(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
24 January 2019 (24.01.2019)

WIPO | PCT

(10) International Publication Number
WO 2019/018342 A1

(51) International Patent Classification:
A61B 17/34 (2006.01) *A61B 5/055* (2006.01)
A61B 90/11 (2016.01) *A61B 34/20* (2016.01)
A61B 90/10 (2016.01) *A61B 34/10* (2016.01)

(21) International Application Number:
PCT/US2018/042391

(22) International Filing Date:
17 July 2018 (17.07.2018)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
62/533,207 17 July 2017 (17.07.2017) US
PCT/US2017/049191
29 August 2017 (29.08.2017) US

(71) Applicants: **VOYAGER THERAPEUTICS, INC.** [US/US]; 75 Sidney Street, Cambridge, Massachusetts 02139 (US). **THE REGENTS OF THE UNIVERSITY OF CALIFORNIA** [US/US]; 1111 Franklin Street, Twelfth Floor, Oakland, California 94607 (US).

(72) Inventor; and
(71) Applicant: **ROSENBLUTH, Kathryn** [US/US]; 1111 Franklin Street, Twelfth Floor, Oakland, California 94607 (US).

(72) Inventors: **KELLS, Adrian Philip**; 75 Sidney Street, Cambridge, Massachusetts 02139 (US). **SCHRECK, Stefan**; 32218 NE 134th St, Duvall, Washington 98019 (US). **LUTTICH, Edward H.**; 1804 Willow Glen Rd, Fallbrook, California 92028 (US). **BLOCH, Kenneth A.**; 14897 Summerbreeze Way, San Diego, California 92128 (US). **BANKIEWICZ, Krystof**; 1111 Franklin Street, Twelfth Floor, Oakland, California 94607 (US).

(74) Agent: **WARD, Donna T.** et al.; 142A Main Street, Groton, Massachusetts 01450 (US).

(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DJ, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JO, JP, KE, KG, KH, KN, KP, KR, KW, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA,

(54) Title: TRAJECTORY ARRAY GUIDE SYSTEM

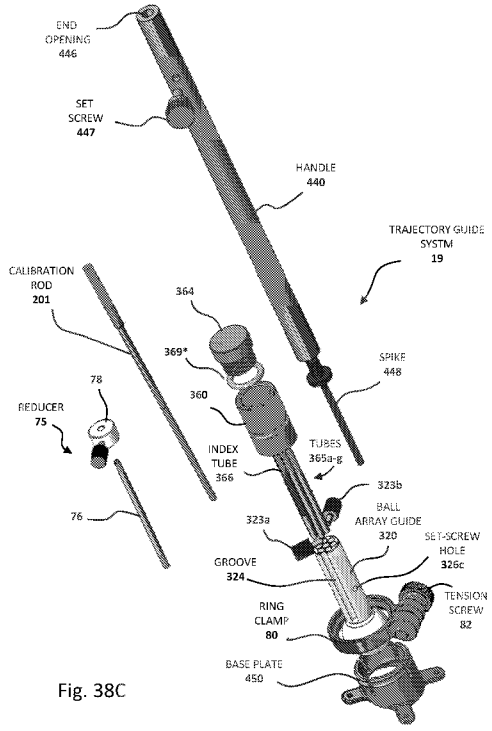


Fig. 38C

(57) Abstract: The present disclosure presents a trajectory array guide system (19) for defining a trajectory to a target location in the brain of a subject and for guiding an elongated tool along the trajectory. The trajectory array guide system (19) can comprise a base (450), an array guide (320), an imaging unit (360), and an elongated handle (440) configured for connection with a stereotaxic navigation system. The present disclosure presents a method of using a trajectory array guide system (19) for defining a trajectory to a target location in the brain of a subject and for guiding an elongated tool along the trajectory.

WO 2019/018342 A1

[Continued on next page]

SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

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

Published:

— *with international search report (Art. 21(3))*

TRAJECTORY ARRAY GUIDE SYSTEM

CROSS REFERENCE TO RELATED APPLICATIONS

[0001] The present application claims priority to U.S. provisional application 62/533,207, filed July 17, 2017, entitled TRAJECTORY ARRAY GUIDE SYSTEM, and to PCT/US2017/049191, filed August 29, 2017, entitled METHODS FOR BIOMEDICAL TARGETING AND DELIVERY AND DEVICES AND SYSTEMS FOR PRACTICING THE SAME, the contents of each of which are hereby incorporated by reference herein in its entirety.

BACKGROUND

[0002] The present disclosure relates to brain surgery and more specifically to the field of trajectory array guides for placement of surgical tools used for delivery of therapeutic agents or measurement devices to specific locations in the brain.

[0003] Precise access to brain structures is frequently required for an assortment of indications, including tissue sampling, catheter or electrode placement, and localized drug delivery. The most common means of performing these procedures is to use either frame based or frameless stereotaxy. In either case, a preoperative imaging session is performed to characterize and localize the specific brain target. Magnetic resonance imaging (MRI) is the preferred technique for preoperative demarcation of brain structures due to the quality and range of tissue contrast that can be achieved. Utilization of previously acquired imaging information during surgery requires some system for registering the image data to the patient on the operating table. This may be achieved with an external frame that is visible on imaging or the identification of implanted markers or characteristic features in the frameless case. In either situation, target points are determined based on the previously acquired images and are used to guide the surgical procedure. This has disadvantages, as the registration process is imperfect and prone to error, and there is no ability to update the images to compensate for dynamic effects such as brain shift. Moreover, there is no opportunity to either confirm that the surgical goals have been met or to monitor deposition of a delivered therapeutic agent, physiological change or instrument operation during the procedure (Martin et al. *J. Magn. Reson. Imaging*, 2008, 27, 737-743).

[0004] An alternative to this traditional means of accessing brain structure is to immobilize the patient's head during imaging and perform the surgery within the magnetic resonance bore. This approach also has obvious disadvantages, most notably the physical presence of the magnet and the corresponding magnetic field. However, it overcomes the

need for registration and permits intraprocedural image updates. It also may provide novel insight into the guidance, administration, and evaluation of interventions and therapies. There are several different means of performing stereotactic procedures within an MRI system. Lower field, open systems, afford some degree of line-of-site and therefore instruments can be tracked in a manner analogous to conventional frameless stereotaxy without moving the head out of the MRI system. The orientation of these tracked devices can further be used to prescribe the slice in which imaging is to be performed. In closed bore systems it is much less practical to track devices via optical means. The magnetic resonance environment itself, however, permits opportunities to track and visualize devices either by passive or active means. The latter is achieved by integrating microcoils into the appropriate surgical tools and tracking their position within the bore via MR methods. Passive methods simply require that the device be visible within acquired images either by positive or negative contrast.

[0005] Prospective stereotaxy is a technique for aligning a trajectory array guide within a magnetic resonance system. The general approach requires that a patient be immobilized within the magnetic resonance scanner and a trajectory array guide be mounted on a rigid surface such as the skull. Imaging is then performed to define the desired trajectory, usually in two orthogonal planes, from the entry point to the remote target. The trajectory array guide is aligned with real-time imaging followed by confirmatory scans to assure the intended path will be followed. This approach has been used to guide brain biopsy and the insertion of deep brain stimulator electrodes (Martin et al. J. Magn. Reson. Imaging, 2008, 27, 737-743).

[0006] The optimal trajectory is established by analyzing the magnetic resonance images of the brain, considering the location of the targeted segment of the brain, suitable entry point on the skull, and critical organs and vessels that need to be avoided (e.g. blood vessels) to minimize the risk of complications. Once the trajectory is established, a mounting system external to the head of the patient is used to position the catheter along the trajectory and guide the insertion of the catheter into the brain. This process tends to be iterative and involves image analysis of the actual trajectory of the mounting system versus the desired trajectory. Repositioning of the mounting system is typically required until the actual trajectory coincides with the desired trajectory.

[0007] A number of efforts have been made to develop trajectory array guide systems for delivery of elongated tools such as catheters to target locations in the brain. Examples of such systems and related tools are disclosed in U.S. Patents 9,042,958, 8,845,665, 7,981,120, 8,845,656, and 8,591,522 and in published U.S. Patent Application Nos. 20150100064 and 20010014771, each of which is incorporated herein by reference in its entirety.

[0008] Many challenges remain with regard to development of trajectory array guide systems. A number of such challenges are addressed by various embodiments of the present disclosure.

SUMMARY

[0009] The present disclosure provides a trajectory array guide system and kit as well as a method for delivering an elongated tool to a target location in the brain of a subject.

[0010] The present disclosure provides a trajectory array guide system for defining a trajectory to a target location in the brain of a subject and for guiding an elongated tool along the trajectory. In some embodiments, the trajectory array guide system includes: a combination of a base and an array guide in a lockable ball-socket pivoting mechanism, wherein the base is configured for attachment to the skull of a subject and the array guide is defined by a series of lumens or is defined by a bore configured to hold a separate array unit defined by a series of lumens; an imaging unit configured for engagement with the array guide and configured to hold and direct imaging fluid along passages which are co-axial with the lumens of the array guide for the purpose of defining a series of trajectories; and an elongated handle having sufficient length for connection to an image-guided stereotaxic navigation system, the handle configured for attachment to either the array guide or the imaging unit.

[0011] In some embodiments, the trajectory array guide system includes an array guide. In some embodiments, the array guide includes a ball component. In some embodiments, the trajectory array guide system also includes a base which includes a socket configured to receive and hold the ball of the array guide. In some embodiments, the socket has a central axis orthogonal to a plane formed by the bottom of the base. In some embodiments, the socket has a central axis which is non-orthogonal with respect to the plane formed by the bottom of the base, thereby providing a tilted socket. In some embodiments, the tilted socket increases the angle range of a series of trajectories. In some embodiments, the central axis of the socket is angled by about 10 to about 30 degrees from the axis orthogonal to the plane formed by the bottom of the base.

[0012] In some embodiments, the trajectory array guide system includes a socket which has an outer sidewall. In some embodiments, the outer sidewall includes threads or one or more grooves configured for attachment to a locking element. In some embodiments, the locking element prevents pivoting movement of a ball within the socket when the locking element is engaged to the outer sidewall of the socket. In some embodiments, the locking

element is a ring-clamp configured for connection to the one or more grooves. In some embodiments, the locking element is a locking nut configured for connection to the threads.

[0013] In some embodiments, the trajectory array guide system includes a base which includes a plurality of attachment members. In some embodiments, the plurality of attachment members are accessible by an attachment tool for attaching the base to the skull of a subject.

[0014] In some embodiments, the trajectory array guide system includes an array guide which is a generally cylindrical or funnel-shaped member with openings at both ends, having a ball formed at one end and a series of lumens extending longitudinally along the length of the array guide between the openings at both ends. In some embodiments, the series of lumens includes seven substantially parallel lumens with six lumens arranged in a symmetrical hexagonal pattern and a seventh lumen located in the center of the symmetrical hexagonal pattern. In some embodiments, the trajectory array guide system further includes an imaging unit which includes an upper reservoir in fluid communication with a series of lower extensions which are co-axial with the lumens of the array guide. In some embodiments, the lower extensions are tubes configured to fit inside the lumens of the array guide. In some embodiments, the array guide includes an outer groove and the imaging unit includes an index tube configured to slide into the outer groove when the imaging unit is engaged with the array guide. In some embodiments, the index tube is provided as a reference point for identification of each of the tubes in magnetic resonance images. In some embodiments, the imaging unit includes a cap to seal the imaging fluid inside the imaging unit. In some embodiments, the array guide includes a locking mechanism for locking the tubes in place within the array guide. In some embodiments, the locking mechanism includes at least one set-screw which penetrates the array guide and makes tightening contact with at least one of the tubes. In some embodiments, the locking system includes three set-screws, each penetrating the body of the array guide to enter two different lumens as well as the seventh lumen. In some embodiments, the three set-screws are placed closer to the ball of the ball array guide than to the upper end of the ball array guide.

[0015] In some embodiments, the trajectory array guide system includes a handle. In some embodiments, the handle includes a connector end configured for attachment to the outside or the inside of an imaging unit. In some embodiments, the connector end is configured for attachment to the outside of the imaging unit and includes an opening for a connector set-screw to lock the handle on the imaging unit. In some embodiments, the handle includes an end spike for insertion into one of the lumens of a ball array guide for direct

connection of the handle to the ball array guide. In some embodiments, the handle is at least partially hollow and has an outer end opening at the end opposite the end spike, the outer end opening configured for connection to a navigation pointer of an image guided surgery system.

[0016] In some embodiments, the trajectory array guide system includes a reducer tube for insertion into one of the lumens of an array guide. In some embodiments, the reducer tube provides a reduced diameter in the lumen for insertion of an elongated tool. In some embodiments, the reducer tube includes an adjustable stop for restraining movement of an elongated tool.

[0017] In some embodiments, the trajectory array guide system includes an array guide defined by a bore configured to hold a guide unit defined by a series of passages which are co-axial with the lumens of the array guide. In some embodiments, the guide unit includes an upper lock tab for connection of the guide unit to the array guide. In some embodiments, the trajectory array guide system includes an imaging unit configured for connection to the array guide at the upper lock tab. In some embodiments, the trajectory array guide system further includes a locking slider configured for insertion into the body of the guide unit to hold an elongated tool in place in one of the lumens.

[0018] In some embodiments, the trajectory array guide system includes an imaging unit engaged with a ball array guide. In some embodiments, the imaging unit includes a series of passages connected to a plenum located at about the center of rotation of the ball in a ball array guide. In some embodiments, the trajectory array guide system includes a handle with a channel for injecting imaging fluid into a central passage of the series of passages. In some embodiments, the imaging fluid flows through the central passage into the plenum, with subsequent upward filling of remaining passages of the series of passages via the plenum. In some embodiments, the passages are seven substantially parallel passages with six passages arranged in a symmetrical hexagonal pattern around the central passage. In some embodiments, one of the six passages is extended downward past the plenum for providing an index passage for identification of individual passages.

[0019] The present disclosure provides a method for delivering an elongated tool to a target location in the brain of a subject. In some embodiments, the method includes: a) providing a trajectory array guide system which includes a base plate, an array guide, an imaging unit, a handle and an image-guided stereotaxic navigation system connected to the handle; b) performing a craniotomy at an entry location; c) connecting the base of the trajectory array guide system to the entry location and engaging the array guide with the base plate; d) engaging the imaging unit with the array guide and aligning the array guide to the

target; e) imaging a series of trajectories towards the target location with magnetic resonance imaging; f) locking the trajectory array guide system and selecting a trajectory from the series of trajectories; g) removing the imaging unit and delivering the elongated tool to the target location using the selected trajectory; and h) removing the trajectory array guide system from the skull of the subject. In some embodiments, the base of the trajectory array guide system is connected to the entry location using bone screws through bottom tabs in the base. In some embodiments, the method includes adding MRI contrast imaging reagent to the imaging unit before the step for imaging the series of trajectories. In some embodiments, the method includes using the stereotaxic navigation system to orient the series of trajectories toward the target location. In some embodiments, the elongated tool is a catheter. In some embodiments, the catheter is configured to deliver a drug to the target location.

[0020] In some embodiments, the method for delivering an elongated tool to a target location in the brain of a subject uses a trajectory array guide system of the present disclosure.

[0021] The present disclosure provides a kit for assembling a trajectory array guide system. In some embodiments, the kit includes: a base and an array guide which can be connected to form a lockable ball-socket pivoting mechanism, wherein the base is configured for attachment to the skull of a subject, and wherein the array guide is defined by a series of lumens or is defined by a bore configured to hold a separate guide unit defined by a series of lumens; an imaging unit configured for engagement with the array guide and configured to hold and direct imaging fluid along axes which are co-axial with the lumens for the purpose of defining a series of trajectories; and an elongated handle having sufficient length for connection to an image-guided stereotaxic navigation system, wherein the handle is configured for attachment to either the array guide or the imaging unit.

[0022] In some embodiments, the kit further comprises instructions for assembly of the array guide system.

[0023] In some embodiments, the kit further comprises a container of imaging reagent.

[0024] In some embodiments, the kit is for assembly of a trajectory array guide system of the present disclosure. In some embodiments, the trajectory array guide system includes a guide unit for insertion into the bore of the array guide. In some embodiments, the kit includes a plurality of guide units configured for guiding elongated tools of different diameters. In some embodiments, the elongated tools include a catheter.

[0025] In some embodiments of the kit, all components of the trajectory array guide system are contained in one or more sterilized packages.

[0026] The present disclosure provides trajectory array guide system which can function to provide or assist with the stereotactic guidance, placement and fixation of surgical instruments or devices during the planning and operation of neurological procedures performed in conjunction with preoperative and perioperative MR imaging. In some embodiments, the procedures can include laser coagulation, biopsies, catheter placement, or electrode placement procedures.

BRIEF DESCRIPTION OF THE DRAWINGS

[0027] Fig. 1A is an illustration of installment of one embodiment of a trajectory array guide system **10** on the skull of an individual for the purpose of showing one orientation of this system during a mode of operation.

[0028] Fig. 1B is a magnified view of the trajectory array guide system **10** of FIG 1A.

[0029] Fig. 2 is an exploded view of an embodiment of a trajectory array guide system **11** which illustrates placement of an imaging unit **60**.

[0030] Fig. 3A is a side view of one embodiment of a ball array guide **120** of the trajectory array guide system **11**.

[0031] Fig. 3B is a cross-sectional view of the ball array guide **120** of Fig. 3A taken along line 3B—3B of Fig. 3A.

[0032] Fig. 4A is a top view of one embodiment of a base plate **150** of the trajectory array guide system **11**.

[0033] Fig. 4B is a cross-sectional view of the base plate **150** of Fig. 4A taken along line 4B—4B of Fig. 4A.

[0034] Fig. 5A is a side view of an imaging unit **60** designed for use in one mode of operation of the trajectory array guide system **11**.

[0035] Fig. 5B is a cross-sectional view of the imaging unit **60** of Fig. 3A taken parallel to line 5B—5B of Fig. 5A.

[0036] Fig. 5C is an arbitrary longitudinal cross-section of the imaging unit **60** with the cap **64** removed.

[0037] Fig. 6A is a side view of the base plate **150** and the ball array guide **120** with the base plate **150** shown in arbitrary cross section to illustrate a socket **153** of the base plate **150**.

[0038] Fig. 6B is a side view of the base plate **150** and the ball array guide **120** with a locking nut **130** in place and indicating pivotable movement of the ball array guide **120** within the base plate **150**.

[0039] Figs. 7A-7B illustrate a process for obtaining an array of projected trajectories **T** using an imaging reagent **IR** in the imaging unit **60** installed in the ball array guide **120**.

[0040] Figs. 8A-8C illustrate a process for inserting a catheter **170** into one of the lumens of the ball array guide **120** with maximal depth limited by the location of an insertion stop **171**.

[0041] Figs. 9A-9C illustrate a process for using a trajectory **T** defined by the trajectory array guide system **11** to reach a target **TG** at a maximum depth **DP** in the brain of a patient via an entry point **E**.

[0042] Figs. 10A-10C illustrate a process for connecting the trajectory array guide system **11** at the site of a craniotomy **C.**

[0043] Figs. 11A-11C illustrate a process for using the trajectory array guide system **11** to generate an array of trajectories **T** in an effort to define an optimal trajectory **OT** to a target **TG.**

[0044] Figs. 12A-12C illustrate a process for insertion of a catheter **170** into the trajectory array guide system **11** to deliver a drug to the target **TG**.

[0045] Fig. 13A is a side elevation view of one embodiment of a trajectory array guide system **12**.

[0046] Fig. 13B is a cross-sectional view of the trajectory array guide system **12** of Fig. 13A taken along line 13B—13B of Fig. 13A.

[0047] Fig. 13C is a bottom view of the trajectory array guide system **12** of Fig. 13A and Fig. 13B.

[0048] Fig. 14A is a perspective view of a ball array guide **220** held and locked in place in a base plate **350** with a ring-shaped locking nut **230** having a grip surface **231**.

[0049] Fig. 14B is a perspective view of a ball array guide **220** held and locked in place in a base plate **350** with a locking nut **330** having cutouts **332a-d**.

[0050] Fig. 14C is a perspective view of a ball array guide **220** held and locked in place in a base plate **350** with a locking nut **430** having opposing lugs **433a-d**.

[0051] Fig. 15A is a side elevation view of an embodiment of a trajectory array guide system **17** indicating that the locking nut **230** limits the angle of trajectory of the ball array guide **620**.

[0052] Fig. 15B is a cross section view of a trajectory array guide system which includes a tilted base plate **450**.

[0053] Fig. 16 is a perspective view of an embodiment of a base plate **50** whose socket **53** is tilted to provide larger angles of trajectory.

[0054] Fig. 17 is a perspective view of base plate **350** whose socket **353** is orthogonal to the plane of the tabs **351a-d**.

[0055] Fig. 18 is a partial cross-sectional perspective view of a ball **221** of a ball array guide **220** held in a socket **553** of a base plate **550** having tapered outer threads **556** which match inner threads **537** on locking nut **530**.

[0056] Fig. 19A is a perspective view of an embodiment of a tilted base plate **450** configured for connection to a ring clamp as shown in FIG 19B.

[0057] Fig. 19B is a perspective view of the tilted base plate **450** of Fig. 19A with a ring clamp **80** attached thereto.

[0058] Fig. 19C is a perspective view of the tilted base plate **450** of Fig. 19A with a ring clamp **80** attached thereto and showing the rotational freedom of the clamp **80** around the outer groove **458** of base plate **450**.

[0059] Fig. 19D is a cross-sectional side elevation view of the tilted base plate **450** and ring clamp **80** showing the ball **221** of a ball array guide held in place.

[0060] Fig. 20A is a perspective view of a handle **140**.

[0061] Fig. 20B is a perspective view of an embodiment of the trajectory array guide system **13** showing the handle **140** attached thereto.

[0062] Fig. 20C is a side elevation view of the handle **140**.

[0063] Fig. 20D is a cross-sectional view of the handle **140** of Fig. 20C taken along line 20D—20D.

[0064] Fig. 20E is a magnified view of the cross-sectional view of the connector **141** of Fig. 20D.

[0065] Fig. 21A is a top perspective view of an embodiment of an imaging unit **360**.

[0066] Fig. 21B is a bottom perspective view of the imaging unit **360** of Fig. 21A.

[0067] Fig. 21C is a top view of the imaging unit **360** of Fig. 21A and Fig. 21B.

[0068] Fig. 21D is a bottom view of the imaging unit **360** of Figs. 21A-21C.

[0069] Fig. 21E is a side elevation view of the imaging unit **360** of Figs. 21A-D.

[0070] Fig. 21F is a cross-sectional view of the imaging unit **360** taken along line 21F—21F of Fig. 21E.

[0071] Fig. 22 is a perspective view of an embodiment of a trajectory array guide system **14**, showing the manner of insertion of tubes **465a-g** and **466** into the ball array guide **620**.

[0072] Fig. 23A is a perspective view of ball array guide **620**.

[0073] Fig. 23B is a side elevation view of ball array guide **620**.

[0074] Fig. 23C is a top view of ball array guide **620**.

[0075] Fig. 23D is a bottom view of ball array guide **620**.

[0076] Fig. 24 is a cross-sectional perspective view of a portion of an embodiment of the trajectory array guide system **15**.

[0077] Fig. 25 is an exploded perspective view of an embodiment of the trajectory array guide system **16**.

[0078] Fig. 26A is a cross-sectional view of an embodiment of a ball array guide **90** which is taken along line 26A—26A of Fig. 26B.

[0079] Fig. 26B is a top view of the same embodiment of the ball array guide **90** shown in Fig. 26A.

[0080] Fig. 26C is an exploded view indicating connection of a handle **240** to the embodiment of the ball array guide **90** of Figs. 26A and 26B.

[0081] Fig. 26D is a cross-sectional view of embodiment of the ball array guide **90** of Figs. 26A and 26B with an imaging unit **960** attached to the ball array guide **90**. This cross-sectional view is taken along line 26D—26D of Fig. 26E.

[0082] Fig. 26E is a top view of the ball array guide **90** of Fig. 26D with imaging unit **960** attached to the ball array guide **90**.

[0083] Fig. 26F is a cross-sectional view of embodiment of the ball array guide **90** of Figs. 26A and 26B with a catheter guide unit **920** attached to the ball array guide **90**. This cross-sectional view is taken along line 26F—26F of Fig. 26G.

[0084] Fig. 26G is a top view of the ball array guide **90** of Fig. 26F with a catheter guide unit **920** attached to the ball array guide **90.**

[0085] Fig. 26H is a top view of a locking slider **926** for holding a catheter in place in the catheter guide unit **920**.

[0086] Fig. 27A includes perspective views of embodiments of a catheter guide unit **1020**, an imaging unit **1060** and a ball array guide **190** placed in a base plate **450**.

[0087] Fig. 27B includes bottom perspective views of the same embodiments of the catheter guide unit **1020**, imaging unit **1060**, ball array guide **190** and base plate **450** of Fig. 27A.

[0088] Fig. 27C includes top perspective views of the same embodiments of the catheter guide unit **1020**, imaging unit **1060**, ball array guide **190** and base plate **450** of Figs. 27A and 27B.

[0089] Fig. 28 is an arbitrary cross-sectional view of an embodiment of a trajectory array guide system **18** including an imaging unit **660** and a handle **340**.

[0090] Fig. 29 is a perspective view of a partial assembly including imaging unit **660** and attached handle **340**.

[0091] Fig. 30 is a transparent perspective view of imaging unit **660** showing internal imaging passages **661a**, **661d** and **661g** as well as plenum **669** and passage extension **661a'**.

[0092] Fig. 31 is a transparent perspective view of the handle **340** showing the internal injection passage **348** and injection port **346**.

[0093] Fig. 32 is a perspective view of imaging unit **660**.

[0094] Fig. 33A includes perspective views of an embodiment of a ball array guide **390** having a central bore **392** and an assembly of ball array guide **390** with imaging unit **660**.

[0095] Fig. 33B includes top perspective views of ball array guide **390** and the assembly of ball array guide **390** with imaging unit **660**.

[0096] Fig. 34 is a perspective view of an embodiment of a catheter guide unit **720** which has an index lobe **766**.

[0097] Fig. 35A includes a perspective view of an embodiment of a ball array guide **490** having a central bore **492** and an index lobe receiver **494** and a perspective view of an assembly of ball array guide **490** with catheter guide unit **720**.

[0098] Fig. 35B includes top perspective views of ball array guide **490** and the assembly of the ball array guide **490** with catheter guide unit **720**.

[0099] Fig. 36A is a cross-sectional view of an embodiment of a ball array guide **590** with an imaging unit **1160** attached to the ball array guide **590**. This cross-sectional view is taken along line 36A—36A of Fig. 36B.

[0100] Fig. 36B is a top view of the ball array guide **590** of Fig. 36A with an imaging unit **1160** attached to the ball array guide **590**.

[0101] Fig. 36C is a cross-sectional view of an embodiment of a ball array guide **590** with a catheter guide unit **1120** attached to the ball array guide **590**. This cross-sectional view is taken along line 36C—36C of Fig. 36D.

[0102] Fig. 36D is a top view of the ball array guide **590** of Fig. 36A with an imaging unit **1160** attached to the ball array guide **590**.

[0103] Fig. 36E is a top view of a locking slider **1126** for holding a catheter in place in the catheter guide unit **1120**

[0104] Fig. 37A is a generalized top view of ball array guide **590** with either imaging unit **960** (straight array) or **1160** (slanted array) attached thereto. This illustration includes clock position markings for the purpose of identifying array locations produced by locking the lock tab **969** or **1169** of imaging unit **960** or **1160**, respectively, at each of the different clock positions.

[0105] Fig. 37B is an illustration indicating the increased array footprint area provided when imaging unit **1160** is placed at the eight different clock positions. Imaging unit **960** (straight array) provides the same array regardless of its clock position connection to the ball array guide **590**.

[0106] Fig. 38A is a perspective view of an embodiment of the handle **440**.

[0107] Fig. 38B is a perspective view of a trajectory array guide system **19** which includes handle **440.**

[0108] Fig. 38C is an exploded perspective view of trajectory array guide system **19**.

[0109] Fig. 38D is a top perspective view of the trajectory array guide system **19** without the handle **440** to indicate penetration of set-screws **323a-c** into the lumens **325a-g** of the ball array guide **320**.

[0110] Fig. 39 is a perspective view of a trajectory array guide system engaged with an image guided surgery system **1200**.

[0111] Fig. 40A is a perspective view of an image guided surgery system **1210** clamped onto a handle **440** of a trajectory array guide system.

[0112] Fig. 40B is a perspective view of an image guided surgery system **1210** clamped onto a ball array guide **320** of a trajectory array guide system.

DETAILED DESCRIPTION

[0113] The present disclosure describes embodiments of a trajectory array guide system which is configured to address a number of shortcomings of known trajectory array guide systems. For example, many such trajectory array guide systems currently in use or under active investigation for use in clinical settings tend to be large, cumbersome and have many separate parts which may be expensive to manufacture and which are prone to damage. Such systems tend to have complicated mechanisms for altering and locking the trajectory paths and as such, tend to require more time to make adjustments than is desirable. In some instances, a contributing factor is that trajectory array guide systems are used while a patient is placed in an MRI system outside of an operating room. This situation increases risk of infection and it is thus desirable to complete the surgical procedure as quickly as possible to minimize patient transportation. It is desirable to have the capability to complete the mounting of the trajectory array guide system and establish an optimal locked trajectory within less than one hour.

