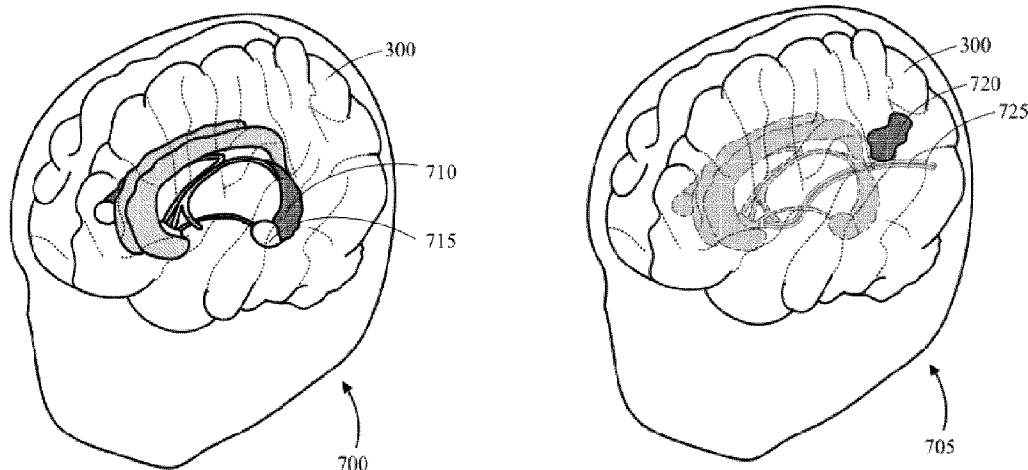




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(57) **Abrégé/Abstract:**

Disclosed herein are physiological phantoms incorporating properties of tissue that respond to laser ablation to replicate a real laser ablation procedure. The materials include waxes, polymers, thermochromic polymer blends or hydrogels, temperature sensitive hydrogels, and photodegradable hydrogels. The materials may mimic tissue as part of the tissue phantom not only in their feel and movement but also in any one or combination of their chemical, physical, mechanical, optical response to a laser ablation application. They may mimic the directionality, density, optical absorption, heat transmittance, heat conductance properties, electrochemical properties, thermochemical properties, and elasticity of the anatomical tissues they may be replicating. The laser ablation responsive materials may change properties such that they provide a measure of the success of a medical procedure.

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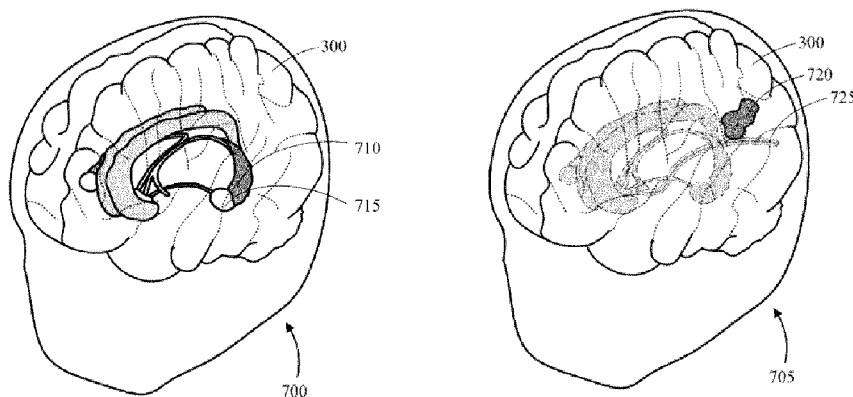


FIGURE 7

(57) Abstract: Disclosed herein are physiological phantoms incorporating properties of tissue that respond to laser ablation to replicate a real laser ablation procedure. The materials include waxes, polymers, thermochromic polymer blends or hydrogels, temperature sensitive hydrogels, and photodegradable hydrogels. The materials may mimic tissue as part of the tissue phantom not only in their feel and movement but also in any one or combination of their chemical, physical, mechanical, optical response to a laser ablation application. They may mimic the directionality, density, optical absorption, heat transmittance, heat conductance properties, electrochemical properties, thermochemical properties, and elasticity of the anatomical tissues they may be replicating. The laser ablation responsive materials may change properties such that they provide a measure of the success of a medical procedure.

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ANATOMICAL PHANTOM FOR SIMULATED LASER ABLATION PROCEDURES

FIELD

5 The present disclosure relates to medical phantoms, imaging phantoms and surgical training phantoms. More particularly the present disclosure relates to life like anatomical phantoms in which some portions of the phantoms are responsive to laser light for simulating laser ablation procedures.

10

BACKGROUND

 In the field of medicine, imaging and image guidance are a significant component of clinical care. From diagnosis and monitoring of disease, to planning of the surgical approach, to guidance during
15 procedures and follow-up after the procedure is complete, imaging and image guidance provides effective and multifaceted treatment approaches, for a variety of procedures, including surgery and radiation therapy. Targeted stem cell delivery, adaptive chemotherapy regimes, thermal ablation, and radiation therapy are only a few examples of procedures
20 utilizing imaging guidance in the medical field.

 Advanced imaging modalities such as Magnetic Resonance Imaging ("MRI") have led to improved rates and accuracy of detection, diagnosis and staging in several fields of medicine including neurology, where imaging of diseases such as brain cancer, stroke, Intra-Cerebral
25 Hemorrhage ("ICH"), and neurodegenerative diseases, such as Parkinson's and Alzheimer's, are performed. As an imaging modality, MRI

enables three-dimensional visualization of tissue with high contrast in soft tissue without the use of ionizing radiation. This modality is often used in conjunction with other modalities such as Ultrasound (“US”), Positron Emission Tomography (“PET”) and Computed X-ray Tomography (“CT”),

5 by examining the same tissue using the different physical principals available with each modality. CT is often used to visualize boney structures, and blood vessels when used in conjunction with an intra-venous agent such as an iodinated contrast agent. MRI may also be performed using a similar contrast agent, such as an intra-venous

10 gadolinium based contrast agent which has pharmaco-kinetic properties that enable visualization of tumors, and break-down of the blood brain barrier. These multi-modality solutions can provide varying degrees of contrast between different tissue types, tissue function, and disease states. Imaging modalities can be used in isolation, or in combination with

15 surgical techniques to provide previously unavailable options for the treatment of disease. An example of this would be laser ablation thermotherapy (referred to as laser ablation) where targeted tissue is destroyed by exposing it to an elevated temperature with laser energy.

An example of this technique in the neurosurgical field would be the

20 guidance of a laser ablation apparatus to a brain tumor using a preoperative scan of the patient in combination with a surgical navigation system followed by imaging the laser ablation procedure using MR thermometry to assure that optimal ablation margins are adhered to. The data collected during these procedures typically consists of CT scans with

25 an associated contrast agent, such as iodinated contrast agent, as well as

MRI scans with an associated contrast agent, such as gadolinium contrast agent. Also during similar procedures, MR imaging (such as a T2, T1, ADC, DWI, or etc.) may be used to differentiate the boundaries of the tumor from healthy tissue, known as the peripheral zone. Tracking of instruments relative to the patient and the associated imaging data is also often achieved by way of external hardware systems such as mechanical arms, radiofrequency, EM, or optical tracking devices. As a set, these devices are commonly referred to as surgical navigation systems.

Brain simulators or brain phantoms can be used as training aids for MRI guided laser ablation. Current methods used for training surgeons in the stereotactic placement of a laser applicator, and subsequent simulation of a laser ablation, are performed either using a cadaver for stereotactic placement training, or a gel phantom for MRI guided thermography.

In the second case of MRI guided thermography, the gel phantom used are either a bottle or a skull filled with a homogeneous gel. This gel does not show thermography changes (i.e., changes in temperature and rate of change in temperature) similar to brain tissue. Further, the skull filled with homogeneous gel do not show any anatomical context to the actual brain.

Thus, it is desirable to have a brain phantom or brain simulator with anatomical structures suitable for laser ablation simulation.

SUMMARY

The present disclosure discloses physiological phantoms incorporating for use during simulated medical procedures.

Disclosed herein is a tissue phantom for performing a simulated laser ablation surgical procedure on an anatomical structure of an organism, comprising:

a tissue phantom made of a material similar to the anatomical structure of the organism; and

a laser responsive material embedded in at least a portion of said tissue phantom, wherein said laser responsive material exhibits a preselected response when irradiated by a laser beam during the simulated laser ablation surgical procedure.

A further understanding of the functional and advantageous aspects of the invention can be realized by reference to the following detailed description and drawings.

BRIEF DESCRIPTION OF THE DRAWINGS

Embodiments disclosed herein will be more fully understood from the following detailed description thereof taken in connection with the accompanying drawings, which form a part of this application, and in which:

FIGURE 1 is an illustration of an example laser ablation based approach in which an ablation needle is inserted into the brain to approach a tumor.

FIGURE 2 is an illustration of an example training model head/brain phantom in an exploded view, illustrating parts of the base component and the training component.

FIGURE 3 is an illustration showing a brain phantom in a skull.

5 **FIGURE 4** is a flow chart describing a typical laser ablation procedure.

10 **FIGURE 5** is an illustration where the left most image is showing an MR scan used to locate a target in an actual patient's brain and the rightmost image is showing an MR scan used to locate a target in a brain shaped laser ablation tissue phantom.

FIGURE 6 is an illustration showing a stereo tactic frame and a tissue phantom having a skull.

FIGURE 7 is an illustration of two exemplary tissue phantoms having ablation targets.

15 **FIGURE 8** is an illustration showing a typical laser ablation approach with the laser ablation probe prior to being inserted shown on the left hand side of **FIGURE 8** and the laser ablation probe inserted into the target being shown on the right hand side of **FIGURE 8**.

FIGURE 9 is an illustration showing a typical ablation sequence.

20 **FIGURE 10** is an illustration showing laser ablative properties of substances that comprise tissue.

FIGURE 11 is an illustration showing a cross section of the two exemplary tissue phantoms having different ablation targets.

25 **FIGURE 12** is an illustration showing a typical laser ablation process on a brain phantom with the upper left section showing the laser

aligned with the target, the upper right showing the laser inserted to the target area and the bottom center showing the ablation procedure complete.

FIGURE 13 is an illustration showing a typical laser ablation with a
5 laser ablation brain phantom having an asymmetrical target.

FIGURE 14 is an illustration showing side by side intraoperative MR thermometry scans derived from the thermography phase portion of the MRI sequence and their corresponding magnitude portion of the sequence with a real time overlaid Arrhenius modeled 'irreversible damage
10 estimate'.

FIGURE 15 is an illustration showing an intraoperative MR thermometry scan on a laser ablation tissue phantom.

FIGURE 16 is an illustration showing various laser ablation responsive materials.

FIGURE 17 is an illustration showing a cross-sectional view of a
15 Facet nerve ablation procedure on a laser ablation tissue phantom.

FIGURE 18 is an illustration showing a side view of a Facet nerve ablation procedure on a laser ablation tissue phantom.

20 **DETAILED DESCRIPTION**

Various embodiments and aspects of the disclosure will be described with reference to details discussed below. The following description and drawings are illustrative of the disclosure and are not to be construed as limiting the disclosure. Numerous specific details are
25 described to provide a thorough understanding of various embodiments of

the present disclosure. However, in certain instances, well-known or conventional details are not described in order to provide a concise discussion of embodiments of the present disclosure.

Disclosed herein are physiological phantoms incorporating
5 properties of tissue that respond to laser ablation to replicate a real laser ablation procedure. The materials include waxes, polymers, thermochromic polymer blends or hydrogels, temperature sensitive hydrogels, and photodegradable hydrogels. The materials may mimic tissue as part of the tissue phantom not only in their feel and movement
10 but also in any one or combination of their chemical, physical, mechanical, optical response to a laser ablation application. They may mimic the directionality, density, optical absorption, heat transmittance, heat conductance properties, electrochemical properties, thermochemical properties, and elasticity of the anatomical tissues they may be replicating.
15 The laser ablation responsive materials may change properties such that they provide a measure of the success of a medical procedure.

As used herein, the terms “comprises” and “comprising” are to be construed as being inclusive and open ended, and not exclusive. Specifically, when used in the specification and claims, the terms
20 “comprises” and “comprising” and variations thereof mean the specified features, steps or components are included. These terms are not to be interpreted to exclude the presence of other features, steps or components.

As used herein, the term "exemplary" means "serving as an example, instance, or illustration," and should not be construed as preferred or advantageous over other configurations disclosed herein.

As used herein, the terms "about" and "approximately" are meant to
5 cover variations that may exist in the upper and lower limits of the ranges of values, such as variations in properties, parameters, and dimensions.

As used herein, the term "patient" is not limited to human patients and may mean any organism to be treated using the planning and navigation system disclosed herein.

10 As used herein the phrase "surgical tool" or "surgical instrument" or "medical instrument" refers to any item that may be directed to a site along a path in the patient's body. Examples of surgical tools may include (but are not necessarily limited to) scalpels, resecting devices, imaging probes, sampling probes, catheters, or any other device that may access a target
15 location within the patient's body (or aid another surgical tool in accessing a location within a patient's body), whether diagnostic or therapeutic in nature.

As used herein the term "tensides" refers to agents that modify interfacial tension of water; usually substances that have one lipophilic and
20 one hydrophilic group in the molecule; includes soaps, detergents, emulsifiers, dispersing and wetting agents, and several groups of antiseptics.

Broadly, tissue phantoms for performing a simulated laser ablation surgical procedure are disclosed herein. The tissue phantom is made of a
25 material designed to mimic an anatomical part of an animal and a laser

responsive material embedded in at least a portion of the tissue phantom.

The laser responsive material exhibits a **preselected response** when being irradiated by a laser beam during the simulated laser ablation surgical procedure.

5 As used herein, the phrase "preselected response" means the material exhibits a predicable change in any one or combination of physical, chemical, physico-chemical, optical, mechanical and structural properties upon being irradiated by the laser light. This predicable change allows a clinician practicing a laser ablation procedure to detect a
10 difference in the laser ablation responsive material due to it being illuminated.

 The change in one or more of the above-noted properties may be induced by one of several mechanisms including an increase in temperature under illumination, a photochemistry induced reaction due to
15 illumination of the laser ablation responsive material by a laser of a specific wavelength which causes a photochemical reaction. An example of this may be light induced cross linking in the material.

 The materials include waxes, polymers, thermochromic polymer blends or hydrogels, temperature sensitive hydrogels, and
20 photodegradable hydrogels. The materials may mimic tissue as part of the tissue phantom not only in their feel and movement but also in their chemical response to a laser ablation application. They may mimic the directionality, density, optical absorption, heat transmittance, heat conductance properties, electrochemical properties, thermochemical
25 properties, and elasticity of the anatomical tissues they may be replicating.

The laser ablation responsive materials may change properties such that they provide a measure of the success of a medical procedure.

Since image-guided medical procedures are complex in nature and the risk associated with use of such procedures in the brain or any other anatomical part is very high, the surgical staff must often resort to performing a simulated rehearsal of the entire procedure. Unfortunately, the tools and models that are currently available for such simulated rehearsal and training exercises typically fail to provide a sufficiently accurate simulation of the procedure.

Understanding and modeling tissue deformations and tissue response to interventional medical instruments is important for surgeons practicing invasive medical procedures on patients. Being able to accurately model how various types of tissue deform and respond to medical instruments may improve a surgeon's ability to approach and apply therapeutic interventions to targets in the patient's body with minimal damage and maximum effectiveness. Being able to produce tissue phantoms which exhibit biomechanical, imaging, and therapeutic response characteristics resembling those of patients is a necessary step in providing a viable life-like tissue phantom on which to practice medical procedures.

When performing surgical and/or diagnostic procedures that involve ablation, neurosurgical techniques such as removing a small section of the superficial tissue to provide access to internal anatomical structures may be executed. In such procedures, as indicated, the medical procedure is invasive of the mammalian body. For example, in the ablation based

surgical method illustrated in **FIGURE 1**, a generally elongated probe **100** is inserted along a planned trajectory into the brain **120** to access a tumor (not shown) or other structures located deep in the brain to undergo laser ablation. The elongated probe **100** provides the surgeon with the ability to
5 ablate the interior portion of the patient's brain being operated on, without significant negative repercussions resultant of more invasive procedures such as those involving sizeable craniotomies.

According to embodiments provided herein, the simulation of such procedures may be achieved by providing an anatomical model that is
10 suitable for simulating the medical procedure through one or more layers of the head. Such a procedure may involve perforating, drilling, boring, punching, piercing, stimulating, ablating, resecting, or any other suitable methods, as necessary for a laser ablation based procedure. For example, some embodiments of the present disclosure such as that shown in
15 **FIGURE 2** provide brain models comprising an artificial skull layer **220** that is suitable for simulating the process of penetrating a mammalian skull. As described in further detail below, once the skull layer is penetrated, the medical procedure to be simulated using the training model may include further steps in the diagnosis and/or treatment of various medical
20 conditions. Such conditions may involve normally occurring structures, aberrant or anomalous structures, and/or anatomical features underlying the skull and possibly embedded within the brain material.

In some example embodiments, the anatomical model is suitable for simulating a medical procedure involving a brain tumor that has been
25 selected for ablation. In such an example embodiment, the brain model

such as that shown in **FIGURE 2** is comprised of a brain material **210** having a simulated brain tumor provided therein. This brain material simulates, mimics, or imitates at least a portion of the brain at which the medical procedure is directed or focused.

