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(54) METHODS AND SYSTEMS FOR ULTRASOUND DELIVERY THROUGH A CRANIAL APERTURE

(76) Inventor: **Henry Nita**, Redwood Shores, CA (US)

Correspondence Address:
Raymond Sun
Law offices of Raymond Sun
12420 Woodhall Way
Tustin, CA 92782 (US)

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Continuation-in-part of application No. 11/203,738, filed on Aug. 15, 2005.
Continuation-in-part of application No. 11/274,356, filed on Nov. 15, 2005.

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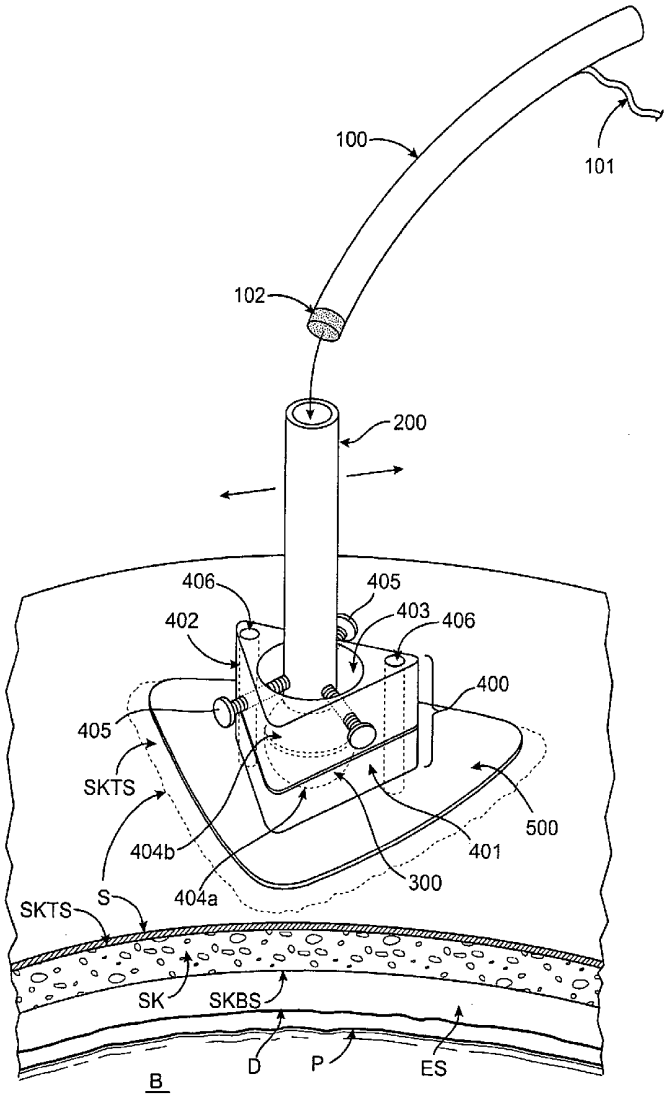
(57) **ABSTRACT**

A method for delivering ultrasound energy to a patient's intracranial space includes forming at least one aperture in the patient's skull, introducing at least one acoustically conductive medium into the intracranial space to contact brain tissue of the patient, advancing an ultrasound device at least partially through the aperture in the skull, and transmitting ultrasound energy to the intracranial space, using the ultrasound device. In some embodiments, the acoustically conductive medium may be cooled to help regulate the temperature of the patient's brain tissue.