[0114] The present presents embodiments of a trajectory array guide system as well as methods and kits to address these and other disadvantages of presently known systems.

Definitions

[0115] As used herein, the term "array guide" refers to a component used to create a series of images of trajectories for insertion of an elongated tool into the brain of a subject and for guiding a path for the elongated tool. The array guide can be adjustable to adjust the angles of the trajectories. The array guide may have an array of lumens formed in its body or alternatively be provided with a wide bore configured for insertion of one or more separate units for creating the trajectories for imaging and guiding of the elongated tool.

[0116] As used herein, the term "ball array guide" is an array guide having a ball formed at one end for the purpose of creating a pivoting ball and socket joint for adjustment of the angles of the trajectories.

[0117] As used herein, the terms "cannula" and "catheter" are considered synonymous, each referring to a tube constructed for insertion into the body for surgical treatment or for delivery of an external substance or extraction of an internal substance.

[0118] As used herein, the term "imaging fluid" refers to a fluid having properties for providing contrast images under a mode of analysis such as magnetic resonance imaging, for example. This term is synonymous with the term "MRI contrast agent." The most commonly used imaging fluids in magnetic resonance imaging include gadolinium-based compounds.

[0119] As used herein, the term "imaging unit" refers to a component intended for use with an array guide for the purpose of directing imaging fluid to generate images representing an array of trajectories.

[0120] As used herein, the term "image-guided stereotaxic navigation" indicates that images generated by an imaging technology such as magnetic resonance imaging, for example, are used to guide stereotaxic navigation.

[0121] As used herein, the term "lumen" refers to an opening or cavity within a body of a system component. More specifically, this term is used to identify channels of an array in an array guide which are provided for guiding the insertion of an elongated tool.

[0122] As used herein, the term "passage," like the term "lumen" above refers to an opening or cavity within a body if a system component. More specifically, this term is used to identify channels of an array in an array guide which are provided to deliver imaging fluid to provide trajectory images.

[0123] As used herein, the term "plenum" refers to an open space within an otherwise solid body.

[0124] As used herein, the term "stereotaxic navigation" refers to provision of three-dimensional navigation within a surgical site using a three-dimensional coordinate system to

locate targets within the body and to perform an action such as ablation, biopsy, lesion, injection, stimulation, implantation, radiosurgery or any other surgical procedure.

[0125] As used herein, the term "trajectory" refers to a potential pathway. More specifically herein, the term is used to identify potential pathways for insertion of a catheter or cannula into the brain.

Overview of One Embodiment of a Ball Trajectory Array Guide System

[0126] The present description presents a ball trajectory array guide system with reference to Figs. 1A to 8C. A number of alternative embodiments are introduced during the course of this description which may be substituted in various compatible combinations according to the knowledge of persons having ordinary skill in the art to arrive at different embodiments of the present invention.

[0127] Fig. 1A illustrates a trajectory array guide system **10** fixed to the skull of a subject for the purpose of showing a one orientation of the system during operation. This placement of the system **10** is shown by way of example only. The placement of the system **10** on the skull will vary according to a number of different factors such as access and avoidance of peripheral equipment as well as the desired trajectory of a surgical tool such as a catheter.

[0128] A magnified perspective view of the trajectory array guide system **10** is shown in Fig. 1B. In some cases, the head of the subject can be inside the bore of an MRI system (not shown). In some cases where a standard stereotaxic navigation system is not used to provide initial alignment, the head of the subject may be inside the bore of an MRI system for the entire procedure. The system **10** includes a base plate **50** which has four attachment tabs **51a-d** with only three **(51a-c)** of the four attachment tabs **51a-d** visible in this perspective view and with the fourth attachment tab **51d** hidden from view in this perspective. Each of the four attachment tabs **51a-d** has a corresponding opening **52a-52d** for insertion of a fastener, typically a bone screw, for fixing the location of the base plate **50** to the skull. The base plate should be located such that an opening made in the skull will be within the central bore of the base plate.

[0129] The base plate **50** can include a hollow cup-shaped interior (not shown) acting as a socket to receive the ball **21** of the ball array guide **20**. The socket may be designed to provide resistance to the ball such that the array will only move under an externally applied force. One of the advantages of using a ball and socket arrangement is that the socket holds the array in an unlocked state and requires intentional force to adjust the trajectory.

[0130] The interior of the ball array guide **20** can include a series of parallel channels or lumens (not shown) which are parallel to the main axis of the ball array guide **20**. These

parallel channels or lumens can establish an array of parallel trajectories for an elongated surgical instrument, such as a catheter, to enter the brain on a selected trajectory and to reach a desired target location within the brain for delivery of a drug.

[0131] The ball-and-socket arrangement allows pivotable movement of the stem **22** of the ball array guide **20**. A locking nut **330** with inner threads is provided in this embodiment to be threaded and tightened against outer threads of the base plate **50**. Engagement of the locking nut **330** with the out threads of the base plate **50** can compress the socket and prevent pivoting motion of the ball array guide **20** when the desired orientation of the stem is attained.

[0132] Also seen in Fig. 1B is a handle **40** with a connector **41** configured for secure attachment to the outward extending end of the ball array guide **20** or to an imaging unit. The connector **41** is joined to an arm **42** which provides an extension of the ball array guide **20** for the purpose of connecting to an image guided stereotactic navigation system. This arrangement allows for manipulation of the position of the ball array guide **20** while viewing a computer monitor with magnetic resonance images of the brain for the purpose of adjusting projected trajectories for catheter placement. Examples of stereotactic navigation systems include: the Varioguide System which is manufactured by BrainLab, AG of Munich; and the Curve Image Guided Surgery system which is manufactured by BrainLab, AG of Munich.

[0133] Fig. 2 shows an exploded illustration of an embodiment of the trajectory array guide system **11**. The ball **121** of the ball array guide **120** is placed inside the socket **153** of the base plate **150**. Base plate **150** is shown as an arbitrary cross section for visualization of the shape of the socket **153** (seen in Fig. 4B) formed by an interior sidewall of the bore of the top portion of the base plate **150**. The base plate **150** of this embodiment includes a socket axis essentially orthogonal to the plane containing the upper surfaces of the tabs (**151a** and **151c** seen in Fig. 4B). In contrast to the orthogonal socket axis of the base plate **150** in Fig. 2, the socket axis of the base plate **50** in Figs. 1A and 1B is tilted away from orthogonality i.e. is non-orthogonal.

[0134] The locking nut **130** is passed over the ball array guide **120** and fixed to the upper portion of the outer sidewall of the base plate **150** to lock the orientation of the ball array guide **120**. Before or after this step, the imaging unit **60** may be connected to or engaged with the ball array guide **120**. The lower portion of the imaging unit **60** has a series of tubes generally labelled in Fig. 2 as **65**. While only four tubes are visible in Fig. 2, this embodiment has eight tubes with seven long tubes **65a-g** and one short tube **66** (shown in Figs. 5A-C). The seven long tubes **65a-g** fit inside seven corresponding cavities or lumens (shown in Fig.

3B) in the stem **122** of the ball array guide **120** and the remaining upper portion of the imaging unit **60** remains above the top of the stem **122**. In some embodiments, these tubes **65a-g** and **66** are formed of a thermoplastic polymer such as polyether ether ketone (PEEK) or another polymer having similar properties. The imaging unit **60** can be locked to the ball array guide **120** by three equi-spaced set screws with only one set screw **123a** shown in Fig. 2 (the remaining set screws **123b** and **123c** are seen in the top view of Fig. 3B).

[0135] In certain modes of operation, the trajectory array guide system **11** uses the imaging unit **60**. In certain modes of operation, the trajectory array guide system **11** does not use the imaging unit **60**. In certain modes of operation, both modes (with and without imaging unit **60**) will be employed at different points during the procedure.

[0136] The connector **41** of the handle **40** is placed over the top of the inserted imaging unit **60** (or without the unit **60** in place) and fixed to the top portion of the ball array guide **120** by threading or another connection mechanism.

[0137] Fig. 3A is a similar view of the ball array guide **120** of Fig. 2. In Fig. 3A, a second set-screw **123b** is present. The ball array guide **120** also includes an outer groove **124** formed in the stem **122** of the ball array guide **120**. Fig. 3B is a cross section of the stem **122** of the ball array guide **120** taken along line 3B—3B of Fig. 3A. It is seen that the stem has seven lumens **125a-g** formed therein. The outer groove **124** is also visible in Fig. 3B as well as the third set-screw **123c**. The set screws **123a-c** can penetrate the body of the ball array guide **120** to enter the spaces of lumens **125b**, **125d** and **125f**, respectively. When corresponding tubes **65** of the imaging unit **60** are inserted into these lumens, **125b**, **125d** and **125f**, the set-screws **123a-c** can be tightened against the outer sidewalls of the tubes **65** to fix the imaging unit **60** in place on the ball array guide **120**.

[0138] Fig. 4A is a top view of the base plate **150** showing the socket **153**, the tabs **151a-d** and holes **152a-d**, and the central bore **154**. Fig. 4B, which is similar to the view of the base plate **150** in Fig. 2, is a cross section taken along line 4B—4B of Fig. 4A.

[0139] Fig. 5A is a side view of the imaging unit **60**. Fig. 5B is a cross-sectional view of the imaging unit **60** taken along line 5B—5B of Fig. 5A. The imaging unit **60** has a reservoir **63** for filling a series of tubes **65a-g** and **66** with an imaging fluid, such as a gadolinium-based MRI contrast reagent for example. In some embodiments, the imaging unit includes tubes constructed of a radiopaque material which is visible under MRI and computerized tomography. When the imaging fluid is added to the reservoir **63**, it enters all of the tubes **65a-g** and **66**. The imaging fluid within the tubes **65a-g** can then provide a means of imaging the trajectory paths defined by the axes of the tubes. Tube **66** (the shorter tube) is an indexing

tube which is provided outside of the hexagonal symmetry of the other tubes **65a-g** for the purpose of easily identifying the seven tubes used for imaging the trajectories. In this side view of Fig. 5A, only tubes **65c**, **65d**, **65g** and **66** are visible with the remaining tubes **65a**, **65b**, **65e** and **65f** being hidden from view. These hidden tubes **65a**, **65b**, **65e** and **65f** are seen in the cross-sectional view of Fig. 5B which is taken along line 5B-5B of Fig. 5A. Also seen in Fig. 5A is a cap **64** to seal and cover the top of the reservoir **63**. Fig. 5C is an arbitrary longitudinal cross-sectional view of the imaging unit **60** with the cap **64** removed.

[0140] Fig. 6A is a side view illustration of the ball array guide **120** installed in the socket **153** of the base plate **150** prior to installment of the locking nut **130**. Fig. 6B shows the same arrangement after installation of the locking nut **130** and additionally shows pivoting rotation of the ball array guide **120** and a projected trajectory **T** corresponding to one of the lumens **125a-g** (not seen in Fig. 6A) in the body of the ball array guide **120**.

[0141] Fig. 7 shows a system and process for defining a series of projected trajectories using the imaging unit **60** in order to identify an appropriate trajectory for insertion of a catheter to reach a target location in the brain (not shown). The tubes **65a-g** and index tube **66** of the imaging unit **60** are filled with an imaging reagent **IR** which subsequently fills the upper reservoir **63**. The imaging unit is inserted into the ball array guide **120** with the tubes **65a-g** (see Fig. 5B) entering corresponding lumens **125a-g** (see Fig. 3B). The index tube **66** slides along the outer groove **124** (see Fig. 3A and 3B). The imaging unit **60** is fully inserted into the ball array guide **120**. The tubes **65a-g** and **66** are filled with imaging reagent **IR** (such as a gadolinium-based contrast reagent which provides a bright white image under MRI) and are used to define a series of projected trajectories **T** into the brain while the head of the subject is placed in an MRI system. One of the trajectories **T** is selected for insertion of a catheter (not shown). The image of the bottom of the reservoir **63** serves as an index point or datum to define the insertion depth of the catheter. There is gap of known dimensions between the bottom of the reservoir **63** and the top of the ball array guide **120** due to the thickness of the bottom of the imaging unit **60**. The index tube **66** is shorter than the other tubes **65a-g**. The image of the index tube **66** (provided by the imaging reagent **IR**) is used as a reference to correctly identify the individual trajectories **T** under MRI (which would otherwise be impossible due to the symmetry of the hexagonal pattern of tubes **65a-g**). The imaging unit **60** is then removed from the ball array guide **120**.

[0142] Fig. 8A-8C illustrates a system and process for insertion of a catheter **170** into the ball array guide **120** after a trajectory is selected and the imaging unit **60** is removed. The free end of the ball array guide **120** serves as the datum **D** for the depth of insertion of the catheter

170. The structure of the catheter **170** is shown in Fig. 8B. The maximum depth of insertion of the catheter **170** is defined by the location of the insertion stop **171** on the catheter **170**. Fig. 8C shows two illustrations of the catheter **170** being partially inserted (left) and fully inserted (right) into the optimal target trajectory as identified by analysis of the trajectory images. In some embodiments, to make the system compatible with 14 and 16-gauge catheters, two separate trajectory arrays with lumens for 14 and 16-gauge catheters can be provided. This will also require two separate imaging units with 14 and 16-gauge tubes, respectively. Alternatively reducing tubes can be used with a 14-gauge array to accommodate small diameter instruments.

[0143] As noted above, MRI images of the patient's brain are obtained to guide the overall procedure. Surgical planning is performed by the surgeon using preferred planning software to pre-plan entry sites and catheter trajectories to the target locations in the brain. In addition, MRI systems typically include software for 3D reconstruction of the images and further image analysis including dimensional analysis to obtain locations, dimensions, planes, and trajectories for catheter insertion to the target location. Standard image-guided stereotactic platforms available to neurosurgeons in combination with software provided by the manufacturer are used to guide the entire procedure. From the analysis of the MRI scans the following dimensions and landmarks are identified: target location(s); entry point on the skull; a preferred trajectory from the entry point to the target location(s); and insertion depth, which is defined as the distance from the entry point to the target location(s).

[0144] The entry point and trajectory are selected to avoid potential damage to blood vessels and brain sections by the catheter. In some cases, the trajectory is chosen to allow for multiple injections into the target along the pathway of the catheter as illustrated in Fig. 9A-9C.

[0145] In some embodiments, components of a trajectory array guide system are sterilized. Suitable sterilization methods for the components include high heat, steam, ethylene oxide or radiation such as gamma sterilization. In some embodiments, components of a trajectory array guide system are made of medical grade materials, including medical grade plastics, medical grade polymers, and medical grade metals. Specific examples of medical grade materials include, but are not limited to: medical grade polyether ether ketone (PEEK); medical grade silicon, medical grade steel (such as medical grade stainless steel); and medical grade aluminum.

Overview of Operation of One Embodiment of the Trajectory Array Guide System

[0146] The present disclosure provides a system and method for delivering an elongated tool to a target location in the brain of a subject which uses a trajectory array guide system of the present disclosure. An example describing the operation of a trajectory array guide system **11** is presented with reference to components illustrated in Figs. 2 to 12C.

[0147] A patient receives general anesthesia in preparation for the procedure. A head stabilization system is used to avoid head motion during the procedure. The placement of the trajectory array guide system **11** is performed in a sterile environment in a surgical operating room or a hybrid operating room with MRI capabilities. The head is shaven and the desired entry point is marked. The incision site is draped and a skin flap is created with a scalpel to expose the skull for placement of the trajectory array guide system **11**. A craniotomy **C** can be made either at this time (see Fig. 10A) or after placement of the base plate **150**. The ball array guide **120** is loosely mounted onto the base plate **150** and the handle **40** is connected to the trajectory array guide system **11**. The imaging unit **60** filled with gadolinium imaging reagent **IR** is inserted into the ball array guide **120**. The assembled trajectory array guide system **11** (see Fig. 2) is then connected via the handle **40** to a guiding system such as the VarioGuide navigation system to correctly orient the trajectory array to the pre-determined trajectory (Fig. 10B).

[0148] Once a suitable orientation of the trajectory array guide system **11** is established, it is lowered to the surface of the skull and the base plate **150** is secured onto the skull by securing up to four bone screws into the four holes **152a-d** of the tabs **151a-d** of the base plate **150**. If a craniotomy was not previously made, the upper portion of the trajectory array guide system **11** including the handle **40** is removed from the socket of the base plate **150** to allow access through the base plate **150** to make a burr hole in the skull according to known surgical procedures. The trajectory array guide system **11** is then reattached to the base plate **150** with proper alignment confirmed by the stereotactic navigation system. The locking nut **130** is then tightened to preserve the orientation and prevent any further movement between the system components. The handle **40** is disconnected from the stereotactic navigation system and removed, as shown in Fig. 10C. In case of a hybrid surgical suite, the patient is ready for MR imaging. In case of a separate imaging suite, the incision site and trajectory array guide system **11** are covered with a sterile drape and the patient is transported to the imaging suite.

[0149] As an alternative workflow, it is envisioned that the entire procedure could be performed within an MRI scanner without use of an alternative imaging system to align the

trajectory array guide system **11**. Some alternative navigation system, or MRI sequences, will be needed to identify the entry point for attachment of the base plate but alignment of the trajectory array guide system **11** would be performed entirely as described below for refinement of the trajectory.

[0150] MRI scans of the patient's brain are performed to confirm that the correct entry point and trajectory have been established. Figs. 11A-11C illustrate the MR imaging and analysis procedure. An illustration of a magnetic resonance image of the brain of the patient and the trajectory array guide system **11** mounted on the skull. The imaging reagent **IR** contained in the reservoir **63** and tubes **65a-g** and **66** of the imaging unit **60** provides bright white images on the MRI scan (see Fig. 11A). 3D reconstruction and subsequent image analysis on the MRI scanner console is used to determine the sagittal and axial plans of each trajectory and to project the trajectories **T** originating from the tubes **65a-g** and **66** of the imaging unit **60** into the brain toward the target location **TG** (see Fig. 11B). The optimal trajectory **OT** is selected from the array of possible trajectories **T** (see Fig. 11C). While it is helpful to use the central lumen **125g** for initial alignment, the surrounding lumens **125a-f** provide alternative parallel trajectories **T** which can be employed if required. The image of the index tube **66** serves as a directional reference to identify each individual lumen in the array of lumens **125a-g** in the ball array guide **120**. If none of the trajectories **T** is deemed suitable, the direction of the trajectories **T** can be adjusted by loosening the anchor lock nut **130** to allow pivoting movement of the ball array guide to provide an improved series of trajectories **T**. The ball array guide **120** should not move without intentional force when the lock nut **130** is loosened. Then the ball array guide **120** is tightened with the lock nut **130** to secure the new orientation. The MR imaging and analysis procedure is then repeated.

[0151] When the optimal trajectory is confirmed, the imaging unit **60** is removed from the ball array guide **120**. From the MRI images the initial and maximum depth of insertion of the catheter **170** is measured using the base of the reservoir of the imaging unit **60** as the datum (a correction equal to the thickness of the imaging unit base must be made). A depth insertion-stop **171** is mounted on the drug delivery catheter **170** at a distance from the tip of the catheter **170** equal to the maximum insertion depth as shown in Fig. 12A (see also Figs. 8A-8C) and a distance equal to the initial depth is marked onto the catheter **170** with a sterile pen. The catheter **170** is carefully inserted through one lumen of the array of lumens **125a-g** in the ball array guide **120** to the initial target depth and secured by a lock screw which is configured to penetrate all lumens **125a-g** of the ball array guide **120**. The correct position of the tip of the catheter **170** is confirmed by MRI and the drug is injected (see Fig. 12B). The

catheter **170** is then withdrawn as shown in Fig. 12C. In situations where one or more targets along the optimal trajectory **OT** can be reached before the insertion stop **171** prevents further insertion, additional boluses of drug may be injected at these targets. Likewise, such targets may receive injections with pausing during the phase of retraction of the catheter **170**.

[0152] The trajectory array guide system **11** is removed from the skull by removing the bone screws. The wound is closed using standard surgical techniques.

[0153] One embodiment of a procedure sequence will now be briefly outlined. This procedure sequence assumes that the entire system **11** may be assembled prior to mounting to the skull of the subject.

[0154] First the entire trajectory array guide system **11**, including the imaging unit **60** and the handle **40**, is assembled. Then a surgical navigation system is connected to the handle **40**. The entry location on the skull is identified and a craniotomy **C** is performed to expose the entry location. Then the base plate **150** is connected to the skull. The handle **40** is removed to add imaging reagent **IR** to the trajectory array guide system **11**. MRI scans are then performed to view the projected trajectories **T** and the optimal trajectory **OT** is selected. The handle **40** is reattached to facilitate additional manipulation of the optimal trajectory **OT**, if required. The imaging unit **60** is then removed with confirmation that the selected optimal trajectory **OT** remains locked in place. The catheter procedure is performed using the optimal trajectory **OT** and then the system **11** is removed from the subject.

[0155] In some embodiments, the screw holes of the base plate can be directly accessed by a screwdriver during the process of assembly and disassembly.

[0156] Commonly used magnetic resonance imaging has a spatial resolution of about 1 mm. Therefore, in some embodiments, the trajectories in the array are spaced between about 1 mm to about 3 mm apart; between about 1.5 mm to about 2.5 mm apart; about 2 mm apart; about 2.15 mm apart; about 2.25 mm apart; or about 2.35 mm apart.

Base Plate and Locking Nut Combination

[0157] Figs. 13A-13C show an embodiment of trajectory array guide system **12** in which a locking nut **230** is disposed directly above screw holes in the tabs **251a-d** of the base plate **250** once the system **12** is assembled. Figs. 13A-13C also show the system **12** with an imaging unit **260**, a ball array guide **220** including the ball **221**, lumens **225a-g** and set screws **223a-c**, as well as features of the imaging unit **60** including the reservoir **263**, tubes **265g** and **266**, and cap **264.**

[0158] In certain embodiments, a trajectory array guide system can be assembled prior to mounting onto a skull. In certain embodiments, the trajectory array guide system provides

unobstructed access to the screw holes in the base plate to place the bone screws. The images in Fig. 14A to 14C show three alternative embodiments that provide unobstructed access to the screw holes of the tabs. In all three embodiments, the base plate **350** is identical and the screw holes **352a-d** of the tabs **351a-d** are moved radially outward by 2 mm, thereby increasing the footprint of the base plate by 4 mm (tab **351d** with screw hole **352d** is not visible in the perspective views of Figs. 14A-14C). While base plate **350** is illustrated in Figs. 14A-14C, other base plate embodiments, such as the tilted base plate **50** of Figs. 1A and 1B, for example may be substituted for base plate **350**.

[0159] In Figs. 14A-14C, the locking nut is modified differently in each of the three illustrated embodiments to provide convenient access to the screw holes **352a-d** of the tabs **351a-d**.

[0160] In Fig. 14A, the locking nut **230** is the same as in Figs. 13A to 13C and has a grip surface **231** to facilitate application of tightening and loosening force.

[0161] In Fig. 14B, the locking nut **330** is modified relative to locking nut **230** to include four cutouts **332a-d** to provide additional space for access of a screwdriver to the screw holes **352a-d** in the tabs **351a-d** of the base plate **350**. This embodiment **330** of the locking nut also has a grip surface **331**.

[0162] In Fig. 14C, the locking nut **430** is provided with four equi-spaced lugs **433a-d** to facilitate application of tightening/loosening leverage against the locking nut **430**.

Tilted Base Plate

[0163] In certain procedures, it is favorable to enter the skull at angles of up to about 45 degrees from the central orthogonal axis of a base plate. Fig. 15A illustrates a trajectory array guide system **17** which includes a ball array guide **620** and imaging unit **460**. The trajectory array guide system **17** also includes a flat base plate **350** with an orthogonally-directed socket and a locking nut **230**. The angular range of the trajectory array guide system **17** shown in Fig. 15A is limited by the flat base plate **350** and the locking nut **230**, and is only about 30 degrees from the centerline.

[0164] Fig. 15B illustrates a trajectory array guide system which includes a ball array guide **220** and a base plate **450** which includes a socket **453**. The axis of the socket **453** relative to the base plate **450** is tilted by about 20 degrees with a with a ring clamp **80**. This tilt provides the capability of expanding the range of trajectory angles up to about 45 degrees from normal centerline.

[0165] Fig. 16 shows an embodiment of a base plate **50**. The base plate **50** is tilted and includes the four tabs **51a-d** with screw holes **52a-d** (screw hole **52d** is hidden from view in

this perspective). The outer sidewall of the socket **53** is provided with outer threads **54** for coupling to inner threads of one or more different embodiments of a locking nut (not shown in Fig. 16). Also seen in Fig. 16 are four compression slots **55a-d** which are provided to provide the socket with additional flexure to improve tightening of the locking nut against the outer sidewall of the socket **53**. The slots **55a-d** make the circumference of the socket **53** less rigid and therefore more easily compressed against the ball of the ball array guide. The bottom of the center bore of the base plate **50** is provided with a chamfer (not shown) to avoid interference of the catheter with the inner rim of the base plate at significantly large angles relative to the axis which is orthogonal to the plane formed by the bottom of the plate.

[0166] For comparison, Fig. 17 shows an embodiment of a base plate **350**. This embodiment **350** has a socket **353** with an axis which is orthogonal to the plane containing the four tabs **351a-d** as well as outer threads **354** and three compression slots **355a-c**. As noted above with reference to Figs. 15A-15B, this embodiment **350** of the base plate is limited to trajectory angles at or less than 31.2 degrees.

[0167] In some embodiments, a base plate of the present disclosure can have a bore diameter of between about 20 mm to about 50 mm, between about 30 mm to about 40 mm, or a bore diameter of about 35 mm.

[0168] In some embodiments, a kit of the present disclosure includes a trajectory array guide system which includes only a tilted base plate. In some embodiments, the trajectory array guide system includes only a flat base plate.

Locking Nut Modifications and Alternatives

[0169] Figs. 14A to 14C show the ball **221** of the ball array guide **220** locked into the socket **353** of the base plate **350** by different embodiments of locking nuts **230**, **330** and **430** which allow access of an attachment tool such as a screwdriver to the holes of the attachment tabs **351a-d**. In each of these three embodiments **230**, **330** and **430**, locking is achieved by the downward force of the lock nut onto the ball **221**. Friction forces created between the rotating lock nut and the ball during the final stages of tightening can cause the ball to rotate and lose its orientation. In some embodiments, the ball array guide **220** is stabilized as the lock nut is tightened.

[0170] In some embodiments, a ball locking mechanisms can use radial inward compression of the base plate socket to lock the ball of the ball array guide into the socket. In some embodiments, the inward compression of the socket does not create any motion between the parts that could misalign the ball array guide.

[0171] Fig. 18 illustrates an arbitrary cross-sectional view of one embodiment of a ball locking mechanisms which uses radial inward compression of the base plate socket to lock the ball of the ball array guide into the socket. Fig. 18 shows a tilted base plate **550** provided with upwardly tapered outer threads **556** for coupling to the lock nut **530** which has complementary tapered inner threads **537** (i.e. the circumference of the outer threads **556** of the base plate **550** become wider from the top towards the bottom of the outer sidewall of the socket **553**). This tightening and locking mechanism provides the required functional effect of compression of the socket **553** without causing significant friction with the ball **221** or creating create motion between the parts that could misalign the ball array guide. In one variation of this embodiment (not shown), the outer rim of the socket is provided with an upwardly projecting ridge and the lower rim of the circumference of the nut is partially cut away. In combination, these features ensure that the nut does not make contact with the ball.

[0172] Figs. 19A-19D illustrate a ring clamp mechanism for providing external compression against the outer sidewall of a socket. Figs. 19A-D show base plate **450** for cooperation with the ring clamp **80**. Base plate **450** is provided with an outer groove **458** which can receive an inner circumferential ridge **81** of a ring clamp **80**, as shown in Fig. 19D. A tension screw **82** (See Figs. 19C-19D) is used to tighten or loosen the ring clamp **80**. Adding more tension will compress the ring clamp **80** and produce radial inward compression on the outer sidewall of the socket **453** to lock the ball **221** in place in the socket **453**. Fig. 19C illustrates an embodiment where the ring clamp **80** has complete rotational freedom around the outer groove **458** of base plate **450** when the tension screw **82** is not tight. The rotational freedom of the ring clamp **80** allows the tension screw **82** to be positioned and tightened at any rotational position necessary for the operation of the trajectory array guide system.

[0173] In some embodiments, the ring clamp has a low profile which increases the maximum deflection angles of the trajectory array from the centerline. In some embodiments, the ring clamp has a low profile which allows direct access to the screw holes without the need to extend the footprint of the base plate.

[0174] Embodiments of the present disclosure describe trajectory array guide systems which generally include a ball unit configured to fit into a socket of a base plate. In some embodiments, a trajectory array guide system can be reconfigured to include a base plate having a ball unit and an array guide having a socket configured to receive the ball unit of the base plate.