5 The simulation of the above described laser ablation medical procedure is achieved through simulation of both the medical procedure and the associated imaging steps that are performed prior to surgery (pre-operative imaging) and during surgery (intra-operative imaging). Pre-operative imaging simulation is used to train surgical teams on co-
10 registration of images obtained through more than one imaging methodology such as magnetic resonance (MR), computed tomography (CT) and positron emission tomography (PET). Appropriate co-registration geometrically aligns images from different modalities and, hence, aids in surgical planning step where affected regions in the human body are
15 identified and a suitable route to access the affected region is selected. Intraoperative imaging assists the surgical team in guiding and confirming a medical instruments position in the patient's body and allows them to better estimate the progression of the procedure.

Referring to **FIGURE 2**, an exploded view of an example model or
20 phantom shown generally at **250** is provided that is suitable for use in training or simulation of a medical procedure which is invasive of a mammalian head. The training model **250** may be adapted or designed to simulate any anatomical structure. It is to be understood that the person to be trained on the phantom may be selected from a wide variety of roles,
25 including, but not limited to, a medical doctor, resident, student,

researcher, equipment technician, or other practitioner, professionals, or personnel. In other embodiments, the models provided herein may be employed in simulations involving the use of automated equipment, such as robotic surgical and/or diagnostic systems. The present disclosure
5 relates to parts or all of a phantom being designed to mimic the response of patient tissue during any of the steps involved of an ablation procedure. Furthermore the present disclosure also relates to parts or all of a phantom designed to provide a mechanism for obtaining a measure success of a mock ablation procedure during or after it has been performed.

10 **FIGURE 3** shows an exemplary embodiment of a tissue phantom that may be used for a brain tissue ablation procedure as will be described in further detail below. The tissue phantom as shown includes a skull portion **310** and an additional brain portion **300** positioned inside the skull portion **310**. The brain portion **300** may contain further portions such as
15 other anatomical parts or sensors, or sensing materials that may be desirable during a mock brain tissue ablation procedure.

FIGURE 4 depicts a flow chart describing a common brain tissue laser ablation workflow as it is performed on a target tissue of interest in the brain. The following sections will describe a laser ablation tissue
20 phantom with features in accordance with the steps of the generic brain tissue laser ablation procedure workflow as shown in the flow chart in **FIGURE 4**. The features of the exemplary laser ablation tissue phantom may be designed to provide a training surgeon using the phantom with a similar response to patient tissue during an actual laser ablation procedure
25 consonant with said workflow.

The exemplary brain tissue laser ablation workflow shown in **FIGURE 4** will be described with respect to its implementations in two procedures that employ brain tissue laser ablation. It should be noted that these procedures and workflow are provided as non-limiting examples only and that the laser ablation tissue phantom as disclosed herein may be used for any applicable medical procedure such as a prostate tumor laser ablation or a Facet (Spinal) Laser Ablation which will be described in further detail below. It should also be noted that any of the features of the laser ablation tissue phantom as described herein may be produced in the laser ablation tissue phantom individually or in combination with one or more alternate features also described herein.

The two exemplary procedures that will be implemented using the exemplary workflow provide in **FIGURE 4** are an amygdalectomy as described in the paper [Willie, Jon T., et al. "Real-time magnetic resonance-guided stereotactic laser amygdalalectomy for mesial temporal lobe epilepsy." **Neurosurgery** 74.6 (2014): 569-585.] and a Glioblastoma thermal laser ablation. Both of these procedures involve inserting a laser ablation probe into the brain of a patient to ablate a volume of brain tissue and follow the workflow as outlined by the flow chart in **FIGURE 4**. An amygdalalectomy is generally performed on patients with epileptic foci found to be within the boundaries of the two adjacently located amygdala and hippocampus brain structures wherein, the ablation of the structures tends to remove the source of the seizure (the epileptic foci). Generally only segments of the adjacent structures showing epileptic

characteristics as determined by cortical mapping may be targeted however in some cases such as the one that will be described as follows dependent on the specific patient, the entire amygdala and hippocampus structures may be targeted.

5 Referring to **FIGURE 4** the first stage **400** of these procedures is to image the patient using an imaging technique such as but not limited to MRI, CT, PET, or any other applicable technique and identify the target of interest. In the case of an amygdalohippocampotomy this would be the hippocampus and amygdala structures located within the brain while for
10 the glioblastoma tumor ablation this would be the tumor of interest. A trajectory corresponding to a path from an entry point to the target structure (tumor, or Hippocampus/Amydala) is also chosen at this stage. To employ the laser ablation tissue phantom as disclosed herein in the replication of this step requires that the phantom have features such that:

- 15 a) the laser ablation tissue phantom may be scanned using an applicable imaging technique such as MRI or those listed above and;
- b) the laser ablation tissue phantom have one or more identifiable target or other volumes that can be used to define a trajectory
20 consonant with the procedure being performed.
- c) the one or more volumes be differentiable in the scanning modality used at this stage in the procedure.

FIGURE 5 shows a side by side comparison of an actual scan of a patient **500** during such a workflow step **400**, having a target and entry
25 point, with an actual scan of an exemplary laser ablation tissue phantom

510 containing two targets (replicating two Glioblastomas) as is apparent from the image. The laser ablation tissue phantom in the scan 510 was produced using methods and apparatus as described in the International PCT patent application Serial No. PCT/ CA2014050659 entitled

5 "SURGICAL IMAGING AND TRAINING BRAIN PHANTOM" which shows two artificial Glioblastomas 515 that may be used to replicate the steps in the stage 400 of the laser ablation workflow as shown in FIGURE 4 (i.e. by allowing a training surgeon to identify an entry point and target).

However, in the case of the amygdalohippocampotomy the
10 structures shown in the scan 510 would have to be replaced by structures mimicking the hippocampi and amygdalae as opposed to the Glioblastomas 515 as shown to allow for a replication of an actual amygdalohippocampotomy employing a thermal ablation probe. In addition whereas Glioblastomas are arbitrarily located in the brain, the hippocampi
15 and amygdalae have specific anatomical locations (shown in FIGURE 7) and it would be beneficial to provide the mimicking structures in locations consonant with an anatomical atlas or if desired with an actual patient anatomy.

Referring again to FIGURE 4 the next stage 410 in both procedures
20 is to align the laser ablation probe guide along a trajectory to be traversed by the probe to access the target. FIGURE 6 shows an exemplary stereotactic frame 600 that may be used to align the guide. As is apparent from the stereotactic frame 600 in the figure the frame is typically attached to a skull 605 and oriented accordingly. The frame 600 is typically aligned

25

in accordance with the trajectory defined by the target and entry point as per the previous stage 400 where the trajectory was chosen. Commonly the alignment of the frame 600 is assisted by a tracking system registered with the patient and having tracked tools such as that described in the International PCT patent application Serial No. PCT/CA2014/050270, entitled "**SYSTEMS AND METHODS FOR NAVIGATION AND SIMULATION OF INVASIVE THERAPY**", which is WO Publication 2014/139022. An alternate option often used is to align the frame 600 in relation to the patients' skull 605 by setting the frame 600 to frame coordinates provided by the planning software, using the graduation marks 610 on the frame 600. Once the trajectory is set a small entry hole for the laser ablation probe 100 (**FIGURE 1**) is burred into the patients' skull 605 coaxially with the trajectory. In typical procedures an MRI compatible probe guide is then anchored into this hole to form a linear channel to allow a laser ablation probe 100 to pass through along the trajectory into the brain towards the target.

To employ the laser ablation tissue phantom as disclosed in this embodiment the replication of this step requires that the phantom have features such that:

- a) a stereotactic frame may be mounted on the phantom or part of the phantom as it would be on a patient (it should be noted that various other types of frames such as a miniframe may be used (Monteris Axiis, <http://www.monteris.com/our-technology/axiis-stereotactic-miniframe/>), or a frameless mount may also be

used in which frameless navigation occurs with a patient secured to the table and a referenced attached to the securing device;

b) the superficial part of the phantom have a layer with similar properties of skull and;

c) an MRI compatible probe guide is able to be anchored into the superficial part of the phantom at the location of the burr hole.

FIGURE 6 shows an exemplary embodiment of a skull part **615** of a head/brain phantom potentially having the required properties of a patients' skull for replicating the burr and probe guide anchoring steps of the stage **410** of **FIGURE 4**. It should be noted that this skull part **615** may also be registered with a tracking system for aligning the frame as described above. The embodiment of the skull shown may be produced as per the International PCT patent application Serial No.

PCT/CA2014/050272, entitled "**PLANNING, NAVIGATION AND SIMULATION SYSTEMS AND METHODS FOR MINIMALLY INVASIVE THERAPY**", which is published as WO Publication 2014/139024.

Referring again to **FIGURE 4** the next stage **425** in both procedures is for the surgeon to advance the laser ablation probe through the MRI compatible guide along the defined trajectory to access the target.

FIGURE 7 shows exemplary embodiments, at **700** and at **705**, of the laser ablation tissue phantom as disclosed herein that may be used for the amygdalohippocampotomy and the Glioblastoma tumor laser ablation procedures respectively. The embodiments of the laser ablation tissue

phantom for the amygdalohippocampotomy procedure **700** and the Glioblastoma tumor laser ablation procedure **705** may be referred to as Phantom A **700** and Phantom G **705** respectively henceforth. When advancing an ablation probe **100** towards the targets along the trajectory in

5 medical procedures it is common for surgeons to analyze the tactile feel of the probe **100** at various stages of advancement for trying to detect inconsistencies with respect to the chosen trajectory and what they “should” be feeling like at a certain point. For example if a trajectory is chosen such that the probe **100** should pass through a ventricle at a

10 particular depth (or within a range of depths) within the brain then the surgeon may expect to feel a reduction in opposing force against the probe **100** when that region is accessed (i.e. they will expect to feel the boundary of the ventricle where the opposing force changes). If this reduction is not felt through the surgeons’ tactile perception it may indicate to the surgeon

15 that perhaps the trajectory is off or some other error has occurred for example a shifting of the ventricular area after the scan.

In addition increased pressure against the probe **100** (**FIGURE 1**) may be indicative of a ruptured vessel releasing blood into the brain thereby increasing the overall pressure. Thus it may be advantageous to

20 produce a laser ablation tissue phantom with boundaries or structures representative of the actual anatomy of a patient and the corresponding tactile properties.

The laser ablation anatomical phantoms disclosed herein may be generic phantoms used simply for training purposes. In addition, the

25 phantoms may be patient specific phantoms, produced based on

preoperative imaging of the anatomical part of the patient undergoing the medical procedure. Thus if a patient has a brain tumor, preoperative imaging of the patient's brain may be used to construct a lifelike brain phantom (or other anatomical structure) including the tumor, with the brain structures and tumor being made of responsive materials selected to mimic selected properties of the brain, and tumor, including but not limited to, mechanical, optical and biomechanical properties of the brain structures and tumor. This phantom will give the clinician an opportunity to practice the medical procedure in a very realistic manner.

10 In the case when surgeons perform an amygdalohippocampotomy they target the same structure every time for each patient. Therefore producing a phantom with target volume structures of the amygdala and hippocampus having similar tactile properties to actual amygdalae and hippocampi may assist in improving a surgeons training in providing them not only directional familiarity but tactile familiarity with the structure volumes to be ablated.

 In the case when surgeons perform a Glioblastoma tumor laser ablation they target a different volume every time for each patient. However eloquent structures for example the optic tract are to be avoided almost always to preserve important functionality in the patient. In this example avoiding the optic tract would preserve the patient's vision. Thus, producing a phantom with structures in addition to the target volumes may assist in improving a surgeons training in providing them not only directional familiarity but anatomical experience as to which areas to avoid.

25 In yet another case targeted Glioblastomas to be ablated at times may be

very dense compared to their surrounding tissue. Thus once again producing a target structure with a similar tactile properties to a dense Glioblastoma may assist in improving a surgeons training in providing them not only directional familiarity but tactile familiarity with the structure volumes to be ablated.

In order to produce the changes in tactile feel between brain structures various attributes of the structures may be altered. One example factor that may be changed is the density of the materials used to produce the structures. **Table 1** as shown below, provides some densities of actual brain structures that may be used to choose or produce artificial brain structures materials to be used in the laser ablation tissue phantom as disclosed herein with tactile properties similar to that of their corresponding actual brain structures. Other non-limiting properties that may be used to produce artificial brain structure materials include, elasticity and, hardness.

<u>Human Brain</u>	<u>Density (g/cm³)</u>
Frontal White	1.073
Frontal Gray	1.090
Parietal White	1.026
Parietal Gray	1.109
Occipital White	1.073
Occipital Gray	1.103
Corpus-callosum	1.093
Thalamus	1.052
Caudate Nucleus	1.075
Putamen	1.081
Global Pallidus	1.084
Brachium Pontis	1.116
Medulla	1.057
Pons	1.069
Cerebellum	1.058

Phantom A **700** shown in **FIGURE 7** on the left hand side of the **FIGURE 7** shows the amygdala **715** and hippocampus **710** structures with differing densities with respect to the surrounding brain tissue **300**.

Therefore when employing this phantom (i.e. Phantom A) for a mock
5 amygdalohippocampotomy, a surgeon may feel a change in density moving from the surrounding brain tissue **300** of the phantom into the hippocampus **710** and again through the hippocampus into the amygdala **715**.

Phantom G **705**, shown on the right hand side in **FIGURE 7** shows
10 a Glioblastoma **720** structure with differing density with respect to the surrounding brain tissue **300**. Therefore when employing this phantom (i.e. Phantom G) for a mock Glioblastoma tumor laser ablation a surgeon may feel a change in density moving from the surrounding brain tissue **300** of the phantom into the tumor **720**.

15 Referring again to **FIGURE 4**, the next stage **430** in both procedures is to move the patient into an MRI machine. Again referring to **FIGURE 4** the following stage **435** in both procedures is to begin MRI imaging and confirm that the ablation is properly placed in the target of interest as described above for both procedures being described herein
20 with respect to the workflow. If the laser ablation probe **800** (seen in **FIGURE 8**) is not found to be in the correct position the procedures may be started over. If the laser ablation probe **800** is in the correct position, then the laser ablation process can begin.

To employ the laser ablation tissue phantom as disclosed herein in
25 the replication of this stage requires that the phantom have all of the

features as required in the initial stage **400** of the workflow (i.e. it must have properties such that it may be imaged with the particular imaging modality used in the procedure etc.).

Once the probe **800** is correctly placed the ablation of the tumor
5 may begin. At this stage both MR thermometry imaging (step **470**) and ablation (step **475**) may occur simultaneously such that the MR thermometry is used to monitor the extent of the ablated region created by the laser thermal ablation probe as it is applied within the target. **FIGURE 8**, left hand side of the Figure, shows a diagram of a simulated commonly
10 performed amygdalohippocampotomy on Phantom A prior to step **425** in the workflow. The trajectory **810** shown in the left hand diagram **820** of this figure is a typical trajectory chosen in most procedures of this kind. The trajectory **810** attempts to avoid the lateral ventricles and enter the hippocampus **710** posteriorly along the long axis of the hippocampus body
15 into the amygdala shown in the image at **715**. The reason this trajectory **810** is commonly chosen is to allow the laser ablation probe **800** to ablate as much of the hippocampus as possible through one pass (achieved by maneuvering the probe along a linear path coincident with the long axis of the hippocampus). The laser ablation probe may have multiple laser light
20 emitters **805** on its distal end or a mechanical assembly to allow for customizable ablative laser emission.

The right hand side of **Figure 8** shows a simulated commonly performed amygdalohippocampotomy on Phantom A, shown generally as area/volume **825**, wherein the laser ablation probe **800** has been
25 advanced to the target(s) of interest prior to step **465** in the workflow. The

highlighted area **815** of the right side **825** of **FIGURE 8** can be seen in **FIGURE 9** which depicts further progression of the simulated commonly performed amygdalohippocampotomy. Referring again to **FIGURE 9**, the left hand side of the figure at **900** shows a general starting location
5 between the hippocampus and amygdala (not to scale) for ablation during a commonly performed amygdalohippocampotomy procedure. In this frame ablation has begun on the most-distal end of the ablation probe as can be seen as the region **915** shown in a darker elliptical shape. The middle frame of the figure **905** shows a further progression where ablation
10 has begun in the body of the hippocampus, the ablation volume of this stage in the progression shown as a second dark elliptical shape **920**. The right frame of the figure **910** shows an even further progression where ablation has reached the posterior portion of the hippocampus, the ablation volume at this stage is shown as a third dark elliptical shape.

15 As described above the specific trajectory chosen to reach the target area is an important factor in determining the effectiveness of the amygdalohippocampotomy. From the progression of the procedure shown in **Figure 9**, it is apparent that the more the trajectory is aligned axially with the long axis of the hippocampus towards the amygdala the more access
20 the laser ablation probe will have to the volume to be ablated (i.e. the hippocampus and amygdala). This is important in that the more of these two structures that are ablated the better the chances are of the procedure being a success (i.e. ablating the epileptic region of the patient's brain). Thus it is vital that when producing a laser ablation tissue phantom that
25 structures be aligned in accordance with actual anatomy.

