aligned. Thus, in some embodiments, when the keying ring is attached to the connector, two sets of slots and protrusions are aligned – the slot 327 of the first side of the connector 305 aligns with the elongated protrusion 328 of the second side of the connector 350, and the keying ring slot 357 of the first side keying ring 360 and the keying ring protrusion 359 of the second side keying ring 375 each align in order for the connection to be made.

[0071] In order to make each connector-keying ring combination unique, the keying ring slot 357/protrusion 359 may be oriented in a particular direction relative to the slot 327 of the first part of the connector 305 and the protrusion 328 of the second side of the connector 350. If either slot/protrusion is misaligned, the connector will not be able to fully connect.

[0072] As shown in **FIGURE 13A**, a first side of the connector 305 may be configured to receive a first side of the keying ring 360. For example, an outer casing 335 of the first side of the connector 305 may have a plurality of ribs 320. The ribs 320 may be equally spaced around the circumference of the outer surface of the outer casing 335. The ribs 320 may extend along the entire length of the first side of the connector 305, or they may be shorter and configured around the circumference on the side where the first side of the connector connects to the second side of the connector (the connection end 340). In some embodiments, the first side of the connector 305 may have twelve ribs 320; in other implementations, the first side of the connector 305 may have fewer ribs (e.g., eight, nine, ten) or more ribs (e.g., thirteen, fourteen, fifteen, twenty, etc.)

[0073] Additionally, as discussed above, the first side of the connector 305 may have a slot 327. In some embodiments, the slot 327 may be configured between two of the ribs 320. The slot 327 may extend up from the connection end 340 of the first side of the connector 305 that is configured to connect to the second side of the connector. The slot 327 may extend up a portion of the first side of the connector 305. The slot 327 may not extend into the sterile portion of the first side of the connector 305 – e.g., it may not extend past the first membrane (not shown).

[0074] The first side of the keying ring 360 may be configured to attach to the first side of the connector 305. For example, the keying ring 360 may be configured to go around the connection end 340 of the first side of the connector 305. The keying ring 360 may have equally spaced slots 365 that are configured to receive the ribs 320. In some implementations, the slots 365 may be configured within an inner perimeter of the keying ring 360.

[0075] Upon assembly, the ribs 320 may slide into the slots 365. Thus, for example, in embodiments having twelve ribs 320 and twelve slots 365, the first side keying ring 360 may be rotated and attached to the first side of the connector 305 in twelve different orientations. As such, the orientation of slot 327 relative to keying ring slot 357 may have twelve unique positions. An exemplary configuration of the keying ring slot 357 relative to the slot 327 is shown in **FIGURE**

13B. **FIGURE 13C** shows the same view as **FIGURE 13B**, however here the keying ring is shown as translucent in order to show orientation of the ribs 320 within slots 365.

[0076] Additionally, the slots 365 may have protrusions 368 that extend radially inwards. These protrusions 368 may lock the keying ring 360 to the first side of the connector 305. In some embodiments, all slots 365 have protrusions 368. In other implementations, protrusions 368 are only within some of the slots 365. For example, protrusions 368 may be within, for example, two slots, three slots, four slots, five slots, six slots, etc. In some embodiments, the protrusions 368 may be configured to fit within notches in the first side of the connector 305. In other embodiments, the protrusions 368 may be configured to lock onto the top of the ribs 320. This way, when the first side of the connector 305 and keying ring 360 are pushed together, the protrusions 368 ride up the ribs 320 and snap into place over the ribs 320. Once the protrusions 368 have snapped into place over the ribs 320, the keying ring 360 may be locked onto the first side of the connector 305. This is also shown in **FIGURES 14A-B**.

[0077] In some embodiments, the outer casing 335 may have a protrusion that extends around the circumference of the first side of the connector 305. The protrusion may prevent the keying ring 360 from sliding too far up the first side of the connector 305. The protrusion may abut the top of the keying ring 360, and/or the keying ring 360 may be configured to receive the protrusion at a certain height within the keying ring 360 (see **FIGURE 14B**).

[0078] As shown in **FIGURE 15A**, the second side of the connector 350 may be configured to receive a second side keying ring 375. The second side of the connector 350 may have a protrusion 372 that extends around the circumference of the second side of the connector 350. The protrusion 372 may be a ring that is configured at the bottom edge of the casing 370, i.e., the side of the casing 370 that receives slider 380. In other embodiments, the protrusion 372 may be close to the bottom of the casing 370 or may be another distance from the bottom of the casing 370.

[0079] The protrusion 372 may have ribs 382 that are configured on protrusion 372 such that they extend in a direction towards second membrane 355. The ribs 382 may be equally spaced around the circumference of the protrusion 372. In some embodiments, the protrusion 372 may have twelve ribs 382. In other implementations, the protrusion 372 may have fewer ribs (e.g., eight, nine, ten) or more ribs (e.g., thirteen, fourteen, fifteen, twenty, etc.). The protrusion 372

may have the same number of protrusions 382 as the number of ribs 320 on the first side of the connector 305.

[0080] The second side keying ring 375 may have a round outer edge and a first end of the second side keying ring 375 may have a flat edge that extends radially inwards from the outer edge. The flat edge may have slots 385 that are configured to receive the ribs 382 of the second side of the connector 350. The second side keying ring 375 may have the same number of slots 385 as the number of ribs 382 on the protrusion 372. Thus, for example, the keying ring 375 may have twelve slots 385, or, in other implementations, the keying ring 375 may have fewer slots (e.g., eight, nine, ten) or more slots (e.g., thirteen, fifteen, twenty, etc.). The orientation of the second side keying ring 375 relative to the second side of the connector 350 may be determined by the orientation of the first side keying ring 360 relative to the first side of the connector 305. This ensures that the alignment functionality of the connector (slot 327/protrusion 328) and keying ring (slot 357/protrusion 359) are synchronized so that the first side of the connector 305 can connect to the second side of the connector 350 when the correct pairing is chosen.

[0081] Additionally, the second side keying ring 375 may have a protrusion 359. The protrusion 359 may extend radially inwards from the inner perimeter of the second side keying ring 375. In some embodiments, the protrusion 359 may be configured between two of the slots 385. The protrusion 359 may extend from the flat edge along an inner perimeter and towards the opposite end of the second side keying ring 375. In some embodiments, the protrusion 359 may extend the entire length of the second side keying ring 375; in other embodiments, the protrusion 359 may extend along only part of the length of the second side keying ring 375. For example, the protrusion 359 may not reach all the way to the flat edge and/or may not reach all the way to the opposite end of the second side keying ring 375. An exemplary configuration of the protrusion 359 relative to protrusion 328 is shown in **FIGURE 15B**. The relative positioning may be determined by the rotation of the second side keying ring 375 when slots 385 are positioned on ribs 382.

[0082] The second side of the connector 350 may have a locking tab 390. The locking tab 390 may include a protrusion that is configured to lock the second side keying ring 375 onto the second side of the connector 350. The locking tab 390 may be spaced apart from the protrusion 372 towards the second membrane 355. The spacing between the locking tab 390 and the protrusion

372 may be substantially the same as or just slightly larger than the height of the flat edge of the second side keying ring 375. This way, once the second side keying ring 375 is pushed onto the second side of the connector 350, the locking tab 390 locks the keying ring 375 onto the second side of the connector 350. In some embodiments, the locking tab 390 may be a ring around the outer perimeter of the casing 370, where the ring does not extend as far radially outwards as protrusion 372. In other implementations, the locking tab may be one or more protrusions that are configured at one or more points around the outer perimeter of the casing 370.

[0083] FIGURE 16A shows a perspective view of the second side keying ring 375 attached to the second side of the connector 350; **FIGURE 16B** shows a cutaway view of the same configuration. The locking tab(s) 390 are shown latched onto the flat edge of the second side keying ring 375.

[0084] FIGURE 17 shows the first side of the connector 305 with the first side keying ring 360 configured thereon and the second side of the connector 350 with the second side keying ring 375 configured thereon. As shown, the first side keying ring 360 has a slot 362 around the outer perimeter of the keying ring 360. The slot 362 is configured to receive the second side keying ring 375 when the first side of the connector 305 and second side of the connector 350 are pushed together. In some embodiments, the second side keying ring 375 may only enter slot 362 when the keying ring protrusion 359 of the second side keying ring 375 is aligned with keying ring slot 357. In some implementations, when the keying ring slot 357 and keying ring protrusion 359 are not aligned, the second side keying ring 375 may enter slot 362 but will travel far enough for the connector 300 to connect. The connector 300 may only connect when the keying ring slot 357 and keying ring protrusion 359 are aligned.

[0085] FIGURE 18 shows the first side of the connector 305 and second side of the connector 350 as they are pushed together. As shown, the first membrane 325 and second membrane 355 are touching. Meanwhile, the leading edge of the second side keying ring 375 has entered the slot 362 of the first side keying ring 360. In some implementations, in order for the first side of the connector 305 and second side of the connector 350 to get close enough for the first membrane 328 and second membrane 355 to touch (as shown in **FIGURE 18**), both sets of alignment slots/protrusions match – i.e., the slot 327 aligns with elongate protrusion 328 and the keying ring slot 357 aligns with keying ring protrusion 359.

[0086] **FIGURE 19** shows an embodiment of the cutaway shown in **FIGURE 18**. (**FIGURE 19** may be an alternative angle of the cutaway of **FIGURE 18** or **FIGURE 19** may be an alternative embodiment.) As shown, the slot 362 of the first side keying ring 360 has at least one locking latch 363. The locking latch(es) 363 may be configured to extend from one wall of the slot 362 towards a central region of the slot 362. In the embodiment shown in **FIGURE 19**, the locking latch(es) 378 may be on the inner wall of the slot 362 and extend towards the outer perimeter; however in other embodiments, the locking latch(es) may be on the outer wall of the slot 362 and extend radially inwards.

[0087] The locking latch(es) 363 of the first side keying ring 360 may be configured to fit within locking notch(es) 378 configured in the wall of the second side keying ring 375. The locking notch 378 may be an indentation in the second side keying ring 375, or it may be a cut out in the second side keying ring 375. When the first side of the connector 305 and second side of the connector 350 are pushed together, the locking latch(es) 363 lock into the locking notch(es) 378 such that the connector 300 cannot be separated.

[0088] **FIGURE 20** shows the embodiment of **FIGURE 19** once the two sides have been fully pushed together. The second side keying ring 375 has been pushed into first side keying ring 360 such that locking latch 363 is situated within locking notch 378. Additionally, once the sides have been pushed together, as shown, the slider 380 may advance cannula through the first membrane, similar to **FIGURE 4**.

[0089] **FIGURE 21A** shows a perspective view of the connector, showing the first side of the connector 305 fitted with first side keying ring 360 and the second side of the connector 350 fitted with the second side keying ring 375. **FIGURES 21B-C** show a view looking along central axis A of the connector (axis shown in **FIGURE 21A**). As shown, elongate protrusion 328 is configured within slot 327 and keying ring protrusion 359 is configured within keying ring slot 357. Thus, the connector can be fully connected.

[0090] In some implementations, whether a keying ring is used or not, the connectors may be marked in order to ensure that a first side of a first connector is not connected to a second side of a second connector. For example, in some embodiments, the matching first and second sides may be labeled, such as with a number. Thus, the first side marked “1” matches with the second side marked “1,” the first side marked “2” matches with the second side marked “2” and so on.

Additionally and/or alternatively, the keying rings may be color coded in order to ensure the first and second sides of the connectors are correctly matched. Thus, for example, a blue first side keying ring may match with a blue second side keying ring; a red first side keying ring may match with a red second side keying ring, and so on.

[0091] In yet another implementation (in addition or as an alternative to the color coding and/or numerical marking), the first and second sides of the connectors may be marked with machine-readable identification. For example, the first and second sides of a connector may be marked with a barcode or RFID, and/or machine vision (e.g., camera and comparison algorithm) may be used as OCR. If the sides of the connector do not match, the machine may not permit the instrument to run and/or an operator of the machine may be alerted that the instrument should not be run. Instead, all or part of the machine can be reassembled before use.

Rigid Bottle/Dual Venting Cannula

[0092] As discussed above, in some embodiments, the connector may be attached to a bottle or medicine vial (or the like). In order to draw fluid out of a solid, rigid container, the container needs to have a vent that allows air into the container. Thus, in such implementations, a vent line may be provided next to and/or concentrically around the cannula.

[0093] **FIGURE 22** shows an embodiment of the connector 500 that is configured to attach to a rigid container (bottle 510). **FIGURE 23** shows a magnified version of the embodiment of **FIGURE 22**. The connector 500 may have a first portion 505 that is configured to attach to bottle 510. The first portion 505 may be a cap for the medicine bottle, vial, or the like. The first portion 505 may have a first membrane 540 and a bottle stopper/septum 520. The first membrane 540 may be an easily frangible sterile barrier, such as foil, laminated paper, plastic, Tyvek, thin polypropylene, and/or the like. The bottle stopper/septum 520 may be an elastomeric material, such as rubber, and the septum 520 may form a boundary between the liquid in the bottle/vial and the connector 500.

[0094] The first membrane 540 may form a side of the first portion 505. In some embodiments, the first portion 505 may have a narrower cylindrical portion that has the first membrane at one end and a wider cylindrical section that is configured to connect to the bottle 510.

[0095] The connector 500 may have a second portion 550 that is configured to attach to first portion 505 and create a connection between the interior of the bottle and an IV line attached to the venting IV spike 590. The second portion 550 may have a second membrane 610. The second membrane 610 may be an easily frangible sterile barrier, such as foil, laminated paper, plastic, Tyvek, thin polypropylene, and/or the like. Additionally, the second portion 550 may have a sliding tunneling needle 570 that is configured below the second membrane 610. A venting IV spike 590 may be configured within the sliding tunneling needle 570.

[0096] The second portion 550 may have an outer casing 560 that surrounds an interior of the second portion 550. In some embodiments, the outer casing 560 may surround at least the second membrane 610, the sliding tunneling needle 570, and at least a portion of the venting IV spike 590. The outer casing 560 may have an indentation at a side of the second portion 550 that contains the second membrane 610. The indentation may be configured to receive the narrower cylindrical portion of the first portion of the connector 505 such that when the first portion is inserted into the indentation, the first membrane 540 and second membrane 610 come into contact with one another.

[0097] An interior area of the outer casing 560 may have a guide rib 620. The guide rib 620 may help to ensure that an area containing the sliding tunneling needle 570 does not move and therefore does not prematurely puncture second membrane 610. Additionally, the guide rib 620 may prevent rotational motion and may prevent the sliding tunneling needle 570 from moving away from a central axis of the second membrane 610.

[0098] To initiate a connection between the first side of the connector 505 and second side of the connector 550, the section of the first portion 505 that contains the first membrane 540 is put into the outer casing 560 of the second portion of the connector 550 such that the first membrane 540 is touching the second membrane 610. Once the first membrane 540 and second membrane 610 are touching, as shown in **FIGURE 24**, slider casing 580 may be pushed towards the touching membranes. The motion may continue until the sliding tunneling needle 570 punctures the two membranes (610, 540), thereby creating a clear and sterile pathway through which the venting IV spike 590 may pass (similar to operation of the embodiments discussed above).

[0099] The guide rib 620 may be configured such that the bottom of the guide rib reaches protrusion 640 after the sliding tunneling needle 570 creates the sterile pathway through the first membrane 540 and second membrane 610. Thus, after the sterile pathway has been created, further

motion of the slider casing 580 causes the guide rib 620 to push the protrusions 640 at least partly out of notches 630, as shown in **FIGURE 25**. Once the protrusions 640 are at least partly dislodged from notches 630, the slider casing 580 can be further advanced and therefore can push the venting IV spike 590 through the sterile pathway and towards bottle stopper/septum 520. The fully connected configuration is shown in **FIGURE 26**.