Handle

[0175] In some embodiments, the orientation of the ball array guide and corresponding series of parallel trajectories is facilitated by a commercially available MRI or CT image-guided navigation system. In some embodiments, a handle can be used to connect the ball array guide with a navigation system. The handle can be engaged directly with the ball array guide. The handle can also be engaged with an imaging unit connected to the ball array guide. Fig. 20A shows one embodiment of a handle **140**. Fig. 20B shows the same handle **140** attached to an imaging unit **360** of an assembled trajectory array guide system **13** which includes a longer embodiment of the ball array guide **620**. In this embodiment, the connector **141** of the handle **140** is configured to be placed over the body of the imaging unit **360**. A set screw **144** is placed in the side opening **143** of the connector **141** to lock the handle **140** to the imaging unit **360**. The arm **142** of this embodiment of the handle **140** is roughly twice the length of the ball array guide **620**. The length of the arm may vary according to the needs of the particular situation. Combinations of handles which have longer and shorter arms may be provided in kits for assembling various embodiments of a trajectory array guide system.

[0176] Figs. 20C to 20E illustrate an embodiment of the handle **140**. Fig. 20C is a side elevation view of the handle **140** and Fig. 20D is a cross-section taken along line 20D—20D of Fig. 20C. Fig. 20E is a magnified view of the connector **141** of the handle showing the opening **143** for insertion of the set screw **144** (see Fig. 20B) and an air hole **145** located near the lower end of the connector **141** in this view. The purpose of the air hole **145** is to provide a passage to allow air to escape when the connector **141** is placed over the outer sidewall of an imaging unit with a tight seal.

[0177] In some embodiments, the handle has a total length of between about 12 to about 18 cm. In some embodiments, the arm portion of the handle has a diameter of between about 6 to about 10 mm.

[0178] In some embodiments, the handle is similar to the embodiment of Figs. 20C to 20D with the exception that the arm is hollow to allow insertion of a pointer probe which can be locked in place with a set screw through the opening in the connector.

Imaging Unit

[0179] An imaging unit can be configured for connection to or engagement with a ball array guide and a handle. In some embodiments where the ball array guide uses an offset index tube (such as tube **66** of Fig. 5A for example), the imaging unit can have an index tube arranged co-axially with the outer index groove of the ball array guide (see for example, Fig. 22). Shown in Figs. 21A and 21B are two perspective views of an embodiment of an imaging unit **360**. In Figs. 21A-21F, the imaging unit is shown without tubes being connected. The

imaging unit **360** can be connected to eight tubes to provide axes for imaging trajectories and indexing.

[0180] Fig. 21A is a top perspective view and Fig. 21B is a bottom perspective view of the imaging unit **360**. Fig. 21C is a top view and Fig. 21D is a bottom view. Fig. 21E is a side elevation view and Fig. 21F is a cross sectional view taken along line 21F—21F of Fig. 21E. This imaging unit **360** is constructed to fit over the top end of a ball array guide. In the top perspective view of Fig. 21A, the top openings of all eight of the passages **361a-g** and **362** (an indexing passage) are visible, as well as the reservoir **363** and a groove **368** formed in the outer sidewall of the imaging unit **360**. This groove **368** is provided to receive a locking set-screw **144** extending through the connector **141** of the handle **140**. Fig. 21B is a bottom perspective view of the same embodiment of the imaging unit **360**. In this perspective view, the index passage **362** is not visible. For further clarity, top and bottom views of the same embodiment of the imaging guide **360** are shown in Figs. 21C and 21D, respectively. Each of these views includes alignment lines to indicate the spatial relationships among the passages **361a-g** and **362**. Passages **361a-f** are equi-spaced and arranged in a symmetrical hexagonal shape with passage **361g** in the center and index passage **262** aligned with the line formed between passages **361c** and **361d** as well as the line formed between passages **361e** and **361f**. It is clearly seen in the cross-sectional view of Fig. 21F that the imaging unit **360** has an upper reservoir **363** for holding a volume of imaging reagent and a lower gap **367** below the intermediate solid section within which the passages **361a-g** and **362** are formed. This cross-sectional view has only one passage **361g** (the central passage) visible. It is seen that the upper part of passage **361g** has a smaller diameter than its lower part. This arrangement is also clearly seen in a comparison of the top view of Fig. 21C with the bottom view of Fig. 21D. The larger bottom diameter is for the purpose of insertion of separate trajectory imaging tubes (not shown). During assembly of a complete imaging unit **360**, the tubes are inserted and bonded into the passages **361a-g** and **362** via the bottom of the imaging unit. The upper reduced diameter of each passage acts as a stop to prevent passage of the tubes into the reservoir **363**.

[0181] Fig. 22 illustrates an embodiment of a trajectory array guide system **14**. An embodiment of an imaging unit **460** is inserted into a longer embodiment of a ball array guide **620** (shown in more detail in Fig. 15A, 15B, 20B and 23A-D). The imaging tubes **465a-g** and **466** being arranged co-axially with the lumens **625a-g** (seen at the bottom of the ball **621** of the ball array guide **620**) and outer groove **624** formed in the outer sidewall of the stem **622** of the ball array guide **620.** The tubes **465a-g** and **466** of the imaging unit **460** will thus enter

the corresponding lumens **625a-g** and outer groove **624** of the ball array guide **620**. The trajectory array guide system **14** includes locking nut **730** and base plate **350**.

[0182] In some embodiments, the process of using the imaging unit **360** to produce images for calculation of trajectories to an identified target in the brain will include insertion of tubes **465a-g** and **466** into each of the passages **361a-g** and **362** of the imaging unit **360**, followed by attachment of the imaging unit **360** to the upper end of the ball array guide **620** with the tubes **465a-g** and **466** extending into the corresponding lumens **625a-g** and outer groove **624**.

Ball Array Guide and Lumens

[0183] In some embodiments, the ball array guide provides for the placement and accuracy of a catheter. The catheter is passed through a selected lumen of the ball array guide to reach a target. To allow for smooth insertion, the array guide can provide sufficient clearance between the outer diameter of the catheter and the inner diameter of each lumen of the trajectory array. The accuracy of catheter placement can be increased by increasing the length of the lumens. In some embodiments, a ball array guide and corresponding lumens have a length between about 30 mm to about 60 mm, between about 40 mm to about 50 mm, or a length of about 45 mm. In some embodiments, a ball array guide includes two parts each having a defined length that are bonded together. Such a combination of parts could be machined, 3D-printed parts, or molded parts.

[0184] Figs. 23A-D illustrates an embodiment of a ball array guide **620**. Fig. 23A is a perspective view of the ball array guide **620** where the ball **621**, stem **622** and lower openings of lumens **625a-g** are visible. The outer groove **624** for placement of the index tube is not visible but is to be understood to be present in this embodiment of the ball array guide **620**.

[0185] The openings of the lumens **625a-g** are at a flat bottom part **628** of the ball. Near the top of the stem are three set-screw holes **627a-c** for insertion of set screws (not shown) to fix tubes of an imaging unit (not shown) engaged with the ball array guide. Fig. 23B is a side elevation view of the ball array guide **620**. Fig. 23C is a top view of the ball array guide **620** and Fig. 23F is a bottom view of the ball array guide **620**. The dashed lines in Figs. 23C and 23D indicate that the lumens **625a-f** are arranged symmetrically in a hexagonal shape and lumen **625g** is in the center of this hexagonal shape.

Embodiments of a Trajectory Array Guide System

[0186] The president disclosure illustrates how compatible components can be assembled in different combinations to produce various embodiments of a trajectory array guide system. Fig. 24 illustrates a cross-sectional perspective view of one embodiment of a trajectory array

guide system **15**. The system includes a ball array guide **220** which has a short stem **222** and a ball **221** which is compatible with the socket of the tilted base plate **550**. The tilted base plate **550** has tapered threads configured to thread to locking nut **530**.

[0187] Imaging unit **360** is attached to the top of the stem **222**. The center passage **361g** and the index passage **362** of the imaging unit **360** are aligned with the center lumen **225g** and the outer groove **224** of the ball array guide **220** (the tubes are omitted in an effort to preserve clarity). The cap **364** of the imaging unit **360** is engaged with the top of the imaging unit to isolate the reservoir **363**. Handle **140** is engaged with the outer circumference of the imaging unit **360** and a set screw (not shown) can be used to lock the connector **141** of the handle **140** via the opening **143** in the sidewall of the connector **141**. Arm **142** extends outward from the connector **141**.

[0188] Fig. 25 is an exploded perspective view of an embodiment of a trajectory array guide system **16** which includes a reducer component **75** which can reduce the diameter of one of the lumens **225a-g** of the ball array guide **220**. This may be necessary if a smaller gauge catheter is used, as the reducer can reduce significant deviations of the catheter from its desired trajectory. The reducer **75** includes a reducer tube **76** with a diameter smaller than the diameter of the lumens **225a-g**. The reducer tube **76** is engaged with a reducer disc **77** which includes a set-screw **78**. The set screw **78** allows the depth of an inserted instrument to be locked in place within the reducer tube. The reducer tube **76** can be locked in place using one of the ball array guide set screws **123a-c**.

Embodiments of a Trajectory Array Guide System with Separate Imaging Units and Guide Units

[0189] In some embodiments, a trajectory array guide system can include an array guide in the form of a wide bore sleeve (instead of a series of lumens). This wide-bore array guide includes a ball joint for connection to a base plate. The bore of the array guide is configured to receive an imaging unit and a matched array catheter guide unit (i.e. the arrangement of imaging unit passages and catheter guide unit lumens are matched such that trajectory images generated by the imaging unit will be co-axial with the lumens in order to ensure that the pathway followed by the catheter matches the selected trajectory). This embodiment of a trajectory array guide system provides a capability to provide independent diameter sizing of the lumens used for imaging (i.e. containing imaging reagent) and the lumens used for guiding the catheter. This embodiment also provides for height alignment of the top of the catheter guide lumens with the bottom of the top imaging chamber. This embodiment can provide more reliable general alignment of components while being less delicate than

embodiments using an imaging unit with imaging trajectory tubes. In general terms, the ball portion of the array guide of this embodiment is expected be larger than the ball portion of other embodiments described herein. The use of a ring-clamp as a locking mechanism is particularly amenable for use with trajectory array guide systems having separate imaging array and catheter array units because it allows greater angles of tilting of the array guide.

[0190] One embodiment of a trajectory array guide system is shown in Figs. 26A to 26H. Fig. 26A illustrates a cross-section (taken along line 26A—26A of the top view of Fig. 26B) of a funnel-shaped ball array guide **90** with a ball **91** at the bottom and a tapered internal bore **92** configured to receive matched imaging and catheter guide units. The top of the array guide **90** has a lock tab **93** with a bolt hole **94** for locking a corresponding imaging unit or catheter guide unit to the array guide **90**. These features are also illustrated in Fig. 26B which illustrates a top view of the array guide **90**.

[0191] Fig. 26C shows an arrangement for the connection of a handle **240** to the array guide **90** using a handle adapter **249** which is adaptable for engagement with different surgical navigation systems.

[0192] Fig. 26D is a cross-sectional view of one embodiment of an imaging unit **960** inserted into the array guide **90**. This cross-sectional view is taken at line 26D—26D of Fig. 26E. The imaging unit **960** has a lock tab **969** which is aligned with lock tab **93** of the array guide **90** for locking the imaging unit **960** in place with a lock bolt **95a**. The imaging unit **960** has a reservoir **963** for holding imaging fluid and a series of passages **961a-g** and a shorter index passage **962** for imaging a series of trajectories.

[0193] Fig. 26F shows a similar arrangement (representing a cross-sectional view taken along line 26F—26F of the top view of Fig. 26G) with a catheter guide unit **920** inserted into the array guide **90**. The catheter guide unit **920** has a series of lumens **925a-g** and a shorter index lumen **924**. Any one of lumens **925a-g** may be selected based on a trajectory identified using the imaging unit **960**. Passages **961a-g** of the imaging unit are matched and aligned with corresponding lumens **925a-g** of the catheter guide unit **920**. For example, if trajectory images provided by the imaging unit **960** indicate that lumen **961c** represents the optimal trajectory to the target, this will be noted and after the imaging unit **960** is removed and the catheter guide unit is inserted, lumen **921c** will be the lumen used to guide the catheter to the target. The catheter guide unit **920** also has a lock tab **929** to lock the catheter guide unit **920** in place within the array guide **90**. The catheter guide unit **920** also includes a locking slider **926** with openings **928a-g** for locking a catheter in place within one of the selected lumens **925a-g**. This locking slider **926** is shown by itself in a top view in Fig. 26H.

[0194] An example describing the operation of a trajectory array guide system is presented with reference to components illustrated in Figs. 26A-26H.

[0195] The system is assembled with the array guide **90** connected to a base plate, such as base plate **450** for example, and with the imaging unit **960** inserted and locked into the bore **92** of the array guide **90** using the lock bolt **95a**. The imaging reagent contained within the passages **961a-g** and **962** is used to visualize the series of trajectories towards the target and the optimal trajectory is selected. With the array guide **90** locked in place in the base plate **450**, the imaging unit **960** is removed and the catheter guide unit **920** is inserted into the bore **92** of the array guide **90** and locked in place using the lock bolt **95a**. The locking slider **926** is placed in the catheter guide unit **920** and held in place using lock bolt **95b** to retain the catheter in place in the selected lumen which represents the selected optimal trajectory.

[0196] Figs. 27A-27C illustrate a generally funnel-shaped ball array guide **190** which is provided with a wide bore **192** to receive both a funnel-shaped imaging unit **1060** and a matched catheter guide unit **1020**. The ball array guide **190** is shown connected to the socket of base plate **450**. The ball array guide has a lock tab **193** for locking to a corresponding lock tab **1069** of the imaging unit **1060** and for locking to a corresponding lock tab **1029** of the catheter guide unit **1020**. The lumens **1025a-g** and index lumen **1024** as well as the passages **1065a-g** and index passage **1066** are visible in Fig. 27C.

[0197] Trajectory array guide systems which include a funnel-shaped array guide and corresponding funnel-shaped units can have advantages over other embodiments of the trajectory array guide system. For example, the array of tubes of imaging units can be difficult to insert into corresponding lumens of a ball array guide. There is also a manufacturing challenge in sealing tubes to an imaging unit. There can also a degree of movement between the ball array guide and the tubes which cause a degree of flexure of the system when a handle is connected. In addition, a reducer (see for example reducer 70 in Fig. 25) is required to handle catheters with reduced diameters, whereas the construction of a funnel-shaped catheter guide unit of the present disclosure can be modified to provide units with different sized lumens. Notably, 14-gauge and 16-gauge catheters can require different correction factors for insertion depth. This is particularly important because lower gauge (reduced diameter) imaging unit lumens may provide the best images. The embodiment described in this section addresses these disadvantages, among others.

Trajectory Array Guide System with Alternative Imaging Fluid Injection Path and Handle Connection

[0198] Fig. 28 is an arbitrary cross-sectional perspective illustration of one embodiment of a trajectory array guide system **18** which uses separate imaging and catheter guide units in a manner similar to the system described in Figs. 26A to Fig. 27C.

[0199] This trajectory array guide system **18** includes base plate **450** with its tilted socket and a ring clamp **80**. This base locking combination is used to retain an embodiment of a ball array guide **290** which like the ball array guide **90** of Fig. 26 has a ball **291** configured to be held in the socket of the base plate **450** and a bore **292** for holding imaging and catheter guide units. In Fig. 28, an imaging unit **660** is shown inserted into the bore **292** of the ball array guide **290**. This imaging unit **660** has a series of seven passages **661a-g** with only passages **661a**, **661d** and **661g** being visible in this perspective view. Lumens **661b-g** terminate at an orthogonal passage-connecting plenum **669** which is located at the center of rotation of the ball **191**. Passage **661a** is extended a short distance downward from the plenum **669** and forms a passage extension **661a'**.

[0200] In this embodiment, the handle **340** is provided with an injection passage **348** along the axis of the arm **342** through to the connector **341** which fits into a cavity in the upper chamber **663** of the imaging unit **660**. The injection passage **348** in the arm **342** of the handle **340** is for injection of imaging fluid via a port (not shown) in the arm **342**. The port may be located at any position along the arm **342** of the handle **340** as long as imaging fluid may be effectively injected into the injection passage **348**. When continuously injected, the imaging fluid moves down the injection passage **348** and enters the center passage **661g**. When the injected imaging fluid reaches the plenum **669**, the imaging fluid then disperses in the plenum **669** and fills the remaining passages **661a-f** from the bottom upwards. The imaging fluid also fills the lower extension **661a'** of passage **661a**. In this manner, all passages **661a-g** are appropriately filled with imaging fluid for identification of the array of parallel trajectories. The lower passage extension **661a'** is easily identified and distinguished from the remaining passages under magnetic resonance imaging and serves as an index image for identification of the trajectory images (this would otherwise be impossible due to the symmetrical hexagonal arrangement of the passages **661a-g**). This arrangement obviates the need for an eighth passage used as an index passage as in the previous embodiments.

[0201] As a result of this arrangement of features, all passages **661a-g** and **661a'** can be filled with imaging fluid via a port (such as a Luer taper injection port) in the handle **340** which is conveniently accessible (see for example, Fig. 31). An air hole (not shown) is

provided in communication with the flow path of injected fluid in order to allow air displaced by the imaging fluid to vent from the flow path. This arrangement also allows the flow path to be purged with fluid or air for cleaning.

[0202] In some embodiments, the connector **341** of the handle **340** slides into the upper chamber **663** of the imaging unit. This provides an improved sealing arrangement and eliminates the need for a cap for the imaging unit **660**. An alternative of this embodiment is an arrangement where the handle **340** is bonded or integrally formed with the upper chamber of the imaging unit **660** during manufacture. This could allow the entire assembly of the imaging unit **660** with the monolithically formed handle **340** to be discarded with the imaging fluid contained therein.

[0203] The handle is provided with distance markers (markers **349a-c** are shown in this partial view and more would be visible in a complete illustration of the handle **340**) which indicate the distance from the center of rotation of the ball **291**. This feature provides a means of identifying sideways movement of the handle **340** at a given distance from the center of rotation of the ball **291**, which creates a known opposite movement of a trajectory of the same length as that distance.

[0204] Fig. 29 is a perspective view of the sub-assembly of the imaging unit **660** and the handle **340**. Fig. 30 is a transparent perspective view of the imaging unit **660** which shows internal features including imaging passages **661a**, **661d** and **661g** (remaining passages **661b**, **661c**, **661e** and **661f** are not visible in this view), passage extension **661a'** plenum **669** and reservoir **663.** Likewise, Fig. 31 is a transparent perspective view of the handle **340** which shows the internal injection passage **348** and the injection port **346**. In addition, distance markers **349a-i** are shown as graduations at and above the connector **341**. The internal injection passage **348** provides a convenient means for filling the imaging unit **660** with imaging fluid while the handle **340** and imaging unit **660** subassembly is assembled.

[0205] Figs. 32 and 33A-33B illustrate one embodiment of imaging unit **660** and one embodiment of the ball array guide **390**. The imaging unit **660** is seen in a perspective view in Fig. 32. The imaging unit **660** has a solid bottom **660'** indicating that all of the imaging passages **661a-g** which begin at the bottom of the reservoir **663** terminate within the body of the imaging unit **660** (see Fig. 33B). The ball array guide **390** and the subassembly of both the ball array guide **390** and the imaging unit **660** are shown in perspective views in Figs. 33A and 33B. The ball array guide **390** has a wide bore **392** which extends from the top through to the bottom of the ball **391**. When the imaging unit **660** is fully inserted into the

ball array guide **390**, the solid bottom of the imaging unit **660'** is seen at the bottom of the ball **391**.

[0206] Figs. 34 and 35A-35B illustrate one embodiment of a catheter guide unit **720** and one embodiment of a ball array guide **490**. The catheter guide unit **720**, shown by itself in a perspective view in Fig. 34, is provided with an outer index lobe **726** to accommodate the presence of a shorter index lumen **724** which is outside of the hexagonal symmetry of the main pattern of lumens **725a-g** (see Fig. 35B). The index lumen **724** is used for identification of the individual lumens **725a-g** during imaging. In Figs. 34 and 35A, the lumens **725a-g** extend all the way from the top to the bottom of the catheter guide unit **720**. These lumens **725a-g** are visible in the bore **492** at the bottom of the ball **491** of the ball array guide in Fig. 35A. The ball array guide **490** is provided with an index lobe receiver portion **494** to accommodate the entry of the index lobe **726** of the catheter guide unit **720**. The presence of the lobe **726** allows the catheter guide unit **720** to be constructed with a smaller diameter lower portion to make a tighter array of lumens **725a-g**. The lobe receiver **494** of the ball array guide **490** provides an improvement over the outer groove arrangement of other embodiments of the ball array guide by protecting the index passage which is used during imaging.

Trajectory array guide System Having Separate Imaging Unit and Guide Units with Slanted Arrays

[0207] A trajectory array guide system can include a funnel-shaped ball array guide which includes matched arrays of lumens and imaging passages which are angled with respect to the longitudinal axis of the ball array guide. Such angled or slanted arrays may be designed to expand the range of possible trajectories outside of the typical straight array in which all lumens and passages are aligned with the longitudinal axis of the array guide. This can create a "footprint" three times the size of the single straight array. The advantage of this approach is that the ball-joint can remain in the locked position (i.e. adjustments of the ball-joint are not required). A single slanted imaging array could provide a wide range of additional trajectories arranged circumferentially around the central array when locked in various positions.

[0208] Fig. 36A shows a cross-sectional view of a subassembly of one embodiment of a funnel-shaped ball array guide **590** with a wide bore to accommodate insertion of a funnel-shaped imaging unit **1160**. Fig. 36B is a top view of the same arrangement shown in Fig. 36A. Ball array guide **590** includes eight equi-spaced lock tabs **593a-h** which are each configured to lock the ball array guide **590** to the imaging unit **1160** and to lock the ball array

guide **590** to the matched catheter guide unit **1120** (see Fig. 36C). The index lock tab **593a** (in the 12:00 position in Fig. 36B) is provided with a differentiating indicator such as a different color (as indicated by the black fill in Fig. 36B) for identification. The imaging unit **1160** has the usual hexagonal pattern of imaging passages **1161a-g** and an index passage **1162** as seen in Fig. 36B. However, each of the passages **1161a-g** is angled away from the longitudinal axis of the imaging unit **1160** as indicated by representative passages **1161a**, **1161d** and **1161g** of Fig. 36A (the remaining passages **1161b**, **1161c**, **1161e** and **1161f** are hidden from view in this cross-section). The angled passages **1161a-g** and index passage **1162** are substantially parallel and extend from the bottom of the reservoir **1163** to a position close to the bottom of the imaging unit **1160**.

[0209] The placement of the single lock tab **1169** of the imaging unit (with locking using lock bolt **595a**) in a position other than the index position shown in Fig. 36B will have the effect of rotating the trajectory direction of the hexagonal array of passages **1161a-g**. Because each of the passages **1161a-g** of the hexagonal array is angled, this rotation has the effect of shifting the direction of the array of potential trajectories to create a wider circle of end points for the potential trajectories as shown in Figs. 37A and 37B.

[0210] Fig. 36C is a cross-sectional view of the subassembly of the ball array guide **590** with a catheter guide unit **1120** inserted into the wide bore of the ball array guide **590**. This catheter guide unit **1120** is matched to the imaging unit **1160** and thus has slanted lumens **1125a-g** and a slanted index lumen **1124** which match the passages **1125a-g** and index passage **1162** of the imaging unit **1160**. Thus, when the imaging unit **1160** is used to identify an optimal trajectory passage, the lumen corresponding to that optimal trajectory passage will be used for injection of the catheter. For example, if imaging passage **1161d** was identified as representing the optimal trajectory to the target, lumen **1125d** of the matched catheter guide unit **1120** would be used as the pathway to inject the catheter. The catheter guide unit **1120** has a lock tab **1129** for locking the catheter guide unit **1120** to any one of the lock tabs **593a-i** of the ball array guide **590** (see Fig. 36D).

[0211] The catheter guide unit **1120** also includes a locking slider **1126** with openings **1128a-g** for locking a catheter in place within one of the selected lumens **1125a-g**. This locking slider **1126** is shown by itself in a top view in Fig. 36E. The locking slider **1126** is secured to the catheter guide unit **1120** using lock bolt **595b**.

[0212] As noted hereinabove, Figs. 37A and 37B are provided to indicate how placement of imaging unit **1160** with its lock tab **1169** locked to any one of the lock tabs **593a-i** will

result in direction of the array of trajectories to a different outward location, which are identified using clock positions.

[0213] In accordance with the angular direction of the passages **1161a-g** and lumens **1121a-g** away from the index lock tab **593a** (12:00 position), it is understood that the trajectories are directed in the opposite direction (towards the 6:00 position). Therefore, according to this arrangement, it is seen in Figs. 37A and 37B that when the lock tab **1169** of imaging unit **1160** is locked to tab **593a** (12:00 position), the array will be directed towards the 6:00 position. This opposing directivity holds for the remaining positions.

[0214] The use of ball array guide **590** may be combined with imaging units and catheter guide units with straight arrays such as those illustrated in Figs. 26A-26H. Therefore, if imaging unit **960** of Figs. 26A and 26B is inserted into the ball array guide **560**, it can be locked to any one of lock tab positions **593a-i** and the trajectory direction of the array will remain centralized with no outward directivity because the array of the imaging unit **960** is straight. Therefore, a combination of imaging and guide units with straight arrays and imaging and guide units with slanted arrays can cover a wide footprint as illustrated in Fig. 37B. Importantly the wide footprint of trajectory coverage may be obtained without adjusting the ball array guide **590** within its socket in the base plate.

Trajectory array guide System with Alternative Handle for Connection to Navigation Pointer for Image-Guided Surgery

[0215] An embodiment of a trajectory array guide system **19** is shown in Figs. 38A-D. This embodiment includes a handle **440** which is constructed to facilitate connections to navigation pointers of image guided surgery systems currently in use. As such, the handle **440** (shown by itself in Fig. 38A) is designed for direct placement on and engagement with a ball array guide **320** which is seen as part of the complete system **19** in Figs. 38B-38D. The placement is made by inserting a spike **448** into one of the selected lumens **325a-g** (see Fig. 38D). The handle **440** is hollow to allow insertion of the spike **448** at one end. The hollow handle **440** also allows for the attachment a navigation pointer to the back end opening **446** of the hollow handle. A set-screw **447** penetrating into the bore of the handle **440** is provided to hold the navigation pointer in place.

[0216] Fig. 38B shows one embodiment of an assembled trajectory array guide system with the handle **440** engaged with an embodiment of the ball array guide **320** which has three set screws **323a-c** positioned closer to the ball **321** than to the upper end of the ball array guide **320**. This arrangement is provided to allow direct connection of certain types of

surgical navigation systems to the upper part of the ball array guide **320**. This system **19** uses base plate **450** in combination with ring clamp **80** as seen in Figs. 38B-D.

[0217] Fig. 38C is an exploded view showing components of a trajectory array guide system **19**, including imaging unit **360**, reducer **75**, and a calibration rod **201**. In some embodiments, the calibration rod **201** can be used to calibrate positioning of the ball array guide **320** with respect to certain image guided surgery systems which can be connected directly to the upper body of the ball array guide **320**. The calibration rod **201** has an upper portion with a wider diameter than the bottom portion to provide two calibration diameters to fit different sized holes. In one embodiment of the calibration rod, the wider portion of the calibration rod **201** has an outer diameter of 2.1 mm to fit the center lumen of the ball array guide **320** and the narrower portion of the calibration rod **201** has an outer diameter of 2.0 mm to fit into a calibration hole on the calibration tool of a Brainlab StarLINK™ image guided surgery system. This calibration rod **201** can also be compatible with the Medtronic SureTrak™ image guided surgery system, and other image guided surgery system known to those in the art. In some embodiments, trajectory array guide system **19** includes an O-ring **369** which creates a seal between the cap **364** and the imaging unit **360**.

[0218] Fig. 38D is a top view of the system without the handle **440**. The ball array guide **320** has three set-screw holes **326a-c** which allow each set screw **323a-c** to penetrate the body of the ball array guide **320** and enter three of the seven lumens **325a-g**. Therefore, set-screw **323a** penetrates into lumens **325a**, **325b** and **325g**; set-screw **323b** penetrates into lumens **325c**, **325d** and **325g**; and set-screw **323c** penetrates into lumens **325e**, **325f** and **325g**. As such, the spike **448** can be fixed in place in any one of the seven lumens **325a-g**.