The ablation step **475** as shown in **Figure 9** and described above will be elaborated on in greater detail as follows to outline further features of the laser ablation tissue phantom as disclosed herein. Referring again to **Figure 9**, the laser **805** as shown in the figure is activated to ablate the

5 target tissue. To perform ablation the laser emits a light beam at a particular wavelength in order to induce thermal heating in the target tissue. The rate of tissue ablation and temperature gradient are important factors when performing laser ablation. Specifically for the case of the rate of tissue ablation, the faster the target tissue may be ablated the better the

10 more beneficial the ablation is to the outcome of the procedure. This result follows from general medical procedural knowledge such as the less time the patient is under general anesthesia the less likely complications are to occur. In addition the less time the doctors spend performing the surgery the more money is saved by the hospital. For the case of the temperature

15 gradient the steeper the gradient is over penetration distance the better, as this allows the application of thermal ablation in focused areas while affecting non-target areas minimally. A method of effectively achieving such a result may be implemented by taking advantage of the phenomenon of thermal confinement as described in further detail below.

20 Examples of wavelengths commonly used in laser ablation procedures to optimally meet the important factors mentioned above are 980nm and 1064nm. The mechanisms through which laser thermal ablation acts on tissue is important in determining how to best produce a laser ablation tissue phantom that may mimic this ablation step **475** of the workflow

25 shown in **FIGURE 4**. Thus a description of the basic mechanisms through

which laser ablation acts on patient tissue and its interaction will be elaborated on below in further detail.

FIGURE 10 (a) taken from [Chu, Katrina F., and Damian E. Dupuy. "Thermal ablation of tumours: biological mechanisms and advances in therapy." *Nature Reviews Cancer* 14.3 (2014): 199-208.]

shows a diagram of a tissue undergoing thermal ablation. The following passage gives a summary of cell death caused by ablation and was retrieved from [Chu, Katrina F., and Damian E. Dupuy. "Thermal ablation of tumours: biological mechanisms and advances in therapy." *Nature Reviews Cancer* 14.3 (2014): 199-208.]

"Hyperthermic injury.

RFA and MWA, as well as laser ablation and HIFU, cause focal hyperthermic injury to ablated cells, which affects the tumour microenvironment and damages cells at the membrane and subcellular levels. The process of tumour destruction occurs in at least two phases, through direct and indirect mechanisms.

Heat-ablated lesions can be thought of as having three zones: the central zone, which is immediately beyond the application tip and which undergoes ablation-induced coagulative necrosis; a peripheral or transitional zone of sublethal hyperthermia, which mostly occurs from thermal conduction of the central area that is either undergoing apoptosis or recovering from reversible injury; and the surrounding tissue that is unaffected by ablation. Direct cellular damage occurs at several levels, from the subcellular level to the tissue level, and it depends on the thermal

energy that is applied, the rate of application and the thermal sensitivity of the target tissue."

From the passage it is apparent that there are two zones of ablation created during a thermal ablation therapy. The first zone (labelled as:

5 **Coagulation necrosis** in **FIGURE 10 (a)**) is the area where immediate cell death occurs through coagulation necrosis, while the second zone (labelled as: **Sublethal damage** in **FIGURE 10 (a)**) is the zone undergoing reversible damage. It should be noted that the first zone occurring "*immediately beyond the application tip*" is equivalent to the targeted area
10 by the laser beam of the laser ablation probe in a thermal laser ablation application as described herein. Thus, the mentioned thermal zones are also induced during laser ablation procedures as shown in the figure similar to the induction of thermal zones that occur using an ablation applicator with the difference being that the thermal energy transferred to
15 the tissue occurs through light absorption during laser ablation thermal therapy as opposed direct thermal conduction which occurs when employing a thermal applicator. Thus, the light absorption properties of the tissue being ablated are essential in determining the effectiveness of the ablation procedure.

20 Generally the optical absorption properties of tissue are dominated by five biomolecules as described in the paper [Vogel, Alfred, and Vasan Venugopalan. "Mechanisms of pulsed laser ablation of biological tissues." Chemical reviews 103.2 (2003): 577-644.]. These molecules are protein, DNA, melanin, hemoglobin, and water. **FIGURE 10 (b)** shows the
25 dependence of the light absorption coefficient of these five molecules on

the wavelength of applied laser light. It is apparent from **Figure 10 (b)** that absorption of laser light in the near-infrared range is primarily due to water and hemoglobin (and deoxyhemoglobin). However hemoglobin is predominantly located in vasculature (also partially in tissue) and thus this must be taken into consideration during ablation.

Given the provided information in order to employ the laser ablation tissue phantom as disclosed herein in the replication of this step (475) requires that the phantom have features such that:

- a) generally the replicated tissue in the laser ablation tissue phantom should respond as similarly as possible to how the tissue it's replicating would respond to the same optical (light) stimulus,
- b) specified further for clarity;
 - i. the material should convert absorbed light energy into heat at a similar rate to the target tissue it's replicating,
 - ii. the material should diffuse and absorb light at a similar rate to the target tissue it's replicating,
 - iii. the material should change chemical properties similarly to the tissue being replicated.

The first criteria b)-(i) regarding the conversion of light into heat by the tissue can occur in two specific modalities such that in the first modality heat absorption occurs under normal conditions and in the second modality heat absorption as dictated by thermal confinement.

The first phenomenon is general heat diffusion through conduction within a tissue. As will be described further below, the process of laser

ablation transfers energy in the form of photons to molecules in the tissue to be ablated where the energy is then converted into heat causing thermal damage to the tissue around it. Most tissues contain dominant light absorbing molecules for specific wavelengths of light as for example

5 shown by **FIGURE 10 (b)** mentioned above and discussed further below. These dominant light absorbing molecules absorb the bulk of the photons of the applied laser light and convert them into thermal energy which is then conducted by the surrounding molecules and/or remains with the dominant light absorbing molecules. The absorption of the thermal energy

10 by the surrounding molecules is dictated by their respective thermal conductivities. And the increase in temperature of the dominant light absorbing molecules is dictated by their (as a whole) specific heat capacity (individually this would be represented as mechanical energy such as an increased atomic vibrational energy).

15 Referring to **FIGURE 10 (c)** the temperature (thermal energy) profile of absorbed laser energy (in water) is shown with the dashed line representing the absorption length of the wavelength of laser light. The absorption length is the average penetrating distance photons of specific wavelength will travel in a medium until 63% ($1/e$) of their initial intensity is

20 absorbed by the medium. The temperature (thermal energy) profiles for durations of laser pulses of 10 μ s or more effectively show the temperature profiles for the first phenomenon, heat absorption under normal conditions. In this absorption regime the thermal energy is dissipated to the surrounding molecules as the thermal diffusion time (t_d) is less than the

pulse duration (t_p). The thermal diffusion time for tissues enduring laser ablation may be defined as:

$$t_d = \frac{1}{\kappa \mu_a^2}$$

Where κ is defined as

$$\kappa = \frac{K}{\rho c_s}$$

Where K is the thermal conductivity, ρ is the density, and c_s is the
 5 specific heat capacity.

The second phenomenon termed thermal confinement refers to specific scenarios where the pulse duration (t_s) of the laser is less than that of the thermal diffusion time (t_d). This is shown in **FIGURE 10 (c)** [Vogel, Alfred, and Vasan Venugopalan. "Mechanisms of pulsed laser ablation of
 10 biological tissues." Chemical reviews 103.2 (2003): 577-644.] for when the pulse durations are equal to or less than $3\mu s$. During this phenomenon as the light energy is absorbed and converted into thermal energy it substantially remains in the area (with the molecules) it was initially absorbed, effectively confining the heat energy to be diffused in that
 15 region. This is apparent from the normalized temperatures of the curves for pulse durations in the thermal confinement regime shown in **FIGURE 10 (c)** such as the curve for the 100ns pulse duration. This curve shows that nearly all of the thermal energy (temperature) is absorbed at the surface of the substance where the thermal laser ablation is applied. This
 20 results from the short duration of the pulse resulting in their not being enough time for the thermal energy to diffuse into the rest of the tissue as is apparent from the figure. Employing this phenomenon allows laser

ablation to be done in more accurate and confined regions providing greater accuracy with respect to the tissue to be ablated. Although **FIGURE 10 (c)** is provided for explanatory purposes a material with the thermal profile response shown may be chosen to replicate a tissue to be ablated with a similar thermal profile response during step **475** of the workflow shown in **FIGURE 4**. However it should be noted that this profile response property may be adjusted accordingly for tissues with lower water content such as grey matter in the brain which is typically composed of 80% water. It should further be noted that temperature response profiles such as the one shown in **FIGURE 10 (c)** (or with different axis providing similar information on characteristic thermal properties as outlined immediately below) may be acquired for tissues on which ablation is commonly performed. These responses may then be used to produce a laser ablation tissue phantom material with a similar temperature response profile to the tissues on which ablation is commonly performed that the laser ablation tissue phantom material is to replicate.

Thus to produce a laser ablation tissue phantom for use in step (**475**) of the workflow depicted in **FIGURE 4** the material should be ideally chosen such that it has a similar net thermal conductivity, net specific heat capacity and net thermal diffusivity to the tissue being replicated. The term "net" as used above refers to the thermal characteristics (such as conductivity and diffusivity) of the material as whole as opposed to its constituent molecule concentrations although this would also be a viable, albeit time consuming option.

The two commonly used wavelengths of typical laser ablation probes mentioned above (i.e. 980nm and 1064nm) are in the near-infrared range. Thus a material having a similar net light absorption coefficient to the tissue being replicated at these wavelengths would suffice in

5 substantially meeting the criteria regarding b)-(ii). The net light absorption may or may not refer to the light absorption (coefficient) of the tissue in its entirety as opposed to the light absorption (coefficient) of its constituent individual biomolecules (for example water or hemoglobin).

Referring to **Figure 10 (b)** the two typically used wavelengths are

10 depicted on the wavelength axis as **1000** and **1100** for the 980nm and 1064nm wavelengths respectively. Thus a material replicating a tissue comprising principally of water would have an absorption coefficient in accordance with the line **1200** when being used in a simulated procedure employing a 980nm laser ablation probe and in accordance with **1300**

15 when being used in a simulated procedure employing a 1064nm laser ablation probe. Although the mentioned absorption coefficients may suffice for some embodiments, generally they may or may not be altered as per the percentage of water content in a particular tissue. For example when a laser ablation tissue phantom material is used to replicate a tissue with

20 40% water content the light absorption coefficient of the material at the specific wavelength may be ideally chosen to be 40% of the light absorption coefficient **1200**. In other embodiments a proportionality constant may be applied to the scaling of the water content to provide the same net light absorption coefficient of the tissue being replicated (for

25 example for tissues with non-linear water content to light absorption

coefficient scaling) for example **(P)X%** where **P** is the proportionality constant and **X** is the water content of the tissue being replicated.

Furthermore although the water content of a tissue may be a dominant factor in determining the light absorption coefficient of the tissue in the infrared wavelength range other biomolecular factors must also be taken into consideration.

For example if the tissue being replicated is highly vascularized than the light absorption coefficient of hemoglobin / deoxyhemoglobin (for example as shown by the light absorption coefficient of the line **1400** at 980nm **1000**) in addition to the light absorption coefficient of water must be taken into consideration in determining the optimal light absorption coefficient for the material being used to replicate the tissue. For example if a 980nm wavelength laser ablation probe is applied to a tissue comprising of 50% vasculature and 50% water than the optimal light absorption coefficient of the material may be 50% of both the light absorption coefficients indicated by lines **1400** and **1200** as these are the intersection points of the 980nm line **1000** with the light absorption coefficient curves of water and hemoglobin as shown in

FIGURE 12 and **FIGURE 13** are provided to illustrate additional scenarios that commonly occur in laser ablation procedures that may be replicated through the addition of features of the laser ablation tissue phantom as disclosed herein. **FIGURE 11** shows the cross-sections about the plane **1105** of both Phantom G **1115** and Phantom A **1120**. The cross-section of Phantom G **1115** is used in **FIGURE 12** to describe the ablation step **475** of the workflow as it pertains to a simulated Glioblastoma tumor

laser ablation procedure executed on Phantom G. The trajectory **1200** to reach the target structure **720** shown in the left diagram **1225** of the figure is an arbitrary trajectory that may or may not be chosen in such a procedure depending on the specific anatomical orientation of the
5 (simulated) patients eloquent structures as per Phantom G. This diagram **1225** shows the state of the simulated Glioblastoma tumor laser ablation procedure prior to step **425** shown in the workflow of **FIGURE 4**.

The laser ablation probe may have multiple laser light emitters **805** on its distal end or a mechanical, pneumatic, electromechanical, electrical,
10 or any other type of assembly to allow for customizable ablative laser emission. The right diagram **1230** of **FIGURE 12** shows a simulated commonly performed Glioblastoma tumor laser ablation procedure on Phantom G wherein the laser ablation probe has been advanced to the target(s) of interest prior to step **465** in the workflow shown in **FIGURE 4**.
15 In the diagram **1230** the ablation of the Glioblastoma tumor **720** has begun and the ablated area of the tumor at this stage is highlighted by the segment **1205**.

As the simulated procedure progresses this ablated region **1205** increases in size until it reaches the boundary **1210** of the tumor as shown
20 in the bottom diagram **1235**. As is common with Glioblastomas this boundary **1210** may be highly vascularized or an edema having different optical properties resulting in a different response to the thermal laser ablation application in comparison to the main body of the Glioblastoma **720**. As per the description of light absorption properties illustrated above
25 in **FIGURE 10 (b)** the absorption properties of this boundary region **1210**

may highly depend on the dominant light absorption biomolecule for the particular wavelength(s) of light being applied by the laser ablation probe to the area.

Typically the tumor volume has a much higher ratio of water to
5 hemoglobin (and deoxyhemoglobin) than does the boundary area which is highly vascularized and thus has a higher ratio of hemoglobin (and deoxyhemoglobin) to water. Thus from the intersection of the 980nm line
1000 with the curves of water and hemoglobin in **FIGURE 10 (b)** it is apparent that the light absorption at the boundary **1210** would greatly
10 increase relative to the light absorption within the body of the Glioblastoma **720** (i.e. because the intersections of the line **1400** has a greater light absorption coefficient than the intersection of the line **1200**). During typically performed surgeries this is a common occurrence and the vasculature tends to form a pseudo heat boundary at which the ablation
15 intensity must increase in intensity to surpass.

The consequence of this occurrence is a desirable one as it increases the steepness of the gradient at the boundary where the tumor ends. Thus when performing such a Glioblastoma tumor laser ablation procedure this occurrence is commonly leveraged by the surgeon to
20 improve the results of the procedure by reducing the left over margins at the boundary. Therefore when producing a laser ablation tissue phantom as disclosed herein in an embodiment it may be advantageous to provide an additional structure in the form of a boundary partially or entirely encompassing a tissue replicating structure. This boundary having
25 different light absorption properties than the structure it's encompassing.

By providing this feature in the laser ablation tissue phantom as disclosed herein a simulated Glioblastoma tumor laser ablation procedure may more closely replicate such an occurrence for a training surgeon and/or a user of the laser ablation tissue phantom.

5 It should be noted that the boundary region being highly vascularized as described above was given as an example only and other boundary regions being replicated such as regions plagued with edema may also be benefitted from such an additional replicating structure. In addition if an edema is replicated it may suffice to provide a liquid barrier
10 as opposed to a solid one by filling the area around the replicated Glioblastoma with a liquid with similar properties to edema. Such a liquid could be injected into a cavity built into the laser ablation tissue phantom as disclosed herein for example such as the cavities **515** surrounding the Glioblastomas built into the main body of the tissue laser ablation phantom
15 **300** shown in diagram **510** of **FIGURE 5**. Other boundary regions to be replicated may be the ventricles of the brain formed with artificial CSF.

FIGURE 13 shows the same ablation step **475** of the workflow described above as it pertains to a simulated Glioblastoma tumor laser ablation procedure executed on Phantom G as shown in **FIGURE 12**. The
20 difference being in this scenario the Glioblastoma tumor being ablated is asymmetrical. To ablate such an asymmetrical tumor when performing a Glioblastoma tumor laser ablation procedure a surgeon must then use specific features provided by their laser ablation probe or other medical instrument. In these scenarios it is common to use a laser ablation probe
25 which can be aimed to ablate the tumor in the chosen direction of the laser

ablation probe. Diagram **1320** of **FIGURE 13** illustrates such a scenario, where an asymmetrical tumor **1320** is to be ablated by the surgeon. The portion outlined by the dashed area **1300** is highlighted in the two diagrams below (**1325** and **1330**) showing the progression of such a procedure. The first diagram **1325** shows the ablation as it is being performed in one arm of the asymmetrical tumor wherein the probe is being directionally aimed **1302** in the direction of the bulk of the tumor at that arm leaving an ablated area **1315** as the procedure progresses. The second diagram **1330** shows a further progression of the procedure where an alternate laser is employed to ablate the bulk of the other arm of the asymmetrical tumor. Given that surgeons may be required to perform ablation procedures on asymmetrical tumors in some scenarios it would thus be advantageous to produce the laser ablation tissue phantom as disclosed herein with Glioblastoma replicating structures being of asymmetrical shape. As a result such a feature may improve a surgeons training in performing the Glioblastoma tumor laser ablation procedure as described herein.