[0100] When the venting IV spike 590 pierces the bottle stopper/septum 520, fluid can flow from the bottle 510 through the venting IV spike 590. In order for fluid to flow out of the bottle 510, however, the volume of the fluid is replaced. As such, the venting IV spike 590 may have two lumens, a liquid lumen 660 and a vent lumen 650. The liquid lumen 660 allows fluid to flow out of the bottle 510 while the vent lumen 650 allows air to flow into the bottle 510. In order to maintain a sterile environment while air flows into the bottle and/or the interior of the connector 500, the air passes through a venting filter 600 in order to remove contaminants from the air. The venting filter 600 may be, for example, a 0.2 μ m filter. In addition to filtering the air passing into the connector 500, the venting filter 600 may also prevent any liquid (e.g., liquid that leaks out of the bottle 510 and into the body of the connector 500) from leaking out of the connector 500.

[0101] Thus, air flows through venting filter 600, through spike vent lumen 650, and into the bottle 510, while liquid flows from the bottle 510, through spike liquid lumen 660, and to a hose/IV line. In some implementations, the vent lumen 650 and liquid lumen 660 are concentric, for example, with the vent lumen 650 being the outer line and the liquid lumen being the inner line. In other implementations, the vent line and liquid line may be separate cannulas that are oriented, for example, side-by-side.

[0102] Any and all references to publications or other documents, including but not limited to, patents, patent applications, articles, webpages, books, etc., presented in the present application, are herein incorporated by reference in their entirety.

[0103] Example embodiments of the devices, systems and methods have been described herein. As noted elsewhere, these embodiments have been described for illustrative purposes only and are not limiting. Other embodiments are possible and are covered by the disclosure, which will be apparent from the teachings contained herein. Thus, the breadth and scope of the disclosure should not be limited by any of the above-described embodiments but should be defined only in

accordance with claims supported by the present disclosure and their equivalents. Moreover, embodiments of the subject disclosure may include methods, systems and devices which may further include any and all elements from any other disclosed methods, systems, and devices, including any and all elements corresponding to target particle separation, focusing/concentration. In other words, elements from one or another disclosed embodiments may be interchangeable with elements from other disclosed embodiments. In addition, one or more features/elements of disclosed embodiments may be removed and still result in patentable subject matter (and thus, resulting in yet more embodiments of the subject disclosure). Correspondingly, some embodiments of the present disclosure may be patentably distinct from one and/or another reference by specifically lacking one or more elements/features. In other words, claims to certain embodiments may contain negative limitation to specifically exclude one or more elements/features resulting in embodiments which are patentably distinct from the prior art which include such features/elements.

Claims:

1. An aseptic connector assembly, comprising:
 - a first portion comprising:
 - a first septum;
 - a first membrane;
 - a tunneling spike configured between the first septum and the first membrane; and
 - an outer casing configured around at least the first membrane and the tunneling spike;
 - and
 - a second portion comprising:
 - a second membrane;
 - a cannula; and
 - a casing configured around the cannula, wherein
 - the second membrane forms at least part of an outer edge of the casing,
 - and
 - the casing comprises at least one first protrusion;
- wherein:
 - the second portion is configured to fit within the first portion outer casing, such that when an edge of the outer casing is in contact with the at least one first protrusion of the second portion casing, the first membrane and the second membrane are in contact with one another,
 - the outer casing is configured to move past the at least one first protrusion when pressure is applied, and
 - when said pressure is applied, the tunneling spike punctures at least the first membrane and second membrane to create an opening.

2. The assembly of claim 1, wherein the tip of the tunneling spike is configured to push the first membrane and second membrane away from the opening when the tunneling spike punctures the first membrane and second membrane.
3. The assembly of claim 1, wherein the first septum is an elastomeric material.
4. The assembly of claim 3, wherein the elastomeric material is rubber.
5. The assembly of claim 1, wherein the first membrane and second membrane are an easily frangible sterile barrier.
6. The assembly of claim 5, wherein the easily frangible sterile barrier is foil.
7. The assembly of claim 1, wherein an interior area of the first portion is sterile and an interior area of the second portion is sterile.
8. The assembly of claim 7, wherein when the tunneling spike punctures the first membrane and second membrane to create the opening, the interior area of the tunneling spike, the cannula, and first septum remain sterile.
9. The assembly of claim 1, wherein the first septum forms a boundary between a liquid container and the connector assembly.
10. The assembly of any of claims 1-9, wherein the casing further comprises at least one second protrusion, and wherein, when further pressure is applied:

the outer casing is configured to move past the at least one second protrusion, and

the cannula travels through the opening and the tunneling spike to penetrate the first septum.

11. The assembly of any of claims 1-9, wherein the outer casing is configured with at least a second protrusion extending towards the interior of the outer casing, and wherein when further pressure is applied:

the inner casing is configured to move past the at least one second protrusion, and

the cannula travels through the opening and the tunneling spike to penetrate the first septum.

12. The assembly of any of claims 1-9, wherein the cannula is sterile.
13. The assembly of any of claims 1-9, wherein the cannula contains two distinct channels.
14. The assembly of claim 1, wherein the cannula contains two distinct channels, and wherein one channel is connected to a vent line and the other is a fluid path.
15. The assembly of claim 14 wherein the two cannula paths are concentric.
16. The assembly of claim 14 wherein the two cannula paths are side-by-side.
17. An aseptic connector assembly, comprising:
a first portion comprising:
a first septum;
a first membrane; and

an outer casing configured around at least the first membrane and the first septum;
and
a second portion comprising:
 a second membrane;
 a tunneling spike;
 a cannula positioned within the tunneling spike; and
 a casing configured around the tunneling spike and the cannula, wherein
 the second membrane forms at least part of an outer edge of the casing,
 and
 the casing comprises at least one first protrusion;
wherein:
 the second portion is configured to fit within the first portion outer casing, such
 that when an edge of the outer casing is in contact with the at least one
 first protrusion of the second portion casing, the membrane and the second
 septum are in contact with one another,
 the outer casing is configured to move past the at least one first protrusion when
 pressure is applied, and
 when said pressure is applied, the tunneling spike punctures at least the first
 membrane and second membrane to create an opening.