[0219] In some embodiments, the position and orientation of a trajectory array guide system can be tracked by an image guided neuronavigational system via instrument trackers clamped to a handle or array guide. In certain embodiments, the trajectory array guide system will have general compatibility with image guided surgery systems including, but not limited to, Varioguide™ and StarLINK™ (Brainlab, AG, Munich, Germany), as well as Vertek™ and SureTrak™ (Medtronic). Fig. 39 shows a perspective view of a trajectory array guide system engaged with an image guided surgery system **1200** which includes a probe **1202**. The probe **1202** can be inserted into or engaged with the end opening **446** of the handle **440**. The image guided surgery system **1200** can be secured to the handle using fastening and locking mechanisms, including the set screw **447**. Fig. 40A shows a perspective view of an image guided surgery system **1210** clamped onto a handle **440** of a trajectory array guide system. Fig. 40B shows a perspective view of an image guided surgery system **1210** clamped directly

onto a ball array guide **320** of a trajectory array guide system, with the assistance of a calibration rod **201**.

Kits

[0220] The present disclosure provides kits for assembly of various embodiments of the trajectory array guide system of the present disclosure. In some embodiments, components of a kit may be separately packaged or packaged together in any configuration rendering a package suitable for sterilization. Steam, ethylene oxide, or gamma sterilization are preferred sterilization methods for the kits.

[0221] In some embodiments, the kit includes instructions for assembly of a trajectory array guide system.

[0222] In some embodiments, the kit includes the following: instructions for assembly of a trajectory array guide system; a container of imaging reagent; and one or more catheters which are compatible with the trajectory array guide system.

[0223] In some embodiments, the kit includes multiple imaging units or guide units for insertion into an array guide. In some embodiments, the kit includes a plurality of separate array units or reducers configured for guiding elongated tools of different diameters.

EXAMPLES

Example 1 – Testing of Locking Mechanism

[0224] Base plates resembling base plate **550** of Fig. 18 and base plate **450** of Fig. 19A were produced as plastic 3D-printed prototypes. A locking nut resembling locking nut **530** of Fig. 18 and a ring clamp resembling ring clamp **80** of Figs. 19B-C were produced as plastic 3D-printed prototypes. The base plates were tested to determine the effectiveness of the locking mechanism.

[0225] The base plates were held in a vise at one of the attachment tabs. A ball array guide resembling the ball array guide **220** in Fig. 18 and Fig. 19D was engaged into the socket of each base plate. A downward force was applied 30 mm from the bottom face of the base plate. The speed of the downward force was set at 50 mm/min. The test was first conducted in the absence of a locking mechanism, and then with the tapered threading locking mechanism (similar to Fig. 18) and with the ring-clamp mechanism (similar to Figs. 19A-19D) on their respective base plates. The peak force required to displace the ball array guide was recorded. The results of the test are summarized in Table 1.

Table 1: Testing of Locking Mechanisms

Locking Mechanism	Peak Force (N)	Peak Torque (N) or (Nmm)	Failure Mode
Absent	1-2	30-60 Nmm	Ball moved

Tapered threading (similar to Fig. 18)	7-8	210-240 Nmm	Ball moved
Ring-clamp (similar to Figs. 19A-19C)	16-18	480-540 N	Base plate tab fractured

[0226] The ring-clamp embodiment (similar to base plate **450** in combination with ring clamp **80** of Figs. 19A-C) was found to yield the best results. The ring-clamp embodiment did not fail at a torque of 480-530 N which is twice the torque needed to fracture the catheter.

Example 2 – Preparation of Imaging Cartridge

[0227] A gadolinium-based contrast solution is prepared by aspirating a gadolinium-based contrast agent into a 0.3 mL syringe. 0.04 mL of the gadolinium-based contrast agent is injected into a 10 mL pre-filled sterile saline syringe. A 2.0 to 5.0 inch, 25- to 30-gauge needle is attached to the sterile saline syringe and inverted multiple times to ensure mixing of the contrast agent with the sterile saline.

[0228] An imagining cartridge is provided which includes 7 imaging tubes in a symmetrical hexagonal pattern and an additional reference imagining tube. The 10 mL syringe containing the gadolinium imaging solution is used to sequentially fill the lumen of each tube by injecting imaging solution into the tube. The tip of the syringe is placed at the bottom of the tube, and the injection begins from the bottom of the tube. To ensure optimum MR visibility of the imaging cartridge tubes, the injection of the gadolinium imaging solution is continued while the syringe is slowly withdrawn from the tube, thereby preventing air from re-entering the tube. Each tube is visually inspected for air bubbles. If air bubbles are observed, the needle is reinserted to the base of the tube and additional gadolinium imaging solution is injected to push out the air bubbles.

[0229] Once all tubes have been filled with the gadolinium imaging solution, a reservoir at the top of the imaging cartridge is filled. An O-ring and sealing cap are then engaged with the top opening of the imaging cartridge to seal the imaging solution into the cartridge.

Example 3 – Assembly of a trajectory array guide system and calibration with an image guided surgery system

[0230] A trajectory array guide system resembling the system shown in Fig. 38C is provided. A ring clamp is engaged with a tilted base plate, such that the ridge of the ring clamp is engaged with the outer groove of the base plate, similar to the configuration shown in Figs. 19B-19D. The tension screw of the ring clamp is maintained in a loose position, and the ball of a ball array guide is engaged into the socket of the base plate. The tension screw is softly tightened.

[0231] A component of an image guided surgery system, such as an instrument tracker, is attached to the handle of the trajectory array guide system in a manner resembling the configuration shown in Fig. 40A. The handle is then engaged with the ball array guide by inserting the spike of the handle into the center channel of the array guide. The set-screws of the ball array guide are tightened to secure the engagement.

[0232] The trajectory array guide system can then be adjusted as necessary, with the tension screw of the ring clamp being fully tightened once the system has been properly aligned.

Example 4 – Assembly of a trajectory array guide system without a handle and calibration with an image guided surgery system

[0233] A trajectory array guide system resembling the system shown in Fig. 38C is provided. A ring clamp is engaged with a tilted base plate, such that the ridge of the ring clamp is engaged with the outer groove of the base plate, similar to the configuration shown in Figs. 19B-19D. The tension screw of the ring clamp is maintained in a loose position.

[0234] A component of an image guided surgery system, such as an instrument tracker, is attached directly to a guide array of the trajectory array guide system, similar to the configuration shown in Fig. 40B. The ball of a ball array guide is then engaged into the socket of the base plate. The tension screw is softly tightened. A calibration rod is inserted into the center channel of the array guide.

[0235] The trajectory array guide system can then be adjusted as necessary, with the tension screw of the ring clamp being fully tightened once the system has been properly aligned.

Example 5 – Surgical preparation of a skull and attachment of trajectory array guide system

[0236] A cranial entry point is identified using image guided neuronavigational systems and MRI scans. The target head area is prepared for cranial entry according to standard medical practice, including cleaning and shaving the scalp around the cranial entry point. A craniotomy is conducted using standard surgical procedures to form a cranial entry at least 14 mm diameter at the planned cranial entry site.

[0237] A trajectory array guide system is provided, such as the system described in Example 3. The base plate is placed against the skull at the cranial entry point, with the bore of the base plate being located directly over the cranial entry hole. The base is rotated to a suitable orientation for attachment to the skull and to ensure that the tilt of the base is aligned with the surgical target. The base is then attached to the skull using self-drilling titanium bone

screws through the holes on the base feet. The ring clamp and array guide are rotated and adjusted as necessary to provide access to the screw holes.

Example 6 – Alignment of trajectory array guide system, selection of target trajectory, and completion of surgical procedure

[0238] A trajectory array guide system attached to a skull is provided, such as the arrangement described in Example 5.

[0239] The ring clamp is maintained in a loose position to allow the array guide to be freely rotated and adjusted as necessary. Using standard surgical procedures, an image guided surgery system is used to align the array guide in the direct of the surgical target. The trajectory and position of the array guide is then secured by gently hand-tightening the tension screw of the ring clamp.

[0240] A surgical probe is used to measure the distance from the top of the array guide to the surgical target, thereby providing the necessary insertion depth of the surgical instrument.

[0241] An imagining cartridge, such as the imaging cartridge prepared in Example 2, is carefully inserted into the array guide. The system is inspected to ensure that there is no gap between the top of the guide and the body of the imaging cartridge. Set-screws in the array guide are tightened to secure the engagement of the imaging cartridge and array guide.

[0242] All MRI unsafe tools, such as a metal handle or metal calibration rod are removed, and the head is placed within an MRI suite. The MRI equipment is turned on, and the resulting images are inspected to ensure that the entire trajectory array guide system and target surgical area are included in the MR images. Each of the seven trajectories is evaluated relative to the reference tube, and the best trajectory for the surgical target is selected. The channel corresponding to the selected trajectory is noted, and the imagining cartridge is removed.

[0243] The surgical procedure is then performed using the array channel of the selected trajectory. If the tube is a 14-gauge tube and the surgical instrument is a 16-gauge instrument, a reduce can be used to adjust the diameter of the array channel.

[0244] Once the surgical procedure is complete, the bone screws are withdrawn, and the trajectory array guide system is removed from the skull and disassembled. The trajectory array guide system can then be discarded as a single-use system, or it can be sterilized for reuse.

EQUIVALENTS AND SCOPE

[0245] Those skilled in the art will recognize, or be able to ascertain using no more than routine experimentation, many equivalents to the specific embodiments in accordance with the disclosure described herein.

[0246] In the claims, articles such as "a," "an," and "the" may mean one or more than one unless indicated to the contrary or otherwise evident from the context. Claims or descriptions that include "or" between one or more members of a group are considered satisfied if one, more than one, or all of the group members are present in, employed in, or otherwise relevant to a given product or process unless indicated to the contrary or otherwise evident from the context. members are present in, employed in, or otherwise relevant to a given product or process.

[0247] It is also noted that the term "comprising" is intended to be open and permits but does not require the inclusion of additional elements or steps. When the term "comprising" is used herein, the term "consisting of" is thus also encompassed and disclosed.

[0248] Methods of the present disclosure are exemplified through discussion of certain embodiments which are not intended to be limiting to the scope of the general methods disclosed herein. Certain embodiments of the methods are discussed with different combinations of steps and different orders of steps. The combinations and order in which steps are presented are not intended to be limiting to the scope of the general methods presently disclosed. Individual steps disclosed herein can be combined in any combination and in any order within operable embodiments of the methods according to the knowledge and skill of those with ordinary skill in the art.

[0249] Where ranges are given, endpoints are included. Furthermore, it is to be understood that unless otherwise indicated or otherwise evident from the context and understanding of one of ordinary skill in the art, values that are expressed as ranges can assume any specific value or subrange within the stated ranges in different embodiments of the invention, to the tenth of the unit of the lower limit of the range, unless the context clearly dictates otherwise.

[0250] Any particular embodiment of the present disclosure that falls within the prior art may be explicitly excluded from any one or more of the claims. Since such embodiments are deemed to be known to one of ordinary skill in the art, they may be excluded even if the exclusion is not set forth explicitly herein. Any particular embodiment of the compositions of the invention (e.g., any nucleic acid or protein encoded thereby; any method of production;

any method of use; etc.) can be excluded from any one or more claims, for any reason, whether or not related to the existence of prior art.

[0251] All cited sources, for example, references, publications, databases, database entries, and art cited herein, are incorporated into this application by reference, even if not expressly stated in the citation. In case of conflicting statements of a cited source and the instant application, the statement in the instant application shall control.

[0252] Section and table headings are not intended to be limiting. Figures included with the present disclosure are intended to be non-limiting depictions of general concepts of the present disclosure.

CLAIMS

1. A trajectory array guide system for defining a trajectory to a target location in the brain of a subject and for guiding an elongated tool along the trajectory, the system comprising:
    a. a base configured for attachment to the skull of the subject;
    b. an array guide which is defined by a series of lumens or is defined by a bore configured to hold a guide unit defined by a series of lumens;
    c. an imaging unit configured for engagement with the array guide and configured to hold and direct imaging fluid along passages which are co-axial with the lumens of the array guide or the lumens of the guide unit, for the purpose of defining a series of trajectories; and
    d. an elongated handle configured for connection with a stereotaxic navigation system and configured for engagement with either the array guide or the imaging unit.
2. The trajectory array guide system of claim 1, wherein the array guide comprises a ball at one end, and wherein the base comprise a socket configured to receive and hold the ball of the array guide to form a ball-socket pivoting mechanism.
3. The trajectory array guide system of claim 1 or claim 2 wherein the socket has a central axis orthogonal to a plane formed by the bottom of the base.
4. The trajectory array guide system of claim 1 or claim 2, wherein the socket has a central axis which is non-orthogonal with respect to the plane formed by the bottom of the base, thereby providing a tilted socket.
5. The trajectory array guide system of claim 4, wherein the central axis of the socket is angled by between about 10 to about 30 degrees from the axis orthogonal to the plane formed by the bottom of the base.
6. The trajectory array guide system of any one of claims 2 to 5, wherein the socket has an outer sidewall comprising threads or comprising one or more grooves, wherein the threads or grooves are configured for attachment to a locking element which can prevent the ball within the socket from pivoting movement.
7. The trajectory array guide system of claim 6 wherein the locking element is a ring-clamp configured for connection to the one or more grooves of the socket.
8. The trajectory array guide system of claim 6 wherein the locking element is a locking nut configured for connection to the threads of the socket.
9. The trajectory array guide system of any one of claims 6 to 8, wherein the base includes a plurality of attachment members for attaching the base to the skull of the subject, and

wherein the attachment members are accessible by an attachment tool when the locking element is engaged to the outer sidewall of the socket.

10. The trajectory array guide system of any one of claims 2 to 9, wherein the array guide is a generally cylindrical or funnel-shaped member having the ball formed at one end, and wherein the series of lumens extending longitudinally along the length of the array guide with openings at both ends.
11. The trajectory array guide system of claim 10, wherein the series of lumens comprises seven substantially parallel lumens with six lumens arranged in a symmetrical hexagonal pattern and a seventh lumen located in the center of the symmetrical hexagonal pattern.
12. The trajectory array guide system of any one of claims 1 to 11, wherein the imaging unit comprises an upper reservoir in fluid communication with a series of lower extensions which are co-axial with the lumens of the array guide.
13. The trajectory array guide system of claim 12, wherein the lower extensions are tubes configured to fit inside the lumens of the array guide.
14. The trajectory array guide system of claim 13, wherein the array guide includes an outer groove and the imaging unit includes an index tube configured to slide into the outer groove when the imaging unit is engaged with the array guide, wherein the index tube is provided as a reference point for identification of each of the tubes in a magnetic resonance image.
15. The trajectory array guide system of any one of claims 1 to 14 wherein the imaging unit includes a cap to seal the imaging fluid inside the imaging unit.
16. The trajectory array guide system of any one of claims 13 to 15, wherein the array guide comprises a mechanism for locking the tubes in place within the array guide.
17. The trajectory array guide system of claim 16, wherein the locking mechanism is provided by at least one set-screw which penetrates the array guide and makes tightening contact with at least one of the tubes.
18. The trajectory array guide system of claim 16, wherein the locking system is provided by three set-screws, each penetrating the body of the array guide to enter two different lumens as well as the central lumen.
19. The trajectory array guide system of claim 18, wherein the three set-screws are placed closer to the ball of the ball array guide than to the upper end of the ball array guide.
20. The trajectory array guide system of any one of claims 1 to 19, wherein the handle comprises a connector end configured for engagement with the outside or the inside of the imaging unit.

21. The trajectory array guide system of claim 20, wherein the connector end is configured for engagement with the outside of the imaging unit and includes an opening for a connector set-screw to lock the handle on the imaging unit.
22. The trajectory array guide system of claim 20, wherein the handle includes an end spike for insertion into one of the lumens of the array guide for direct engagement of the handle with the ball array guide.
23. The trajectory array guide system of claim 22, wherein the handle is at least partially hollow and has an outer end opening at the end opposite the end spike, and wherein the outer end opening is configured for connection to a navigation component of an image guided surgery system.
24. The trajectory array guide system of any one of claims 1 to 21, further comprising a reducer tube for insertion into one of the lumens to provide a reduced diameter for the tube.
25. The trajectory array guide system of claim 24, wherein the reducer tube comprises an adjustable stop for restraining movement of an elongated tool within the reducer tube.
26. The trajectory array guide system of any one of claims 2 to 9, wherein the array guide is defined by a bore configured to hold a guide unit defined by a series of passages which are co-axial with the lumens, and wherein the guide unit comprises an upper lock tab for connection of the separate array unit to the array guide.
27. The trajectory array guide system of claim 26, wherein the imaging unit is configured for connection to the array guide at the upper lock tab.
28. The trajectory array guide system of claim 26 or 27, further comprising a locking slider configured for insertion into the body of the guide unit to hold an elongated tool in place in one of the lumens.
29. The trajectory array guide system of any one of claims 26 to 28 wherein the passages connect to a plenum located within the ball, wherein the handle comprises a channel for injecting imaging fluid into the plenum through a central passage of the series of passages, and wherein imaging fluid flows into the remaining passages from the plenum.
30. The trajectory array guide of any one of claims 26 to 29, wherein the passages are seven substantially parallel passages with six passages arranged in a symmetrical hexagonal pattern around a central passage.
31. The trajectory array guide system of claim 30, wherein one of the six passages is extended downward past the plenum for providing an index passage for identification of individual passages.

32. The trajectory array guide system of any one of claims 26 to 31 wherein the passages and the lumens are parallel with the main axis of the array guide or wherein the passages and the lumens are angled with respect to the main axis of the array guide.
33. The trajectory array guide system of claim 32, wherein the array guide comprises a plurality of lock tabs around its circumference for changing the direction of the series of trajectories defined by the lumens and the passages with respect to the main axis of the array guide.
34. The trajectory array guide system of claim 33, wherein the plurality of lock tabs comprise eight equi-spaced lock tabs.
35. The trajectory array guide system of any one of claims 26 to 31, comprising at least two guide units and at least two imaging units matched to the guide units to form pairs wherein one pair of matched guide and imaging units has lumens and passages parallel with the main axis of the array guide and another pair of matched guide and imaging units has lumens and passages which are angled with respect to the main axis if the array guide.
36. The trajectory array guide system of claim 35, wherein the array guide comprises a plurality of lock tabs around its circumference for changing the direction of the series of trajectories defined by the lumens and the passages with respect to the main axis of the array guide.
37. The trajectory array guide system of claim 36, wherein the plurality of lock tabs is eight equi-spaced lock tabs to provide eight different arrays of angled trajectories.
38. A method for delivering an elongated tool to a target location in the brain of a subject, the method comprising:
    a. providing a trajectory array guide system comprises a base plate, an array guide, an imaging unit, a handle, and a stereotaxic navigation system connected to the handle;
    b. performing a craniotomy at an entry location;
    c. connecting the base of the trajectory array guide system to the entry location;
    d. engaging the array guide with the base plate to form a pivoting mechanism;
    e. engaging the imaging unit with the array guide and aligning the array guide to the target;
    f. imaging a series of trajectories towards the target location with magnetic resonance imaging;
    g. locking the trajectory array guide system and selecting a trajectory from the series of trajectories;

h. removing the imaging unit and delivering the elongated tool to the target location using the selected trajectory; and

i. removing the trajectory array guide system from the skull of the subject.

39. The method of claim 38, wherein step of connecting the base of the trajectory array guide system to the entry location comprises connecting the base to the entry location using bone screws through bottom tabs of the base.

40. The method of claim 38 or claim 39, wherein the method further comprises adding MRI contrast imaging reagent to the imaging unit prior to the imaging of the series of trajectories.

41. The method of any one of claims 38 to 40 wherein the step of aligning the array guide to the target comprises using the surgical navigation system to orient the series of trajectories toward the target location.

42. The method of any one of claims 38 to 41 wherein the elongated tool is a catheter.

43. The method of claim 42, wherein the catheter is configured to deliver a drug to the target location.

44. The method of any one of claims 38 to 43 wherein the trajectory array guide system is the trajectory array guide system of any one of claims 1 to 37.

45. A kit for providing a trajectory array guide system, the kit comprising:

a. an array guide which is defined by a series of lumens or is defined by a bore configured to hold a guide unit defined by a series of lumens, and wherein the array guide comprises a ball at one end;

b. a base configured for attachment to the skull of the subject, wherein the base comprise a socket configured to receive and hold the ball of the array guide to form a ball-socket pivoting mechanism;

c. an imaging unit configured for engagement with the array guide and configured to hold and direct imaging fluid along passages which are co-axial with the lumens of the array guide or the lumens of the guide unit, for the purpose of defining a series of trajectories; and

d. an elongated handle configured for connection with a stereotaxic navigation system and configured for engagement with either the array guide or the imaging unit.

46. The kit of claim 45, further comprising instructions for assembly and operation of the array guide system.

47. The kit of claim 45 or 46 further comprising a container of imaging reagent.

48. The kit of any one of claims 45 to 47, wherein the array guide system is the system of any one of claims 1 to 37.
49. The kit of claim 48, wherein the trajectory array guide system is the system of any one of claims 26 to 37 and the kit further comprises a plurality of guide units configured for guiding elongated tools of different diameters.
50. The kit of claim 49 wherein the elongated tools comprise one or more catheters.
51. The kit of any one of claims 45 to 50, wherein all components are contained in one or more sterilized packages.

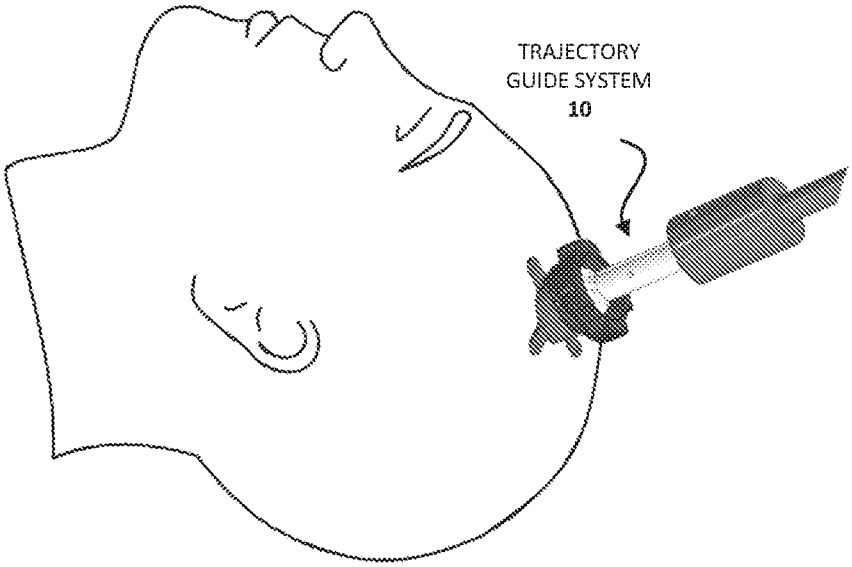

TRAJECTORY
GUIDE SYSTEM
10

Fig. 1A

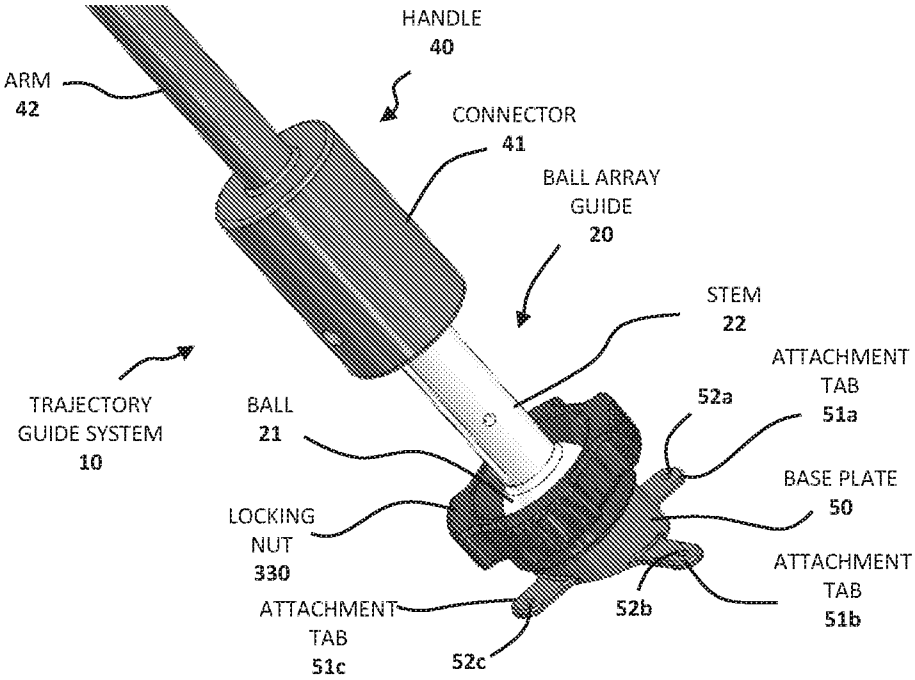

HANDLE
40
ARM
42
CONNECTOR
41
BALL ARRAY
GUIDE
20
STEM
22
ATTACHMENT
TAB
51a
52a
TRAJECTORY
GUIDE SYSTEM
10
BALL
21
BASE PLATE
50
LOCKING
NUT
330
ATTACHMENT
TAB
51b
52b
ATTACHMENT
TAB
51c
52c

Fig. 1B

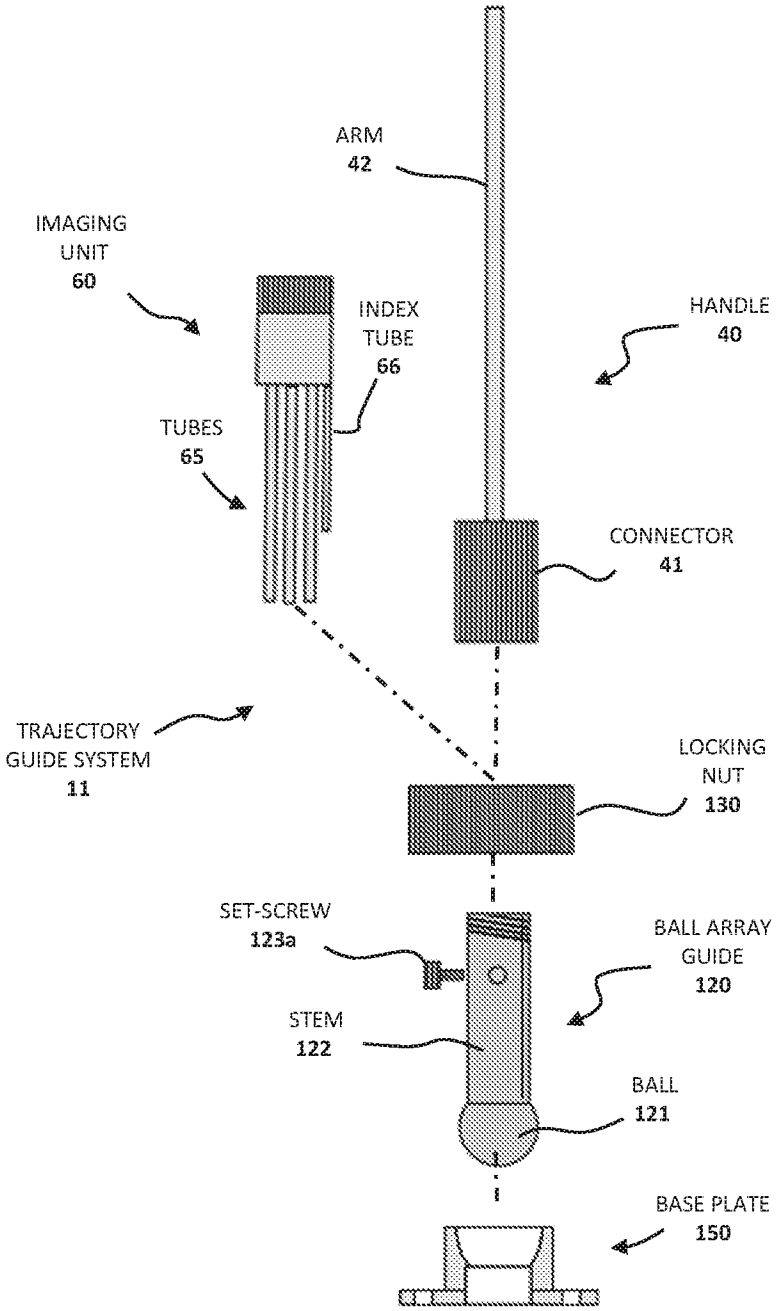

ARM
42
IMAGING
UNIT
60
INDEX
TUBE
66
HANDLE
40
TUBES
65
CONNECTOR
41
TRAJECTORY
GUIDE SYSTEM
11
LOCKING
NUT
130
SET-SCREW
123a
BALL ARRAY
GUIDE
120
STEM
122
BALL
121
BASE PLATE
150