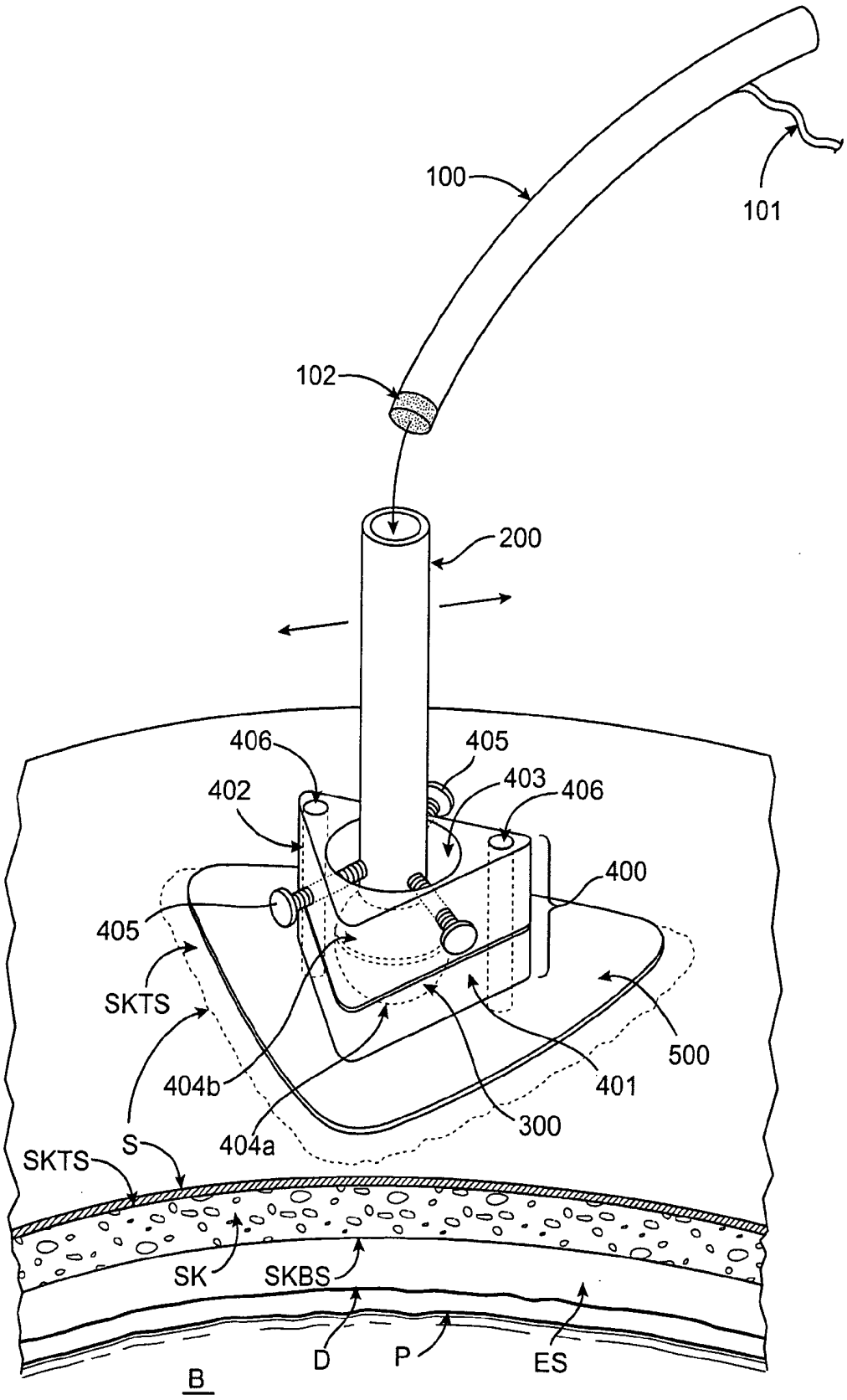

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FIG. 1

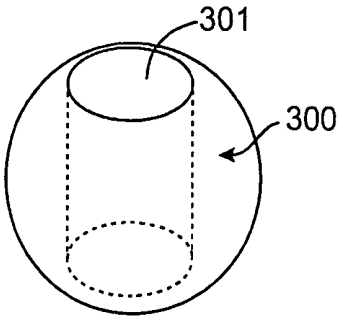