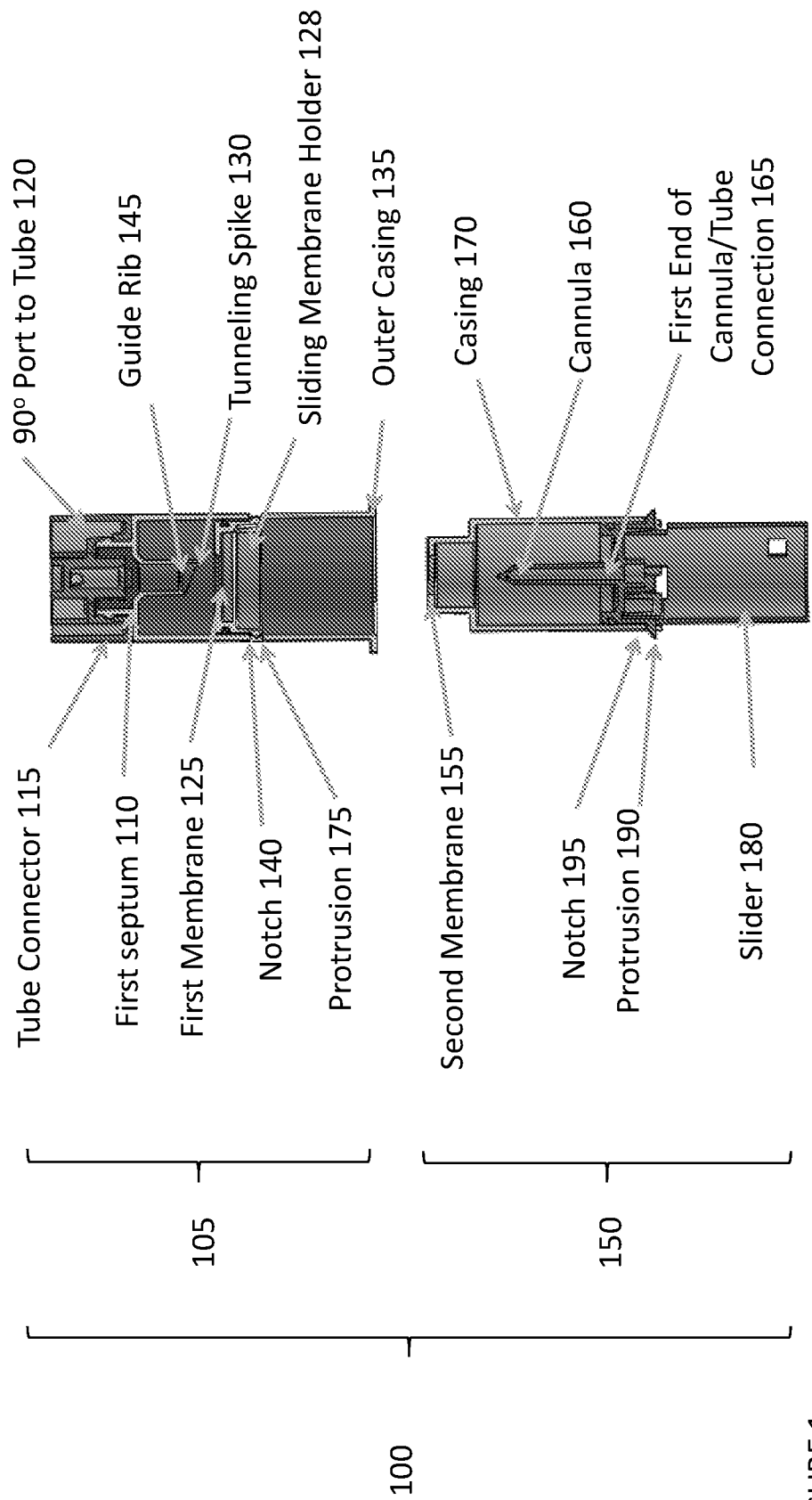


FIGURE 1

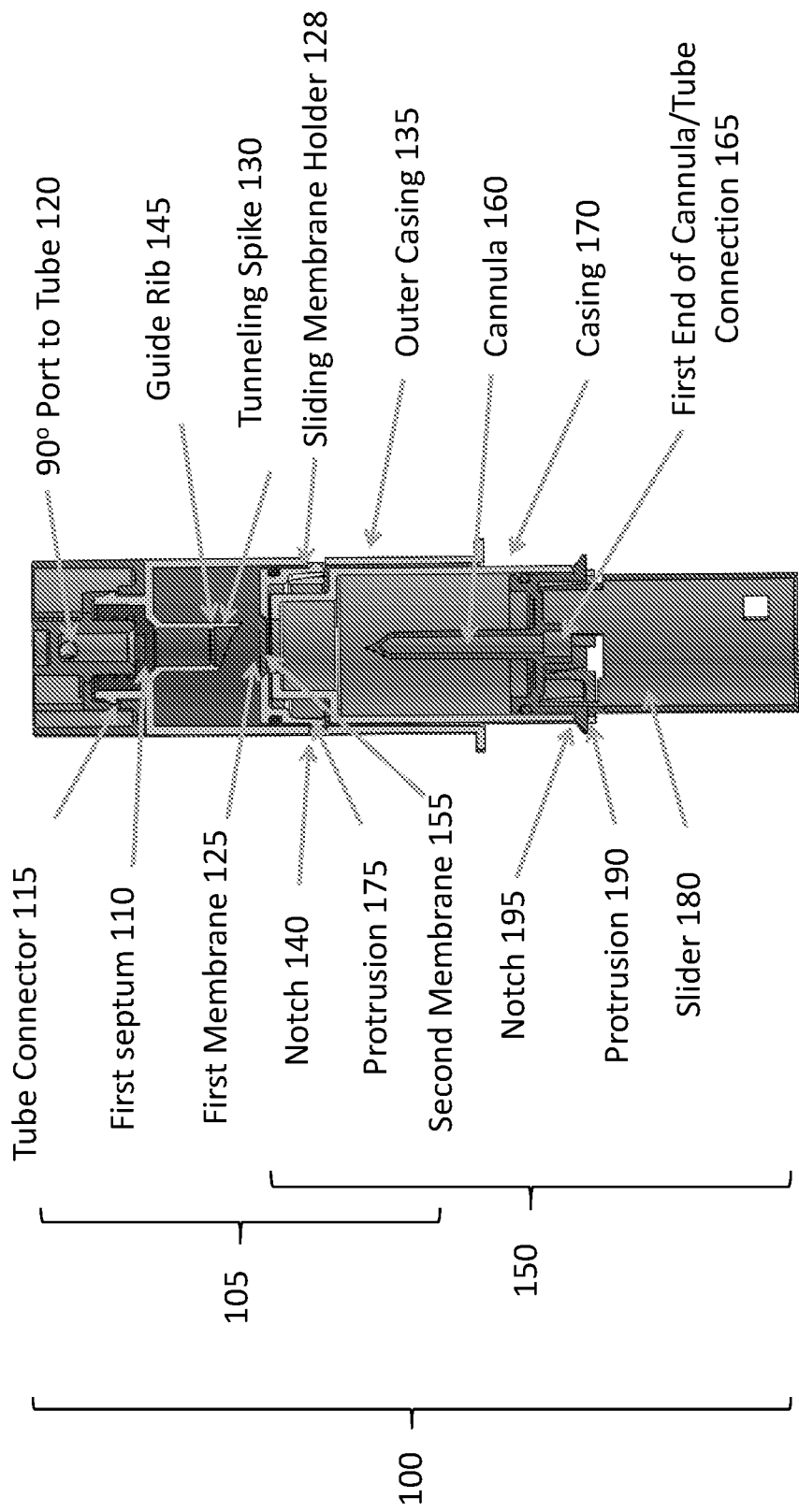


FIGURE 2

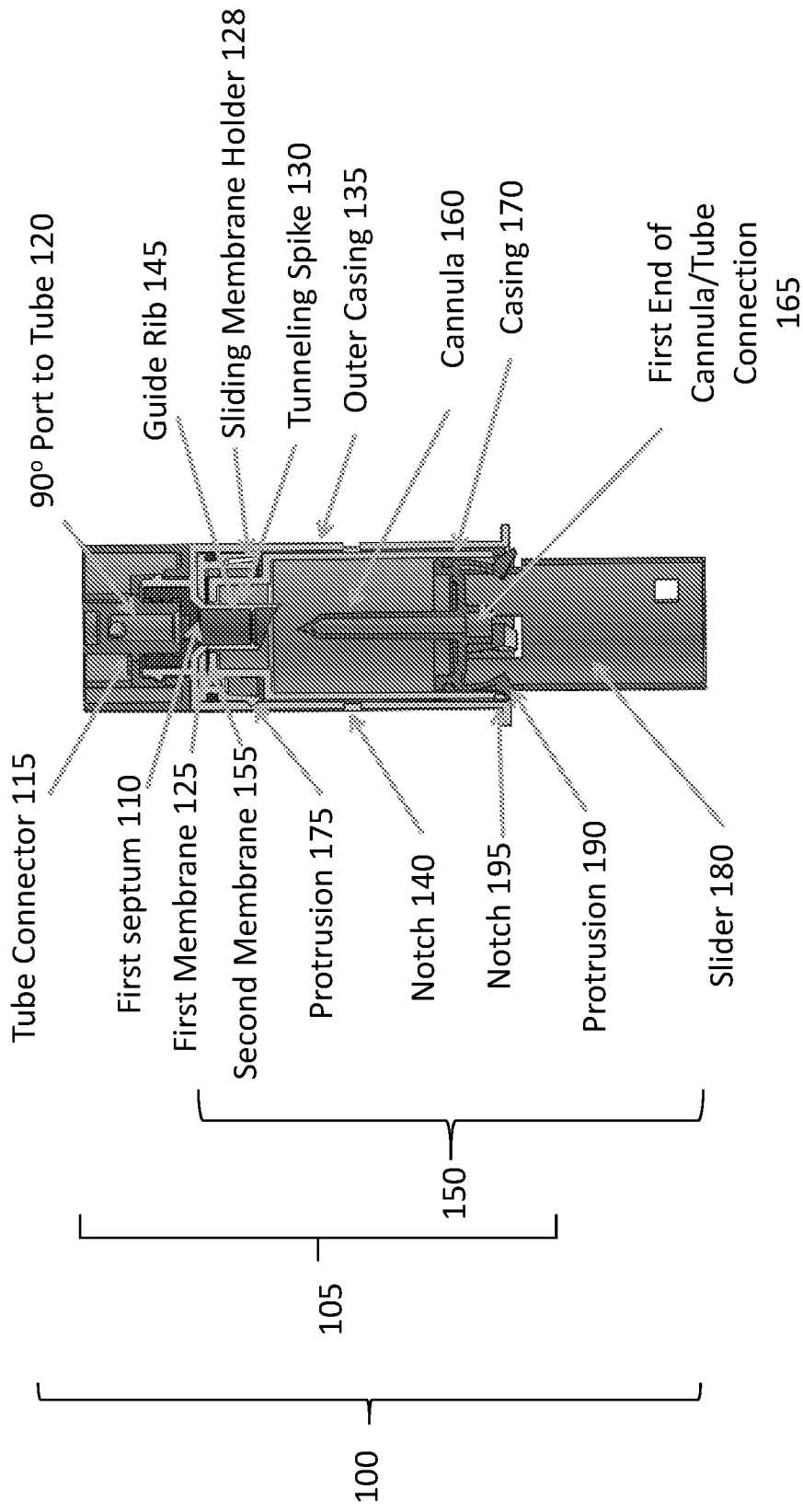


FIGURE 3

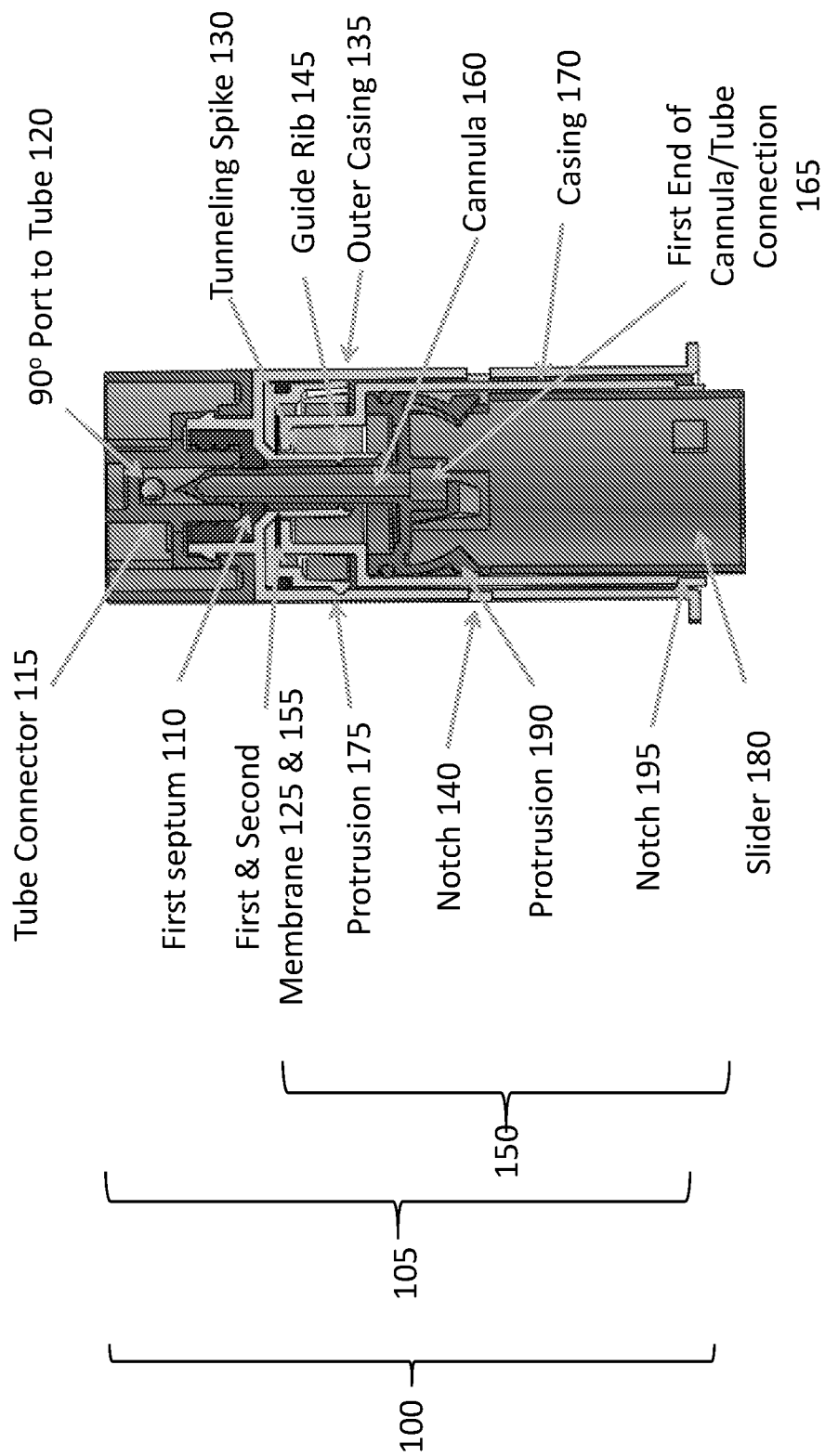


FIGURE 4

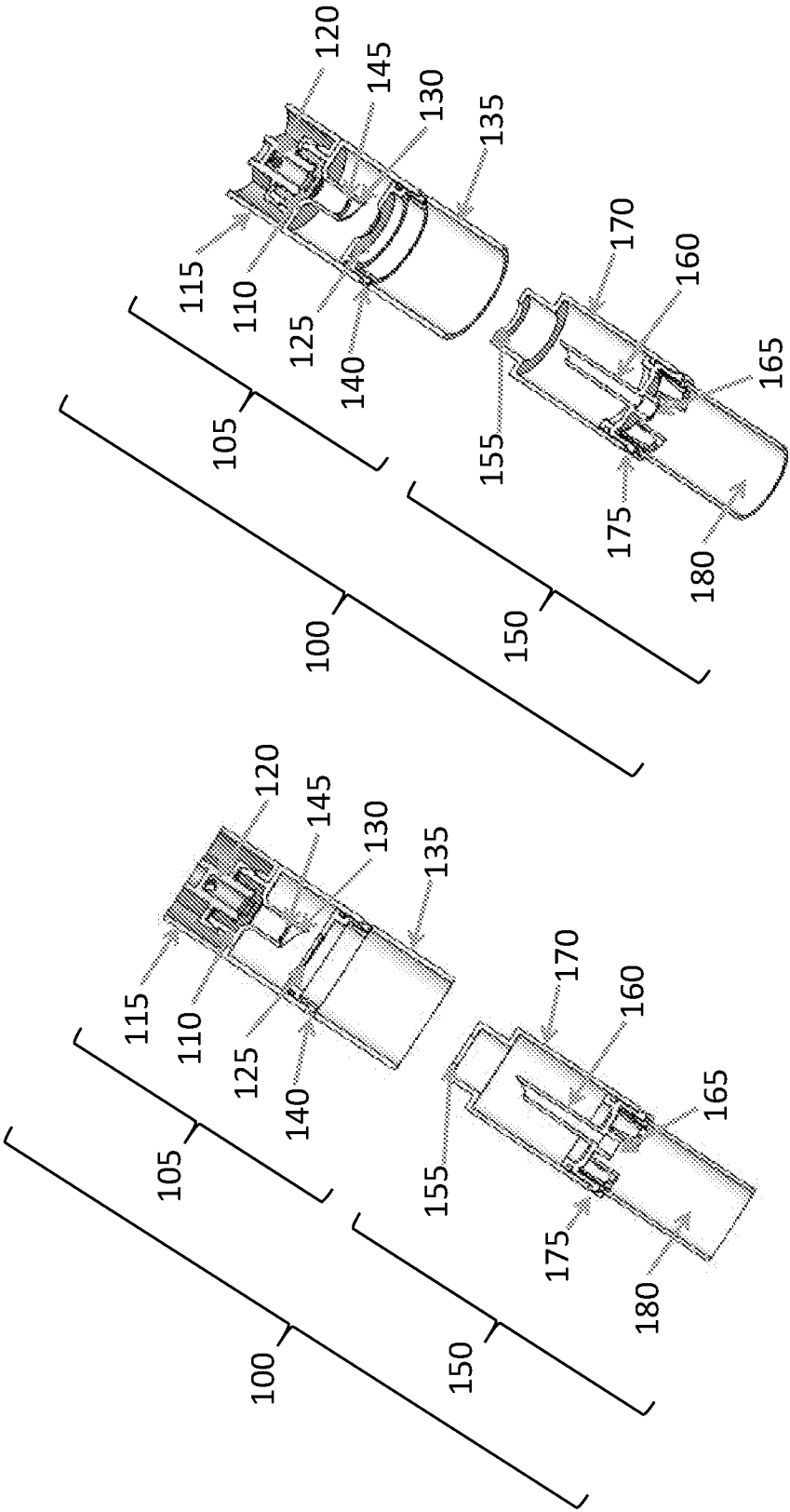
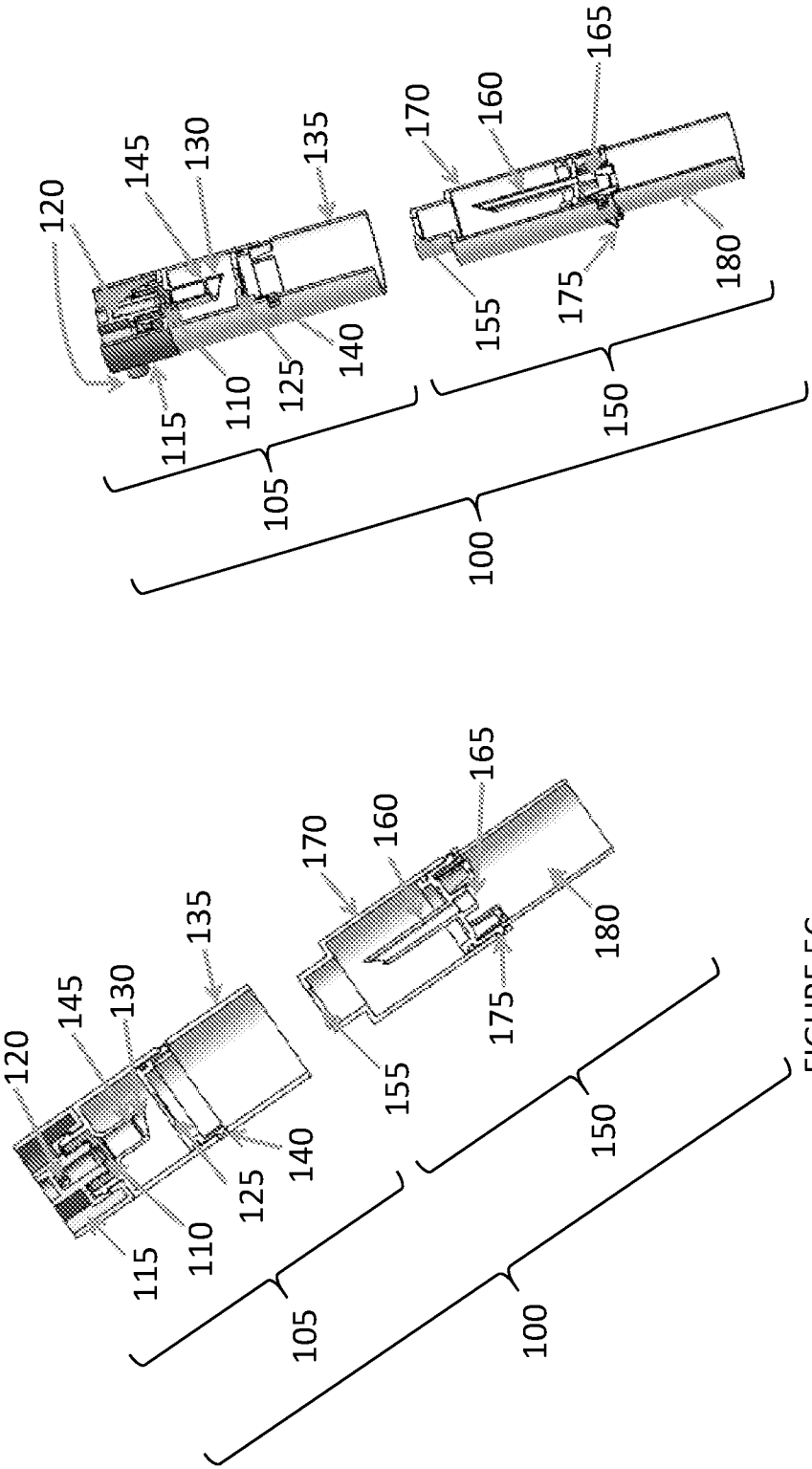