Fig. 2

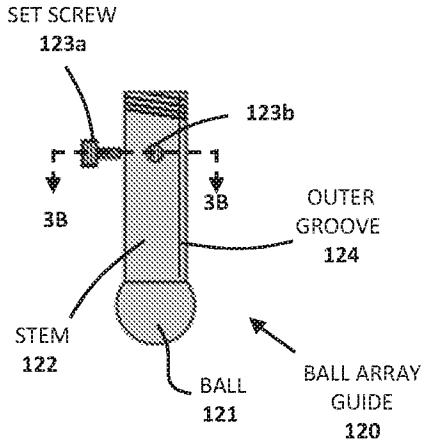


Fig. 3A

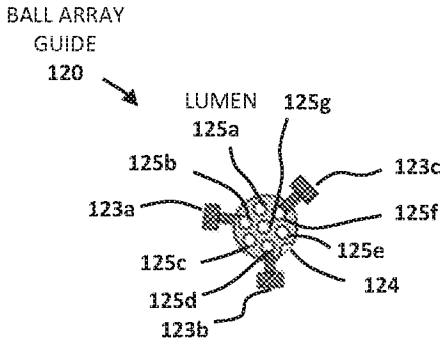


Fig. 3B

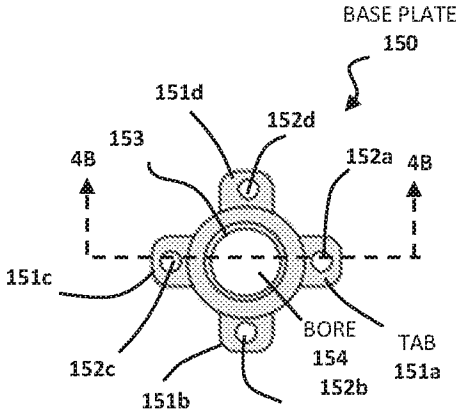


Fig. 4A

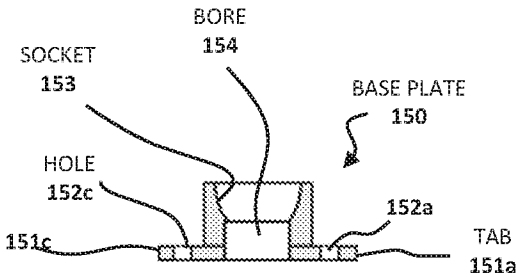


Fig. 4B

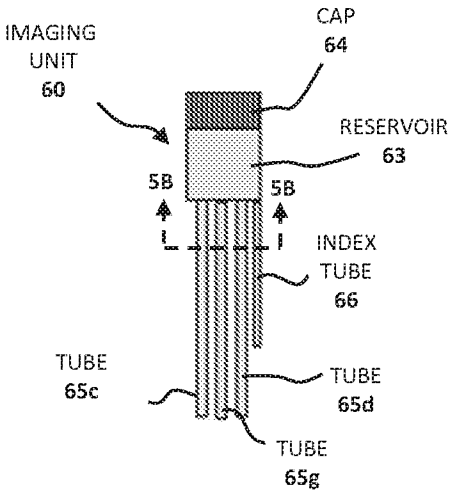


Fig. 5A

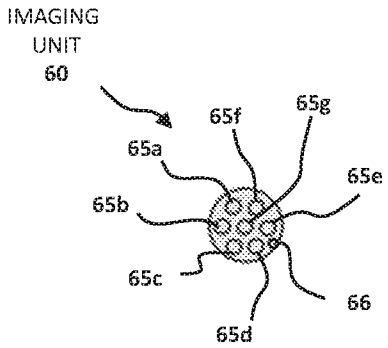


Fig. 5B

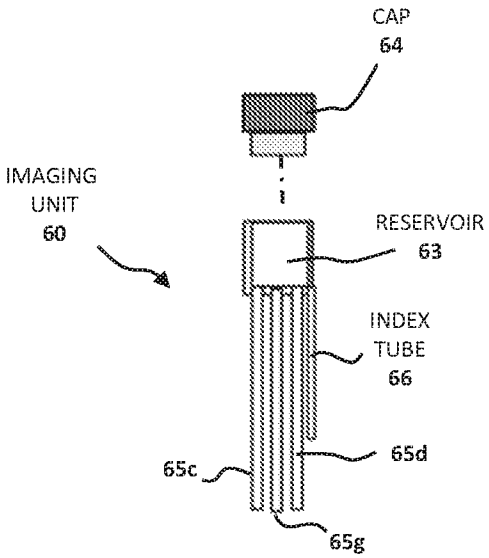


Fig. 5C

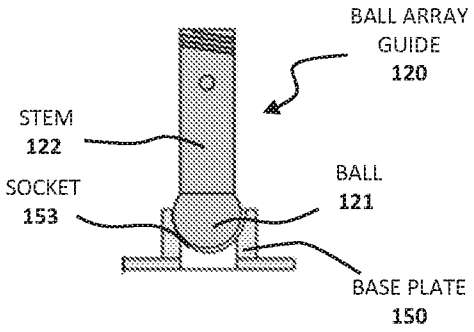


Fig. 6A

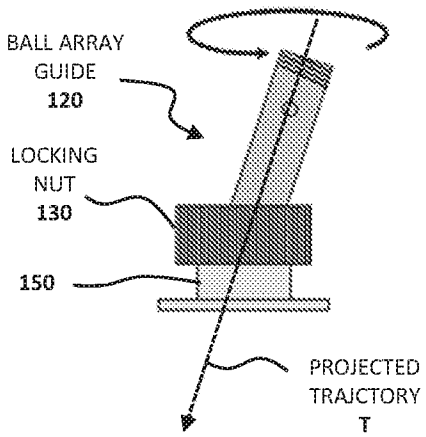


Fig. 6B

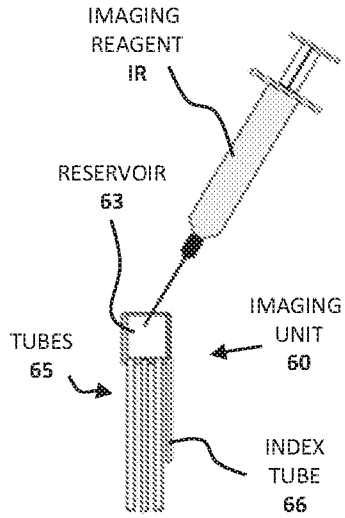


Fig. 7A

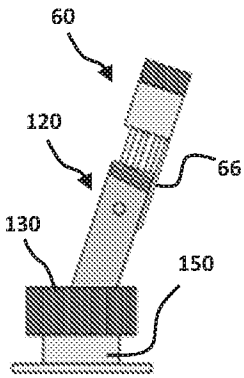


Fig. 7B

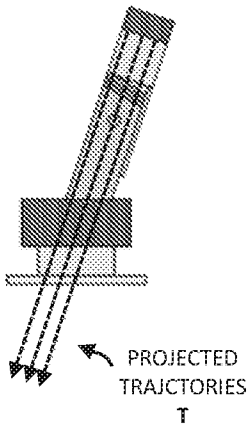


Fig. 7C

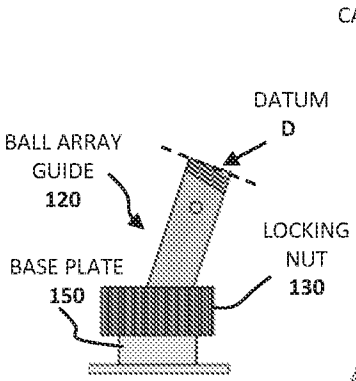


Fig. 8A

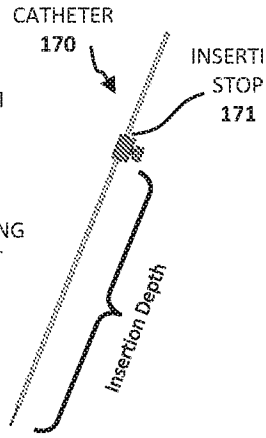


Fig. 8B

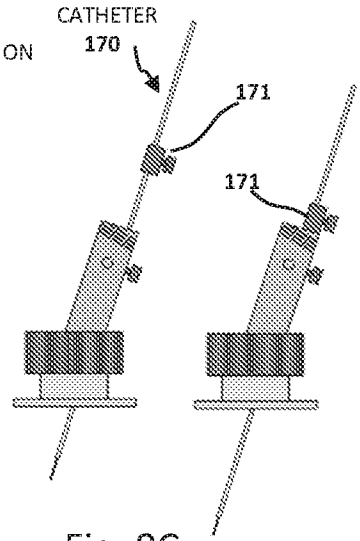


Fig. 8C

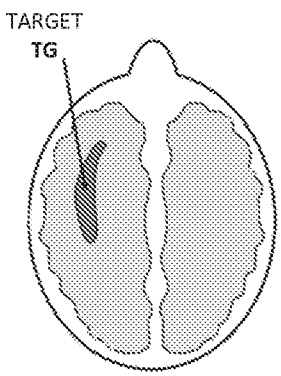


Fig. 9A

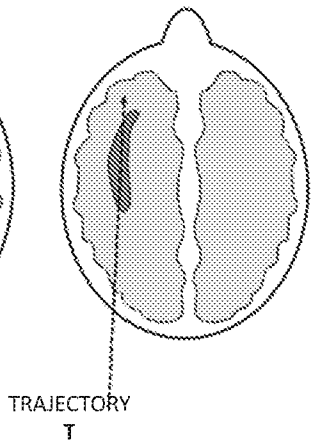


Fig. 9B

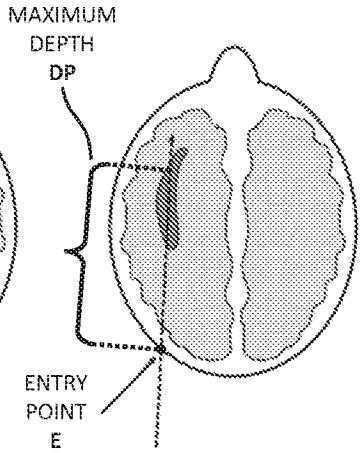


Fig. 9C

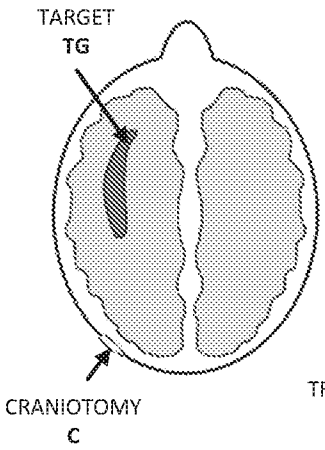


Fig. 10A

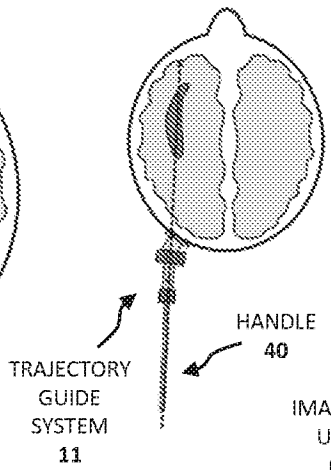


Fig. 10B

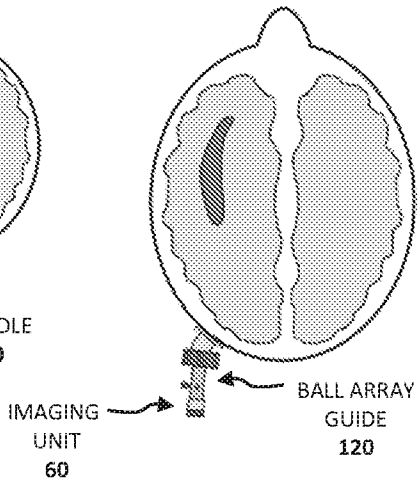


Fig. 10C

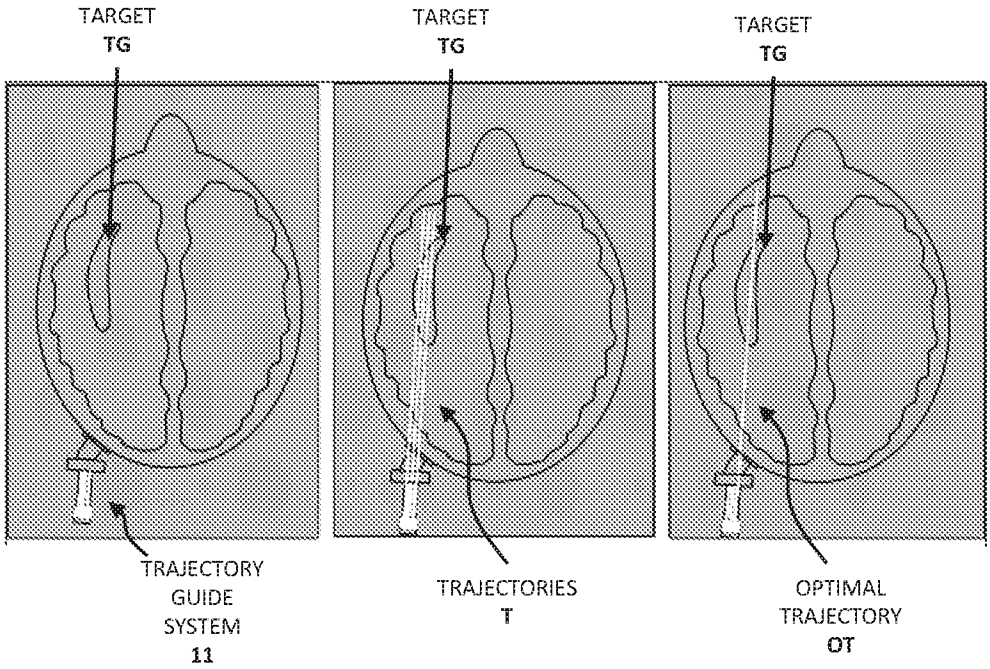


Fig. 11A

Fig. 11B

Fig. 11C

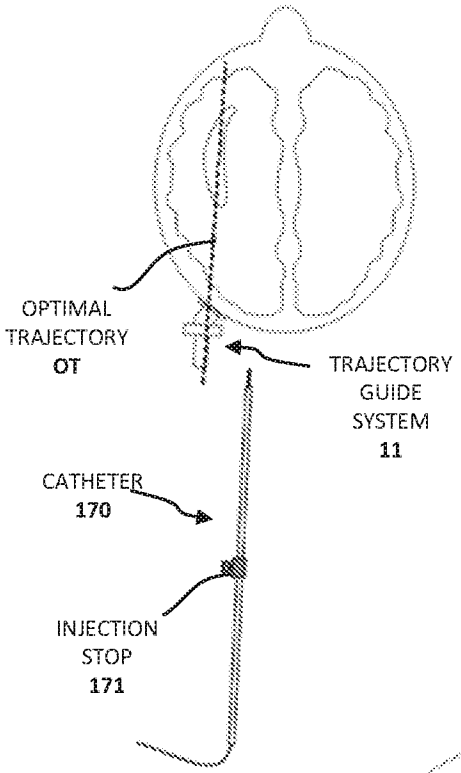


Fig. 12A

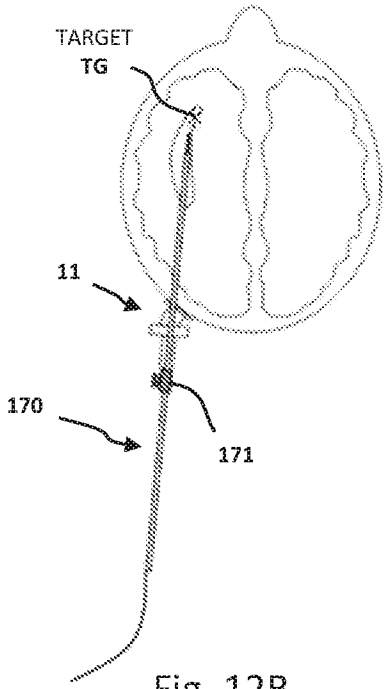


Fig. 12B

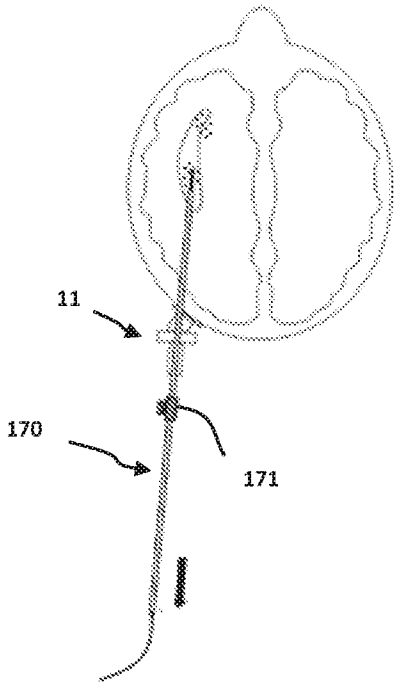


Fig. 12C

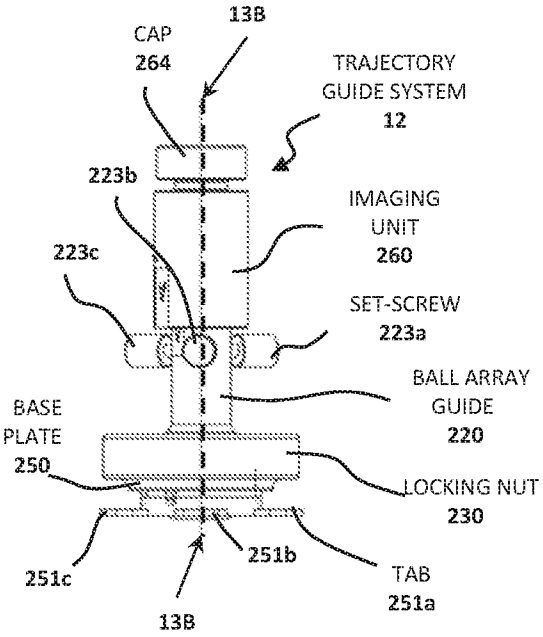


Fig. 13A

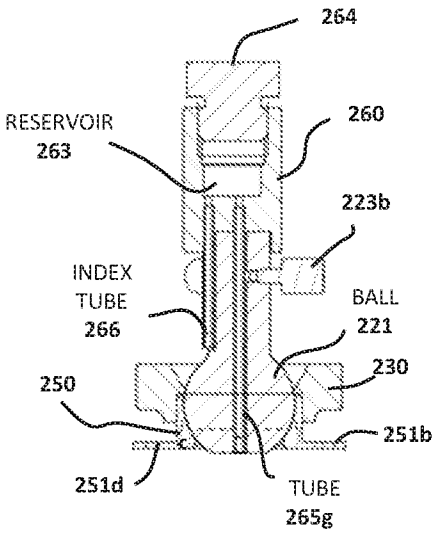


Fig. 13B

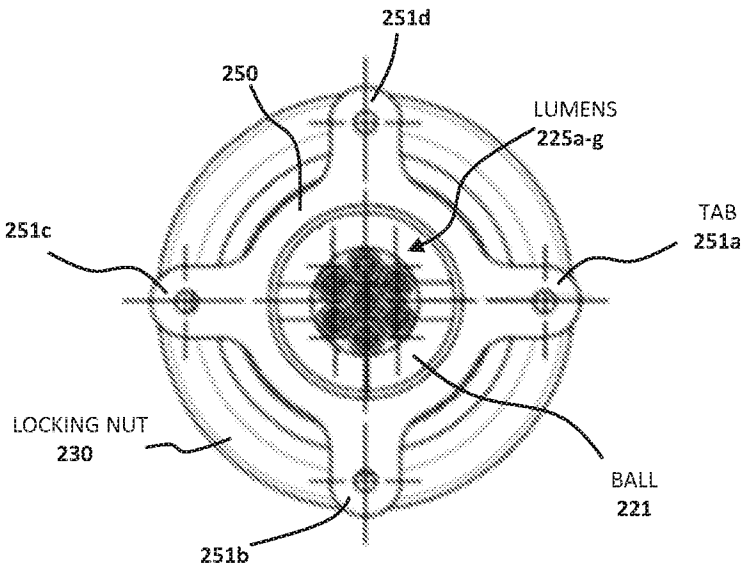


Fig. 13C

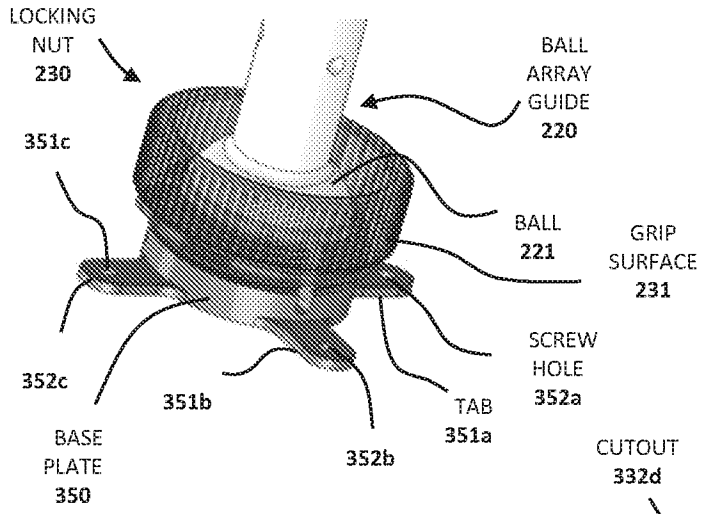


Fig. 14A

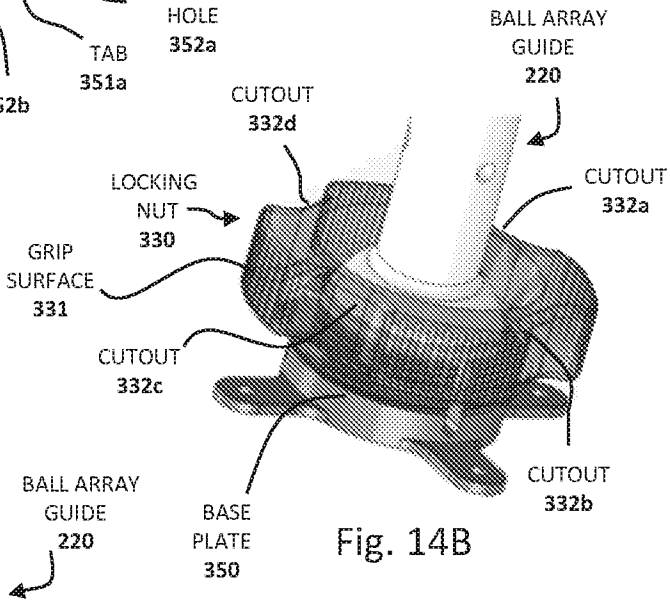


Fig. 14B

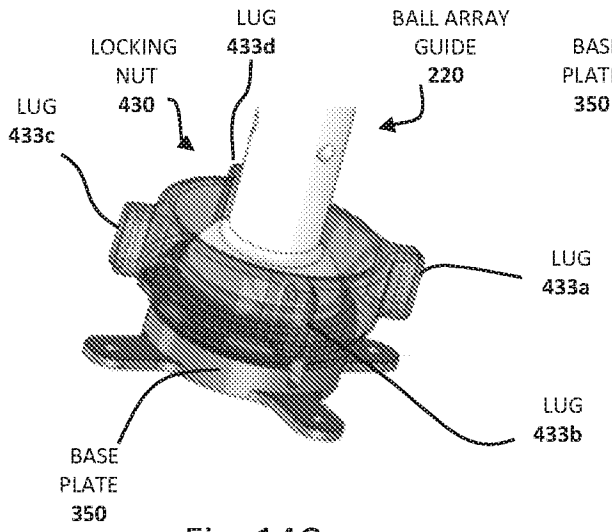


Fig. 14C

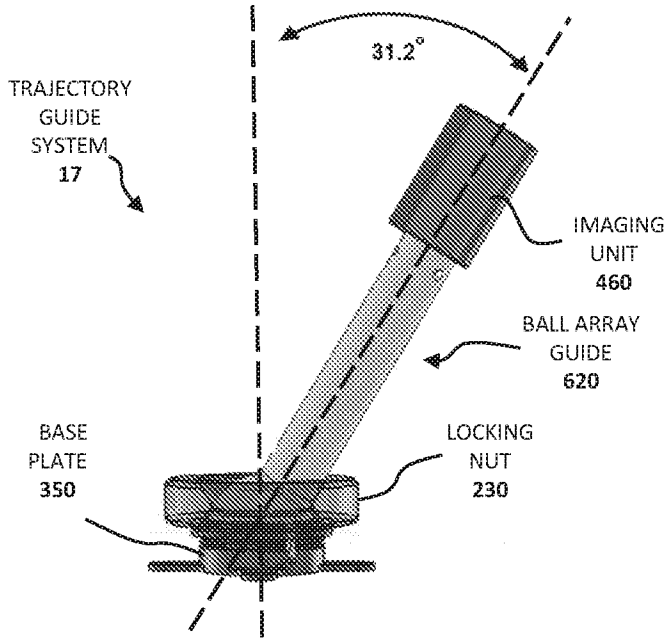


Fig. 15A

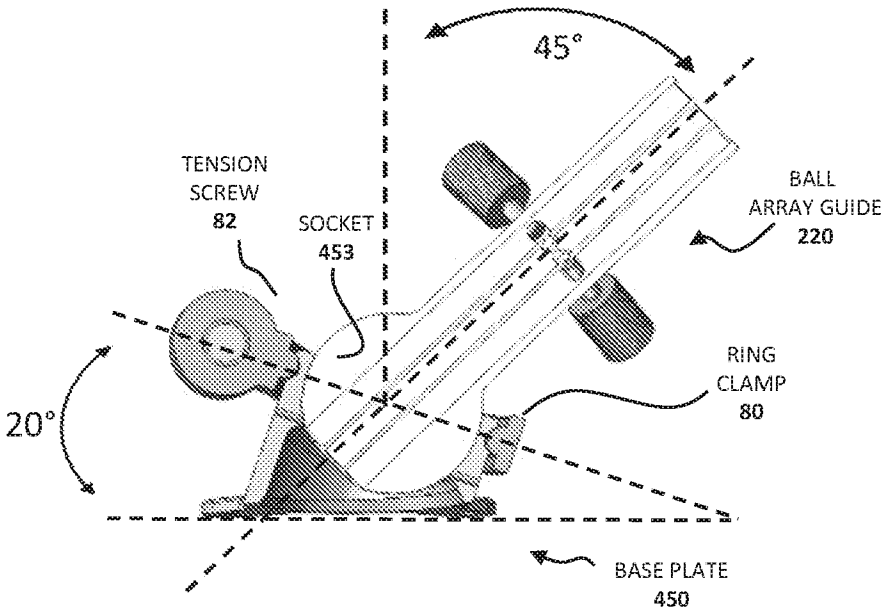


Fig. 15B

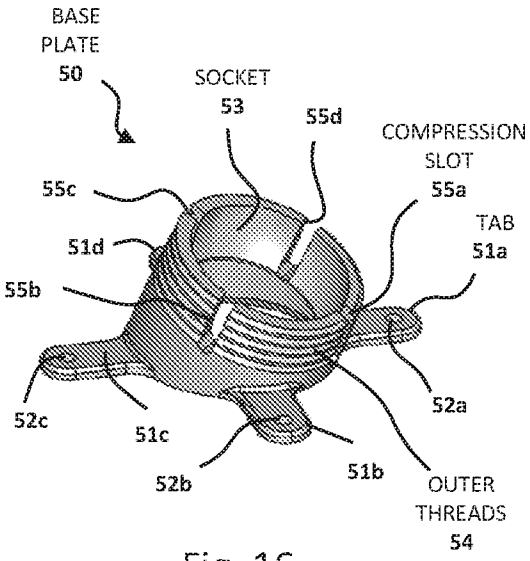


Fig. 16

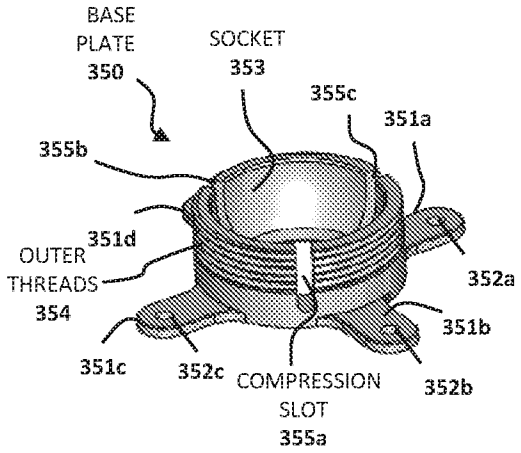


Fig. 17