Referring again to **FIGURE 4** the next stage **470** occurs in a loop with the previous step **475** in the workflow. This stage **470** in both procedures is to monitor a thermometry map of the patient as the ablation probe is applying the laser to the target tissue and to progressively estimate the boundary of the ablated lesion to assure it does not surpass the boundary of the target tissue. **FIGURE 14** shows an exemplary progression of an ablation procedure and the corresponding MR thermometry images of the patient as the procedure progresses. The

figure is provided by the paper [Willie, Jon T., et al. "**Real-time magnetic resonance-guided stereotactic laser amygdalohippocampotomy for mesial temporal lobe epilepsy.**" *Neurosurgery* 74.6 (2014): 569-585].

In general MR thermometry works by measuring the proton
5 resonance frequency shift in protons of water molecules of a tissue to
determine their temperature. The proton resonance frequency of the
protons in water molecules is dependent upon the water molecules
temperature. As a result the temperature of the water molecule may be
inferred from its proton resonance frequency that may be detected by an
10 MR scan of the patient. The MR images provided in **FIGURE 14** are time
stamped at 25s, 75s, and 135s during the laser ablation procedure being
performed providing a visual cue of the temperature of the tissue about the
region being ablated. The figure also contains a diagram showing the
temperature of the thermal ablation area over the elapsed time of the
15 procedure. This diagram also provides information regarding the
temperatures of the ablated area in accordance with the time stamped
images. Using this technique of simultaneously imaging with MR
thermometry and performing laser ablation on the patient intraoperatively
allows for the surgeon to obtain real time feedback as per the progression
20 of their surgery and allows them to adjust their plan accordingly if any
unforeseen circumstances arise.

To employ the laser ablation tissue phantom as disclosed herein in
the replication of this MR thermometry monitoring step **470** requires that
the phantom have features such that:

- a) the laser ablations tissue phantom may be imaged using MR thermometry, and
- b) the laser ablation tissue phantom has a water content high enough such that it may be imaged using MR thermometry during a simulated laser ablation procedure.

The exemplary laser ablation tissue phantom shown in the right frame **510** of **FIGURE 5** is provided again in **FIGURE 15** depicting it in use during step **470** of the workflow shown in **FIGURE 4**. The right frame of **FIGURE 15** depicts an embodiment of the phantom under MR thermometry imaging at the ablation location(s) provided as an example embodiment only where the red area **1505** is indicative of temperatures over 60°C outlining the area of immediate thermal necrosis of tissue. The yellow area **1515** is indicative of temperatures between 43°C and 59°C where thermal damage is time dependent and the beige area **1520** is indicative of temperatures lower than 43°C but higher than body temperature where thermal exposure to the cells wouldn't cause them to sustain any permanent damage. Using this MR thermometry temperature profile an ablation zone estimate may be made by either a computer (as shown as section **1500** in the left side of **FIGURE 15**) and/or a user on the MR thermometry image set. This zone may then be transferred to an alternate image set of the patient using a different protocol or modality. The transfer may be done directly given that the alternate image set is registered with the MR thermometry image set. The transfer may allow for an overlaid area to be outlined on the alternate image identifying on that image the estimated extent of the ablation. This may allow the surgeon to

use the information available in the alternate image to judge if the extent of the ablated area are sufficient for the procedure.

During a laser ablation procedure, in addition to estimating the extent of the ablation and assuring it does not cross the target regions
5 boundary, it is common to set markers at anatomical positions on a patient's scan such that their temperature may be monitored to avoid unintended thermal damage. For example, when performing an amygdalohippocampotomy it is typical for the surgeon to place a virtual position marker on the optic nerve such as **725** shown in the right hand
10 side of **FIGURE 7** to track its temperature using MR thermometry or thermography. If during the ablation procedure the position markers temperature rises above a certain threshold for example 43 °C when potential damage may be incurred by the optic nerve the ablation probe will automatically turn off. This safety feature allows the surgeon to protect
15 vital eloquent brain structures while maximizing the extent of the desired ablation.

In order to employ the laser ablation tissue phantom as disclosed herein in replicating this feature the phantom may be designed with not only MR visible ablation target anatomical structures such as a
20 Glioblastoma, amygdala, and a hippocampus but also with important anatomical structures to be avoided such as the optic tract, motor cortex, or language centers.

Referring to the workflow depicted in **FIGURE 4** the final stages **450** and **445** in both procedures is to remove the laser ablation probe and scan
25 the patient to verify how successful the ablation was.

Thus in order to employ the laser ablation tissue phantom as disclosed herein in the replication of this step requires that the phantom have features such that the success of the surgical ablation may be measured post ablation. Some features that may provide a measure of the relative progression or success of a simulated surgical procedure such as that depicted in **FIGURE 4** will be further described as follows.

One way to produce such a measure of the relative progress of success is to fabricate the target structures or surrounding structures of a laser ablation responsive material. This material being designed such that a measurable/detectable change in properties of the material would result from exposure to an application of laser ablation. The resulting changes in the laser ablation responsive materials could then be interrogated and a measure of success of the procedure derived from the results.

Following a simulated laser ablation medical procedure the laser ablation tissue phantom having ablation responsive materials may be interrogated in one or more ways, two of which will be provided as follows for examples to determine the efficacy of the mock laser ablation procedure. The first manner in which the laser ablation tissue phantom may be interrogated is by scanning the patient using an imaging modality that would allow the user to see the subsurface structures of the laser ablation tissue phantom. In an embodiment, these structures would be the target structures or the surrounding structures at least one of which may be formed from a laser ablation responsive material. A second manner in which the laser ablation tissue phantom may be interrogated is by dissecting the laser ablation tissue phantom and observing or removing

the section of mimic tissue which were targeted by the laser ablation procedure. Some exemplary descriptions of laser ablation responsive materials and their use in concordance with the interrogation methods described will be provided as follows.

5 **FIGURE 16** illustrates some exemplary laser ablation tissue phantom structures that have undergone property changes due to exposure to laser ablation during a simulated laser ablation procedure.

 The scan **1620** on the right hand side of **FIGURE 16** shows an embodiment of a tissue ablation phantom wherein two artificial
10 Glioblastoma tumor structures **1624** and **1622** made of laser ablation responsive materials have been ablated in a simulated laser ablation procedure. For illustrative purposes this exemplary scan includes two separate laser ablation responsive materials for each of the artificial tumors **1624** and **1622**.

15 In this embodiment the first laser ablated artificial tumor **1624** formed of a laser ablation responsive material has properties such that on exposure to an applied ablation laser the artificial tumor melts leaving a cavity in the laser ablation tissue phantom where the artificial tumor had been ablated. This may be seen at the area **1624** of the post-procedure
20 scan **1620** indicative of a cavity because of its signal (or lack thereof) being characteristic of air, such as the area **1625** outside the laser ablation tissue phantom body in the scan **1620**. Thus a comparison of the artificial tumor **1624** area on the post-procedure scan **1620** with the artificial tumor area on the pre-procedure scan should be reflective of the success of the
25 procedure based on the size and location of a cavity. An example of laser

ablation responsive material that melts on exposure to laser ablation would be a paraffin wax (melting point from 50 to about 75 °C) or a polymer such as poly(ϵ -caprolactone), poly(ethylene oxide), or polyvinyl acetate with literature melting point ranges of between about 60 to about 65 °C.

5 In this embodiment the second laser ablated artificial tumor **1622** formed of a laser ablation responsive material has properties such that on exposure to an applied ablation laser the artificial tumor density decreases. In general a decrease in density of material in an MR, ultrasound, or any type of imaging with a characteristic signal strength dependence on
10 density may result in a reduction of signal acquired from that material. Thus if the artificial ablated tumor **1622** formed of the laser ablation responsive material has a lower density and corresponding reduction in signal strength than its original density and signal strength before a simulated laser ablation procedure this should be reflective of the success
15 of the procedure based on the size and location of the area with a reduced signal strength (such as **1622** shown in **Figure 16**). An example embodiment of a laser ablation responsive material that reduces density on exposure to laser ablation as described above may be a hydrogel containing a temperature sensitive cross-linker such as PVA cross-linked
20 with borax or Poly(2-acrylamido-2-methyl-1-propanesulfonic acid) cross-linked with N,N'-methylenebisacrylamide^{xx} (E. A. Karpushkin, "Anionic Polymer Hydrogel Degradation by Ascorbic Acid" Russian Journal of General Chemistry, 2013, 83, 1515-1518) where at higher temperatures the hydrogel will convert back to a solution irreversibly.

Referring to **FIGURE 16** the diagram **1600** shows a dissected laser ablation tissue phantom embodied in the form of a brain after a simulated laser ablation procedure. Where the simulated laser ablation procedure performed, targeted the artificial hippocampus **1604** and amygdala **1606** structures in the laser ablation tissue phantom. In this embodiment the targeted structures (hippocampus **1604** and amygdala **1606**) are formed of a laser ablation responsive material that changes chromaticity (colour) on exposure to a laser ablation application. The area that was ablated by the laser ablation procedure in this embodiment can be seen as the area **1602** in the diagram and is characterized by a change in chromaticity (colour) in comparison to its surrounding structures (i.e. the amygdala **1606** and the hippocampus **1604**). Thus by analytically observing the dissected laser ablation tissue phantom **1600** the success of the laser ablation procedure may be inferred from the volume of pre-procedure target areas that remained at their original chromaticity (i.e. were not ablated and thus did not change chromaticity). It should be noted that not only target structures but surrounding structures such as the main body of the brain mimic material **300** may also be fabricated with a laser ablation sensitive material, such as a material that changes chromaticity as described, in order to allow the training surgeon to infer the amount of peripheral damage that has been potentially done. A nonlimiting example embodiment of a laser ablation responsive material that changes chromaticity on exposure to laser ablation as described above would be a material containing an irreversible thermochromic pigment (i.e. OliKrom smart pigments) that is typically used for thermal mapping that will change

colour as the temperature increases reaching a maximum colour change at the desired temperature (50-80 °C).^{xx} (A Seeboth, et al. "Thermotropic and Thermochromic Polymer Based Materials for Adaptive Solar Control". *Materials*, **2010**, 3, 5143-5168.) The material incorporating the pigment
5 may be a hydrogel of various densities, or a viscous solution. Another example is the use of hydrogels that can achieve reversible color change by adding suitable pH sensitive indicator dyes in combination with tensides. This thermochromic behavior is based on the interaction between the dye's molecules and the hydrogel's micro-environment.

10 Another example is a polymer blend containing dyes that have an irreversible colour change once the melt temperature of the blend has been reached.^{xx} (A Seeboth, et al. "Thermochromic Polymers- Function by Design" Chem Reviews, 2014, 114, 3037-3068) (Page 3055 explains polymer melt blends).

15 Referring to **FIGURE 16**, element **1610** shows a dissected laser ablation tissue phantom embodiment where the target structure has been removed from the surrounding structures of the phantom. In this embodiment the targeted structure (artificial Glioblastoma) is formed of a laser ablation responsive material that changes chemical properties such
20 that it becomes dissolvable by a particular solution after exposure to a laser ablation application. The volume of the target structure that was ablated by the simulated procedure in this embodiment of the laser ablation tissue phantom can be seen as the area **1614** in the diagram and is characterized by a change in dissolvability in comparison to the
25 unexposed segment of the remaining target structure **1612**. Given the

change in chemical properties of the exposed area the target structure may be bathed in a solution to dissolve away any area that had been exposed to the ablation laser leaving behind the mass of target structure that had not been exposed. Thus by comparing this remaining mass of

5 target structure with the original mass of the target structure the success of the simulated ablation procedure may be determined quantitatively. An example embodiment of a laser ablation responsive material that changes its chemical properties such that it becomes dissolvable upon illumination from a laser ablation application would be a polymer hydrogel with a

10 photosensitive cross-linker that will produce a water-soluble polymer after it has been exposed to light at the desired wavelength.^{xx} (R. P. Narayanan "Photodegradable Iron(III) Cross-Linked Alginate Gels" Biomacromolecules, 2012, 13, 2465-2471).

In general any material changing properties after exposure to laser

15 ablation application may suffice for use as a target or surrounding structure in an embodiment of the laser ablation tissue phantom as disclosed herein given the phantom may be fabricated with the material. Furthermore the success of a laser ablation procedure may be determined quantitatively in the case where measurable metrics are provided. Such as when

20 determining the success of the procedure by comparing a pre-procedure and post-procedure weight in the case of the dissolvability changing laser ablation responsive material target or surrounding structure. Or a volume in the case of the melting or density changing laser ablation material target or surrounding structure. For example if 80% of the desired volume of the

25 artificial tumor was ablated they may conclude that the simulated laser

ablation procedure was 80% successful or if 80% of the desired volume was ablated but 10% of undesired volume was ablated they may conclude the simulated laser ablation procedure was 70% successful.

It should be noted that these measures of success of a surgery are being provided as examples only and should not be construed as limiting and may be defined arbitrarily by any user of the laser ablation tissue phantom disclosed herein. The success of a laser ablation procedure may also be determined qualitatively in the case where qualitative metrics are measured such as when determining the success of the procedure by comparing a pre-procedure and post-procedure amount of tumor that has changed colour in the case of the chromaticity changing laser ablation responsive material target or surrounding structure.

In addition to embodiments where the laser ablation tissue phantom takes the form of a brain, in some embodiments the laser ablation tissue phantom as disclosed herein may take the form of other anatomical parts for other anatomical procedures. For example when performing a Facet nerve laser ablation as shown in **FIGURE 17**, the phantom may replicate spinal bone surrounded by the soft and nervous tissue relating to the spine. **FIGURE 17** shows a cross section of such a laser ablation phantom during a Facet nerve laser ablation. In the figure a laser ablation probe **800** is inserted through the ligaments of the spine and has gained access to the Facet **1702** on which the Facet nerve **1700** lies. In order to complete the procedure the Facet nerve must be ablated such that it no longer functions. Once in place the laser **800** may be activated forming an

ablation region **1706** around the tip **805** of laser **800** encompassing the peripheral Facet nerve **1700**.

FIGURE 18 illustrates a side view of the phantom in **FIGURE 17** for further clarification. In addition to the embodiment of the laser ablation tissue phantoms provided in **FIGURES 17** and **18**, other anatomical laser ablation tissue phantoms may include a prostate phantom. It should be noted that all of the features of the laser ablation tissue phantom mentioned above may be applied to any of the laser ablation tissue phantoms described herein. In doing so it should also be noted that all of the requirements of the features given above such as tissue density or light absorption coefficients are given as examples only for the tissues described herein and are not to be construed as limiting. Furthermore when applying these features or equivalent features individually or in any combination thereof to laser ablation tissue phantoms of alternate anatomical parts, correct information regarding those anatomical parts with respect to the mentioned features may be acquired and used to provide applicable requirements to produce a laser ablation tissue phantom of that alternate anatomical part. Some examples of correct information may be the bone densities of the spine for the spinal phantom as shown in **FIGURE 18**. Another example may be the optical absorption spectra, of bone and nerves located in the spine, or tumor tissue formed on a prostate.

While the Applicant's teachings described herein are in conjunction with various embodiments for illustrative purposes, it is not intended that the applicant's teachings be limited to such embodiments. On the

contrary, the applicant's teachings described and illustrated herein encompass various alternatives, modifications, and equivalents, without departing from the embodiments, the general scope of which is defined in the appended claims.

- 5 Except to the extent necessary or inherent in the processes themselves, no particular order to steps or stages of methods or processes described in this disclosure is intended or implied. In many cases the order of process steps may be varied without changing the purpose, effect, or import of the methods described.

10

THEREFORE WHAT IS CLAIMED:

1. A tissue phantom for performing a stereotactic simulated laser ablation surgical procedure on an anatomical structure of an organism, comprising:
 - a tissue phantom made of a material similar to the anatomical structure of the organism; and
 - a laser responsive material embedded in at least a portion of said tissue phantom, wherein said laser responsive material comprises any one or combination of:
 - (a) a hydrogel containing pH sensitive indicator dye in combination with tensides and exhibits thermochromatic behaviour, or
 - (b) a polymer hydrogel with a photosensitive cross-linker that produces a water-soluble polymer after said polymer hydrogel has been exposed to light at a preselected wavelength,wherein said laser responsive material exhibits a preselected response when irradiated by a laser beam during the simulated laser ablation surgical procedure.
2. The tissue phantom according to claim 1 wherein said at least a portion of said tissue phantom is mimicking one or more preselected parts of said anatomical structure, wherein said laser responsive material in said preselected parts is selected to behave in a preselected manner when being irradiated by a laser beam during the simulated laser ablation surgical procedure.

3. The tissue phantom according to claim 2 wherein said laser responsive material is selected to mimic a response of said one or more preselected parts of said anatomical structure during an actual laser ablation surgical procedure.
4. The tissue phantom according to claim 3 wherein said one or more preselected parts include any one or combination of healthy anatomical tissue making up the anatomical structure, anomalous tissue present in the anatomical structure, and bodily fluids present in the anatomical structure.
5. The tissue phantom according to claim 4 wherein said anomalous tissue is one or more tumors present in the anatomical structure.
6. The tissue phantom according to claim 2 wherein said laser responsive materials are made of materials which exhibit light absorption characteristics of said one or more preselected parts.
7. The tissue phantom according to claim 2 wherein said laser responsive materials are made of materials which exhibit thermal characteristics of said one or more preselected parts.
8. The tissue phantom according to any one of claims 1 to 7 wherein said laser responsive material embedded in at least a portion of said tissue phantom exhibits properties selected to mimic any one or combination of feel, movement, temperature, optical, physical and chemical response to a laser ablation application of the anatomical tissues the laser responsive material is mimicking.