FIG. 2

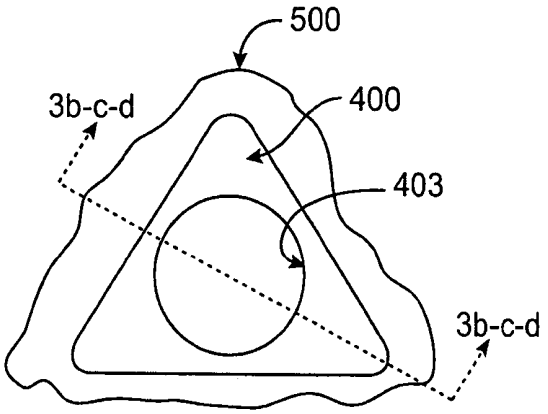

FIG. 3a

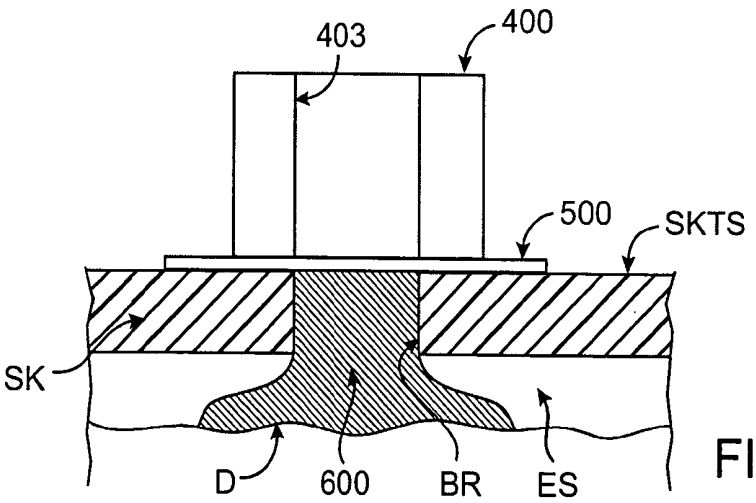