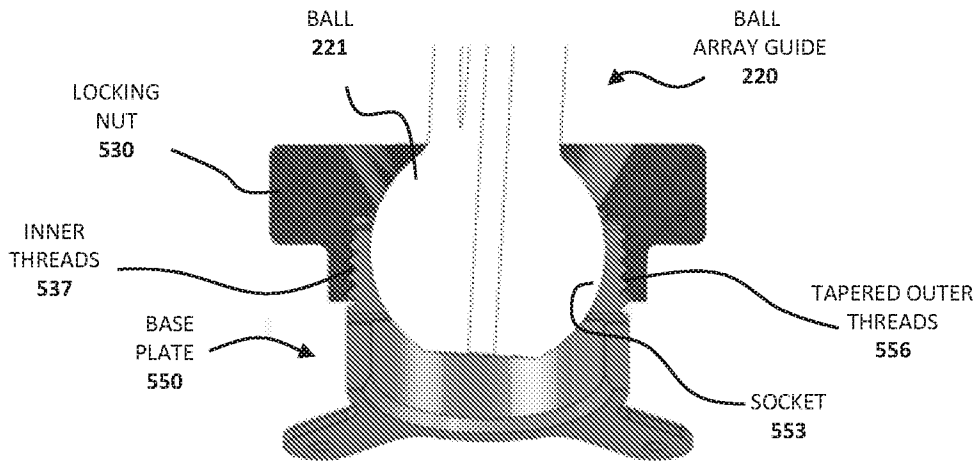


Fig. 18

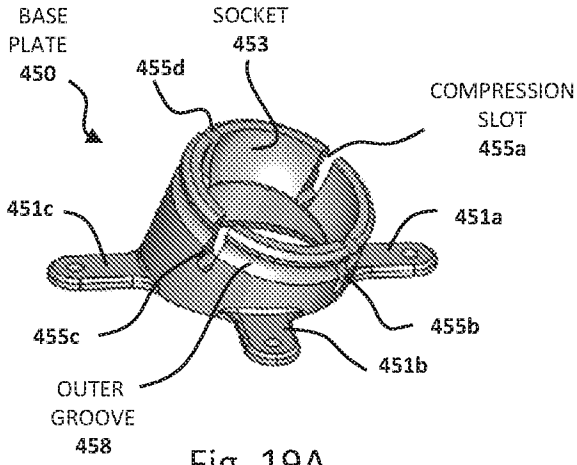


Fig. 19A

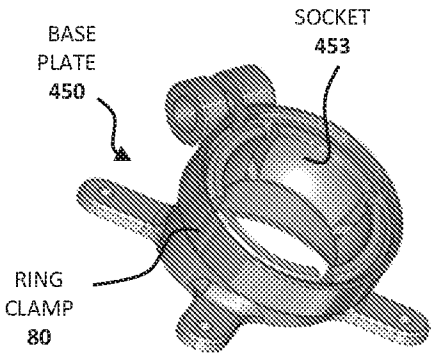


Fig. 19B

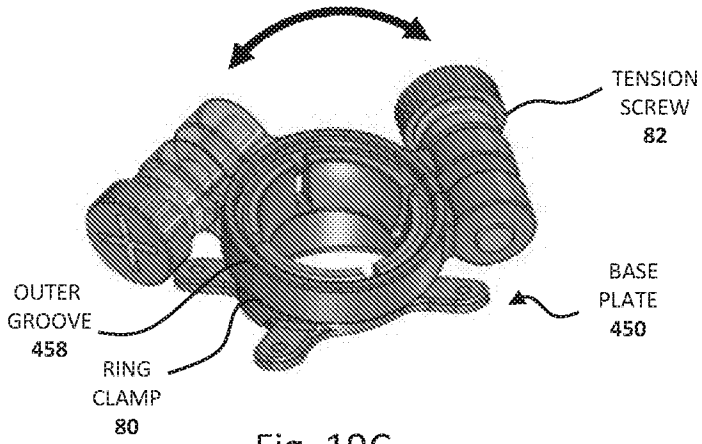


Fig. 19C

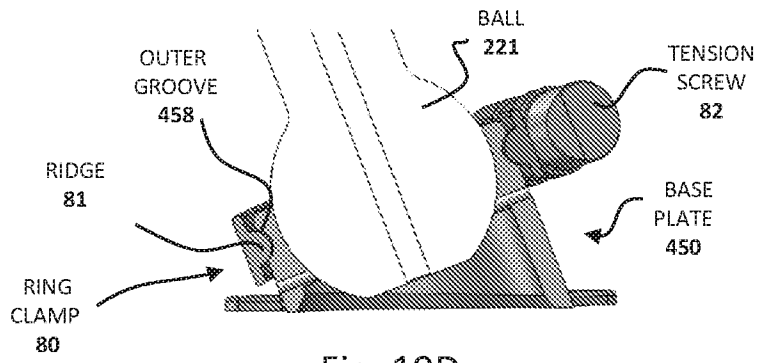


Fig. 19D

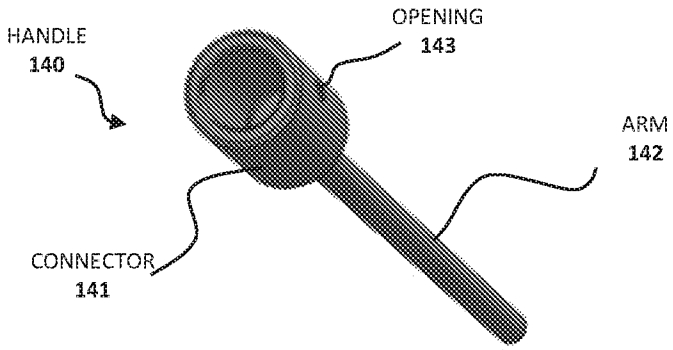


Fig. 20A

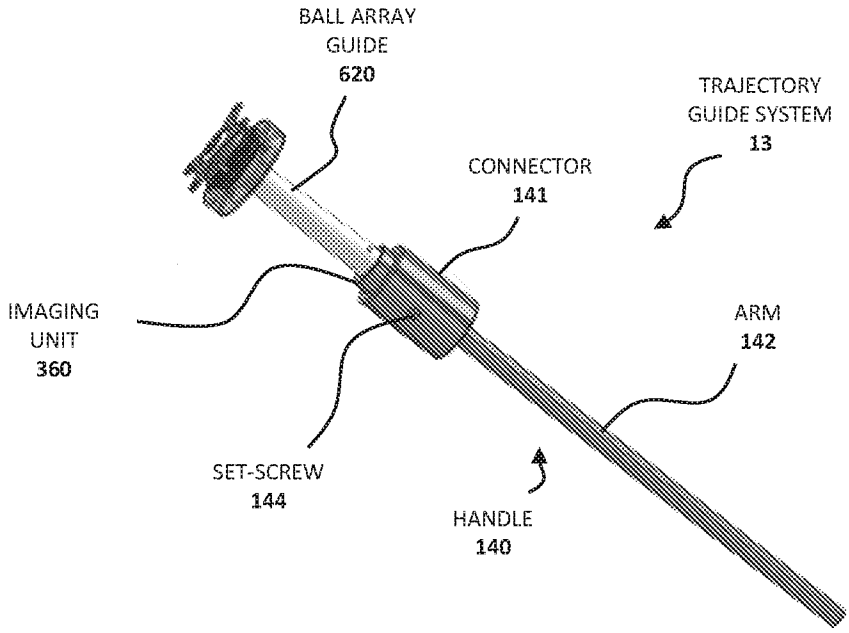


Fig. 20B

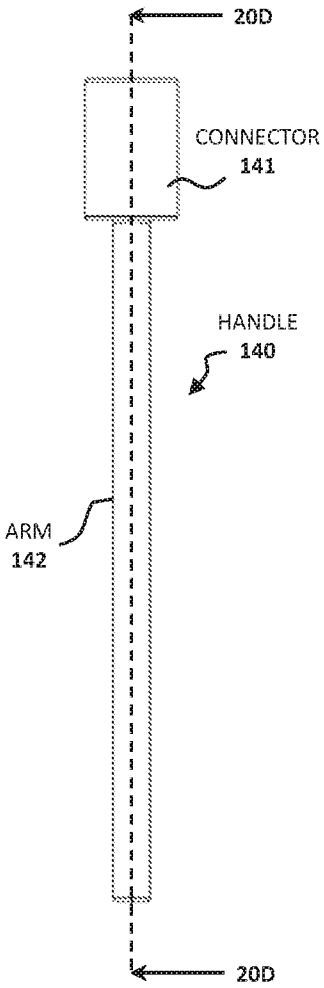


Fig. 20C

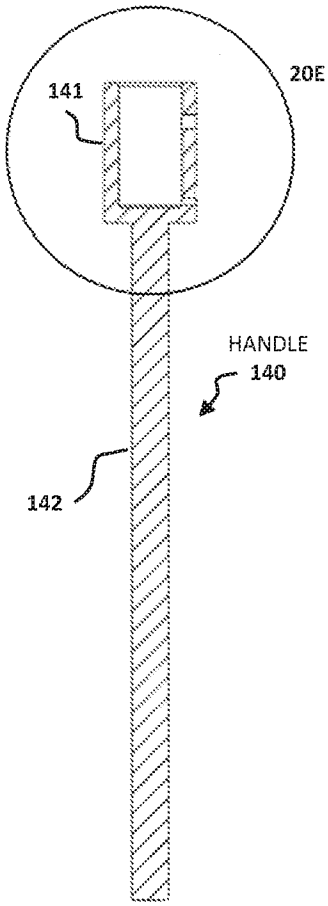


Fig. 20D

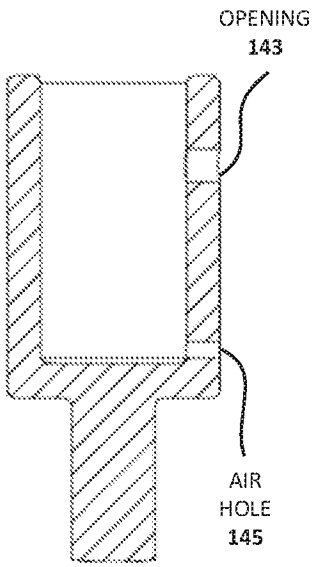


Fig. 20E

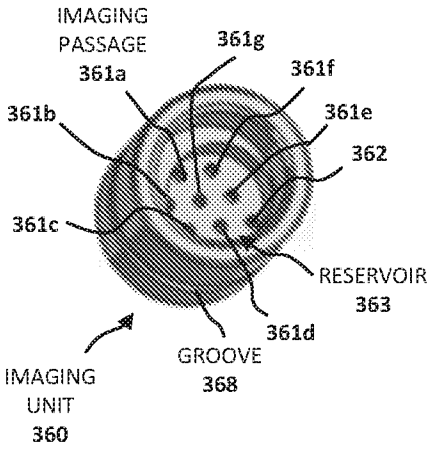


Fig. 21A

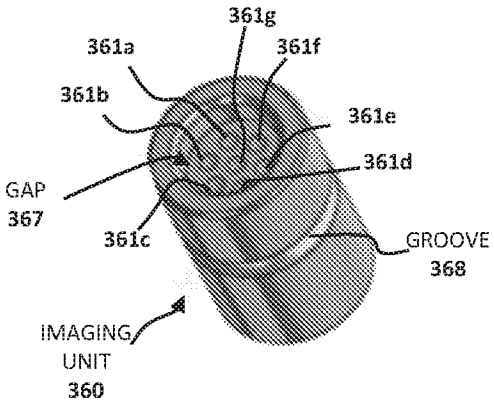


Fig. 21B

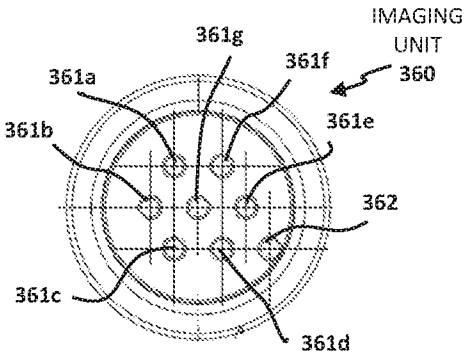


Fig. 21C

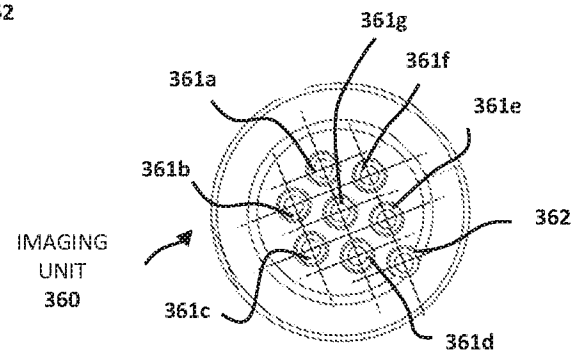


Fig. 21D

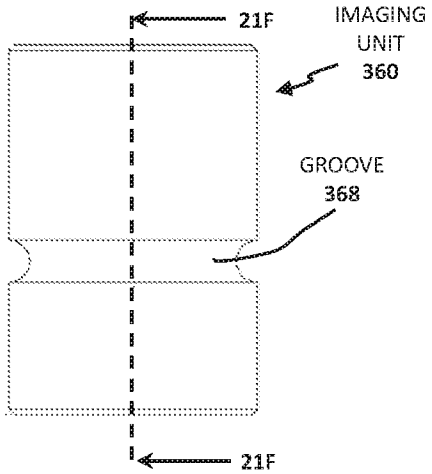


Fig. 21E

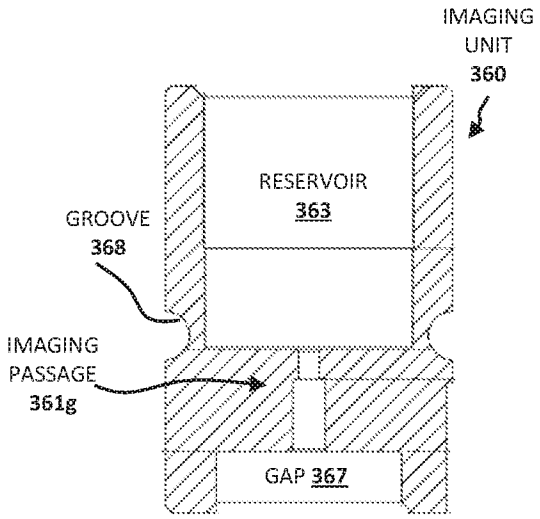


Fig. 21F

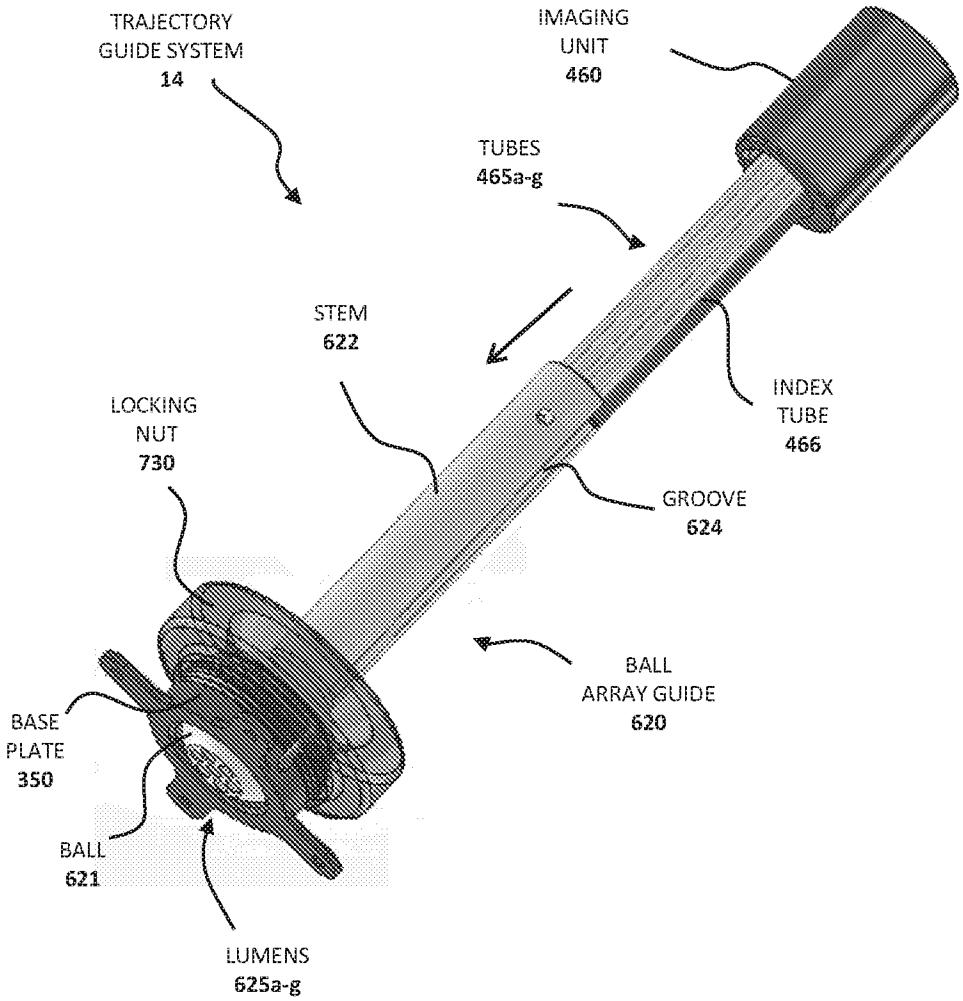

TRAJECTORY GUIDE SYSTEM 14
IMAGING UNIT 460
TUBES 465a-g
STEM 622
INDEX TUBE 466
LOCKING NUT 730
GROOVE 624
BALL ARRAY GUIDE 620
BASE PLATE 350
BALL 621
LUMENS 625a-g

Fig. 22

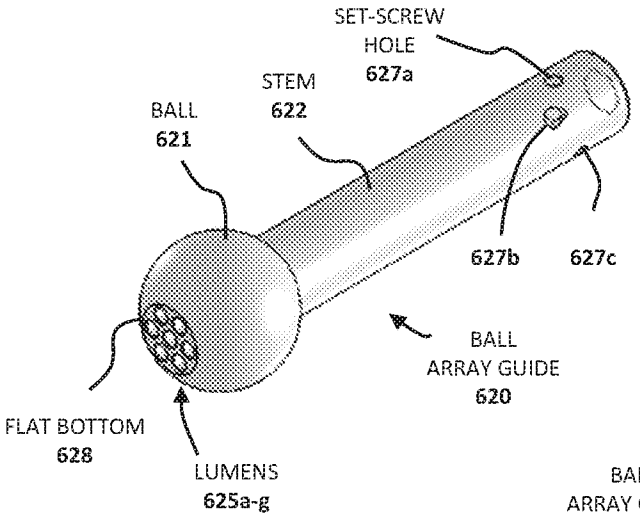


Fig. 23A

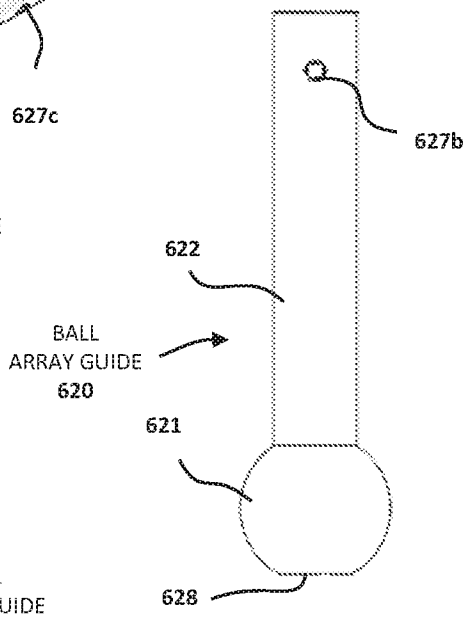


Fig. 23B

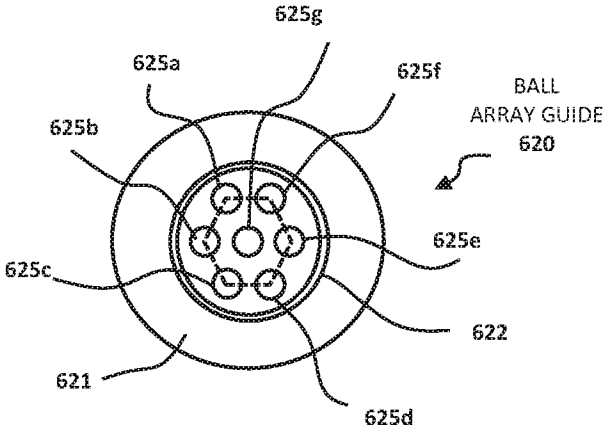


Fig. 23C

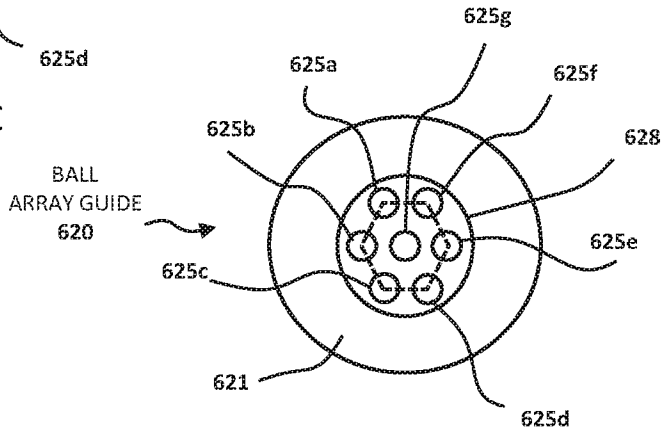


Fig. 23D

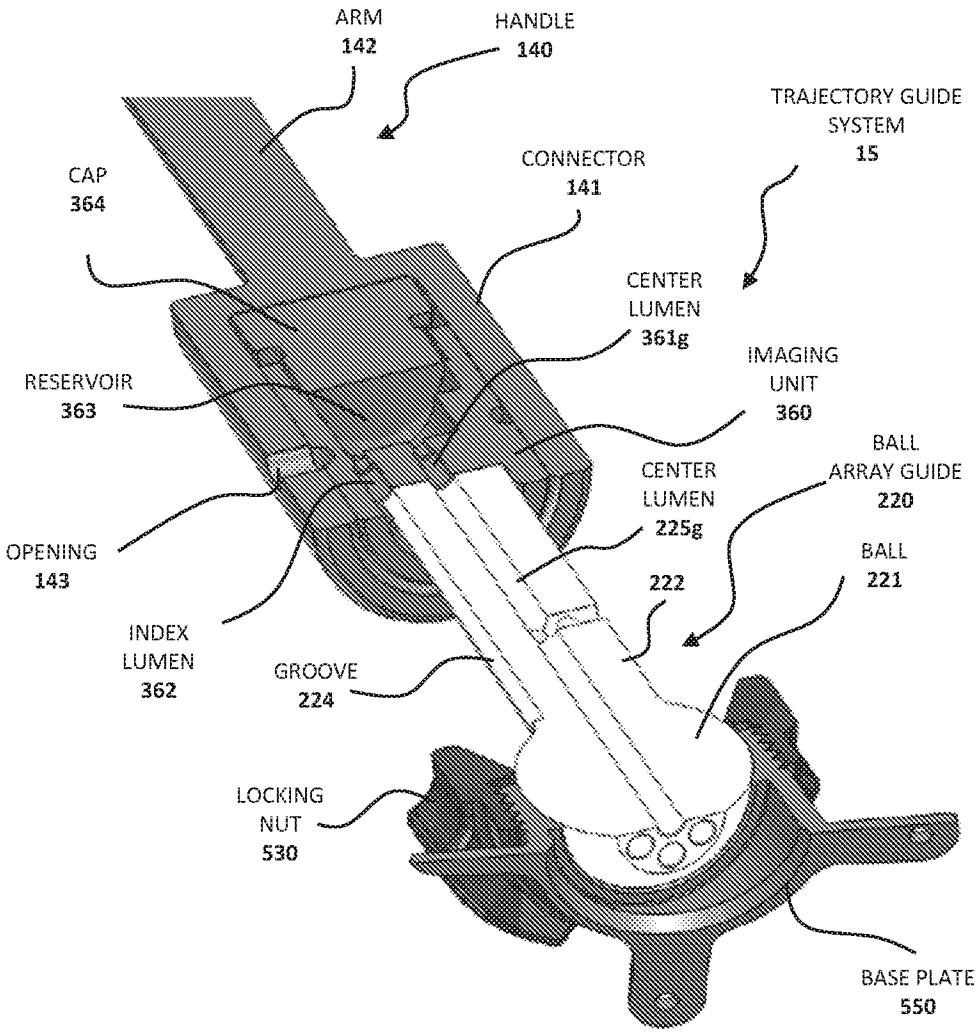
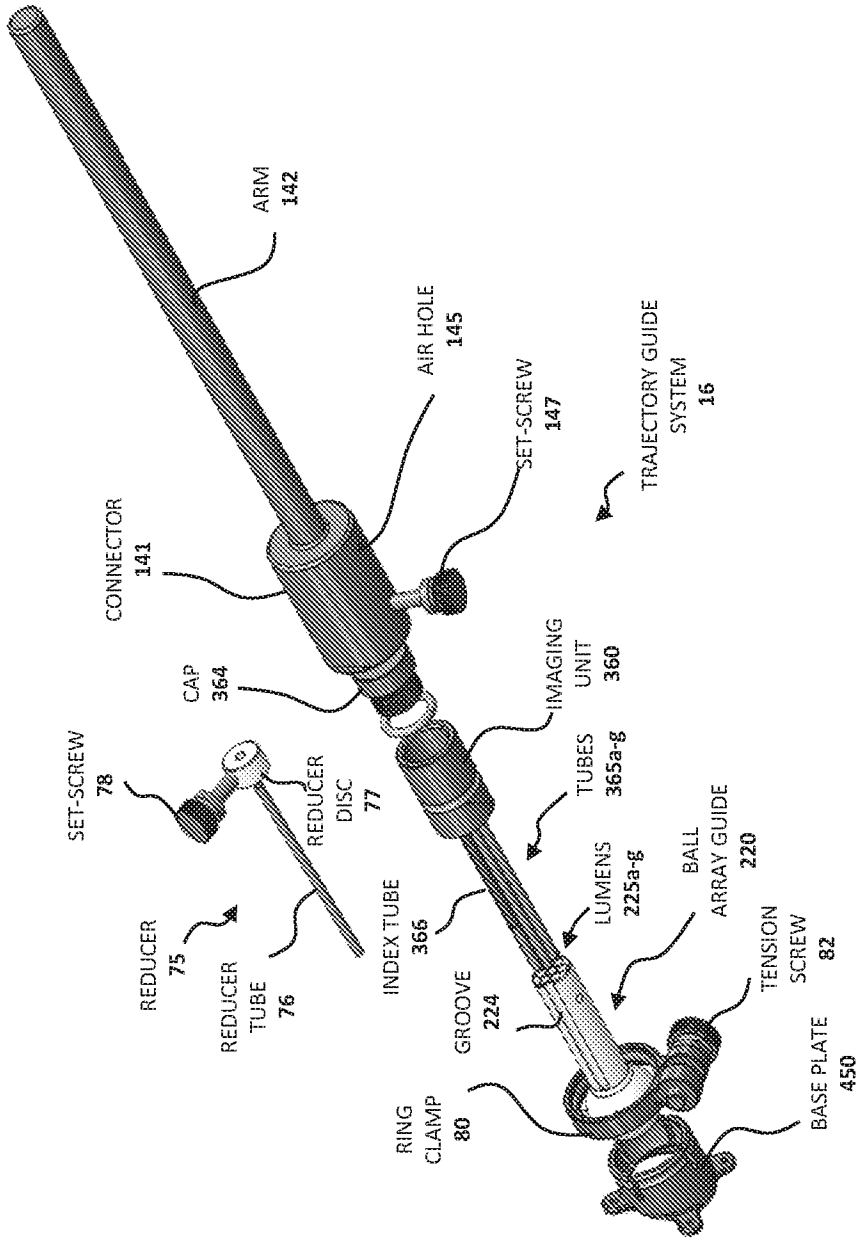

ARM
142
HANDLE
140
TRAJECTORY GUIDE
SYSTEM
15
CONNECTOR
141
CAP
364
CENTER
LUMEN
361g
IMAGING
UNIT
360
RESERVOIR
363
BALL
ARRAY GUIDE
220
CENTER
LUMEN
225g
OPENING
143
BALL
221
222
INDEX
LUMEN
362
GROOVE
224
LOCKING
NUT
530
BASE PLATE
550

Fig. 24

Fig. 25


ARM
142
AIR HOLE
145
SET-SCREW
147
TRAJECTORY GUIDE
SYSTEM
16
CONNECTOR
141
CAP
364
IMAGING
UNIT
360
SET-SCREW
78
REDUCER
DISC
77
TUBES
365a-g
REDUCER
75
REDUCER
TUBE
76
INDEX TUBE
366
LUMENS
225a-g
BALL
ARRAY GUIDE
220
GROOVE
224
TENSION
SCREW
82
RING
CLAMP
80
BASE PLATE
450