9. The tissue phantom according to any one of claims 1 to 8 wherein said laser responsive material embedded in at least a portion of said tissue phantom exhibits properties selected to mimic any one or combination of directionality, density, optical absorption, heat transmittance, heat conductance properties, electrochemical properties, thermochemical properties, and elasticity of the anatomical tissues the laser responsive material is mimicking.

10. The tissue phantom according to any one of claims 1 to 9 wherein said laser responsive material is any one or combination of waxes, polymers, thermochromic polymer blends, hydrogels, temperature sensitive hydrogels, and photodegradable hydrogels.

11. The tissue phantom according to any one of claims 1 to 10 wherein said preselected response is any one or combination of change of state from solid to liquid, change of state from solid to vapor, change of color, change in shape, and change in density.

12. The tissue phantom according to any one of claims 1 to 9 wherein said laser responsive material is a hydrogel containing a temperature sensitive cross-linker constituent.

13. The tissue phantom according to claim 12 wherein said hydrogel containing a temperature sensitive cross-linker constituent comprises polyvinyl alcohol (PVA) cross-linked with borax and Poly(2-acrylamido-2-methyl-1-propanesulfonic acid) cross-linked with N,N'-methylenebisacrylamide.

14. The tissue phantom according to any one of claims 1 to 9 wherein said laser responsive material is a polymer blend containing one or more dyes that undergo an irreversible colour change once a melt temperature of the blend has been reached under illumination by the laser light.

15. The tissue phantom according to any one of claims 1 to 9 wherein said laser responsive material is a hydrogel having a preselected density containing an irreversible thermochromic pigment which changes colour as temperature increases reaching a maximum colour change at a temperature in a range from about 50°C to about 80°C.

16. The tissue phantom according to any one of claims 1 to 9 wherein said laser responsive material is a solution having a preselected viscosity containing an irreversible thermochromic pigment which changes colour as temperature increases reaching a maximum colour change at a temperature in a range from about 50°C to about 80°C.

17. The tissue phantom according to any one of claims 1 to 16 wherein said tissue phantom is a life sized tissue phantom of the anatomical structure of the organism.

18. The tissue phantom according to any one of claims 1 to 17 wherein said tissue phantom is a life sized tissue phantom of a brain of a human being.

19. The tissue phantom according to claim 18 wherein said tissue phantom of a human brain is a brain phantom of a human patient produced based on preoperative imaging of the human patient's brain.

20. The tissue phantom according to any one of claims 1 to 17 wherein said tissue phantom is a life sized tissue phantom of a section of a human patient's spine.

21. The tissue phantom according to claim 20 wherein said section of a human patient's spine includes spinal bone mimic material surrounded by soft and nervous tissue mimic material relating to the spine.

22. The tissue phantom according to claim 20 or 21 wherein said section of a human patient's spine is produced based on preoperative imaging of the human patient's brain.

23. The tissue phantom according to any one of claims 1 to 16 wherein said tissue phantom is a life sized tissue phantom of a selected anatomical structure of a non-human animal.

24. The tissue phantom according to claim 23 wherein said tissue phantom of selected anatomical structure is produced based on preoperative imaging of the selected anatomical structure.

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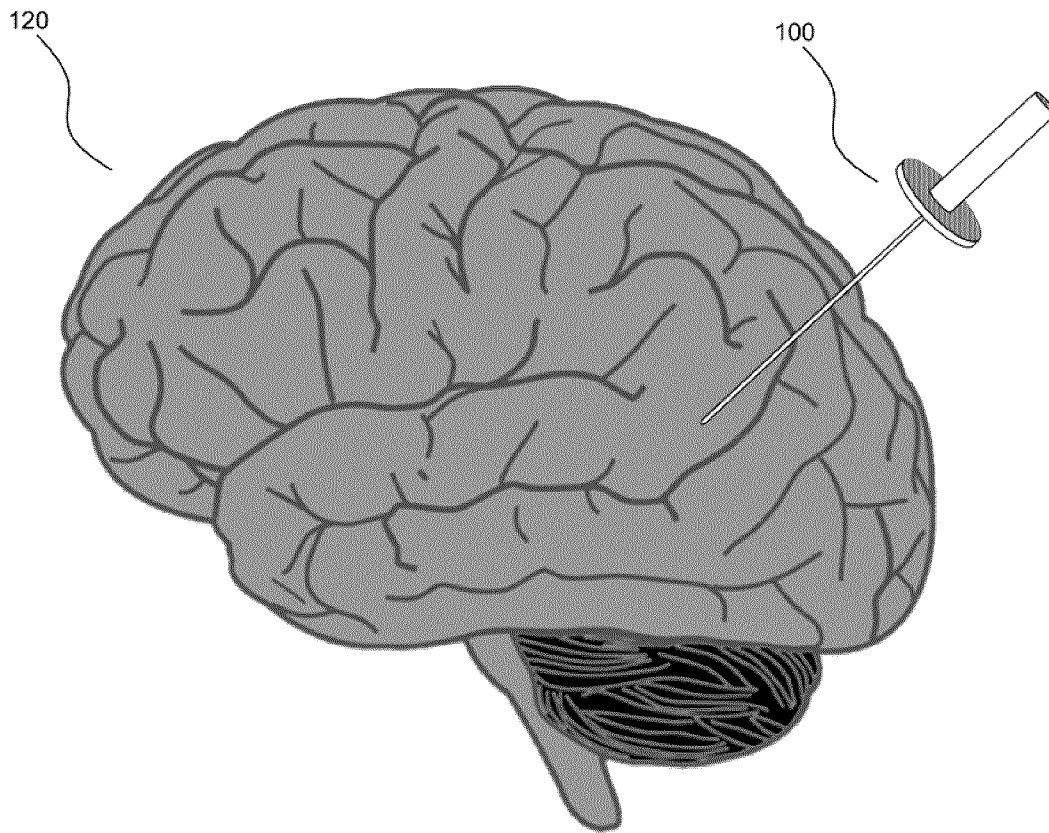


FIGURE 1

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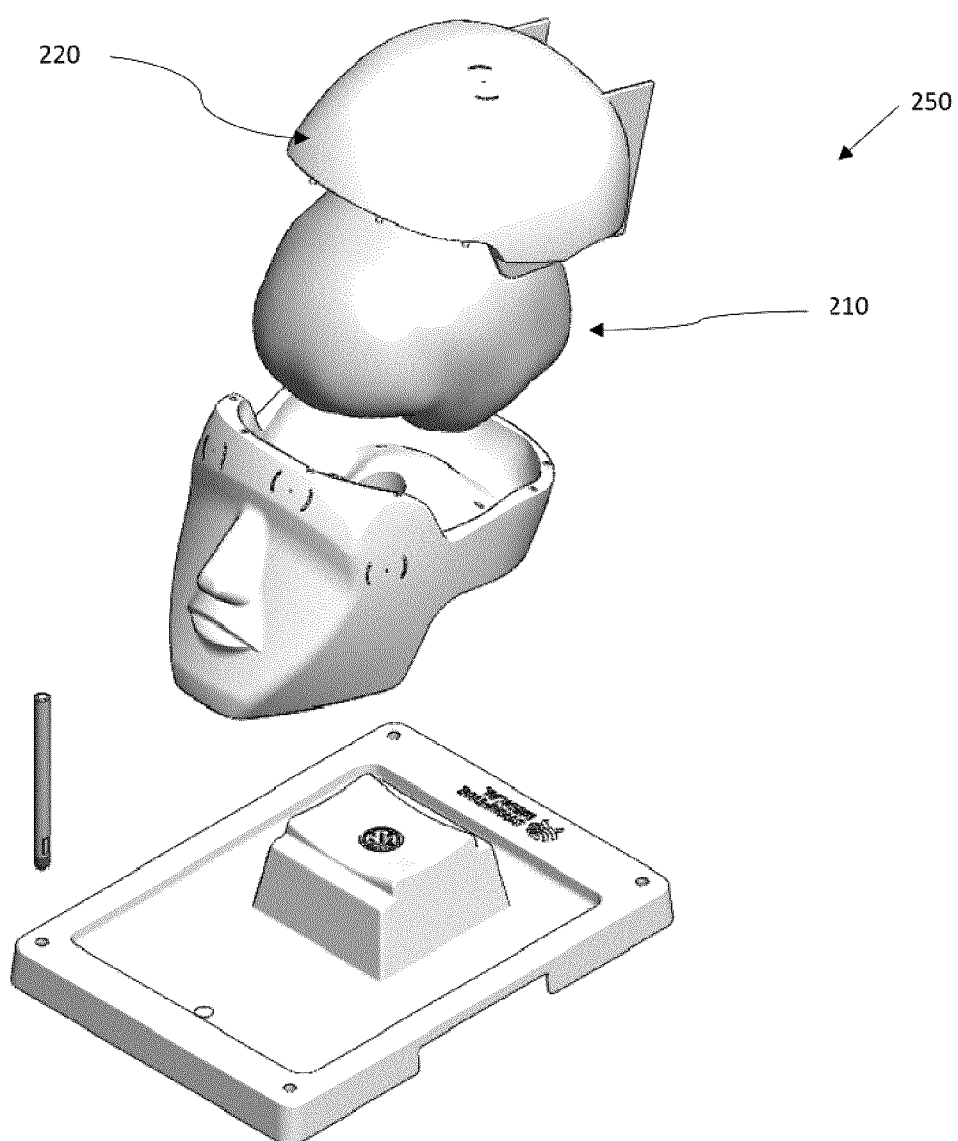


FIGURE 2

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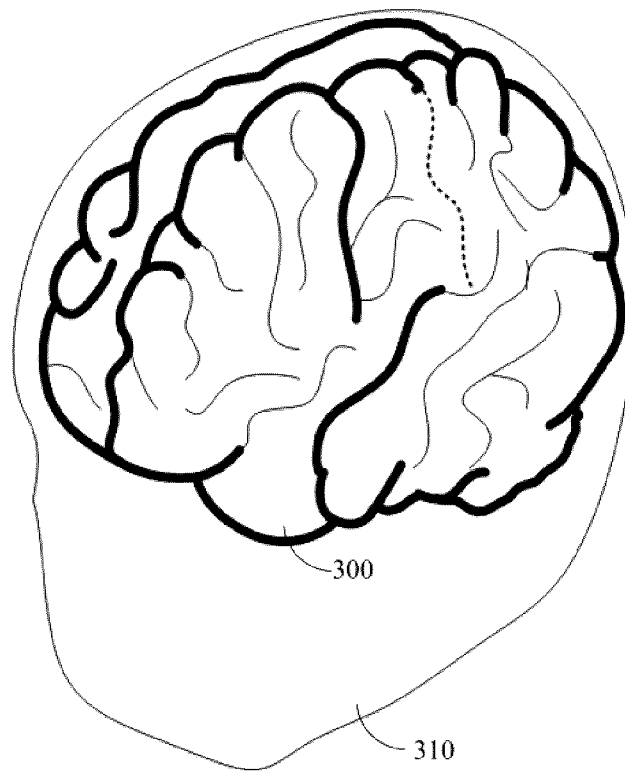


FIGURE 3

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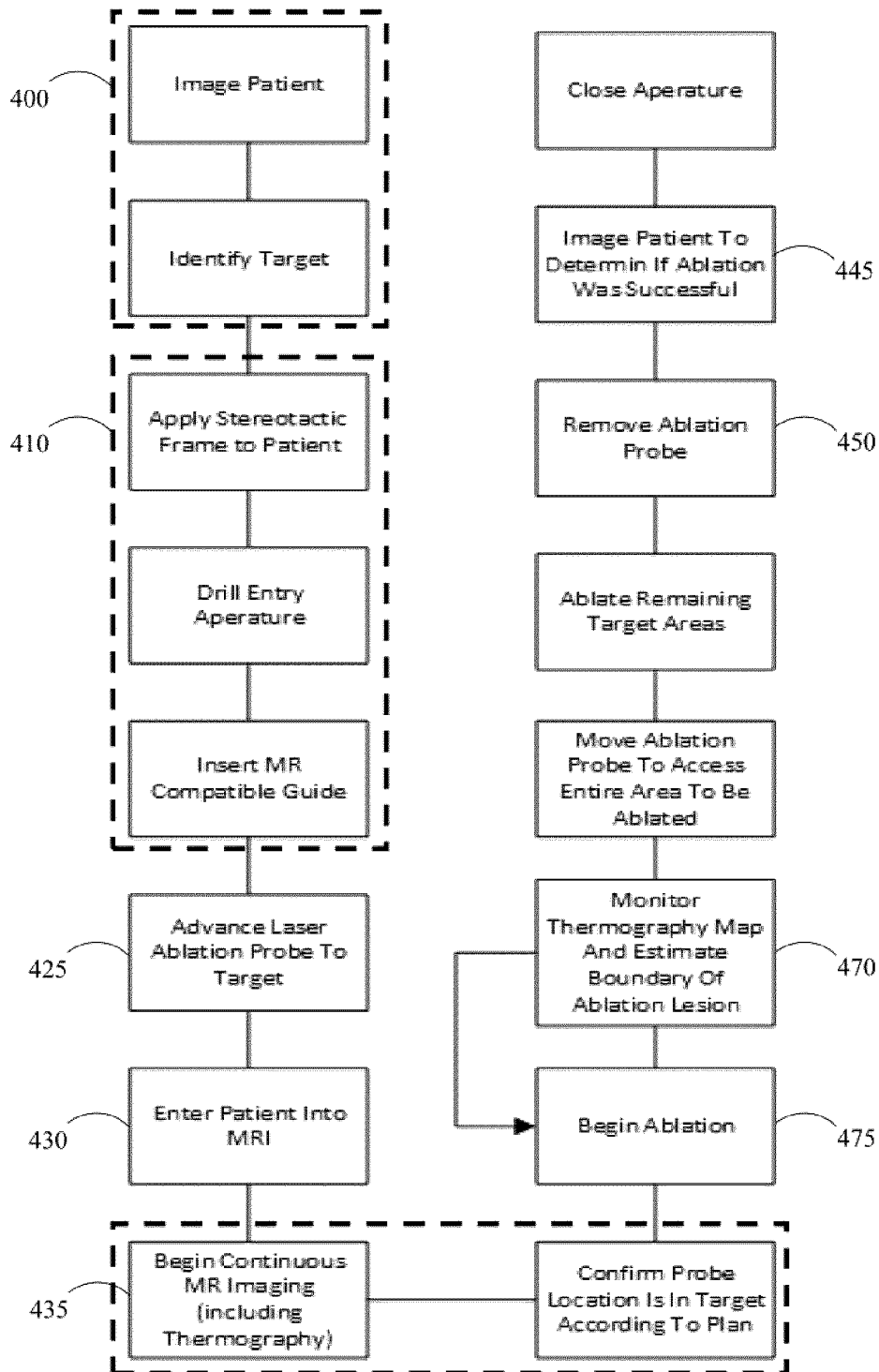
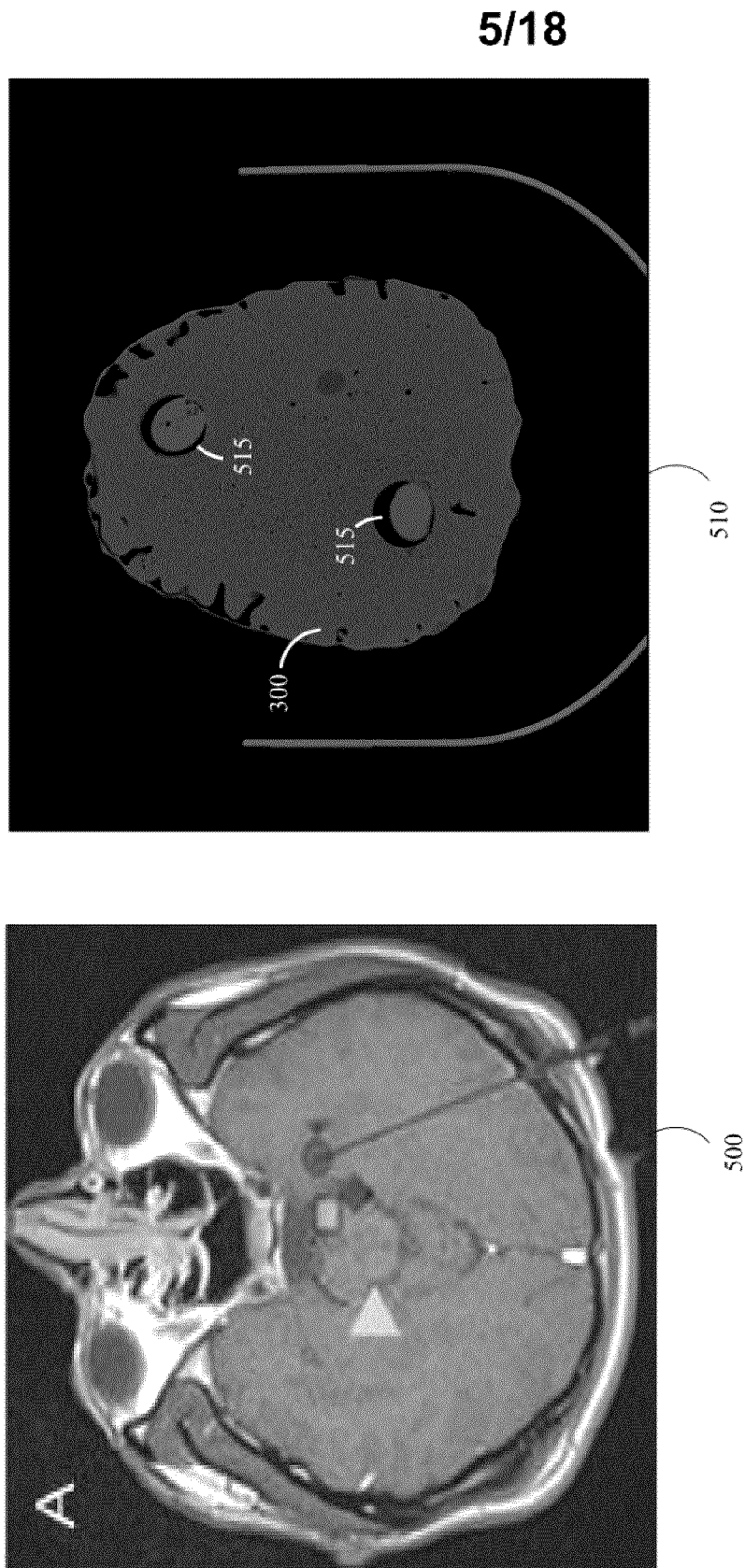


FIGURE 4

**FIGURE 5**

Willie, Jon T., et al. "Real-time magnetic resonance-guided stereotactic laser amygdalohippocampotomy for mesial temporal lobe epilepsy." *Neurosurgery* 74.6 (2014): 569-585.