FIG. 3b

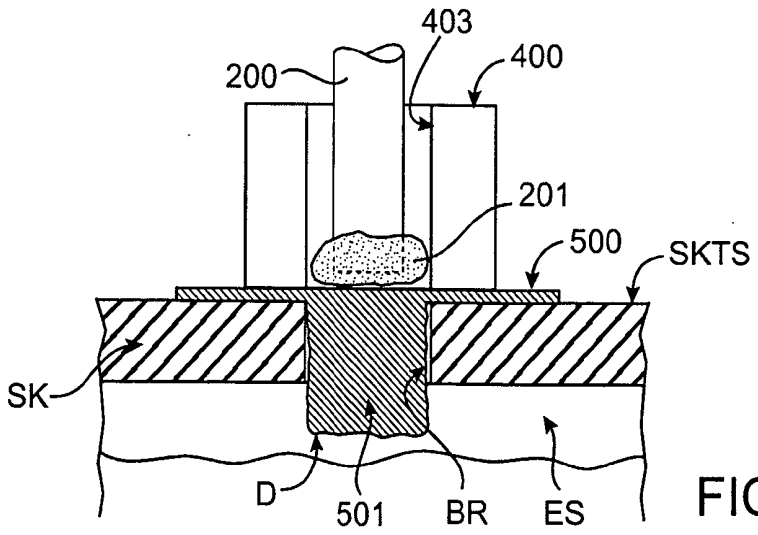

FIG. 3c

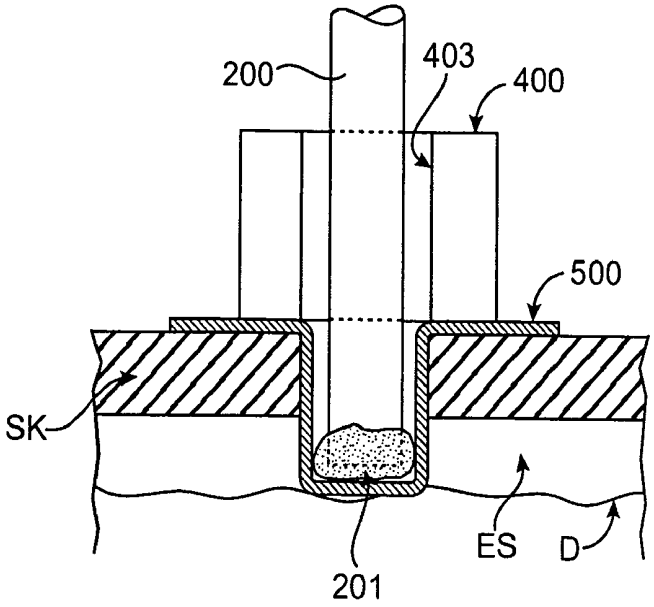

FIG. 3d