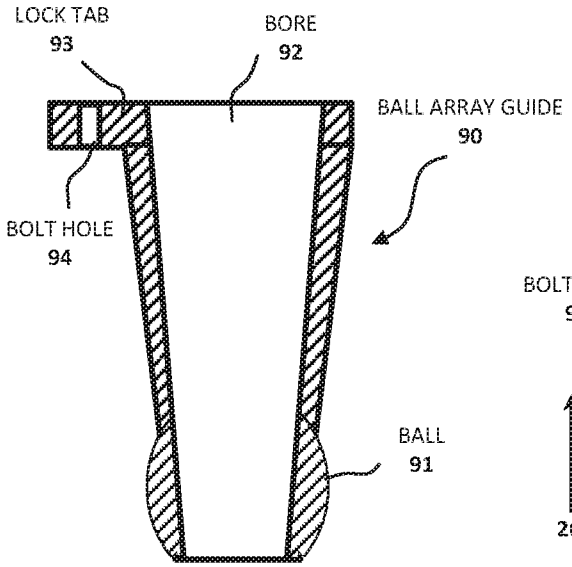


Fig. 26A

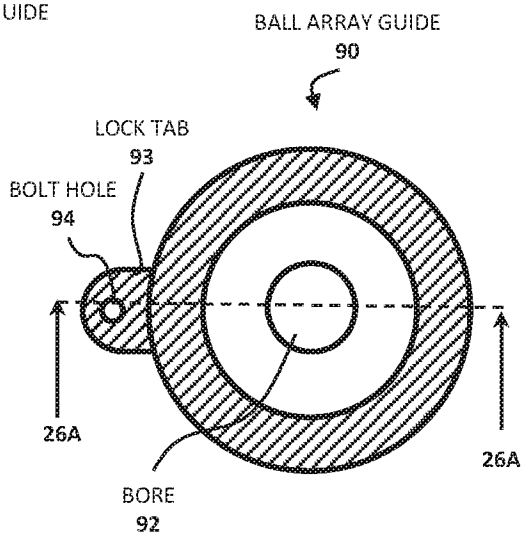


Fig. 26B

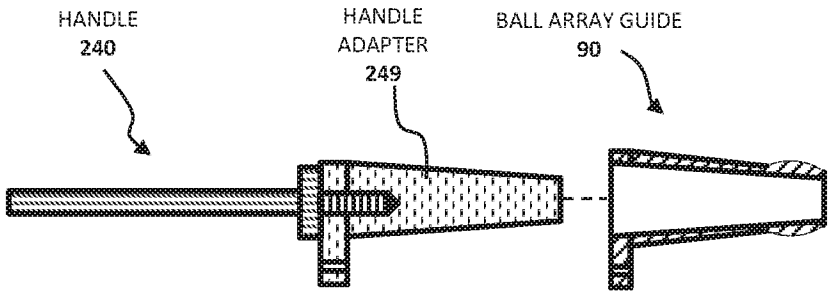


Fig. 26C

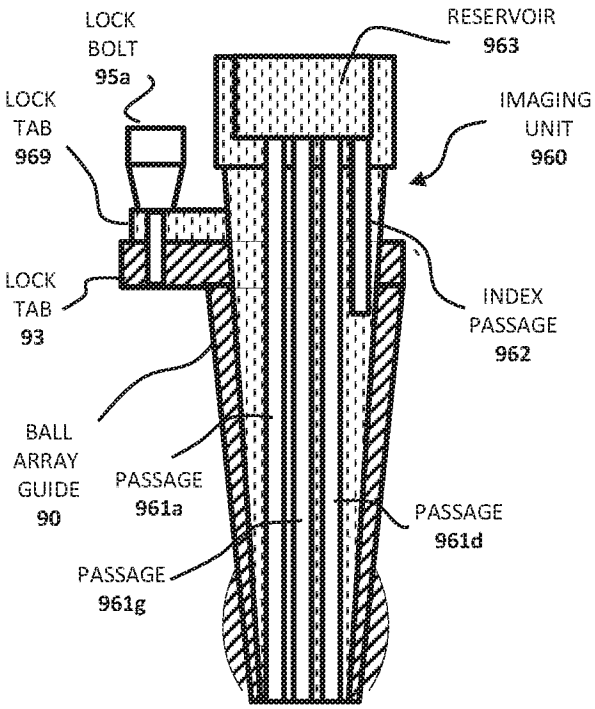


Fig. 26D

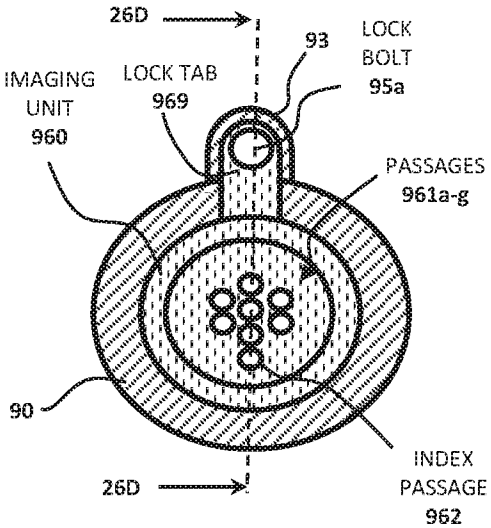


Fig. 26E

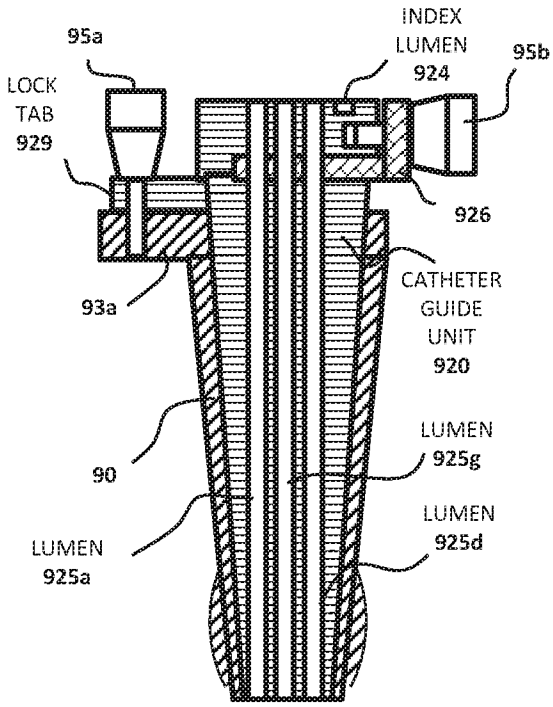


Fig. 26F

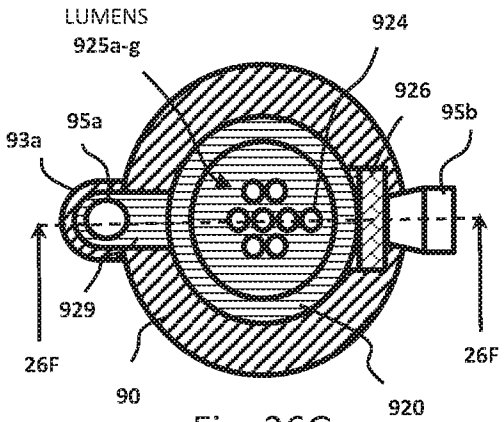


Fig. 26G

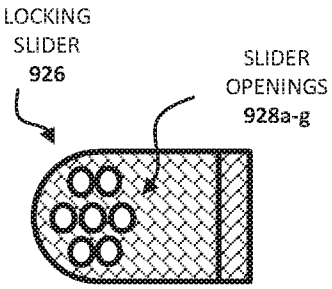


Fig. 26H

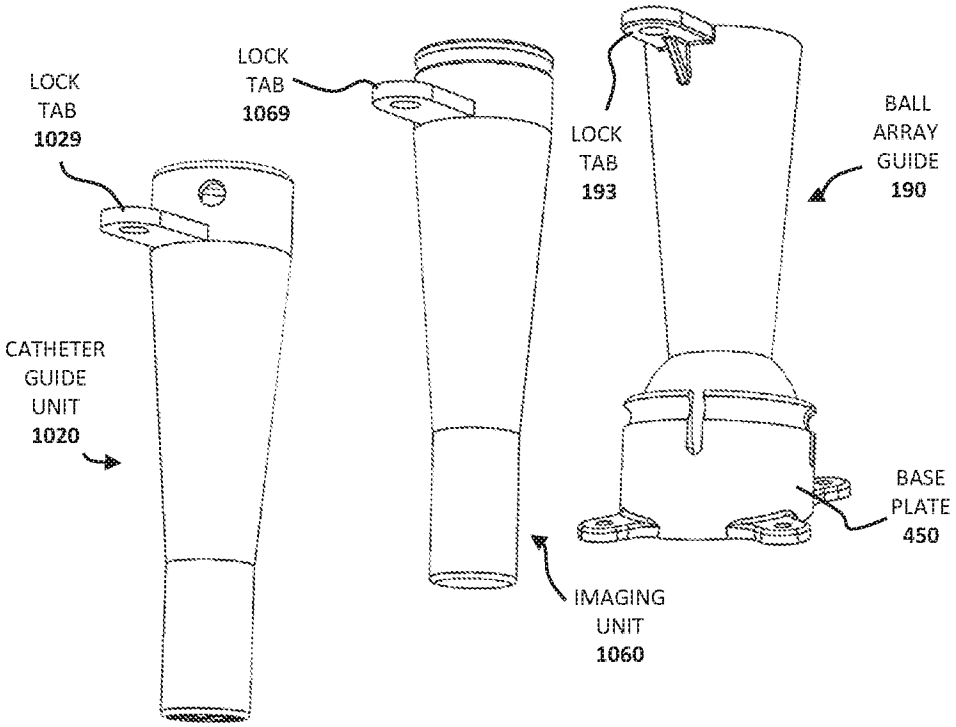

LOCK
TAB
1029
LOCK
TAB
1069
LOCK
TAB
193
BALL
ARRAY
GUIDE
190
CATHETER
GUIDE
UNIT
1020
BASE
PLATE
450
IMAGING
UNIT
1060

Fig. 27A

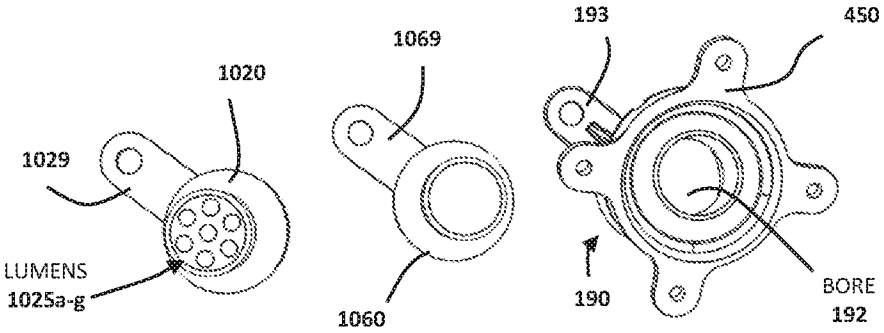


Fig. 27B

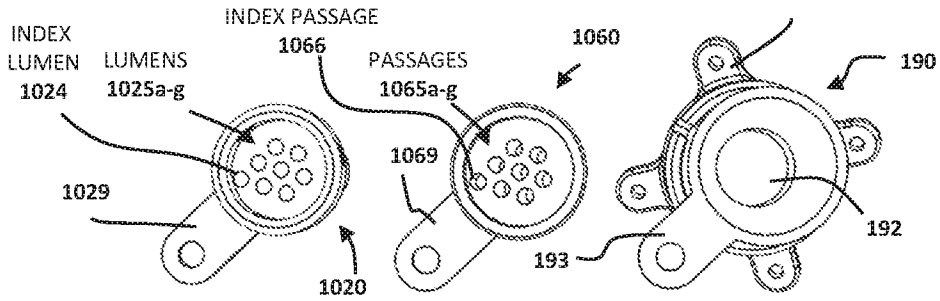


Fig. 27C

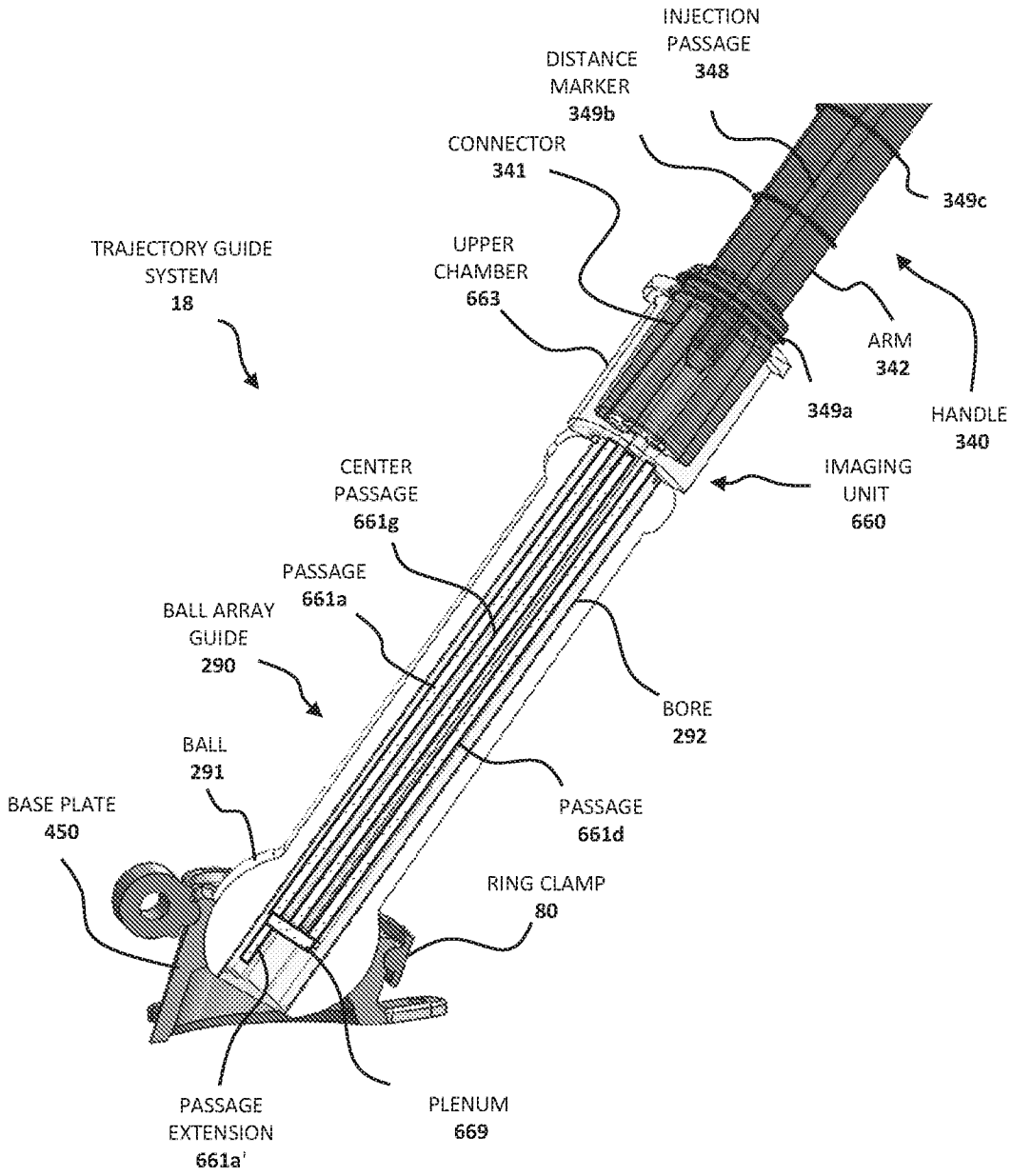

INJECTION PASSAGE 348
DISTANCE MARKER 349b
CONNECTOR 341
349c
TRAJECTORY GUIDE SYSTEM 18
UPPER CHAMBER 663
ARM 342
349a
HANDLE 340
CENTER PASSAGE 661g
IMAGING UNIT 660
PASSAGE 661a
BALL ARRAY GUIDE 290
BORE 292
BALL 291
BASE PLATE 450
PASSAGE 661d
RING CLAMP 80
PASSAGE EXTENSION 661a'
PLENUM 669