FIGURE 5B

FIGURE 5A



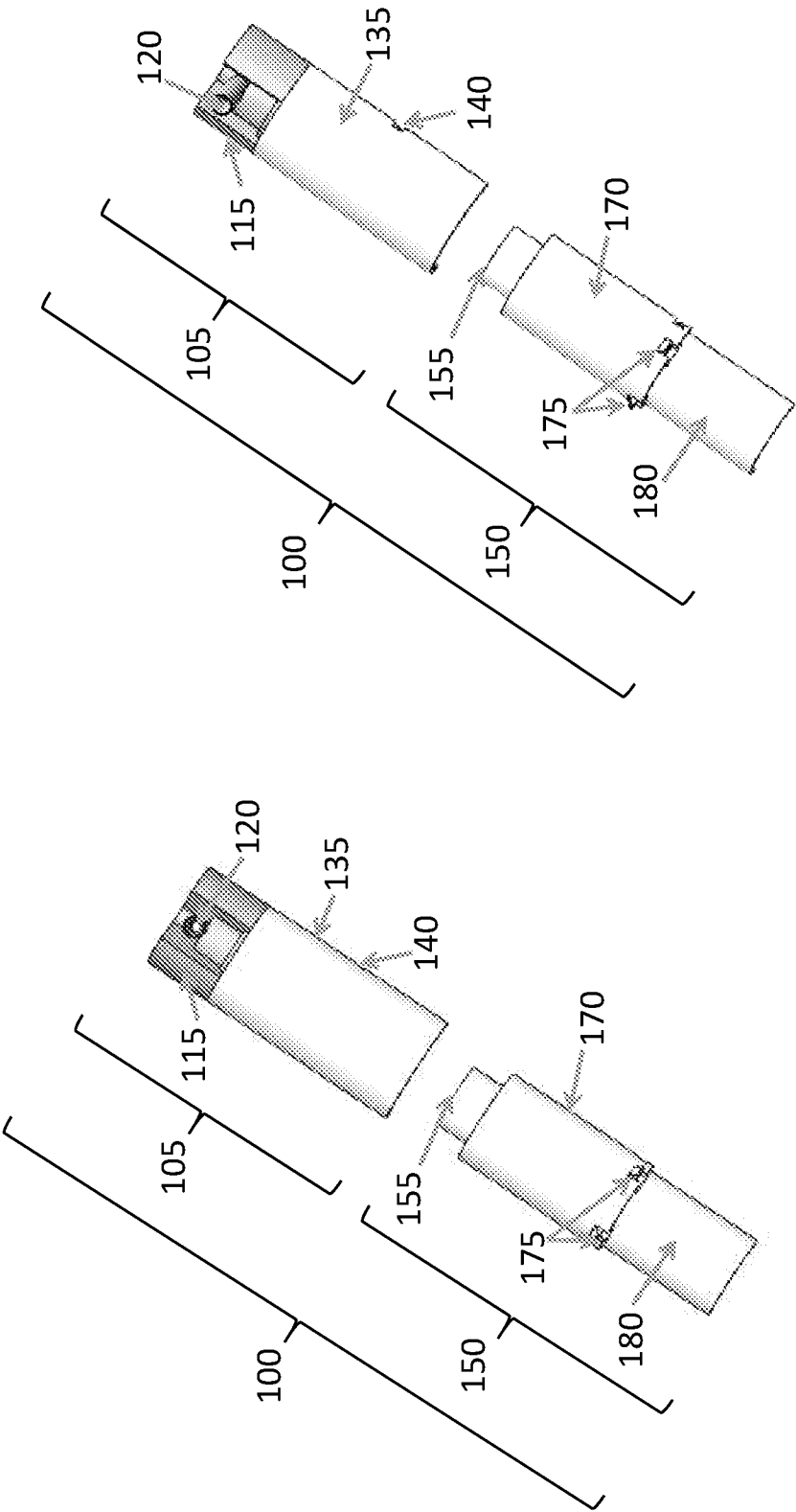


FIGURE 6B

FIGURE 6A

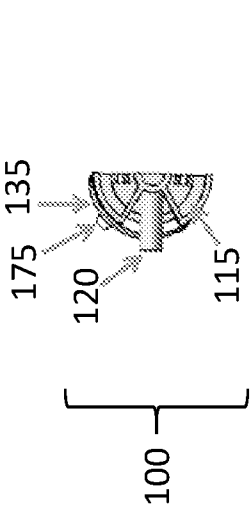


FIGURE 7A

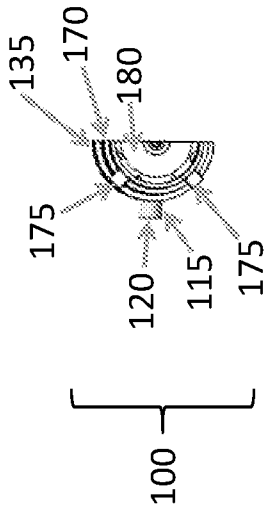


FIGURE 7B

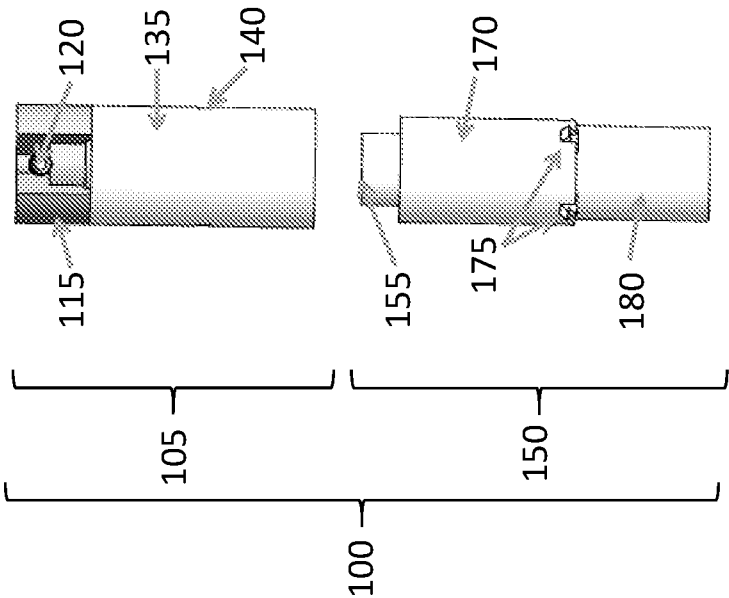


FIGURE 6C

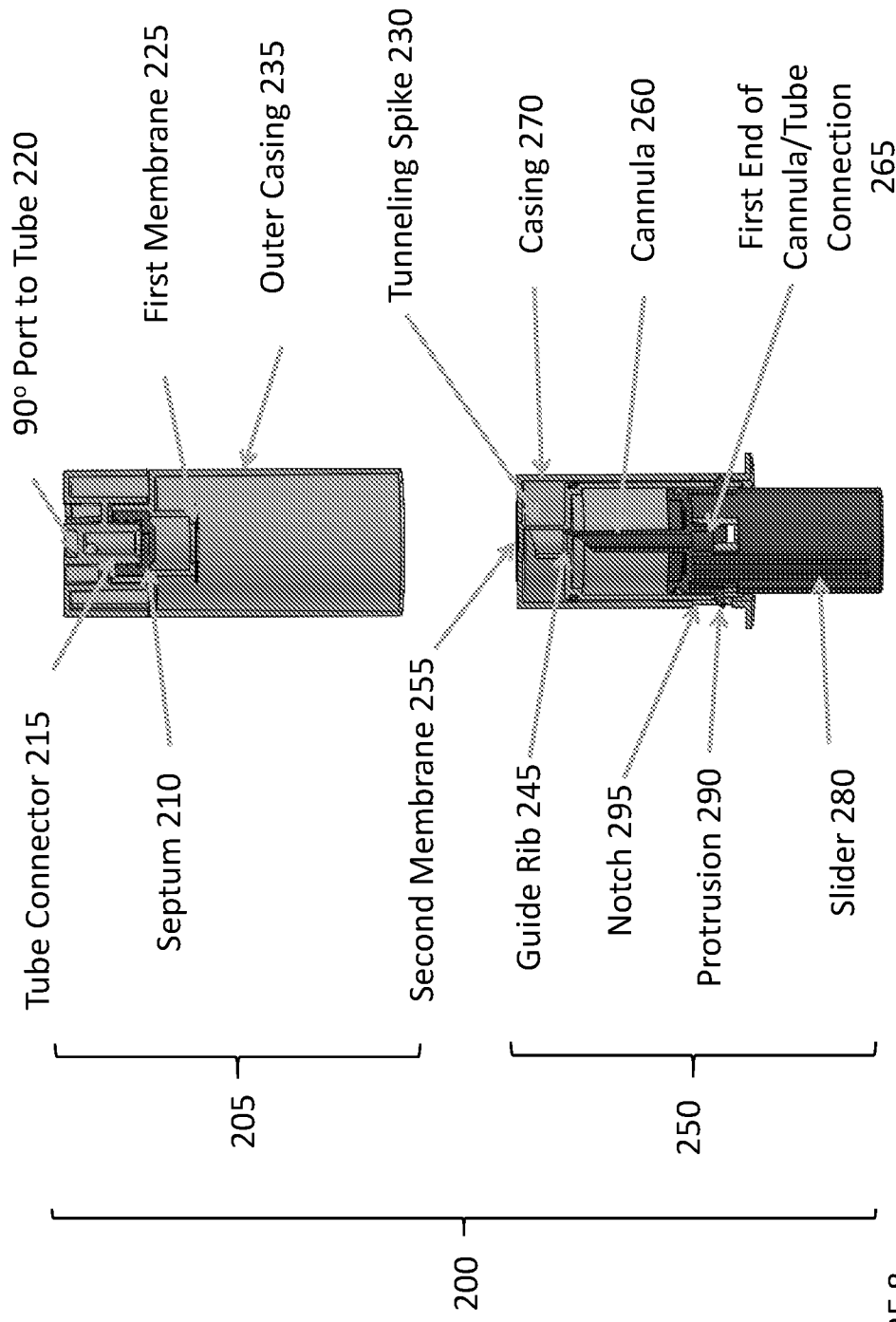


FIGURE 8

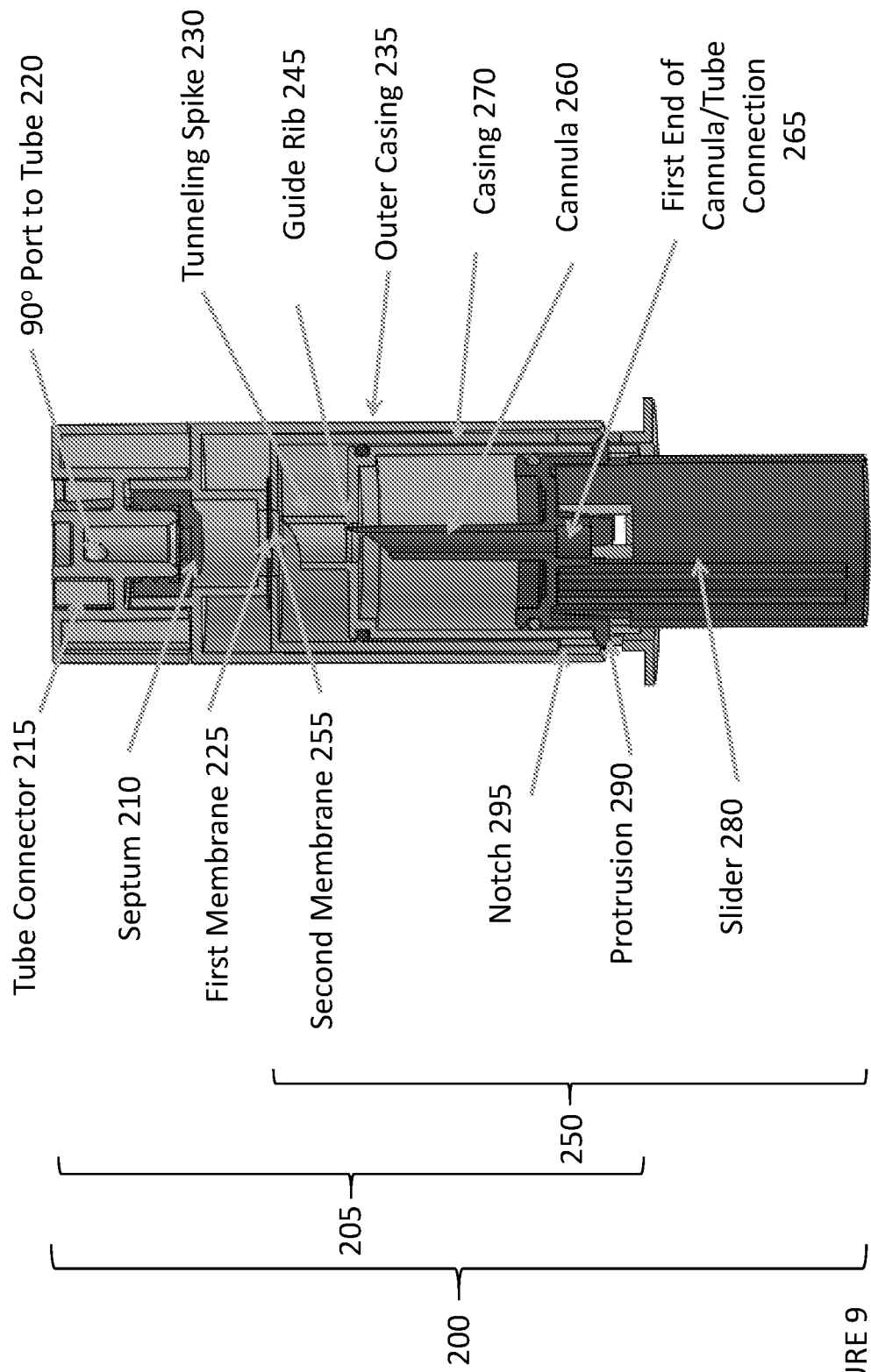


FIGURE 9

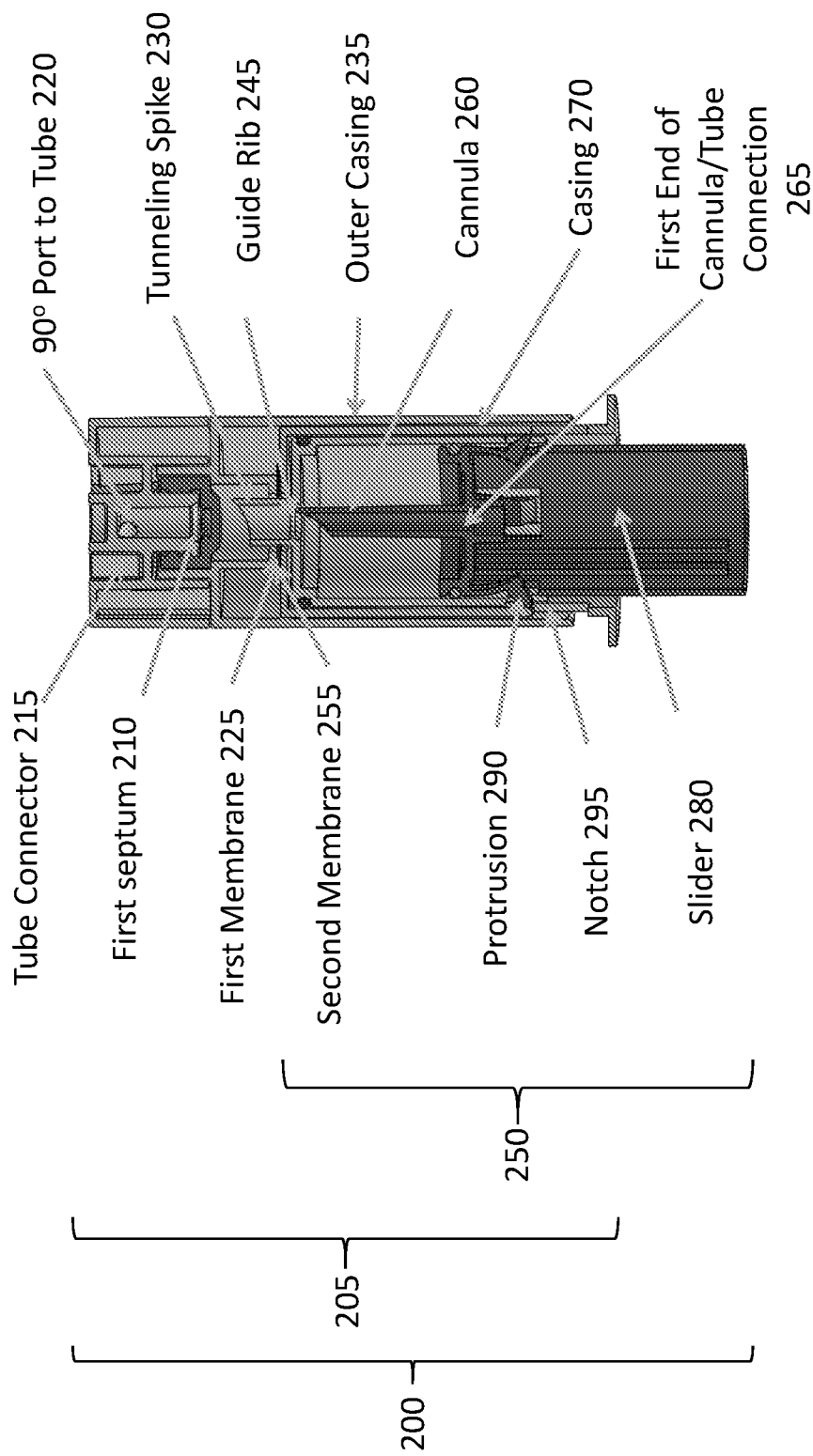


FIGURE 10

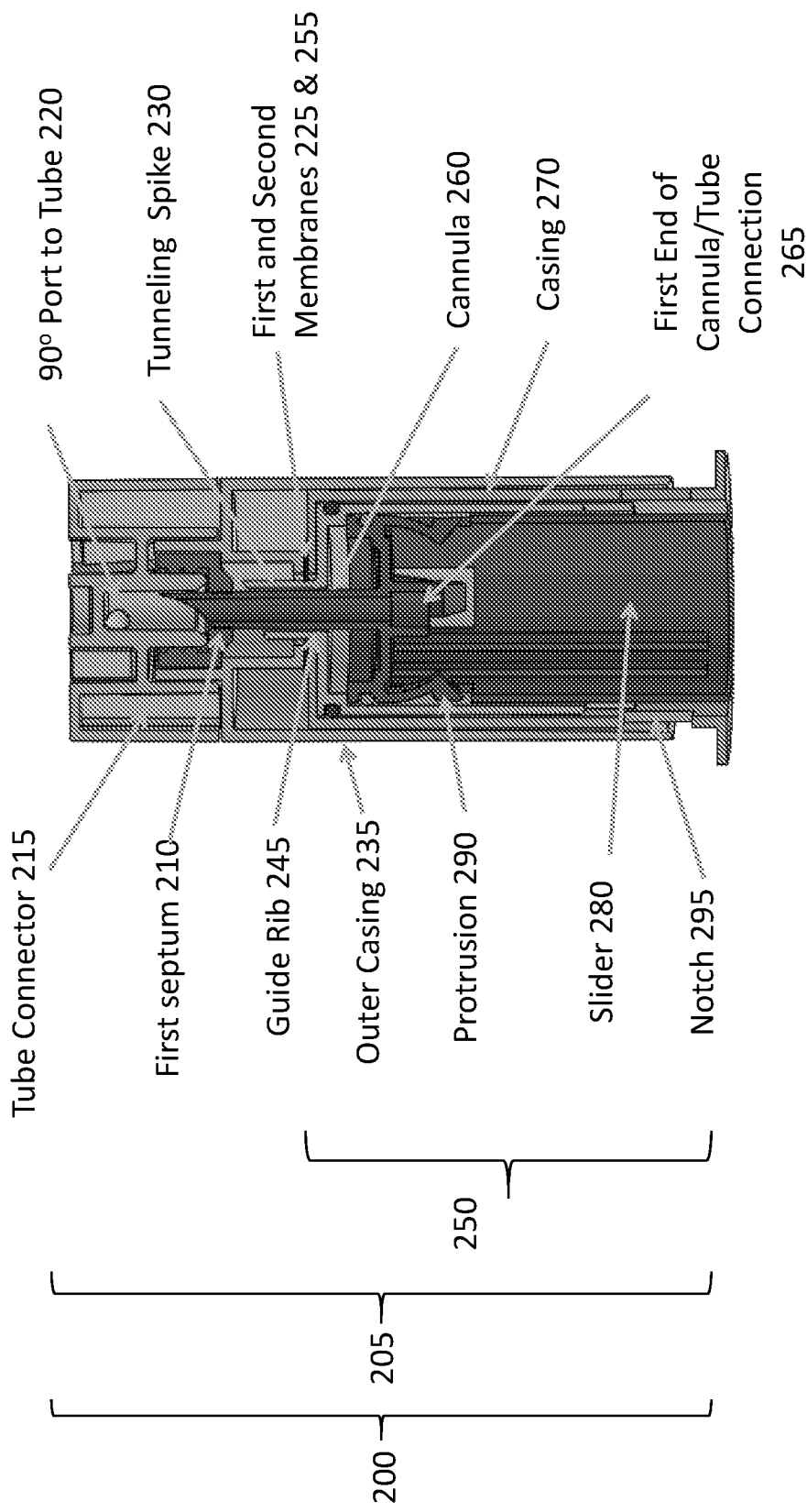


FIGURE 11

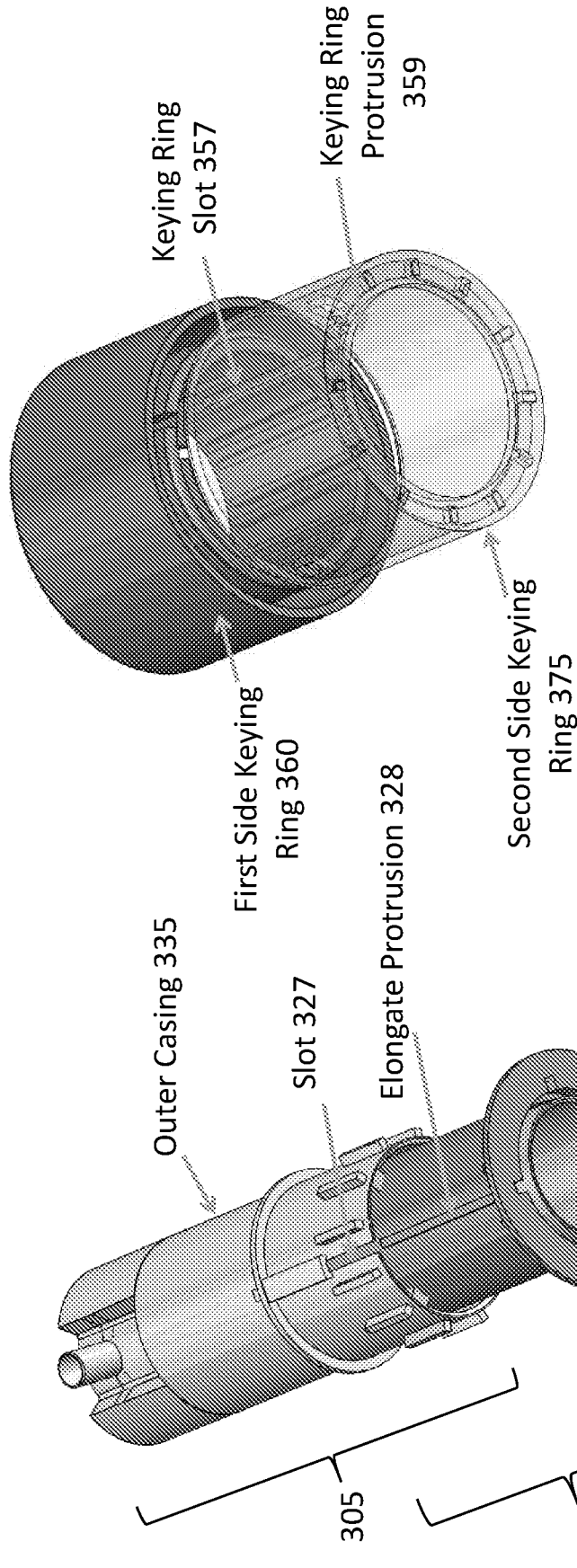


FIGURE 12A

FIGURE 12B

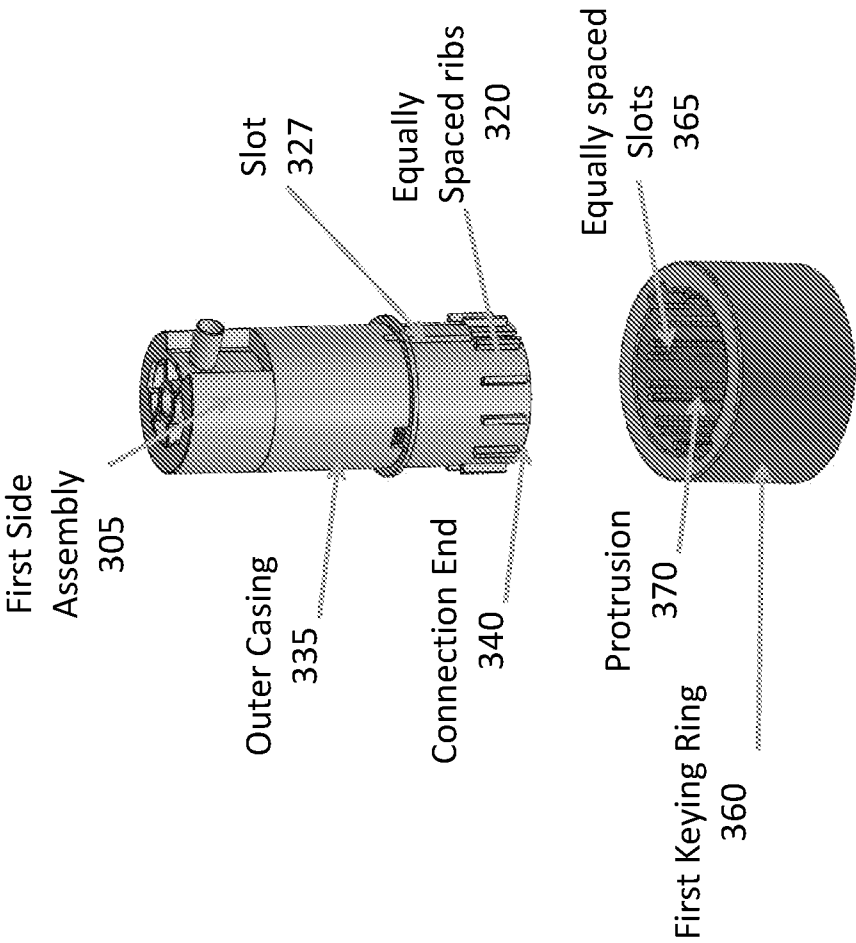


FIGURE 13A

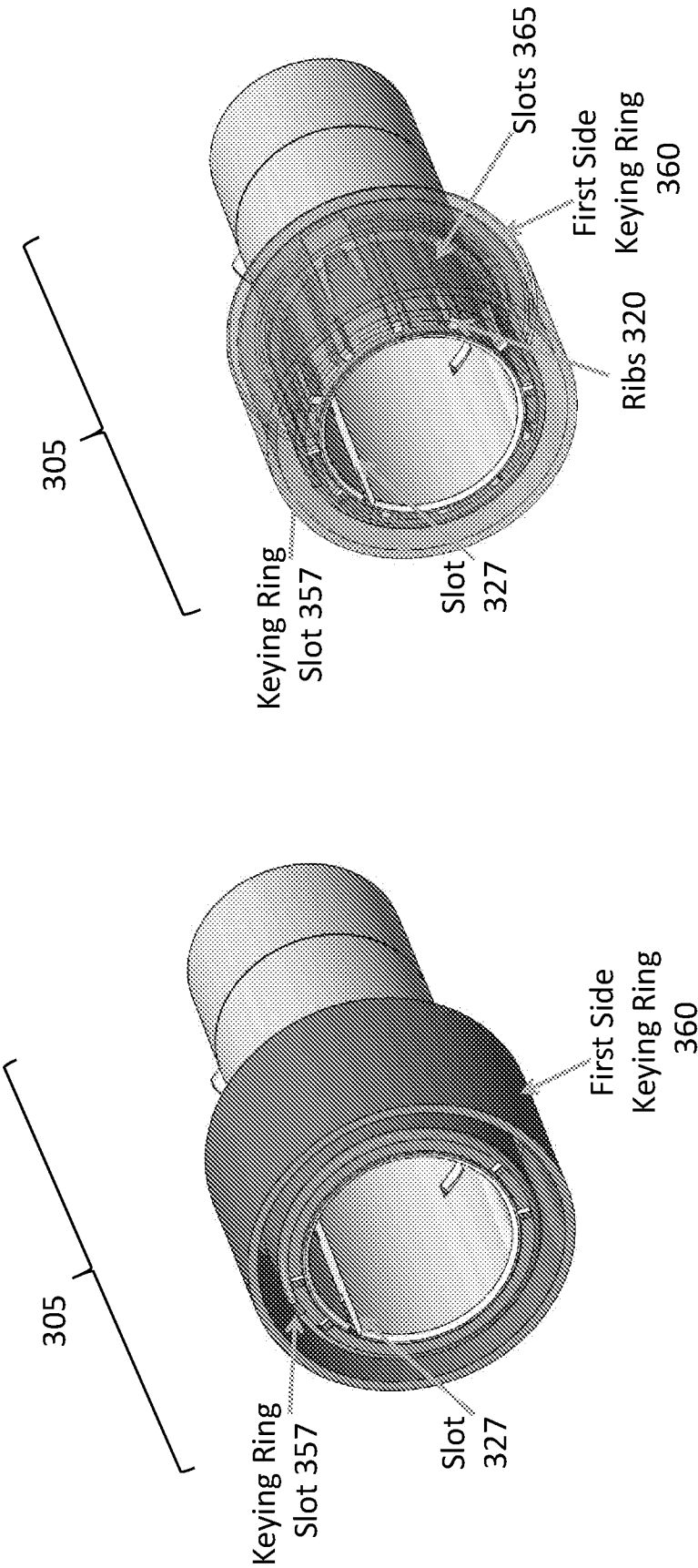


FIGURE 13C

FIGURE 13B