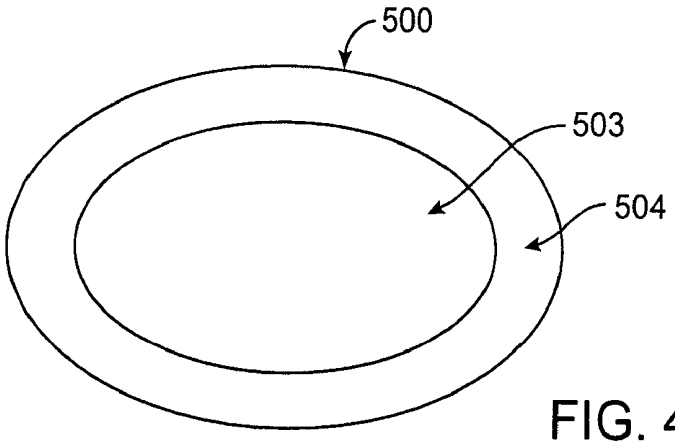

FIG. 4a

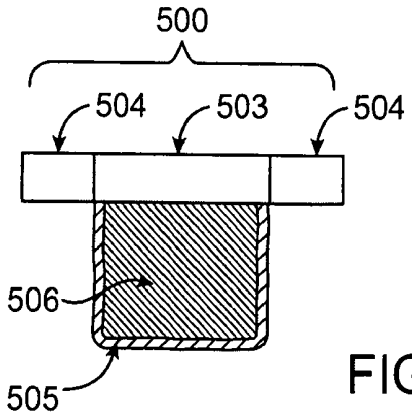

FIG. 4b

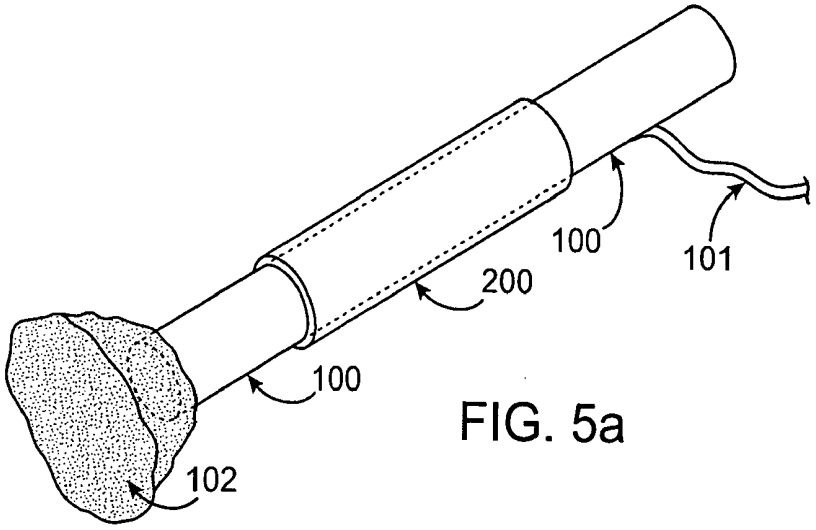