Fig. 28

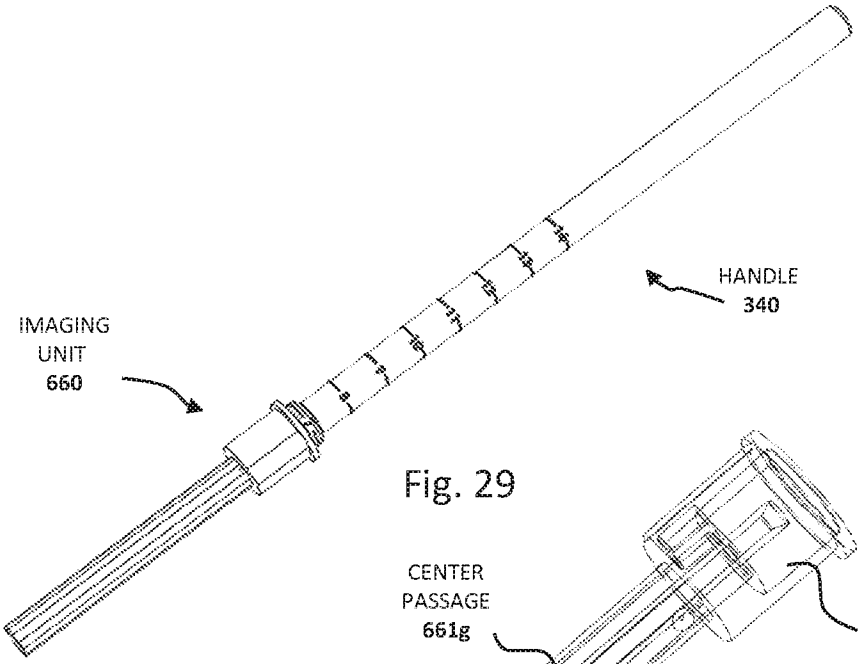


Fig. 29

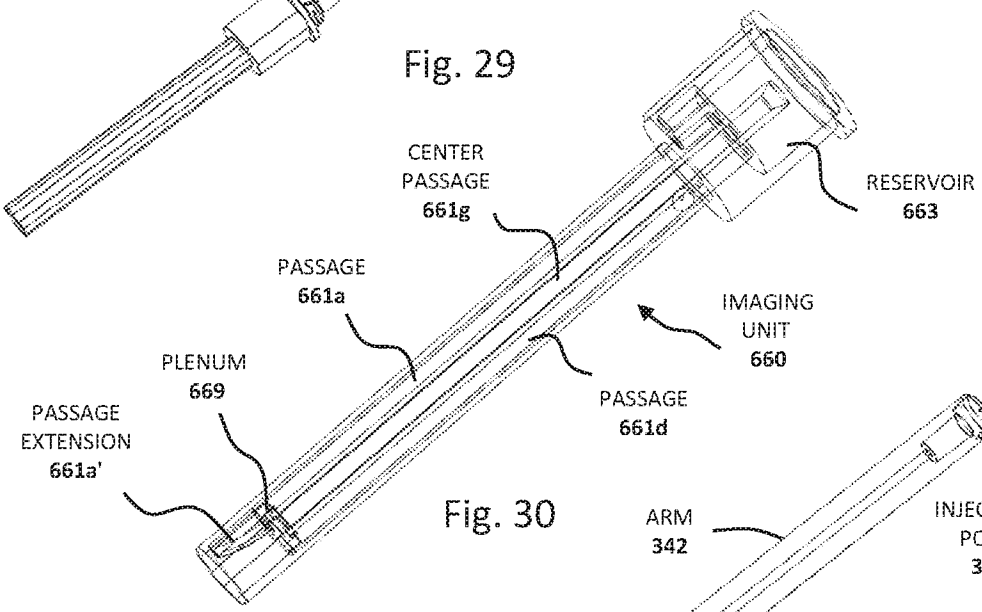


Fig. 30

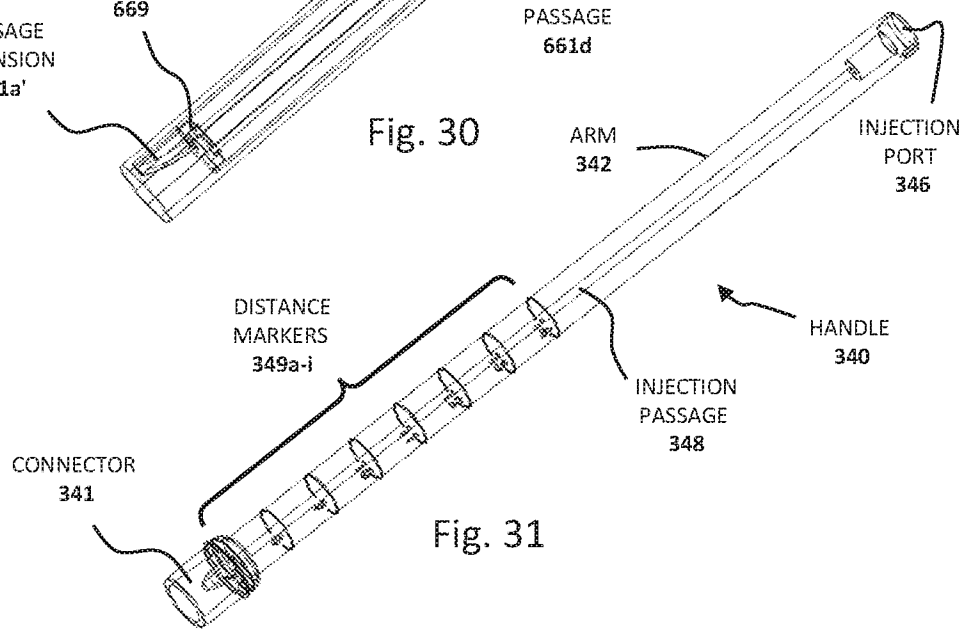


Fig. 31

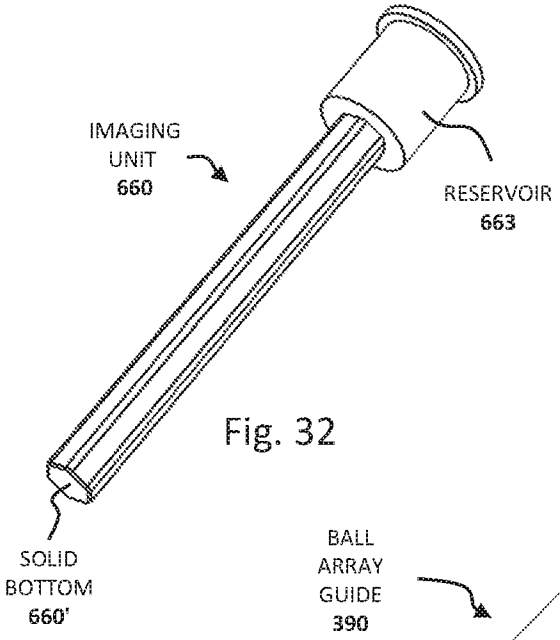


Fig. 32

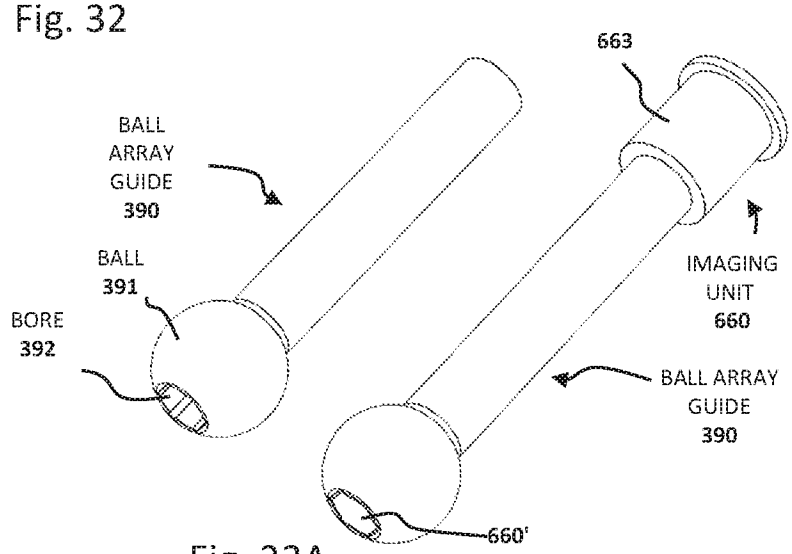


Fig. 33A

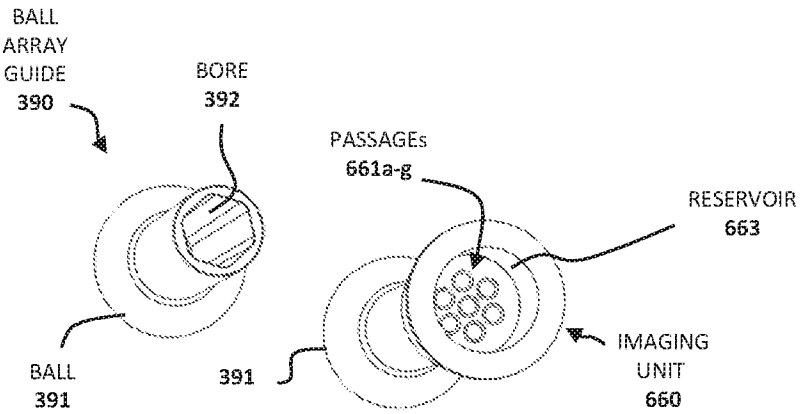


Fig. 33B

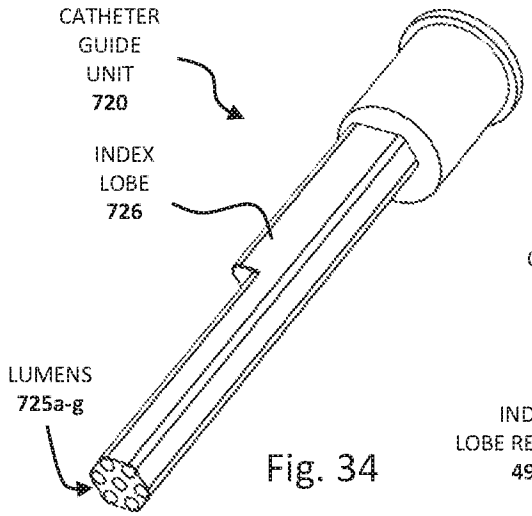


Fig. 34

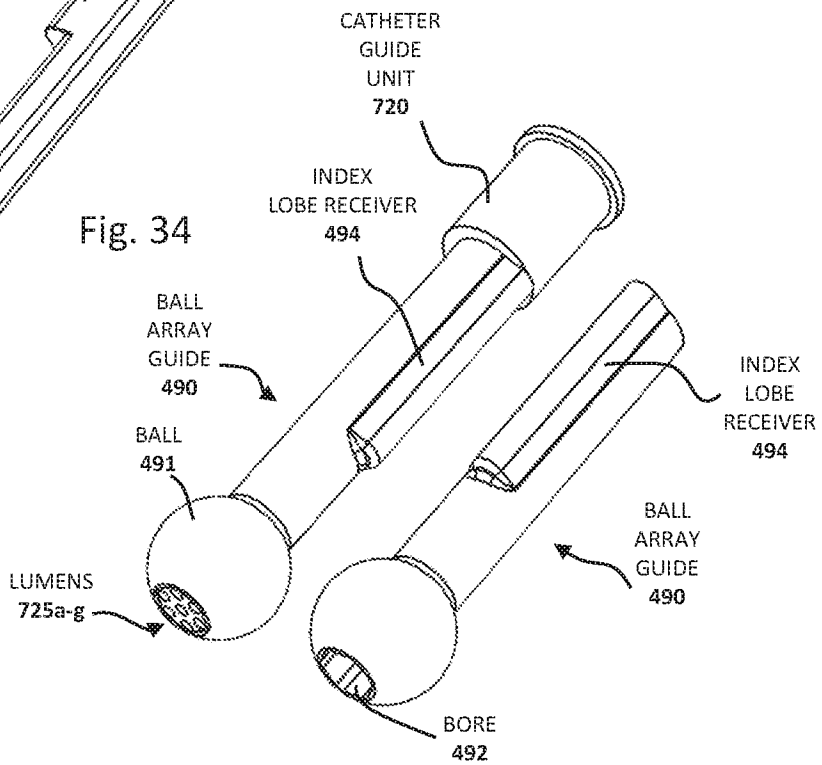


Fig. 35A

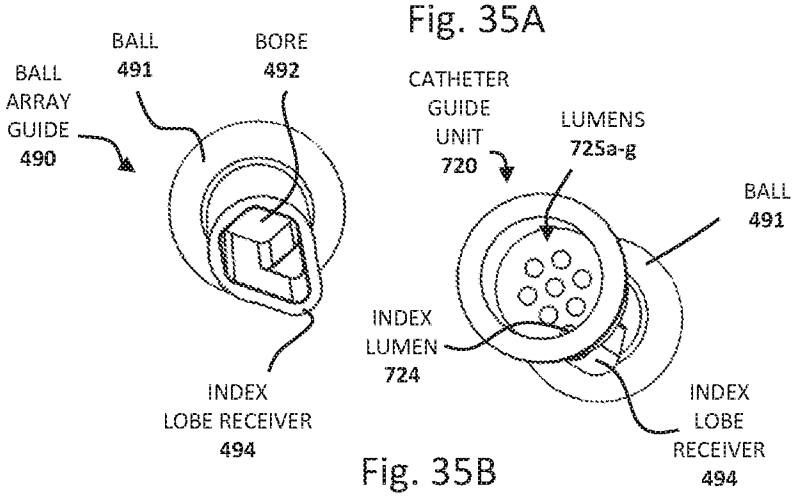


Fig. 35B

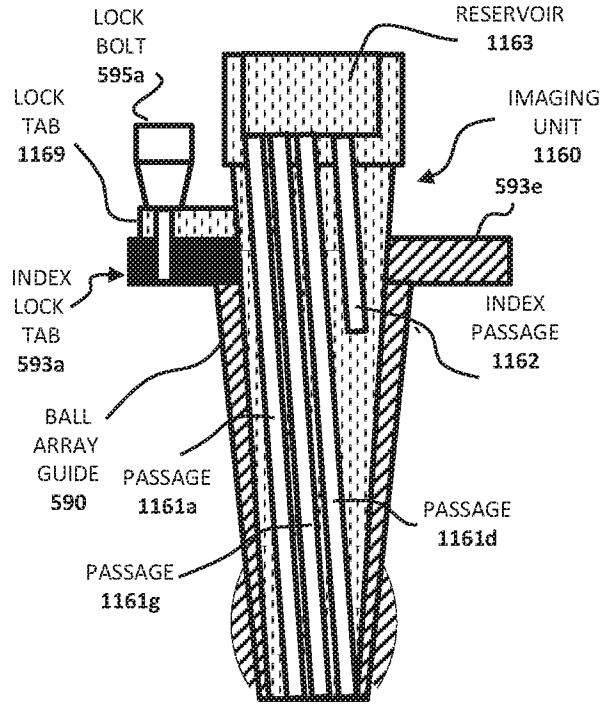


Fig. 36A

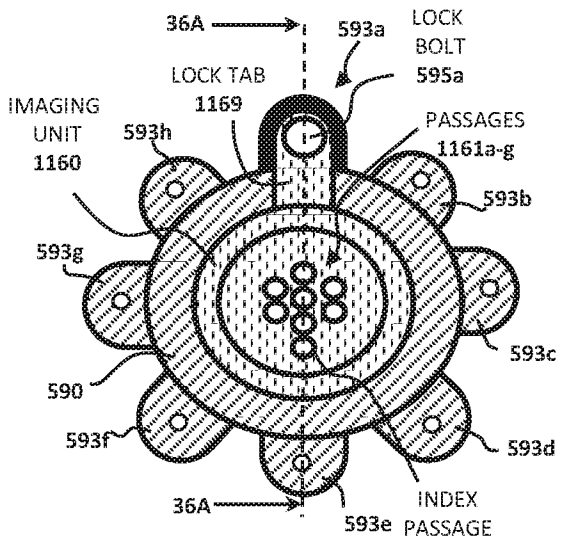


Fig. 36B

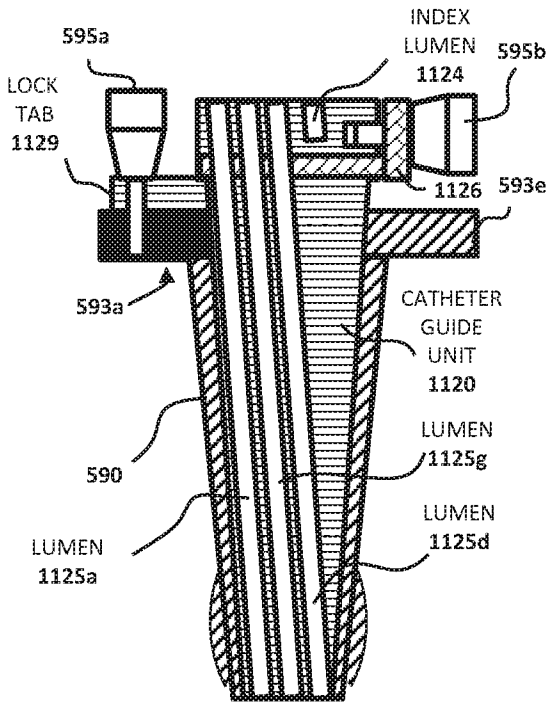


Fig. 36C

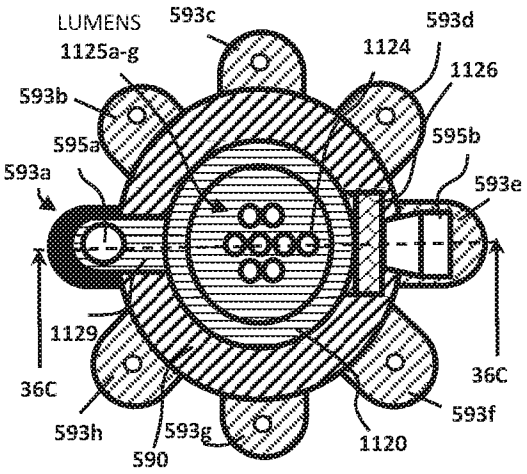


Fig. 36D

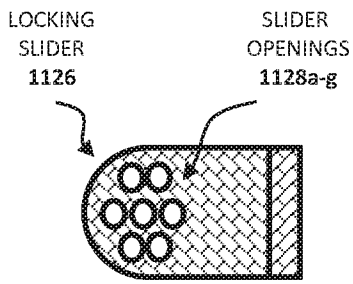


Fig. 36E

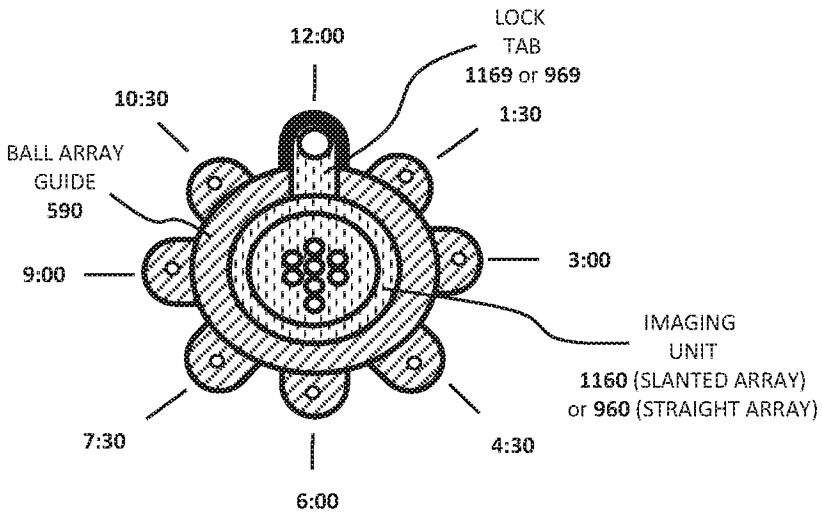


Fig. 37A

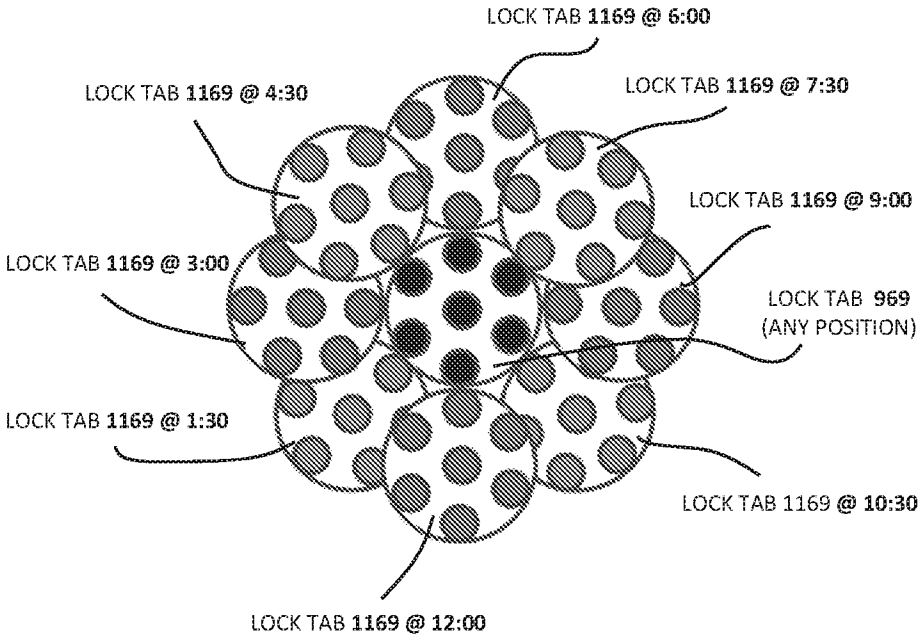


Fig. 37B

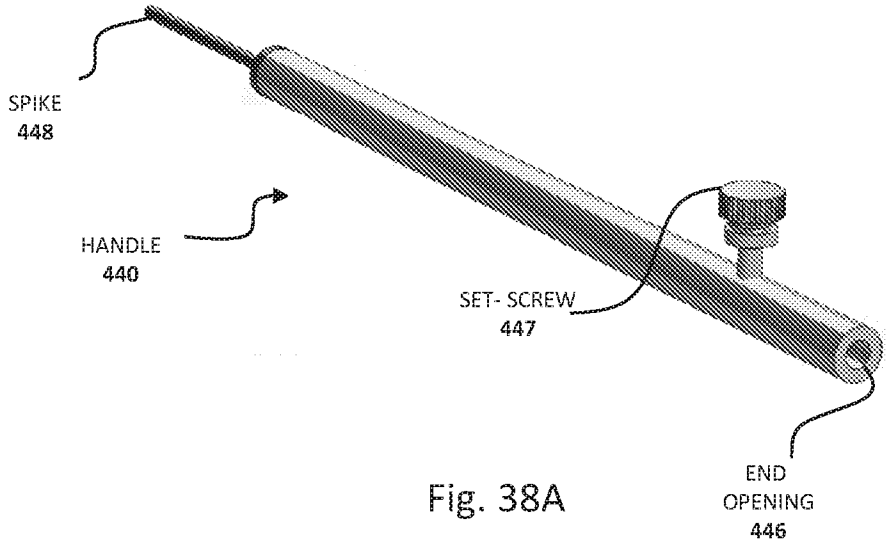


Fig. 38A

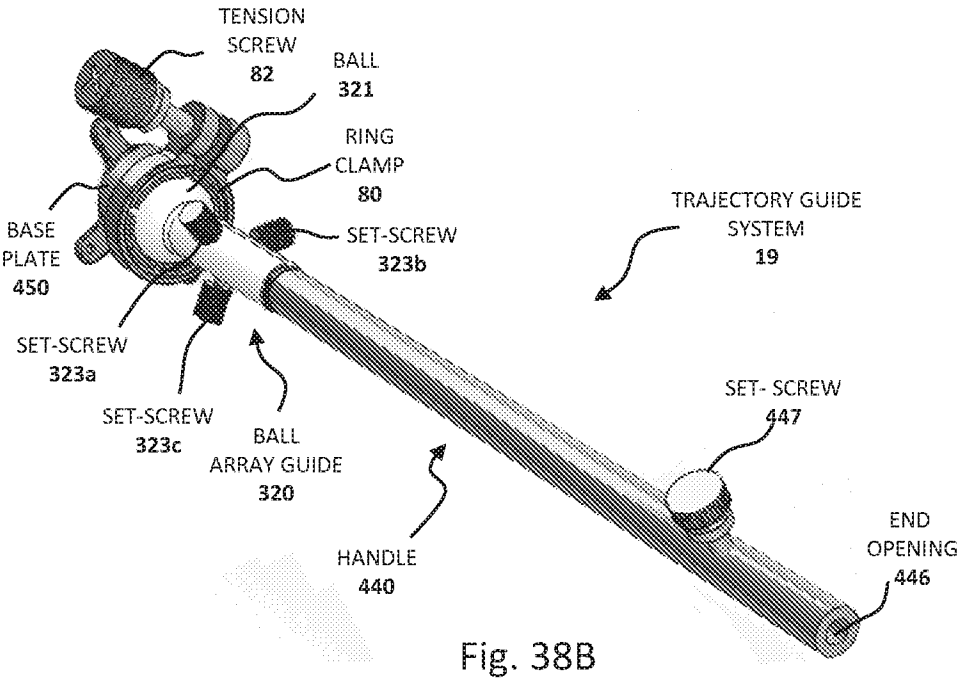


Fig. 38B

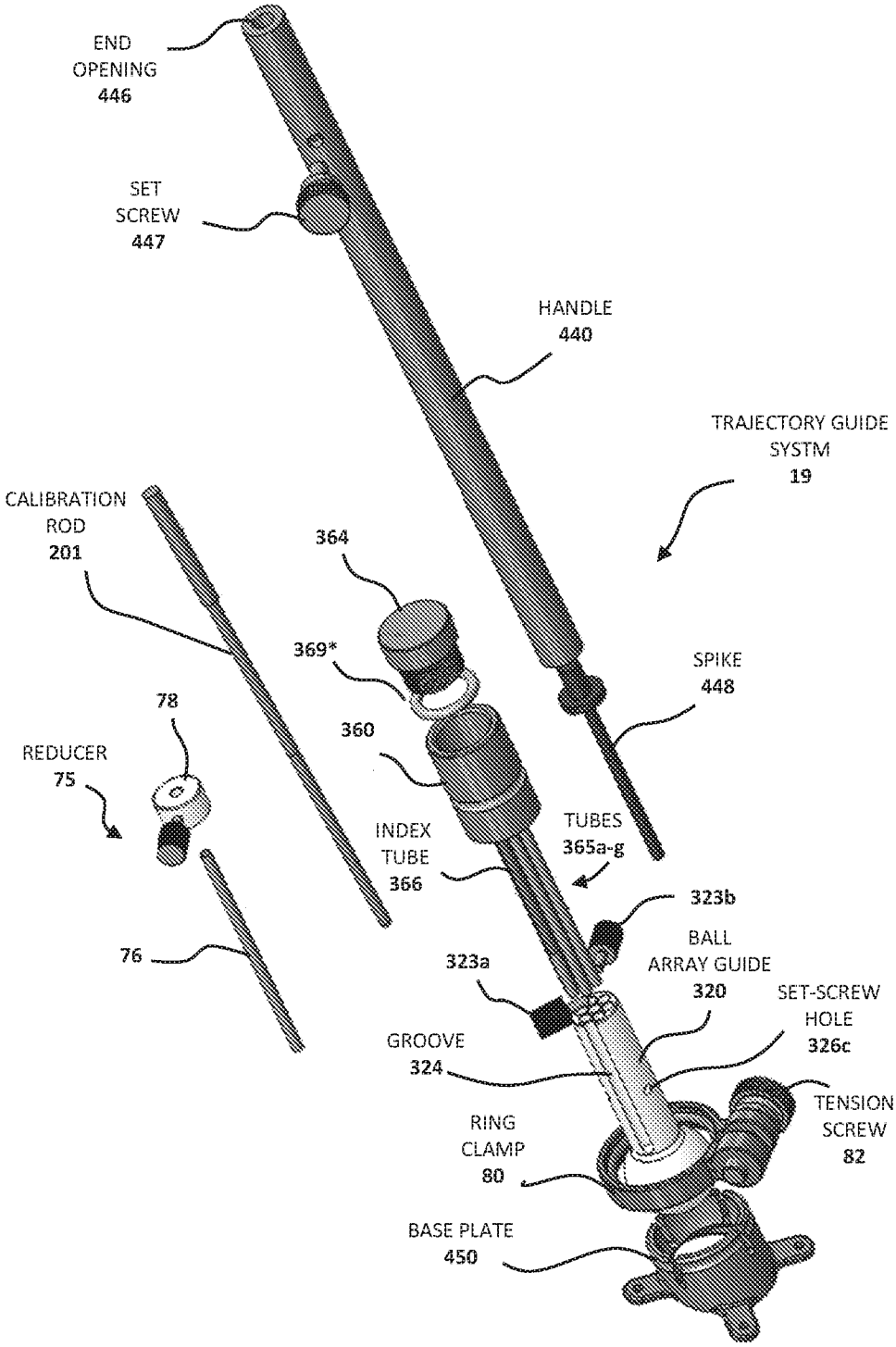

END OPENING 446
SET SCREW 447
HANDLE 440
TRAJECTORY GUIDE SYSTM 19
CALIBRATION ROD 201
364
369*
360
78
REDUCER 75
SPIKE 448
INDEX TUBE 366
TUBES 365a-g
323b
BALL ARRAY GUIDE 320
323a
SET-SCREW HOLE 326c
76
GROOVE 324
TENSION SCREW 82
RING CLAMP 80
BASE PLATE 450

Fig. 38C

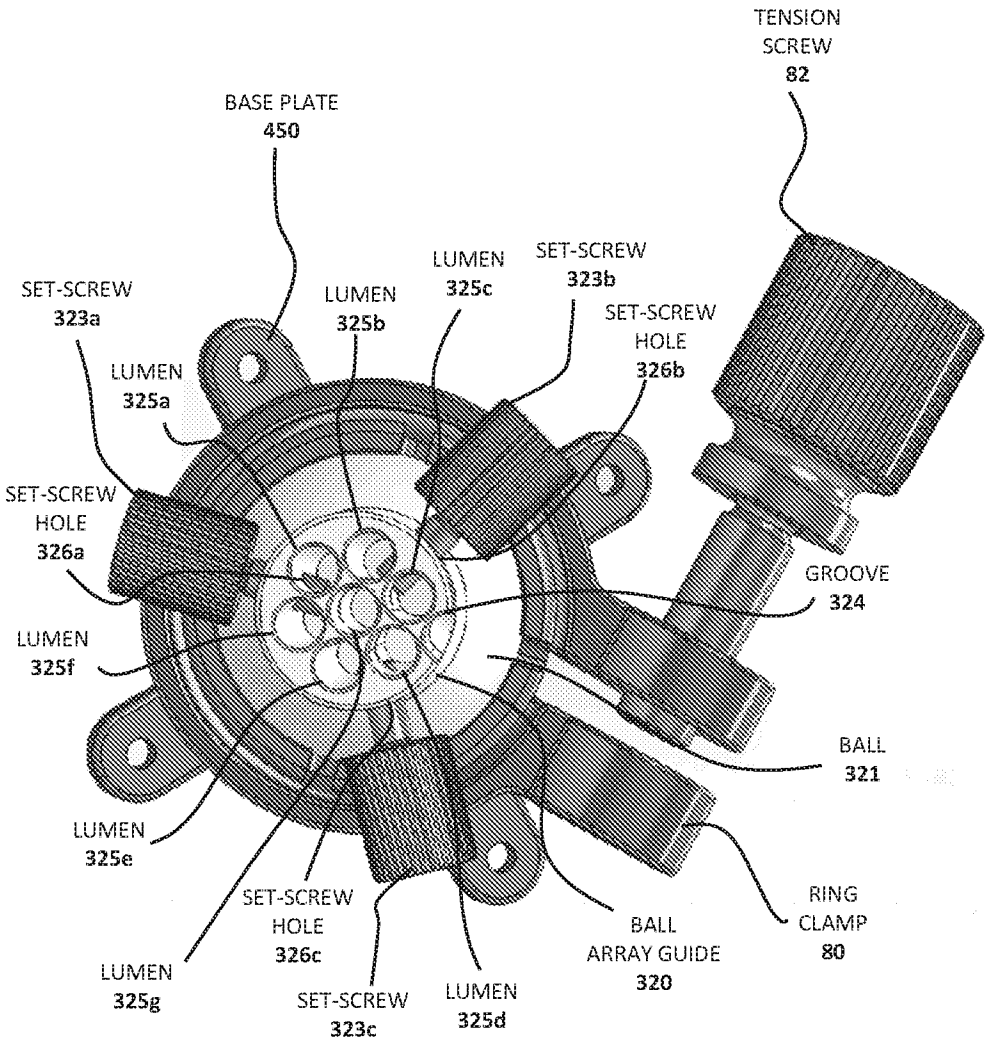

TENSION SCREW 82
BASE PLATE 450
SET-SCREW 323a
LUMEN 325b
LUMEN 325c
SET-SCREW 323b
SET-SCREW HOLE 326b
LUMEN 325a
SET-SCREW HOLE 326a
GROOVE 324
LUMEN 325f
BALL 321
LUMEN 325e
RING CLAMP 80
SET-SCREW HOLE 326c
BALL ARRAY GUIDE 320
LUMEN 325g
SET-SCREW 323c
LUMEN 325d

Fig. 38D

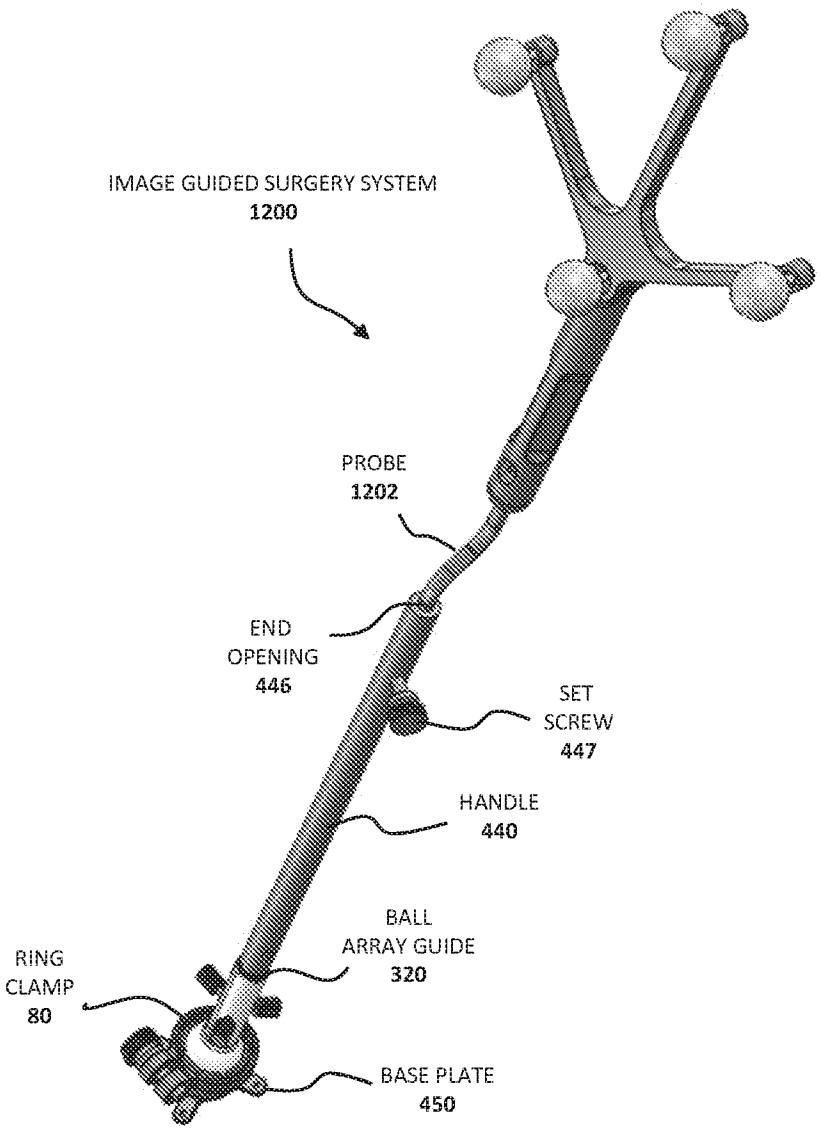

IMAGE GUIDED SURGERY SYSTEM
1200
PROBE
1202
END
OPENING
446
SET
SCREW
447
HANDLE
440
BALL
ARRAY GUIDE
320
RING
CLAMP
80
BASE PLATE
450

Fig. 39

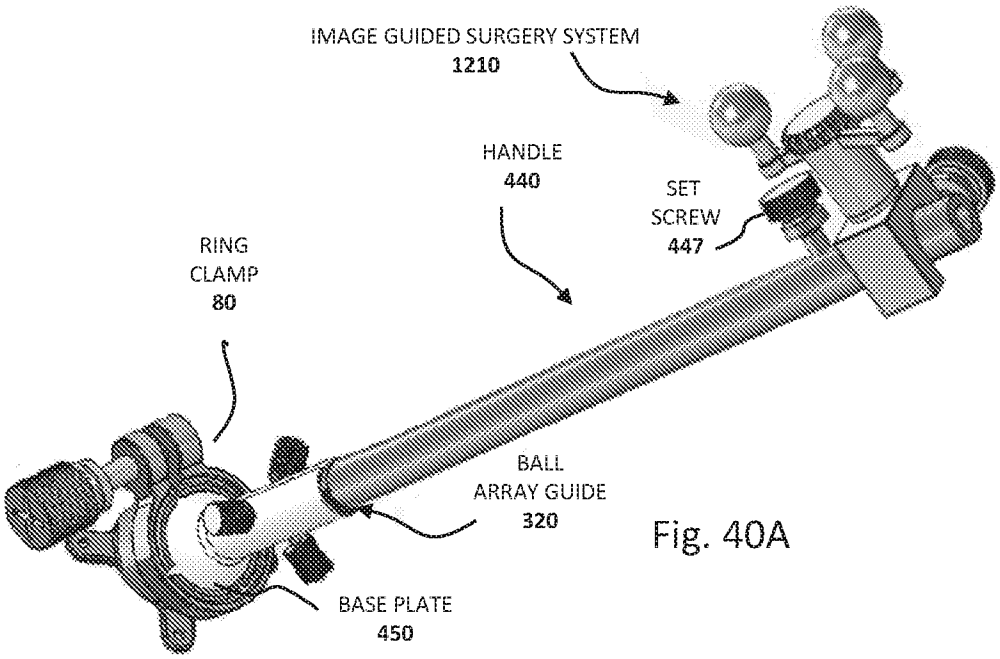


Fig. 40A

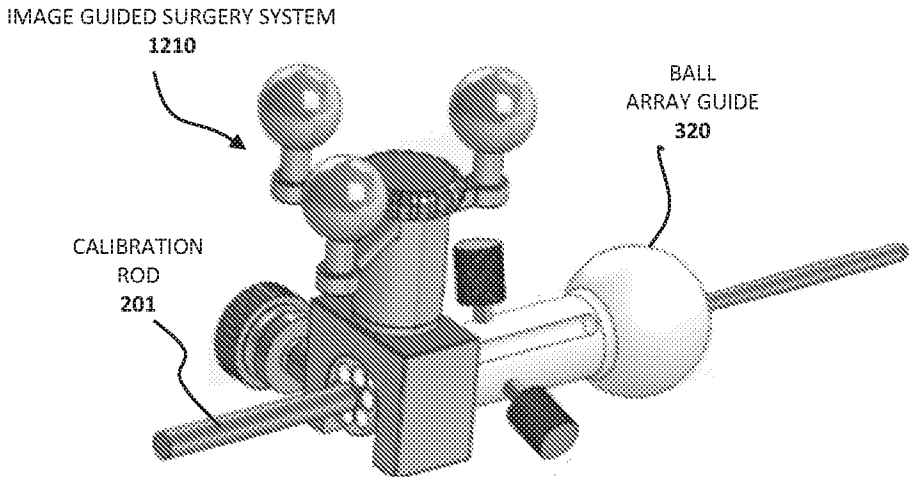


Fig. 40B

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2018/042391

A. CLASSIFICATION OF SUBJECT MATTER
INV. A61B17/34 A61B90/11 A61B90/10
ADD. A61B5/055 A61B34/20 A61B34/10

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)
A61B

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.
Y	WO 2007/064739 A2 (SURGIVISION INC [US]; KARMARKAR PARAG V [US]; JENKINS KIMBLE [US]) 7 June 2007 (2007-06-07) figures 12-16B page 36, line 27 - page 39, line 2	1-37, 45-51
Y	WO 2015/057807 A1 (MRI INTERVENTIONS INC [US]) 23 April 2015 (2015-04-23) figures 18A-B, 19A-G paragraph [0177] - paragraph [0181]	1-37, 45-51
A	US 2007/106305 A1 (KAO CHANGQUING C [US] ET AL) 10 May 2007 (2007-05-10) figures 1-5B paragraph [0058] - paragraph [0069]	1-37, 45-51

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

☒ See patent family annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
5 October 2018	12/10/2018

Name and mailing address of the ISA/	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016	Emirdag, Eda

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2018/042391

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. [X] Claims Nos.: 38-44
because they relate to subject matter not required to be searched by this Authority, namely:

The subject-matter of claims 38-44 relates to a method for treatment of the human or animal body by surgery. No search has been performed for the subject-matter of these claims (Rule 39.1(iv) and Rule 67.1(iv) PCT).

2. [ ] Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. [ ] Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. [ ] As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.

2. [ ] As all searchable claims could be searched without effort justifying an additional fees, this Authority did not invite payment of additional fees.

3. [ ] As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. [ ] No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

[ ] The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.

[ ] The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.

[ ] No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/US2018/042391

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 2007064739 A2	07-06-2007	AU 2006320611 A1	07-06-2007
		CA 2623616 A1	07-06-2007
		EP 1956975 A2	20-08-2008
		EP 2062530 A2	27-05-2009
		EP 2305109 A1	06-04-2011
		US 2009118610 A1	07-05-2009
		US 2015223905 A1	13-08-2015
		US 2017215981 A1	03-08-2017
		WO 2007064739 A2	07-06-2007
WO 2015057807 A1	23-04-2015	EP 3046500 A1	27-07-2016
		WO 2015057807 A1	23-04-2015
US 2007106305 A1	10-05-2007	EP 1945124 A2	23-07-2008
		US 2007106305 A1	10-05-2007
		US 2010298846 A1	25-11-2010
		WO 2007056458 A2	18-05-2007