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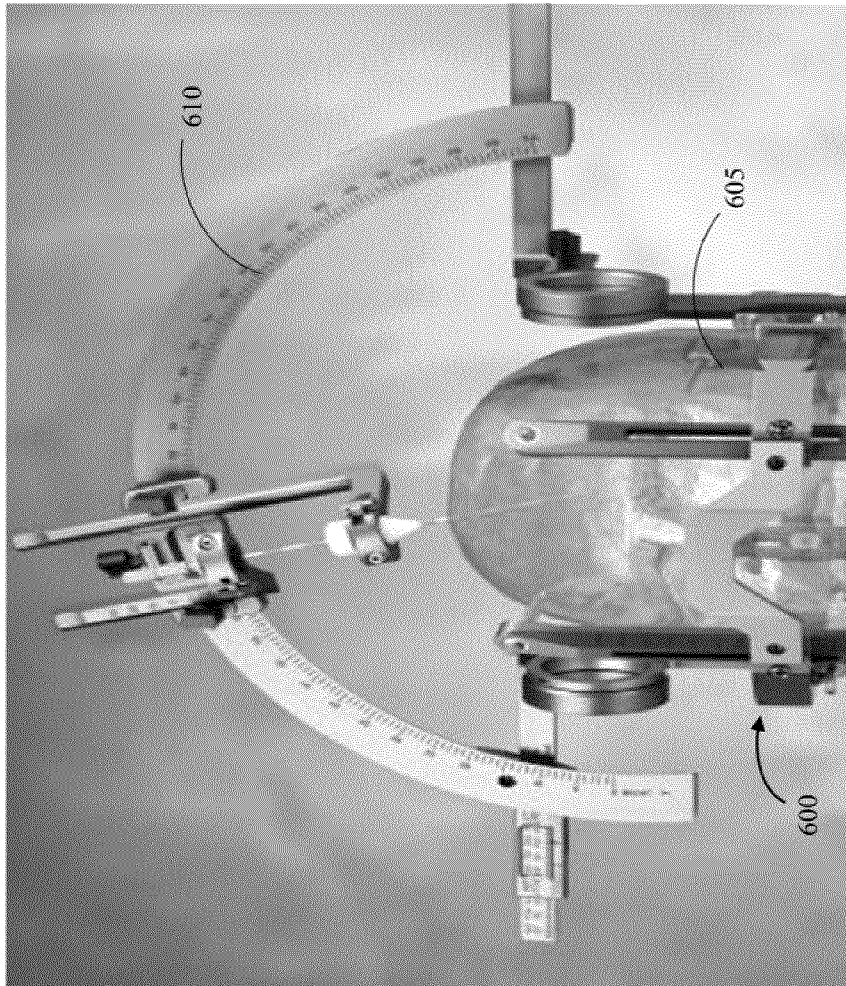
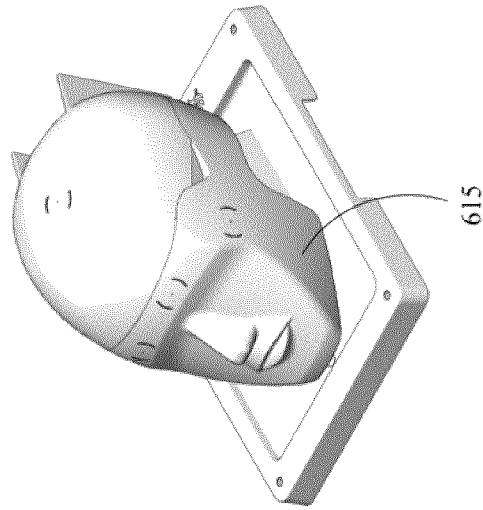


FIGURE 6

[*"Elekta Neuroscience in Hong Kong."* Elekta Oncology Neuroscience Blog. N.p., n.d. Web. 27 Jan. 2015.]

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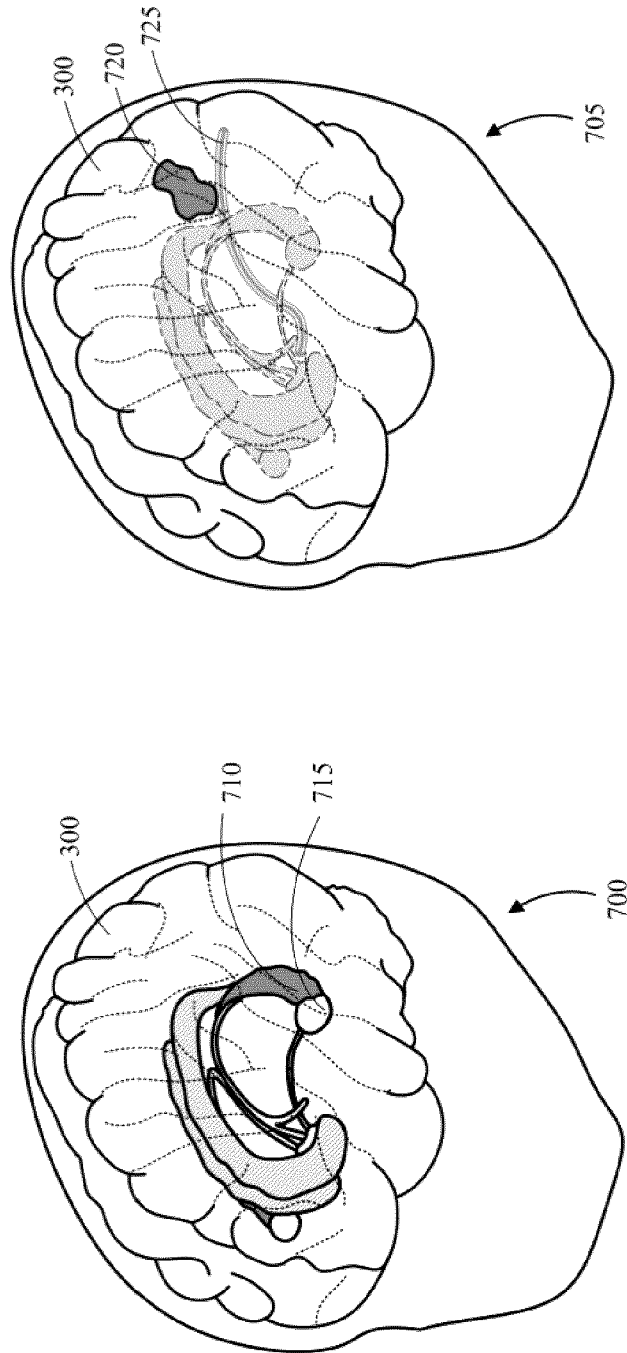


FIGURE 7

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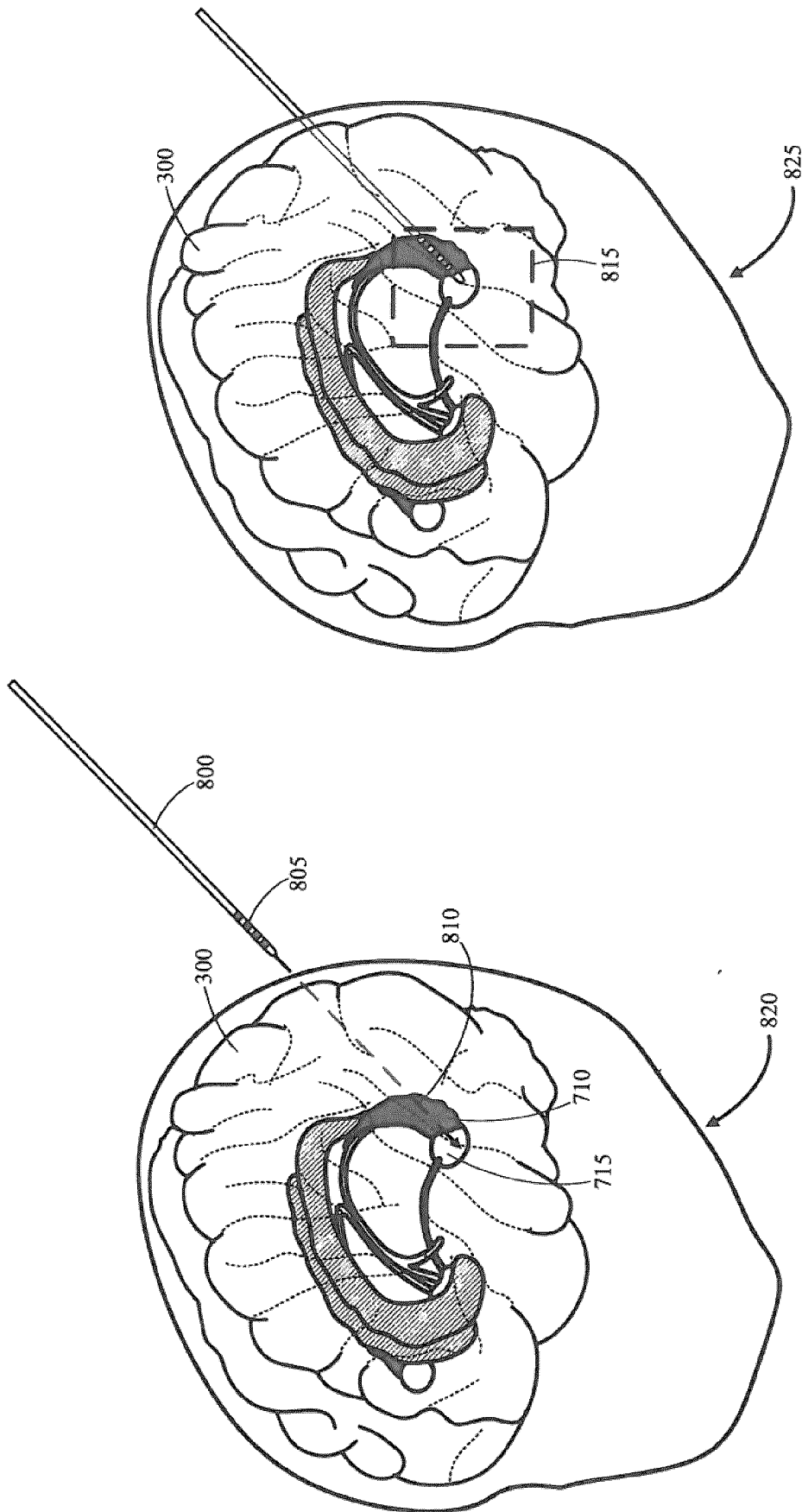


FIGURE 8

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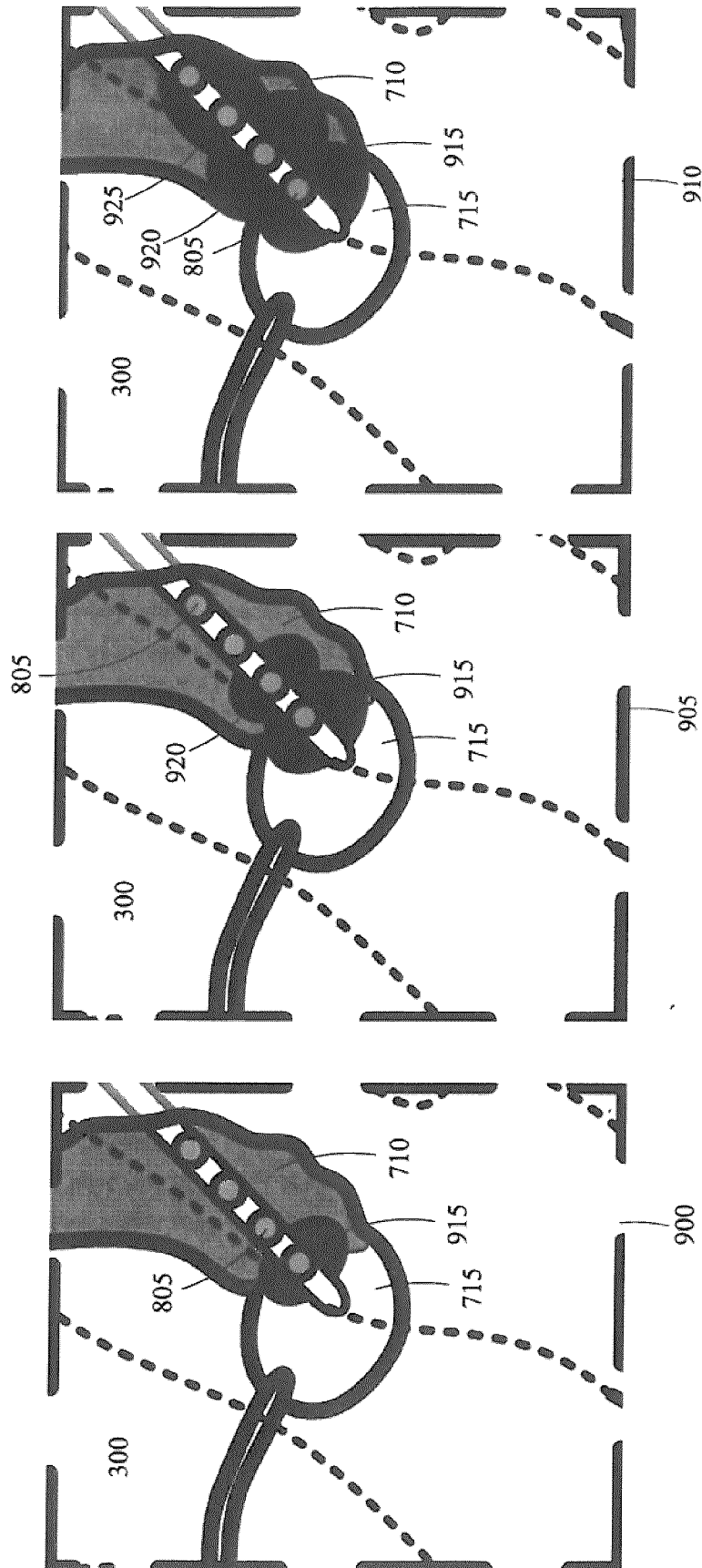