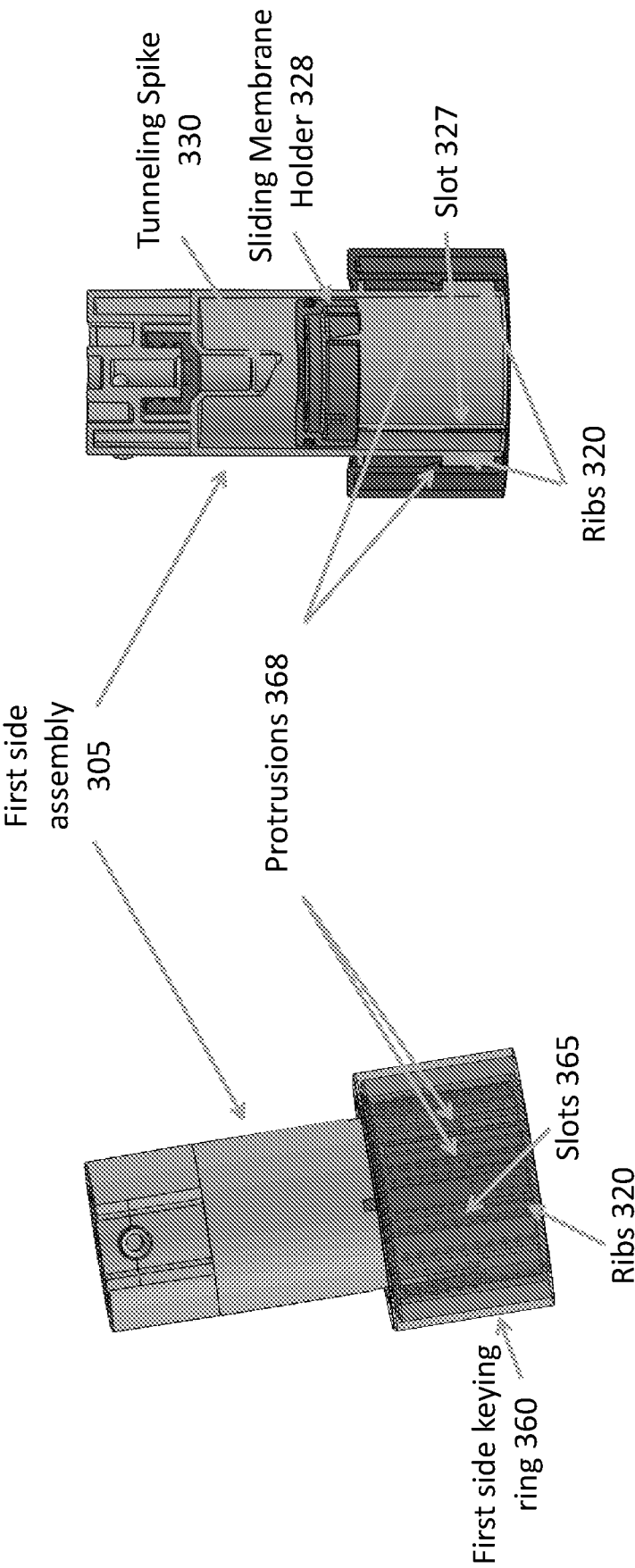


FIGURE 14B

FIGURE 14A

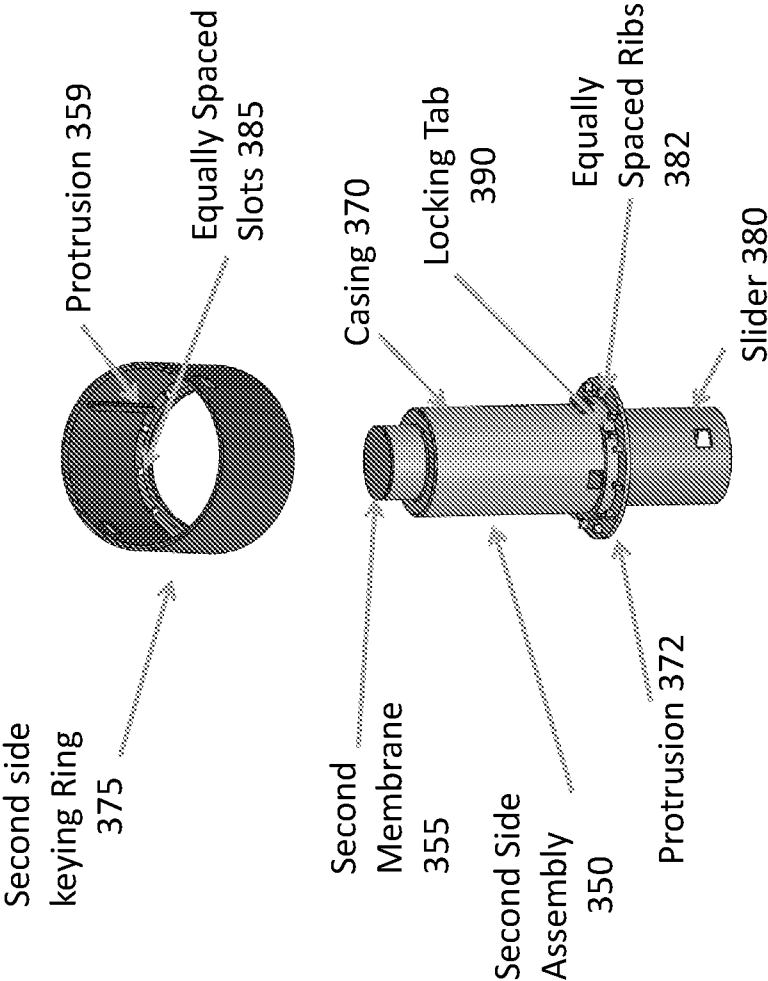


FIGURE 15A

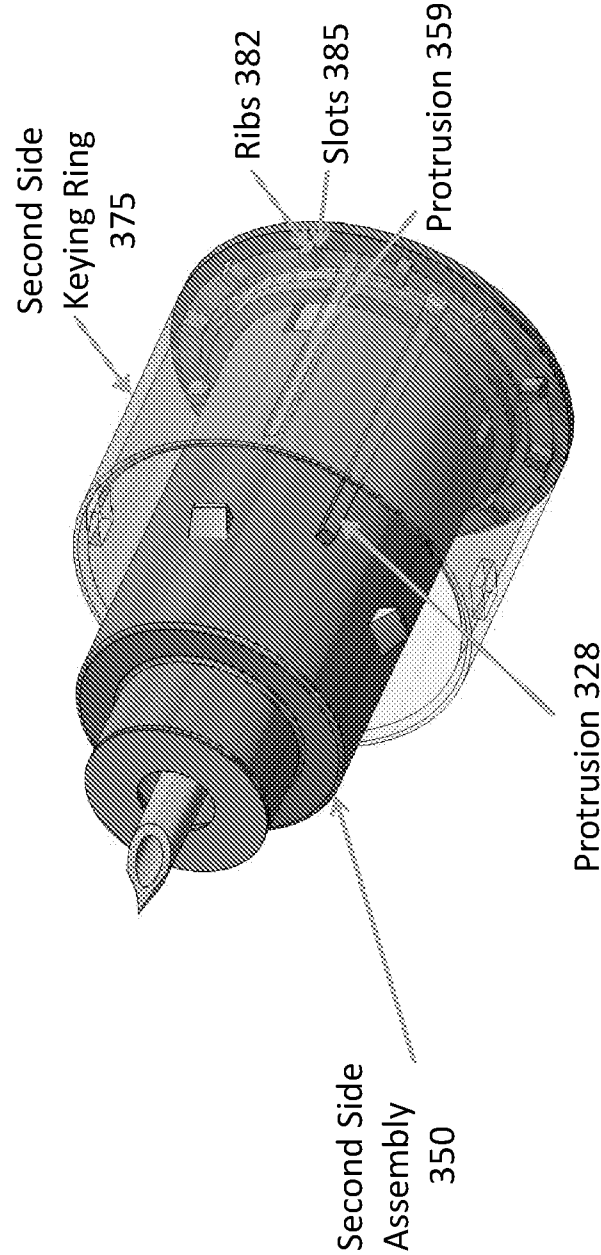


FIGURE 15B

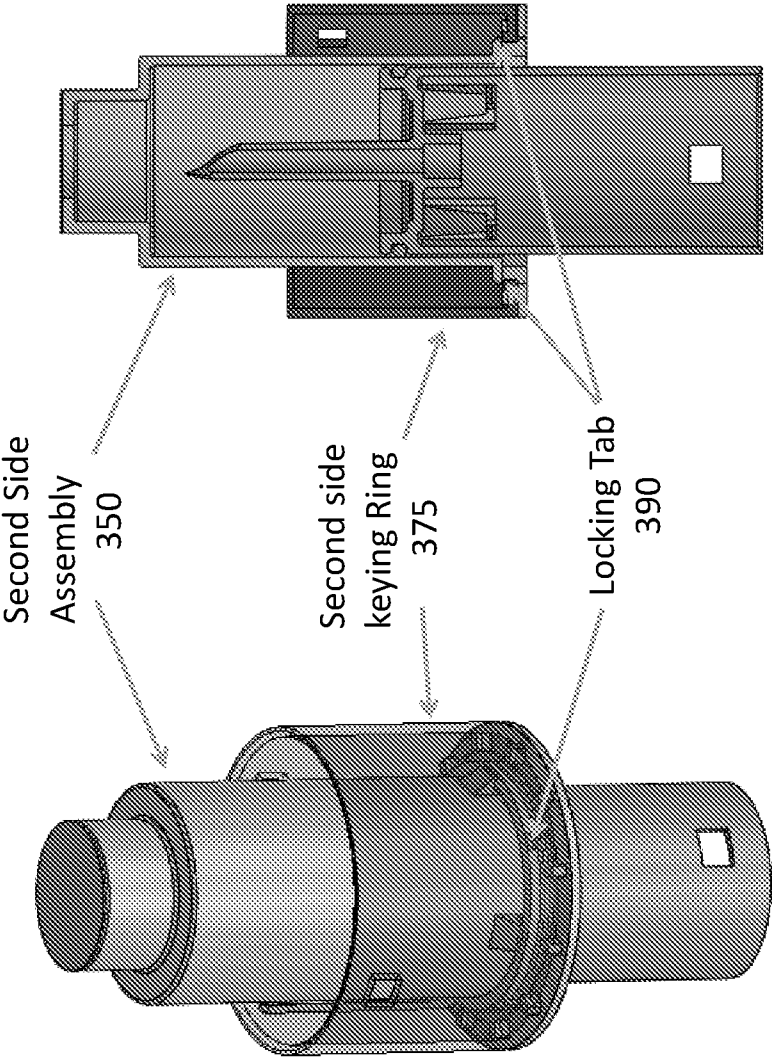


FIGURE 16A

FIGURE 16B

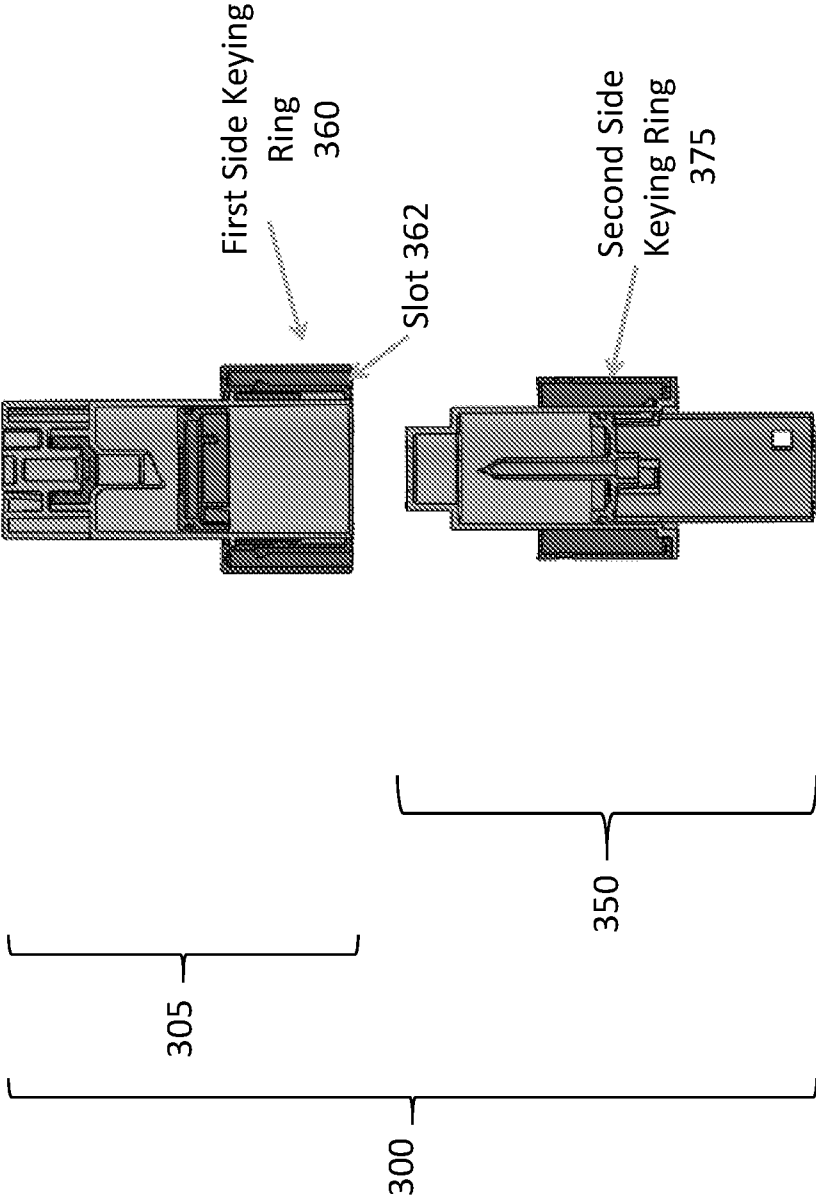


FIGURE 17

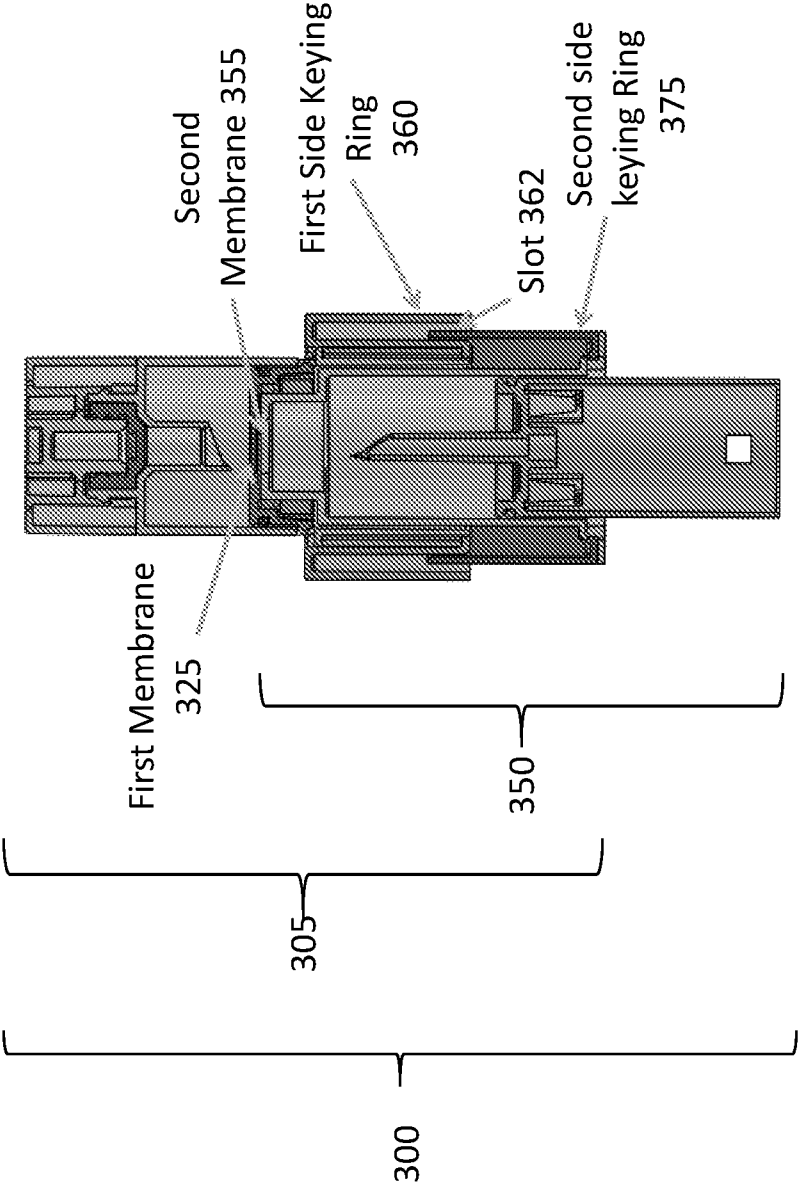


FIGURE 18

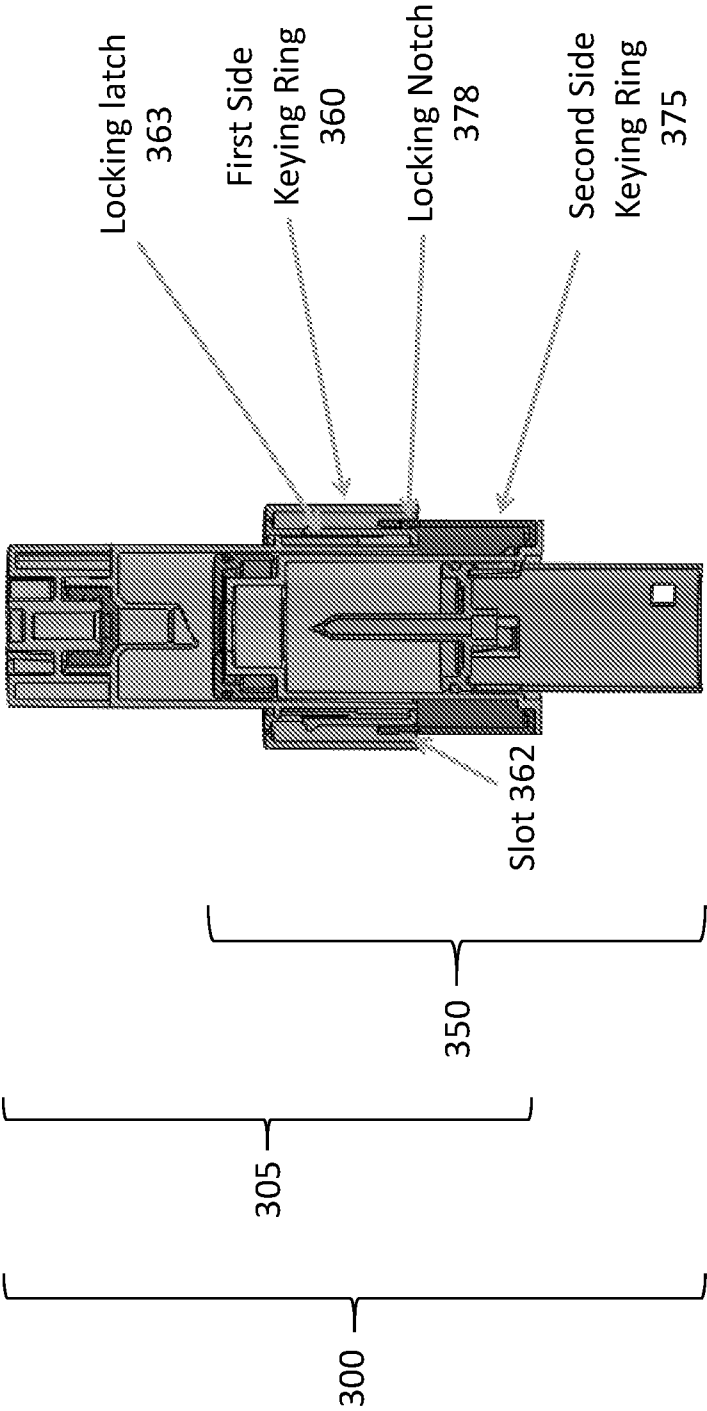


FIGURE 19

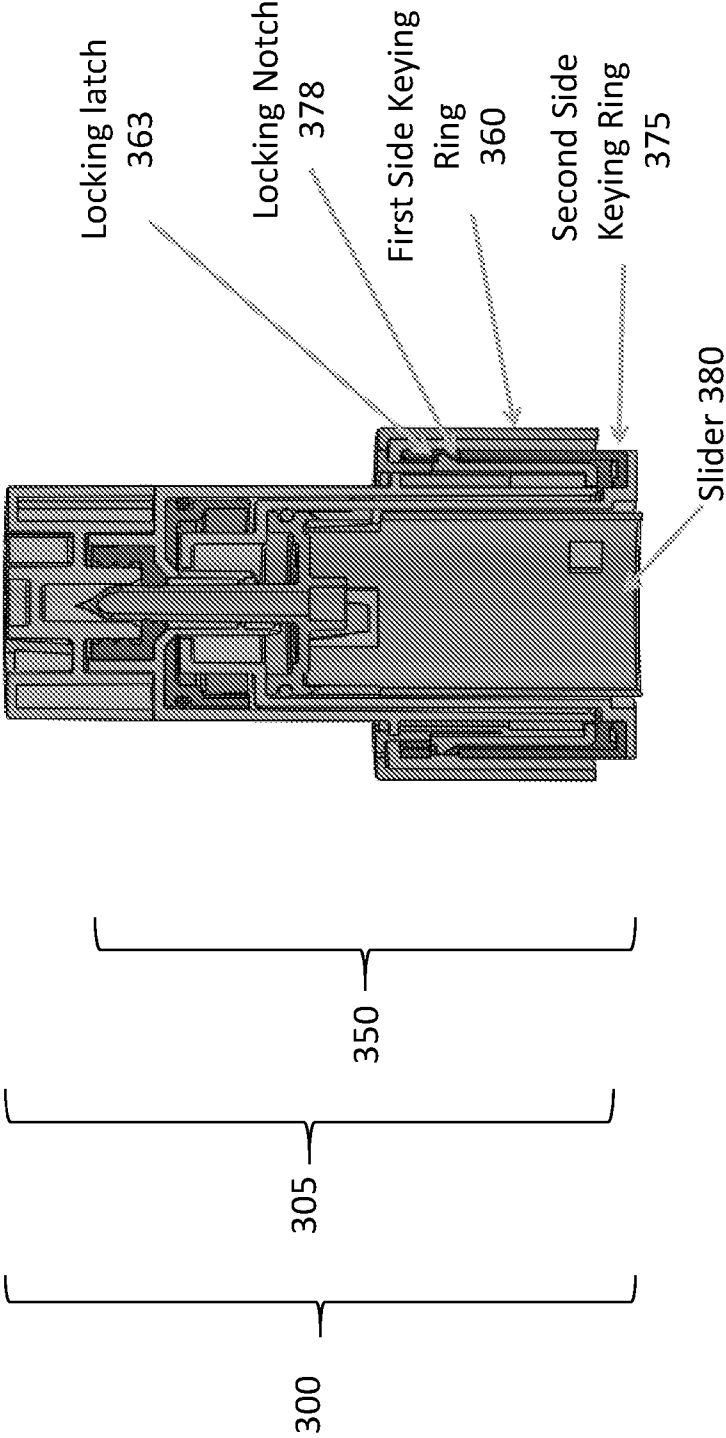


FIGURE 20

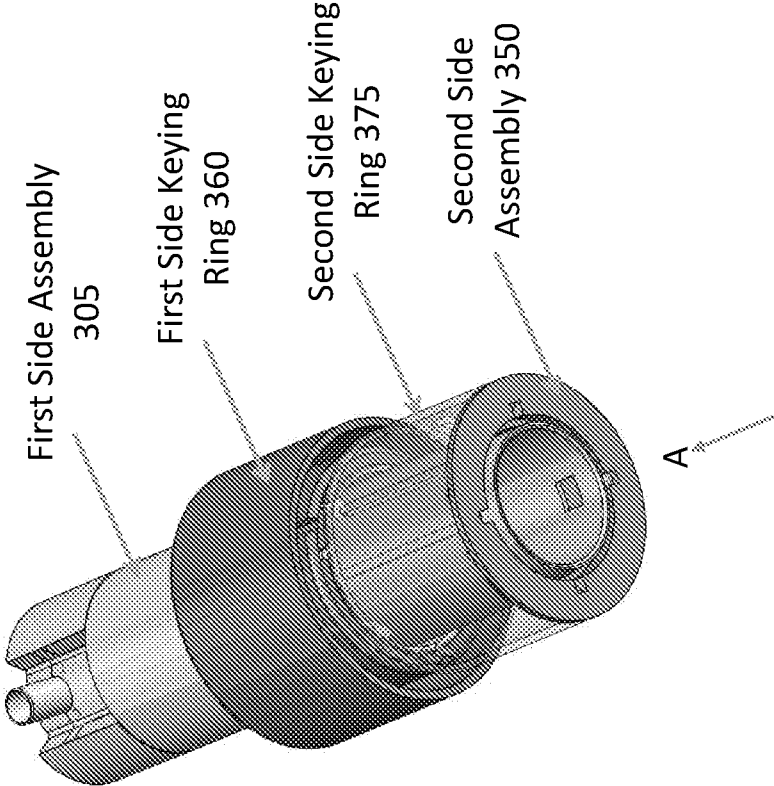


FIGURE 21A

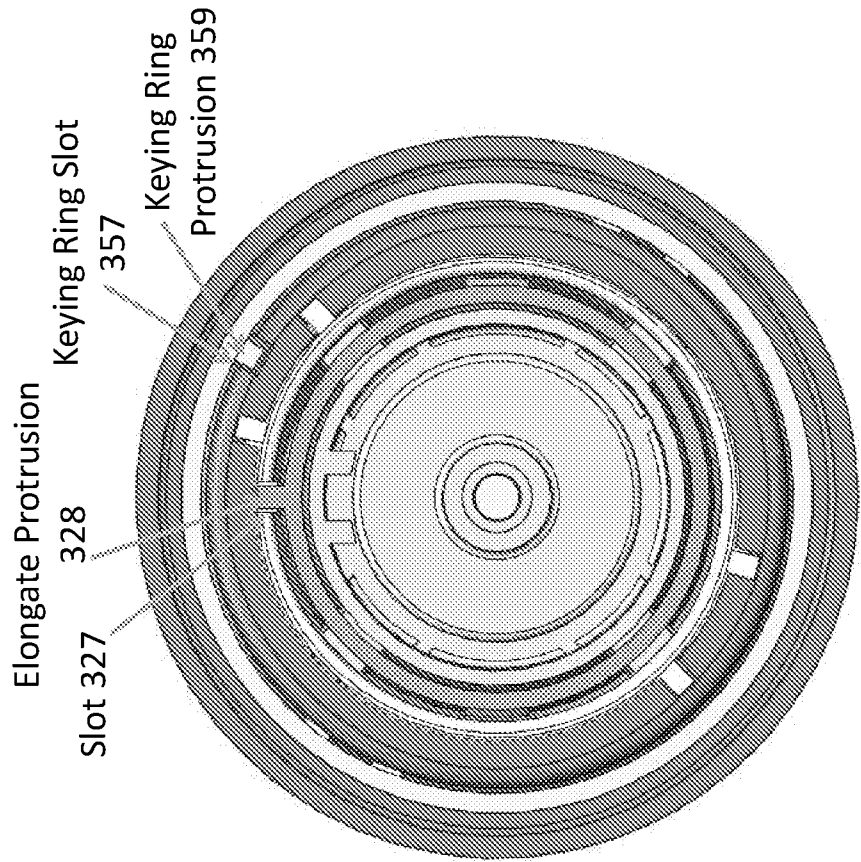


FIGURE 21B

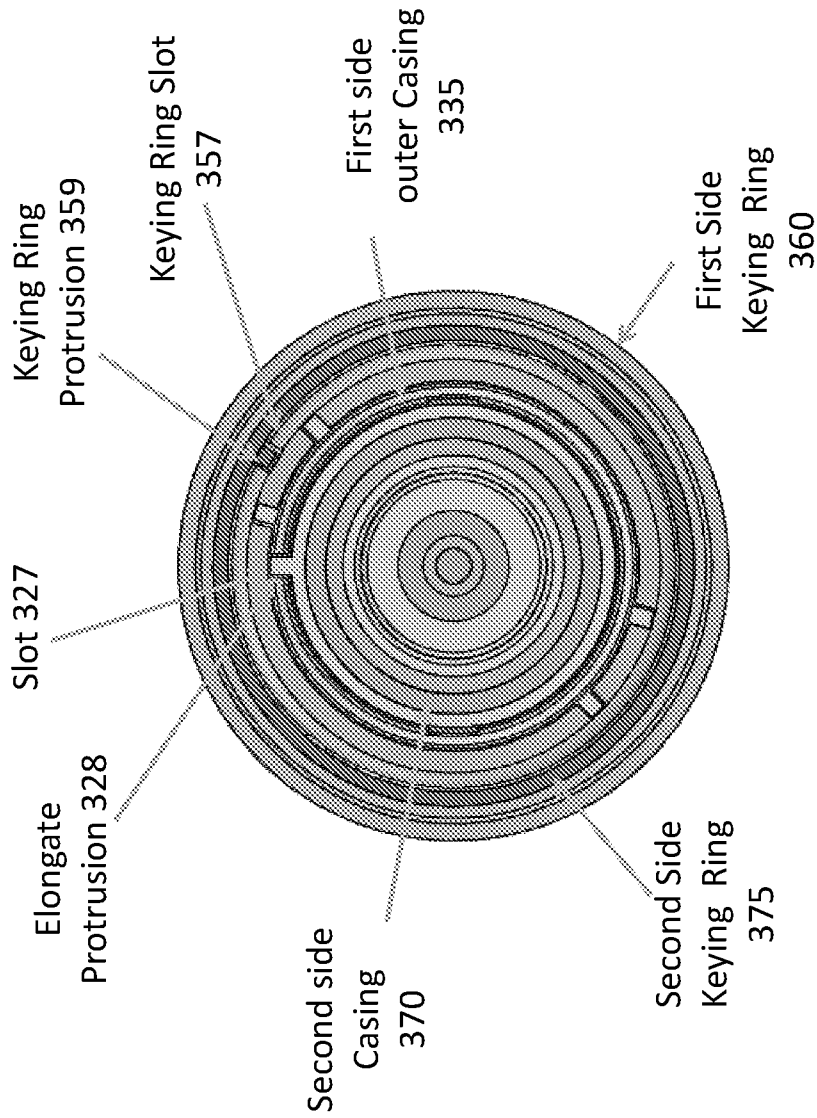


FIGURE 21C

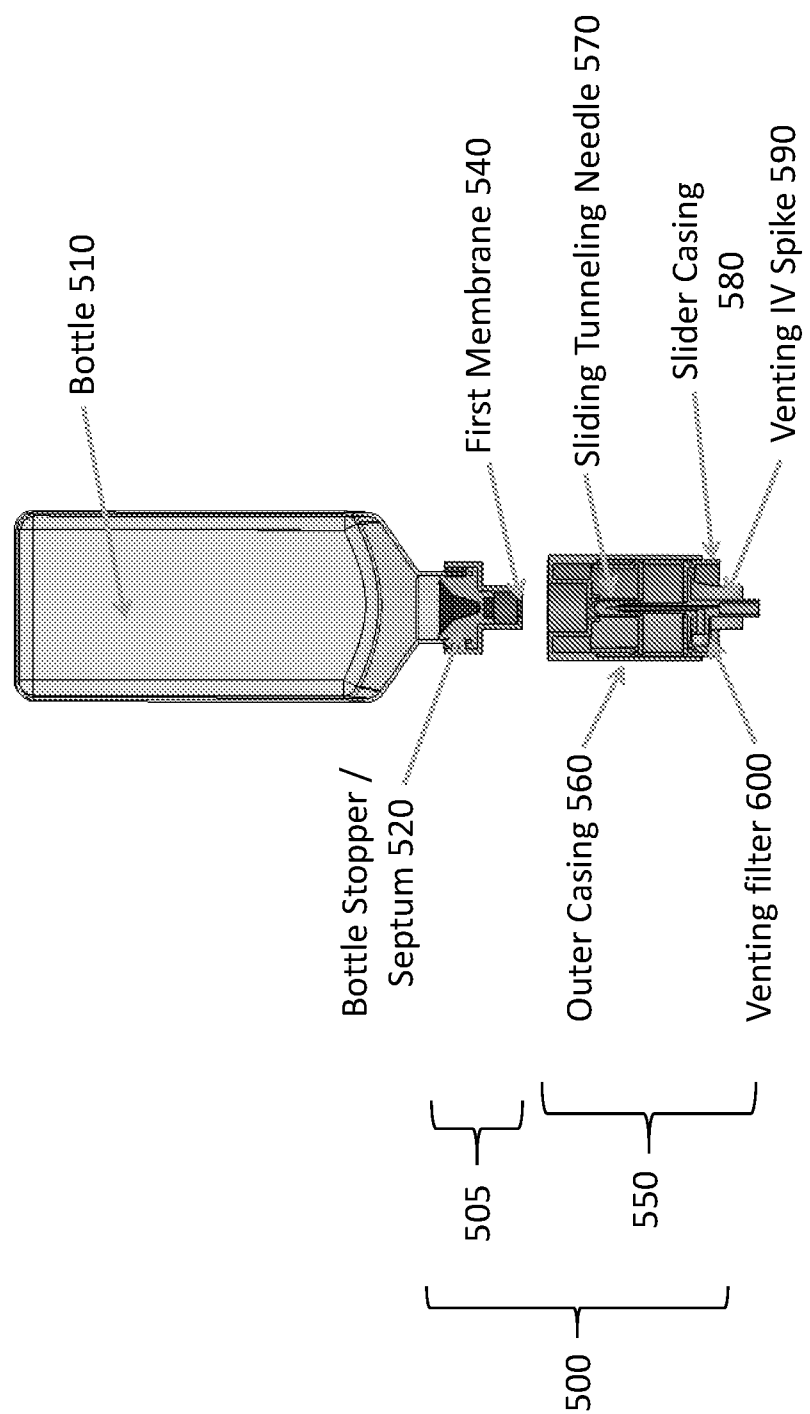


FIGURE 22