FIG. 5a

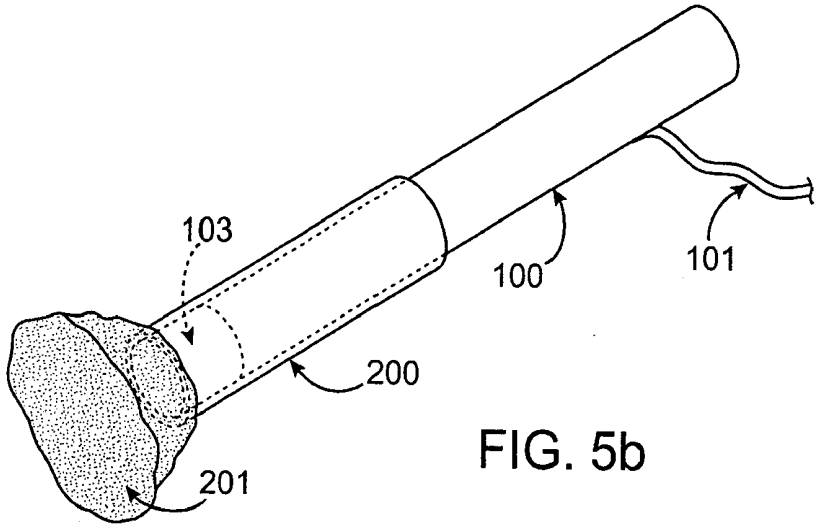

FIG. 5b

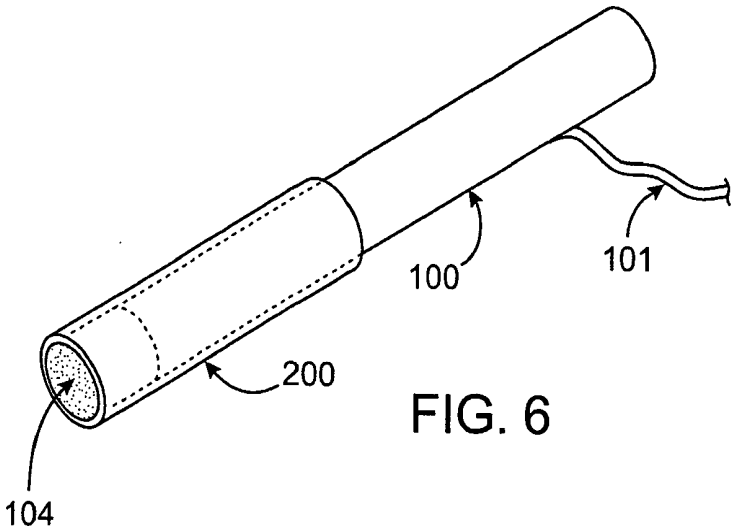

FIG. 6