FIGURE 9

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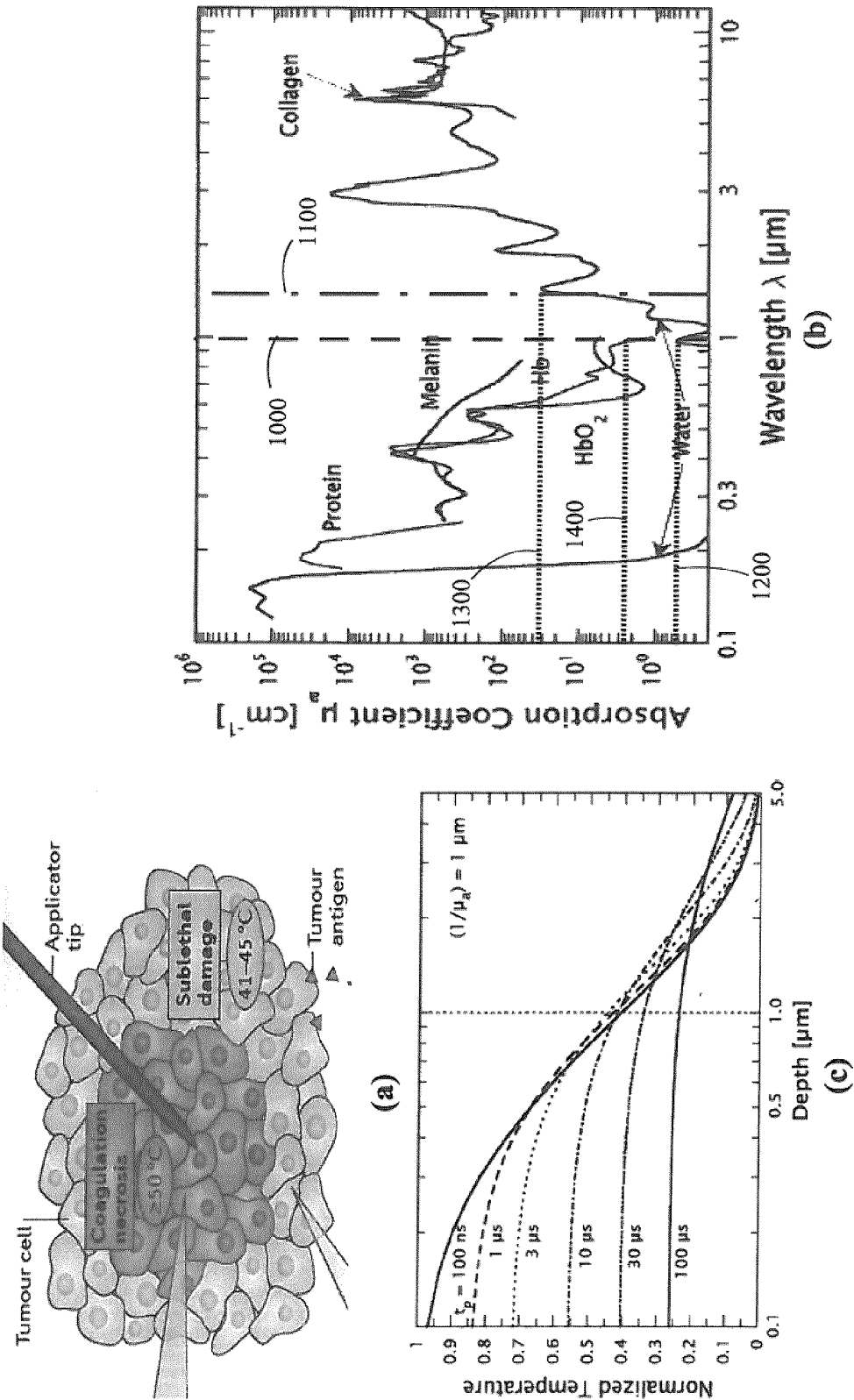


FIGURE 10

- (a) [Chu, Katrina F., and Damian E. Dupuy. "Thermal ablation of tumours: biological mechanisms and advances in therapy." *Nature Reviews Cancer* 14.3 (2014): 199-208.]
- (b) [Vogel, Alfred, and Vasan Venugopalan. "Mechanisms of pulsed laser ablation of biological tissues." *Chemical reviews* 103.2 (2003): 577-644.]

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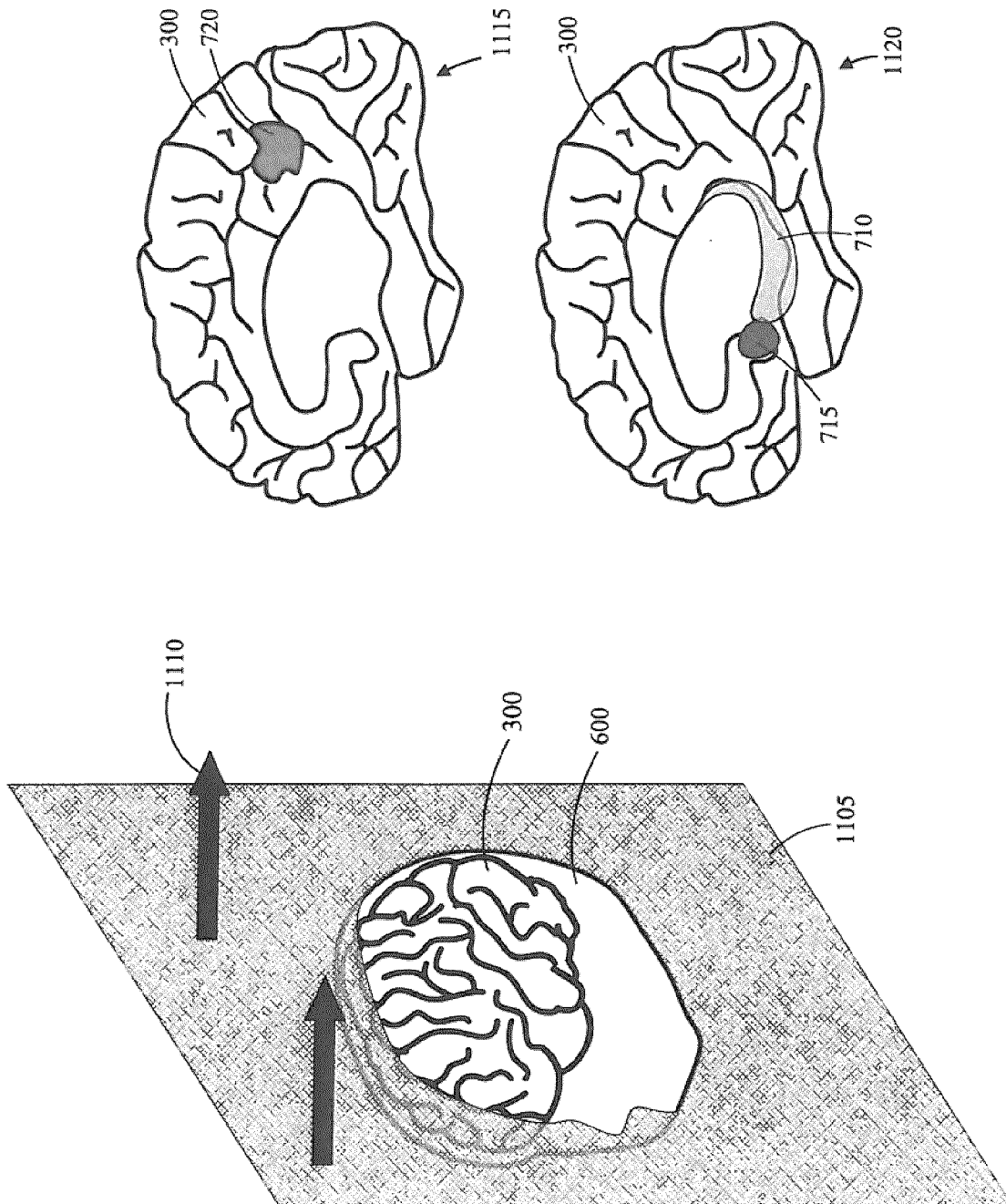


FIGURE 11

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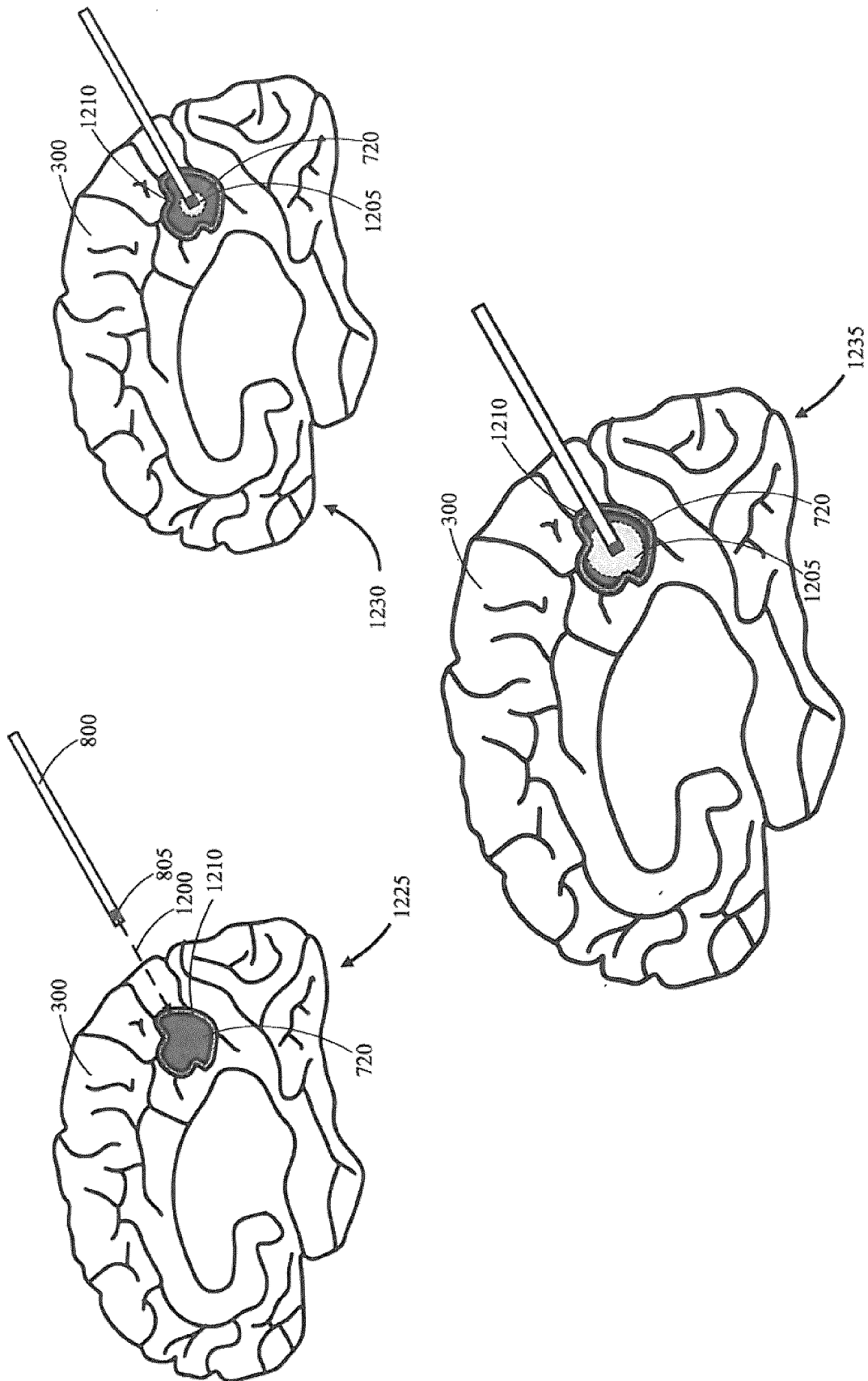


FIGURE 12

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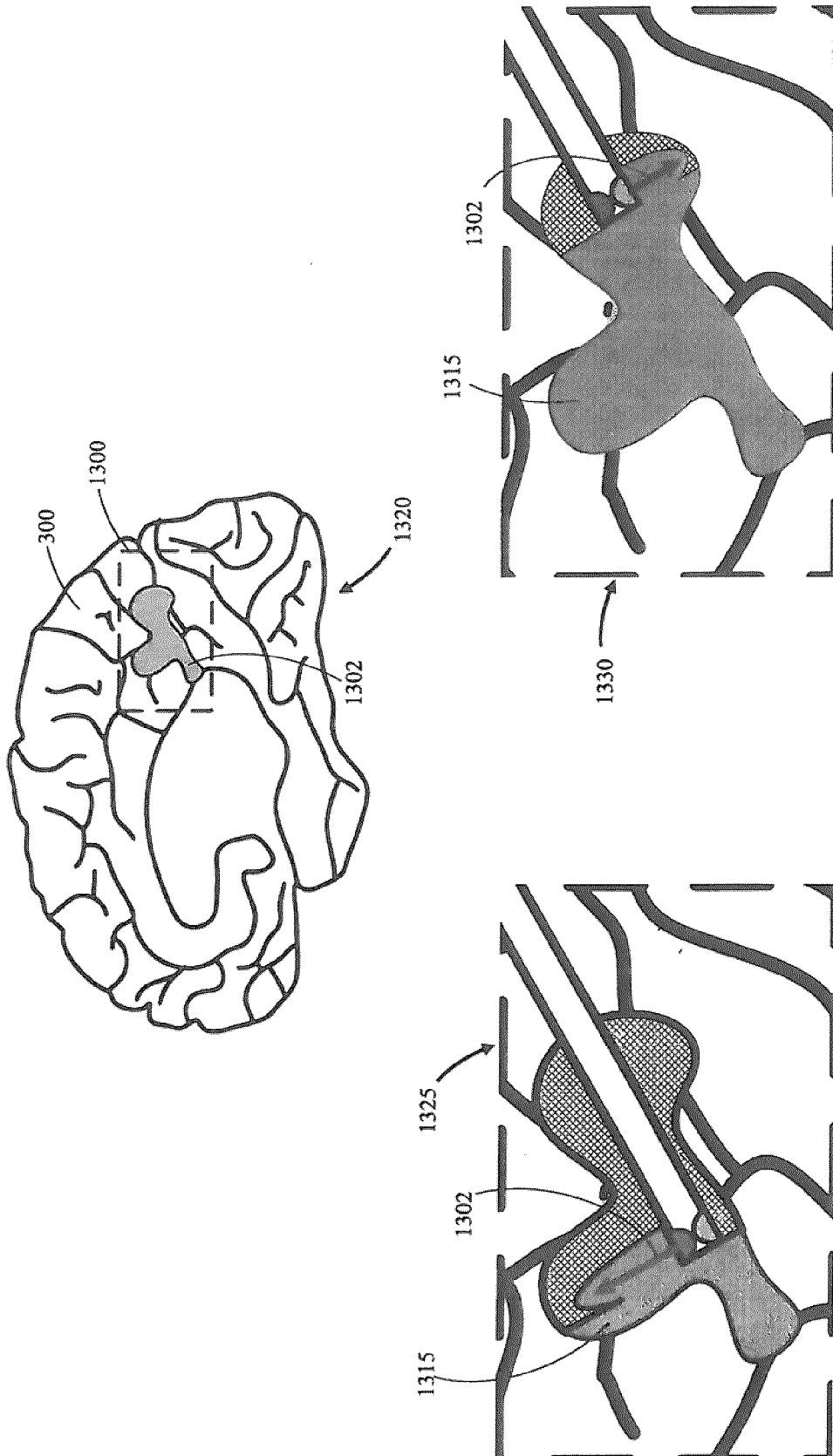


FIGURE 13

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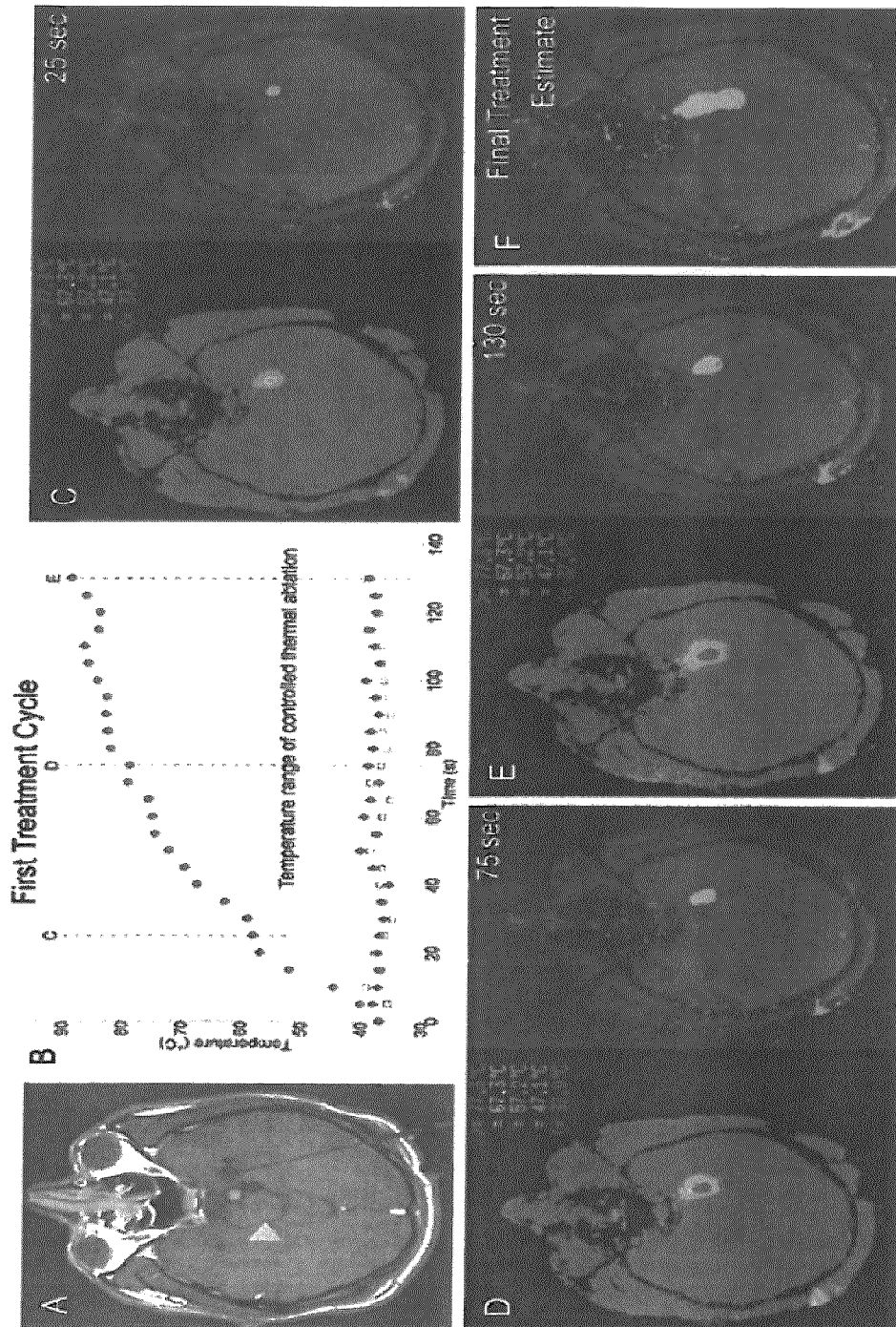


FIGURE 14

[Willie, Jon T., et al. "Real-time magnetic resonance-guided stereotactic laser amygdalohippocampotomy for mesial temporal lobe epilepsy." *Neurosurgery* 74.6 (2014): 569-585.]