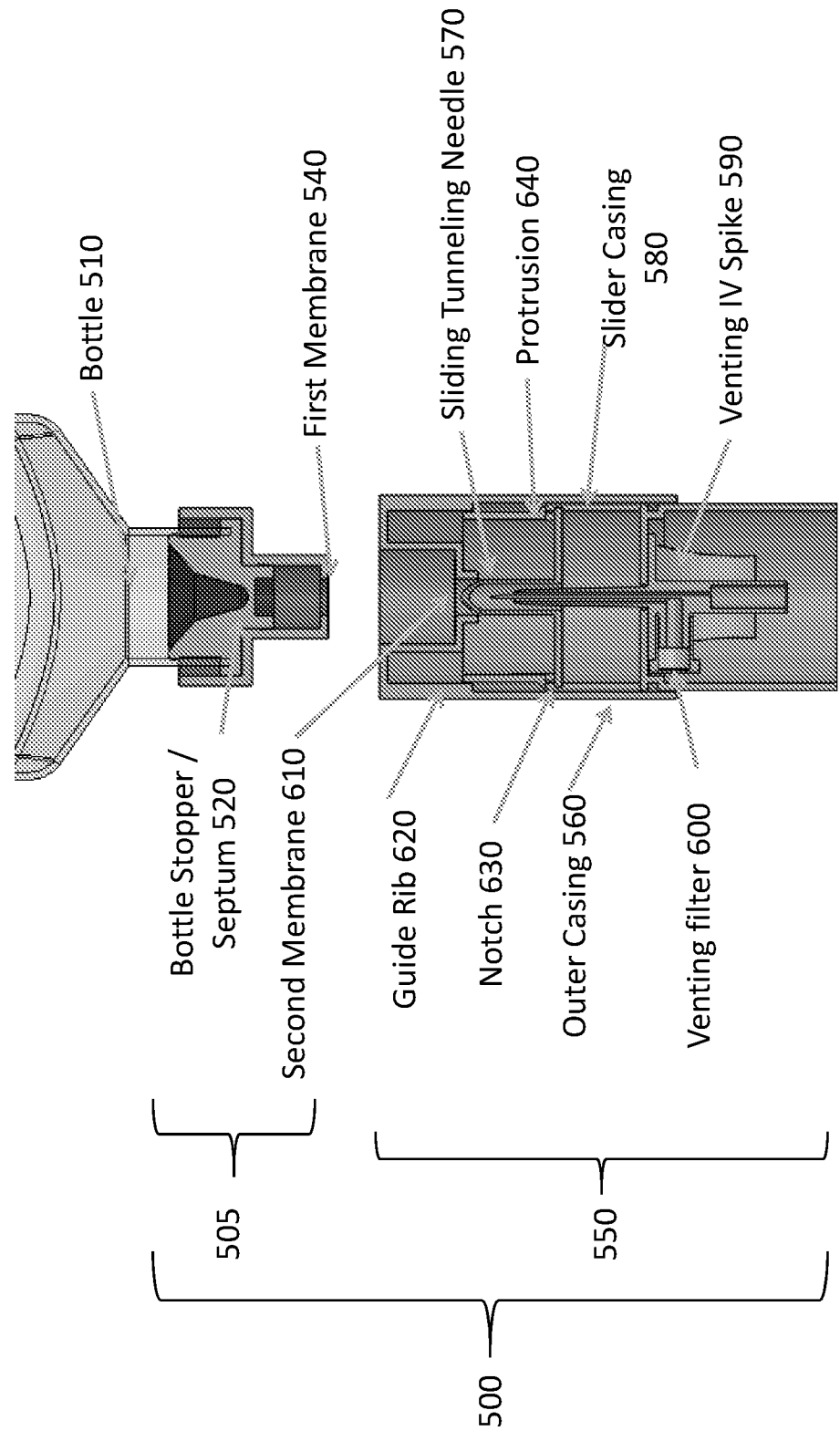


FIGURE 23

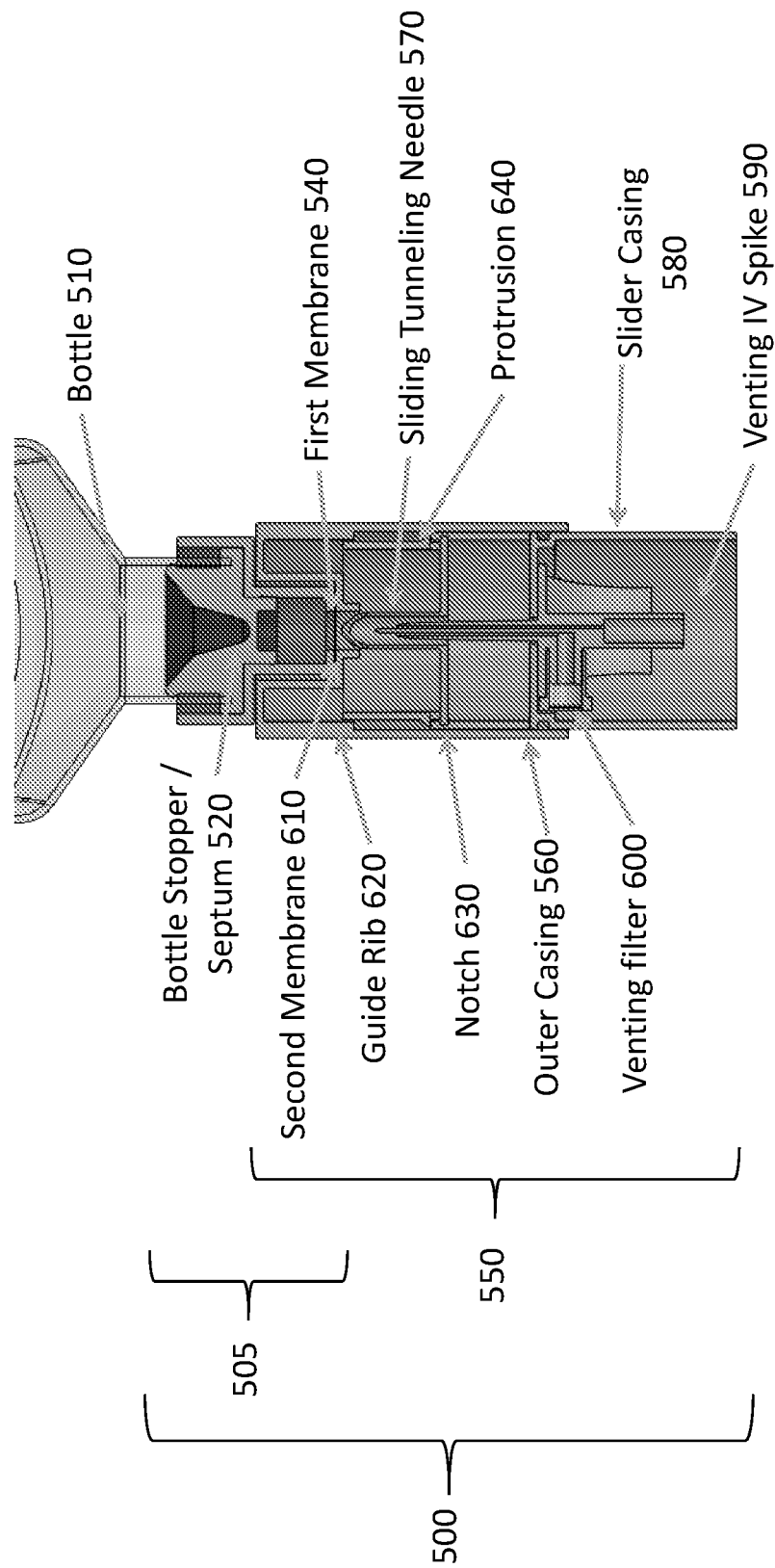


FIGURE 24

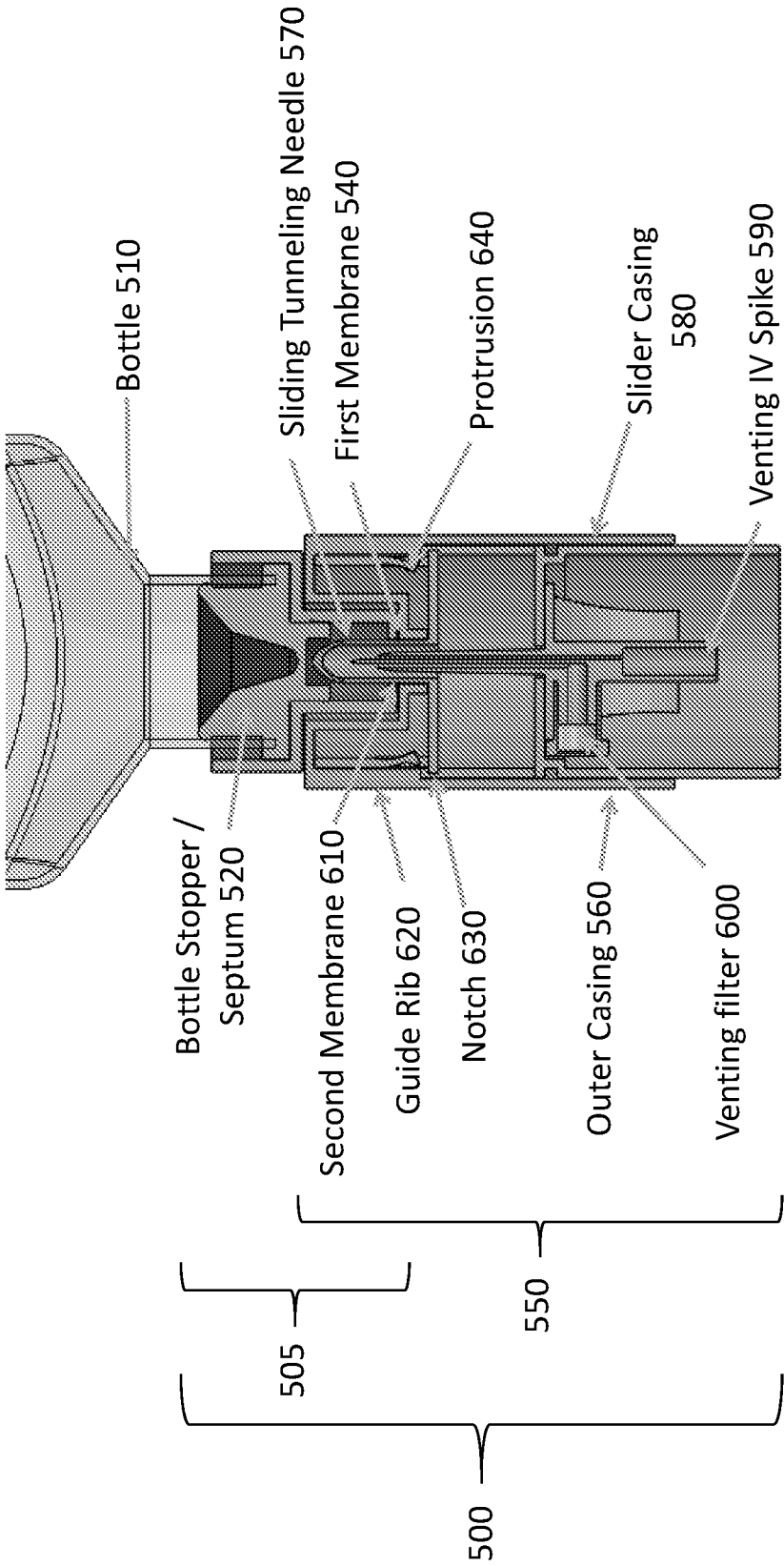


FIGURE 25

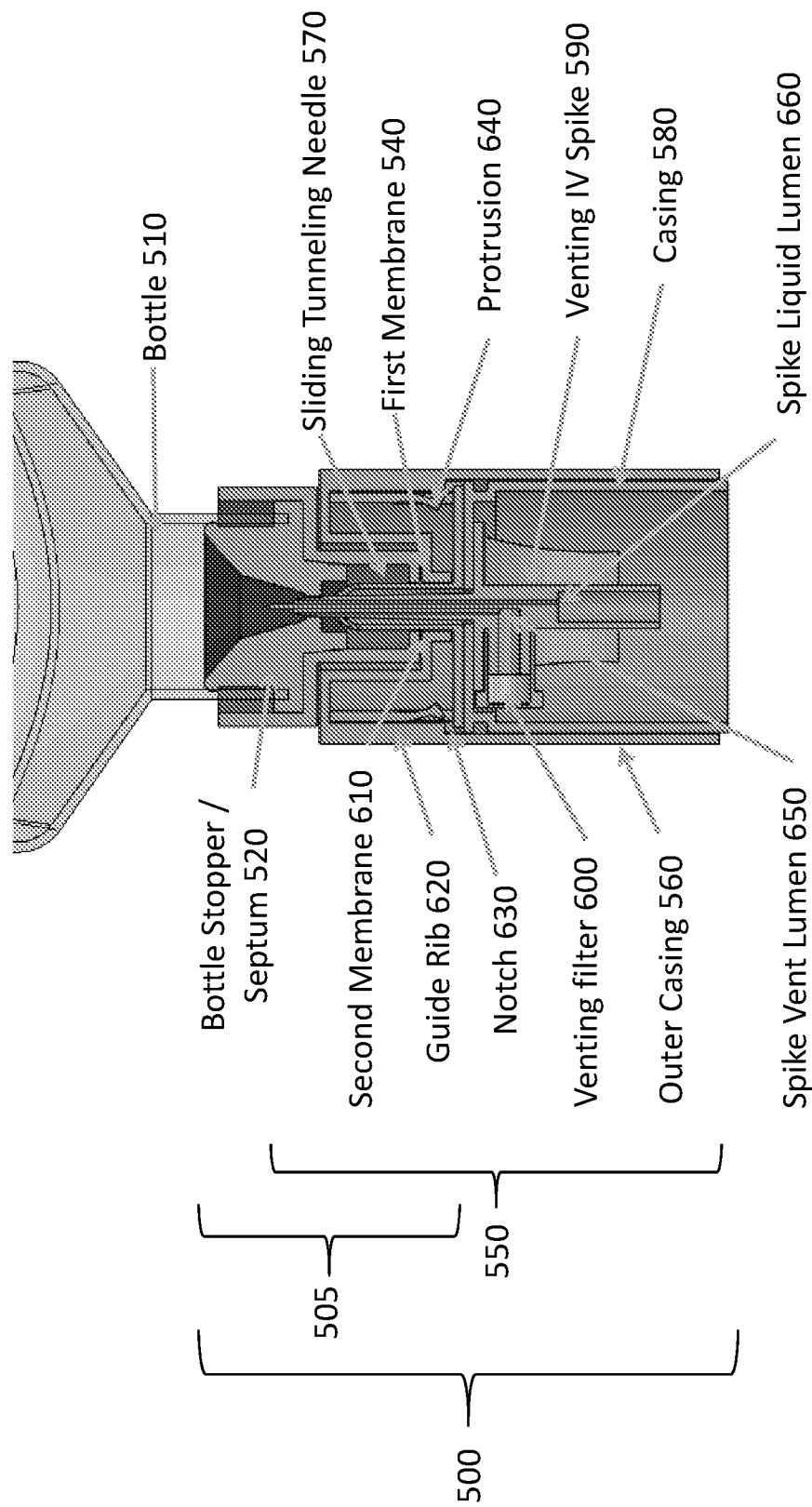


FIGURE 26

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2018/046278

A. CLASSIFICATION OF SUBJECT MATTER
INV. A61M39/10 A61M39/16 A61M39/18 A61M39/26
ADD.

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
A61M

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

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

EPO-Internal, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	EP 0 256 640 A2 (BETABROOK LTD [GB]) 24 February 1988 (1988-02-24) the whole document -----	1-17