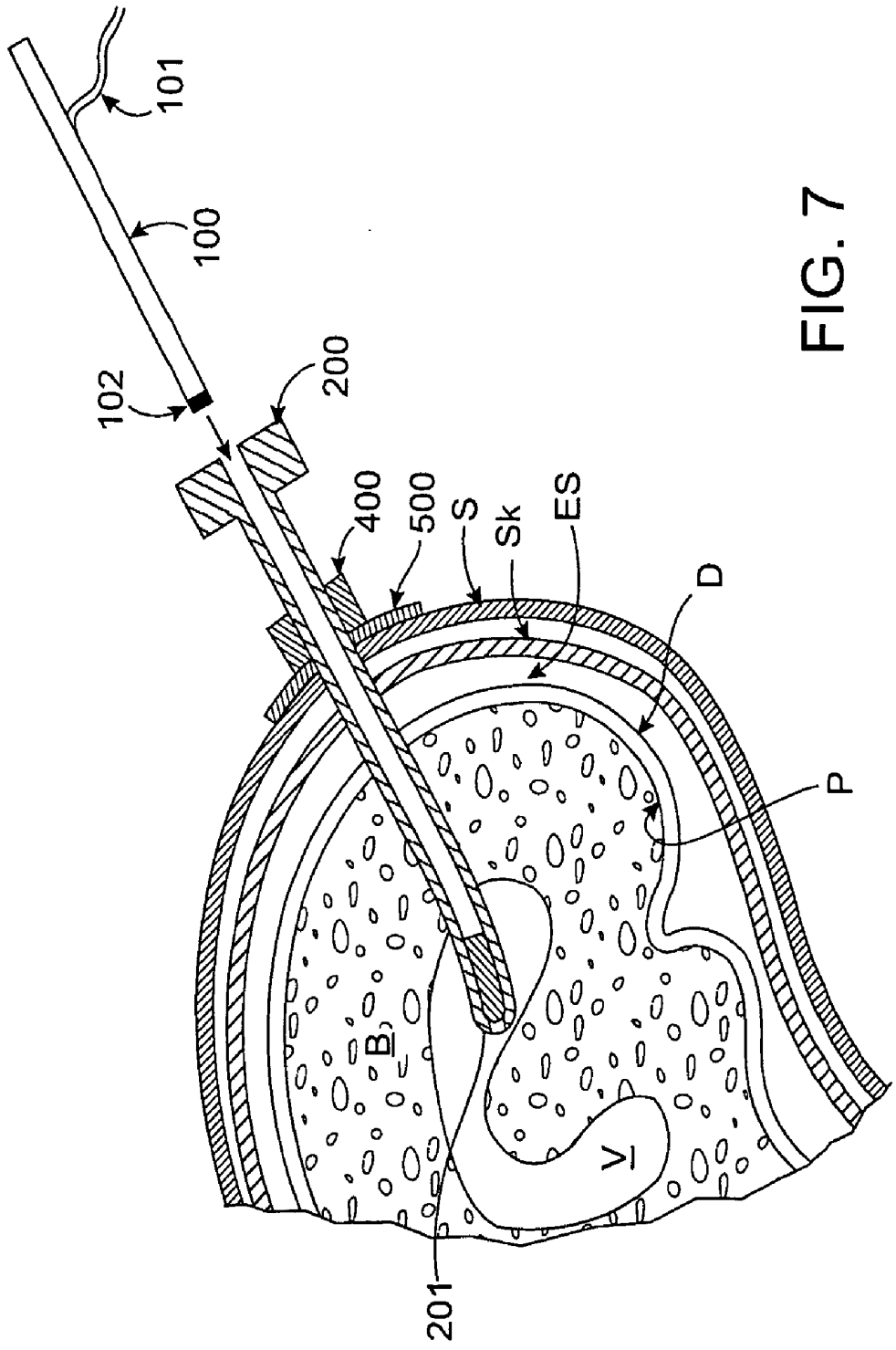

FIG. 7

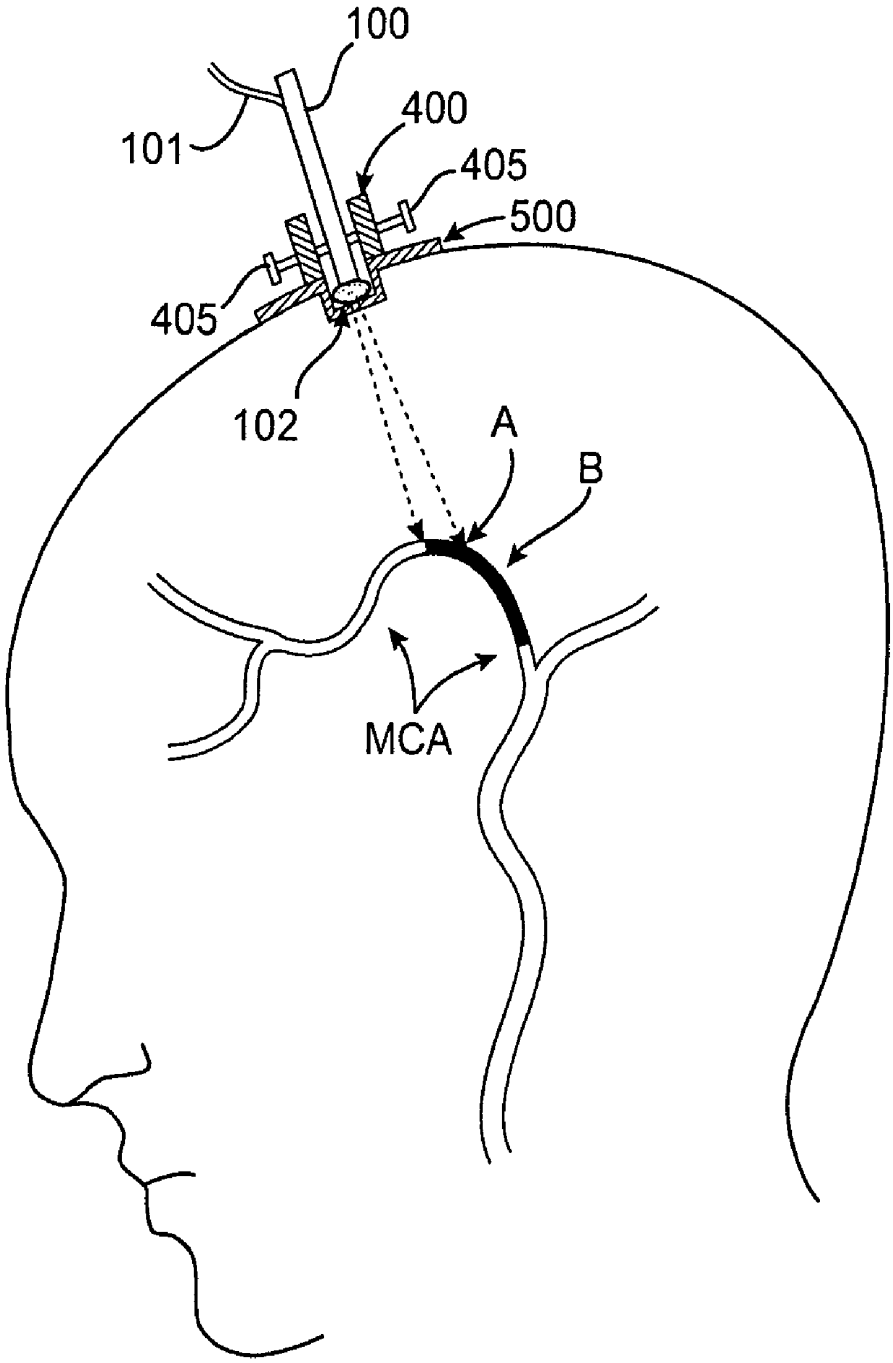

FIG. 8a

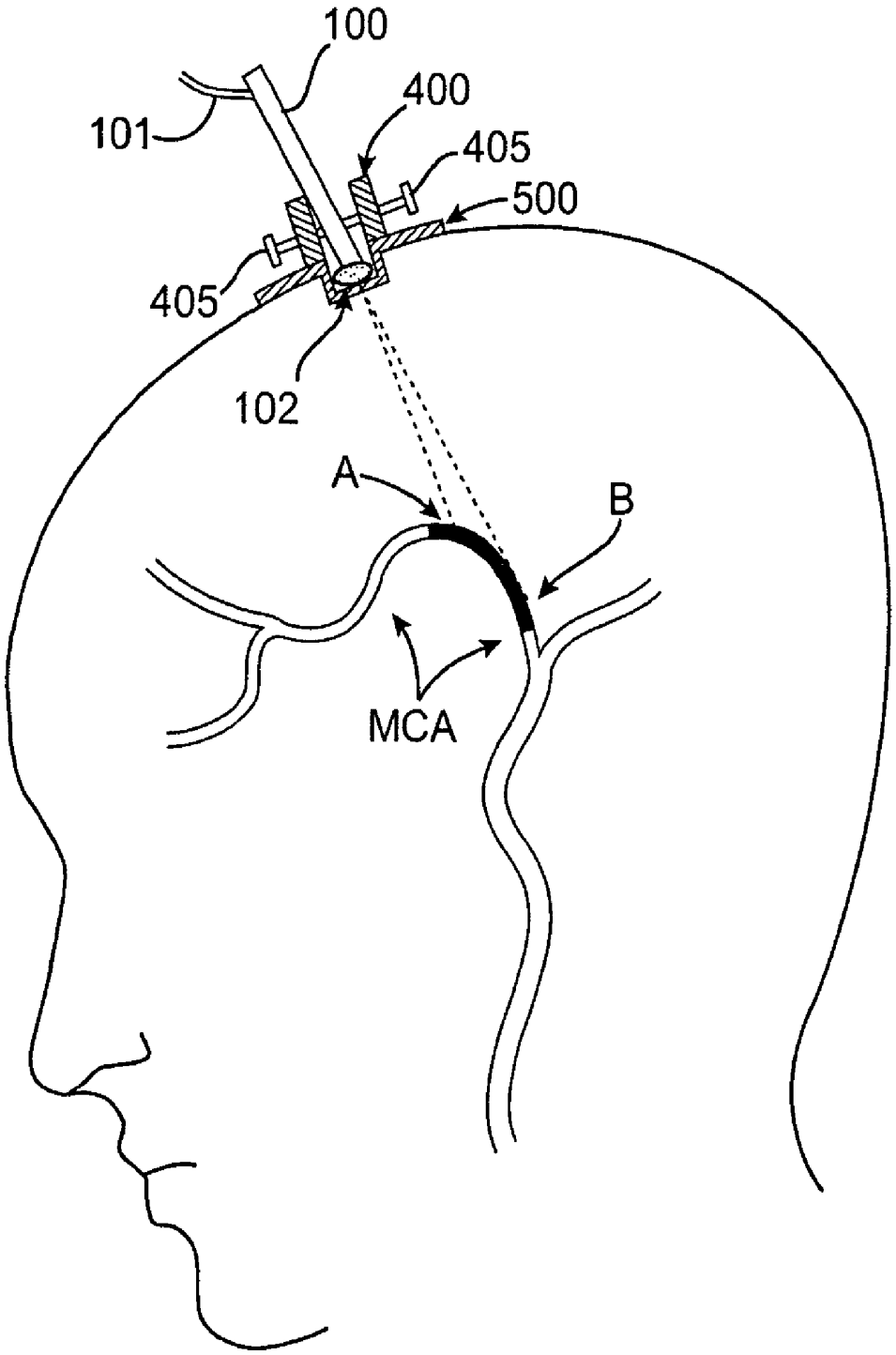