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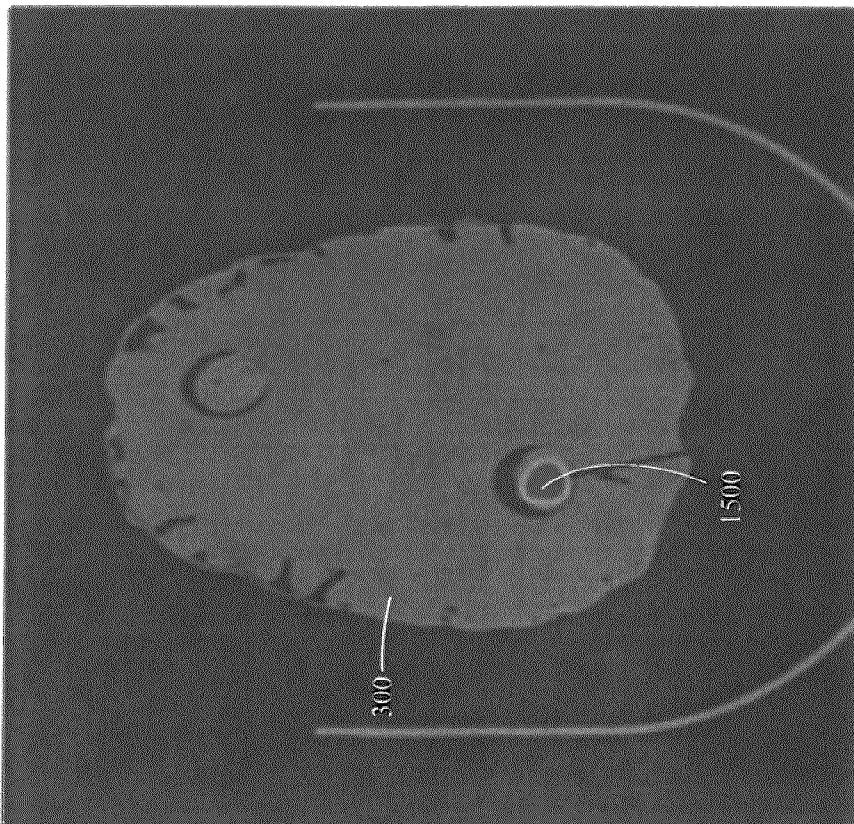
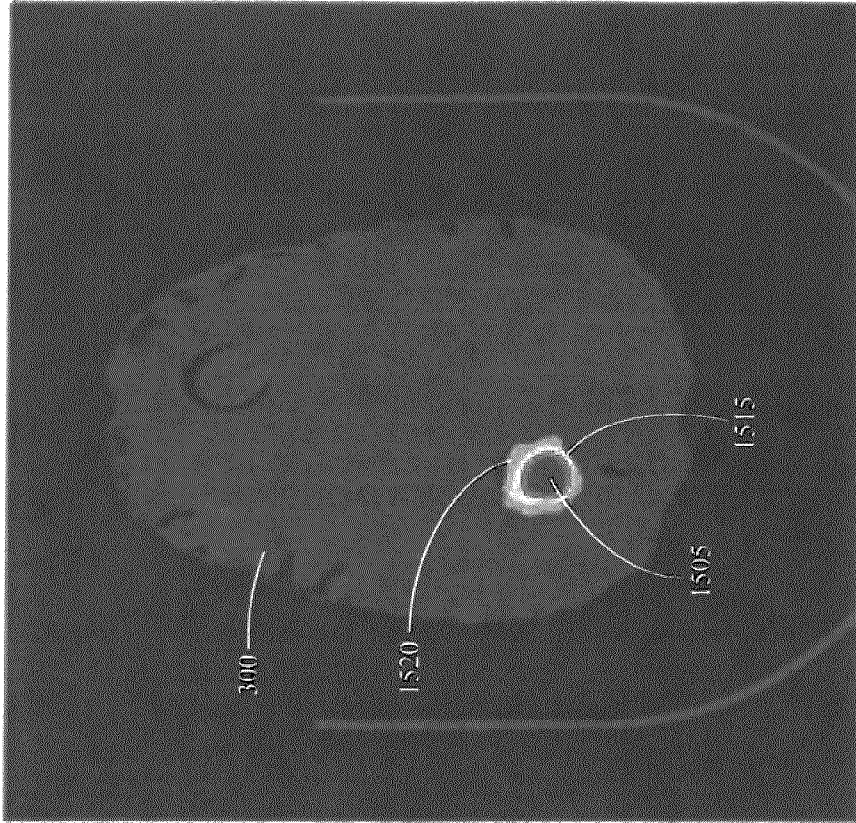


FIGURE 15

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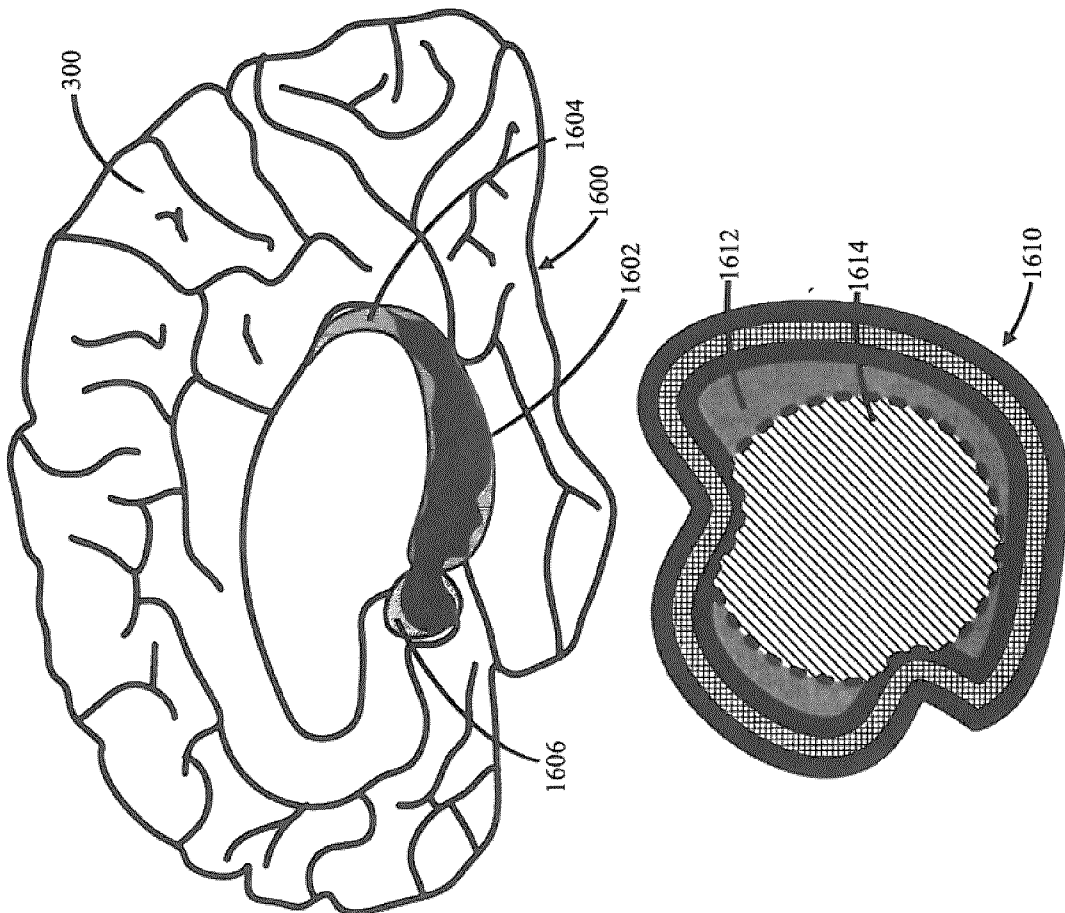
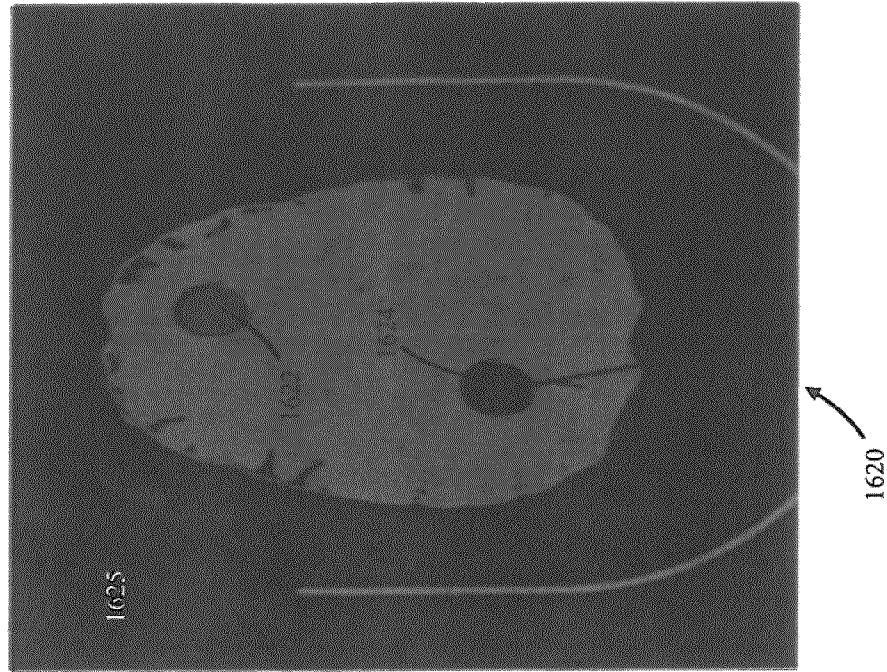


FIGURE 16

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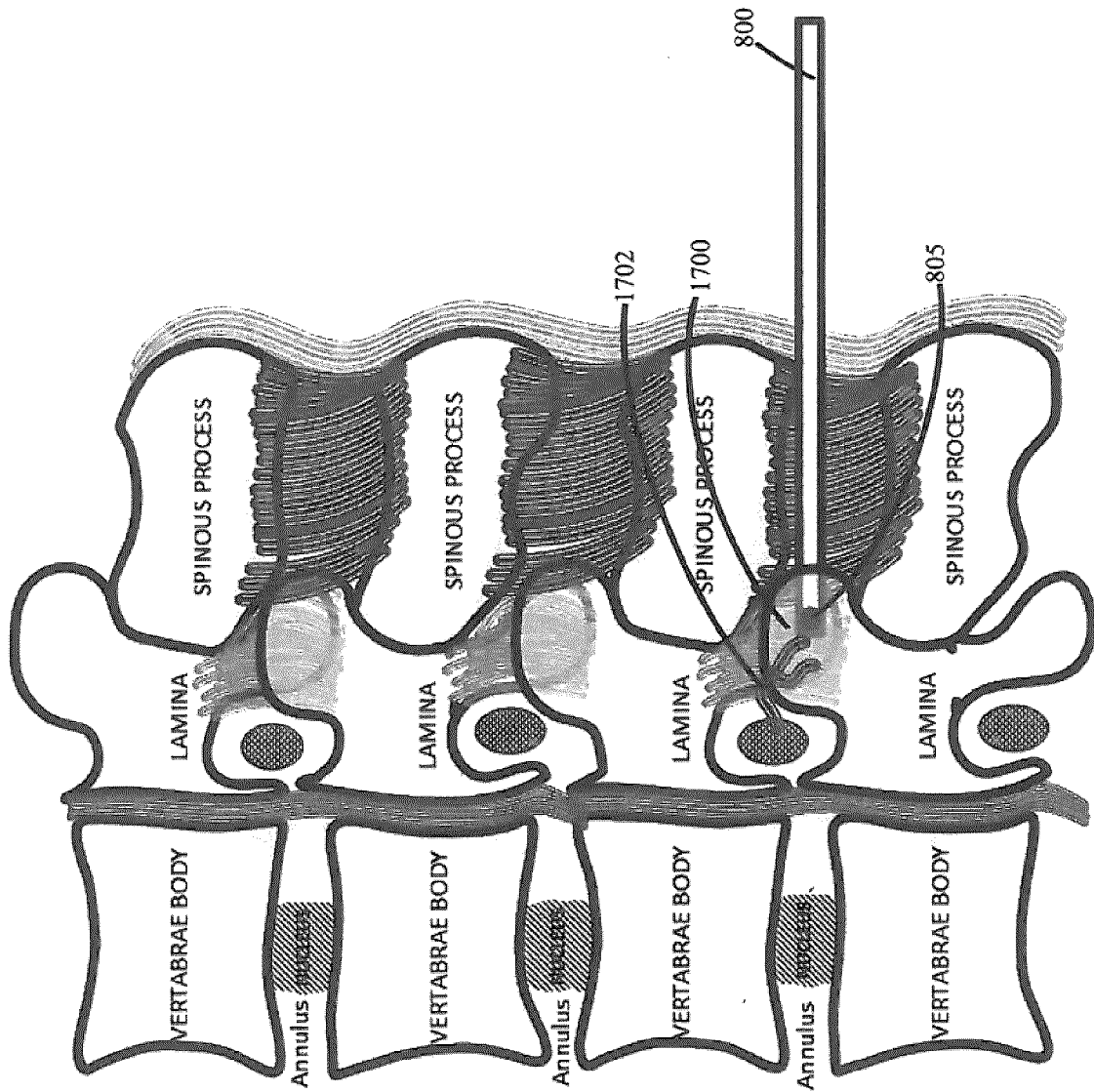


FIGURE 18

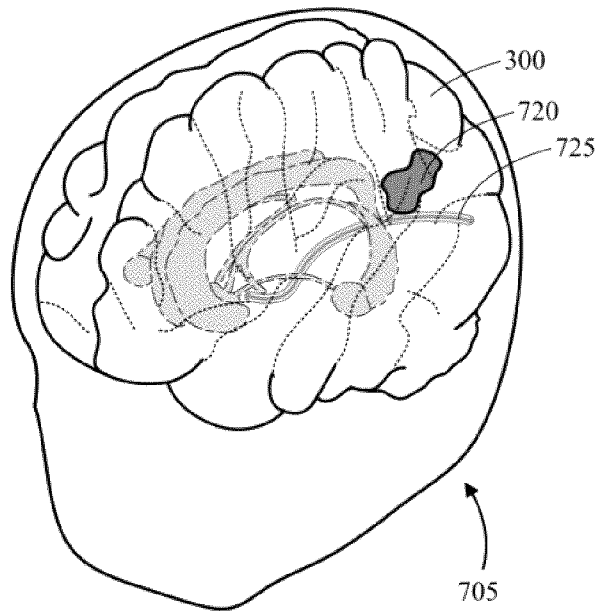
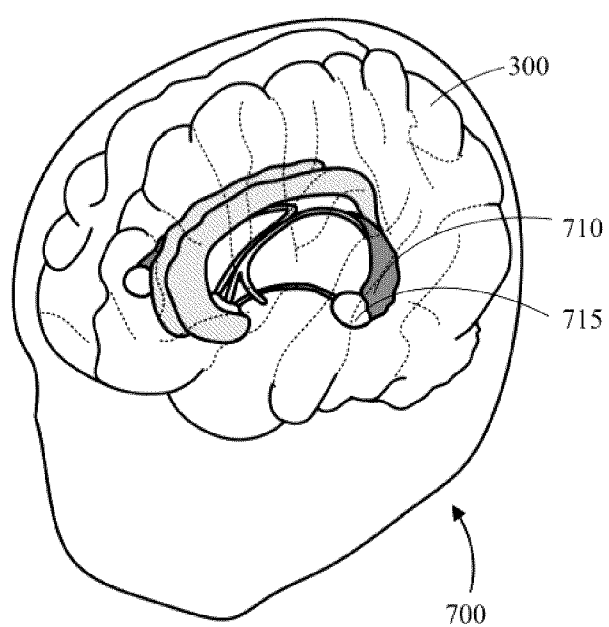


FIGURE 7