A	EP 0 792 661 A2 (PROMEDICAL S R L [IT]) 3 September 1997 (1997-09-03) the whole document -----	1-17
A	WO 2006/122406 A1 (B & D RES AND DEV INC [CA]; COAMBS DAVID [CA]; WRIGHT BRIDGET ADELE [C] 23 November 2006 (2006-11-23) the whole document -----	1-17
A	FR 2 685 209 A1 (AGUETTANT LAB [FR]) 25 June 1993 (1993-06-25) the whole document -----	1-17



Further documents are listed in the continuation of Box C.



See patent family annex.

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Date of the actual completion of the international search

16 October 2018

Date of mailing of the international search report

24/10/2018

Name and mailing address of the ISA/

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040,
Fax: (+31-70) 340-3016

Authorized officer

Neiller, Frédéric

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/US2018/046278

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
EP 0256640	A2	24-02-1988	DE 3779515 D1 09-07-1992
		DE 3779515 T2 11-02-1993	
		EP 0256640 A2 24-02-1988	
		ES 2032824 T3 01-03-1993	

EP 0792661	A2	03-09-1997	NONE

WO 2006122406	A1	23-11-2006	AU 2006246933 A1 23-11-2006
		CA 2607998 A1 23-11-2006	
		EP 1896118 A1 12-03-2008	
		JP 2008539992 A 20-11-2008	
		US 2008197626 A1 21-08-2008	
		WO 2006122406 A1 23-11-2006	

FR 2685209	A1	25-06-1993	NONE