FIG. 8b

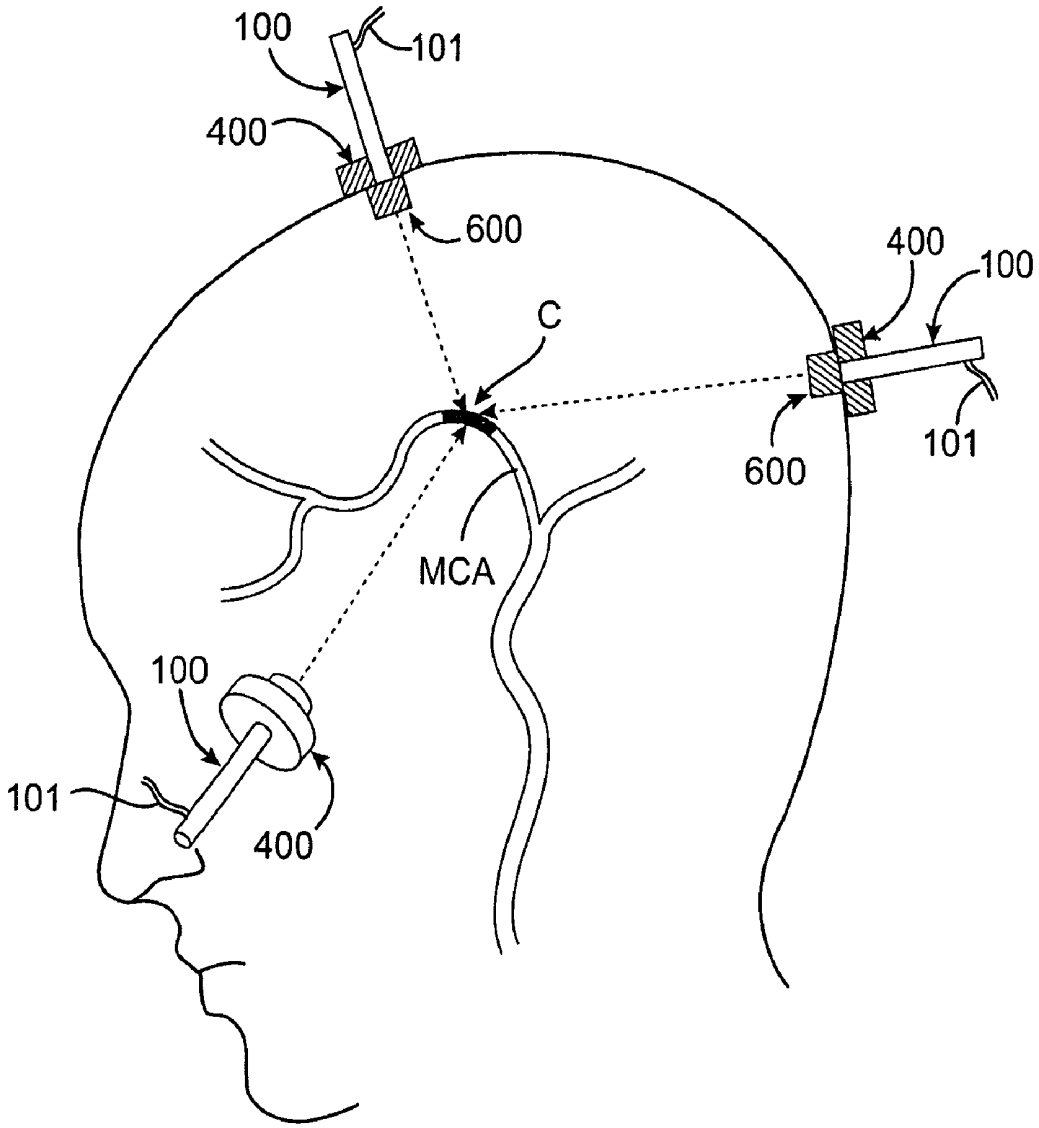

FIG. 9

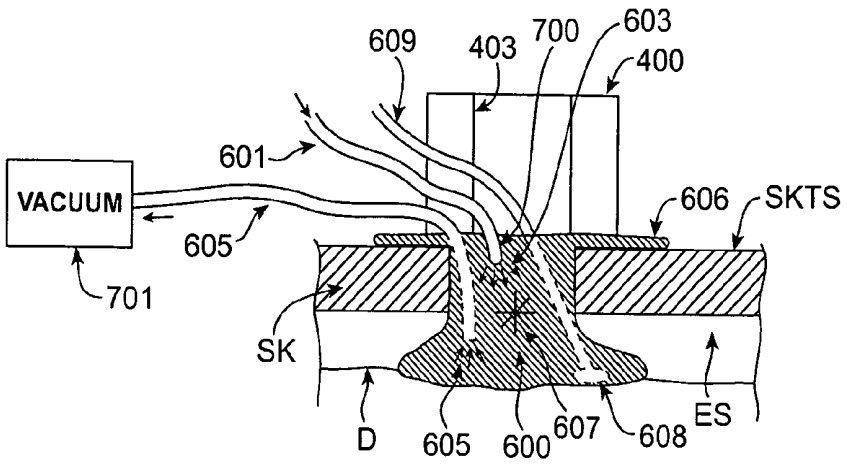

FIG. 10a

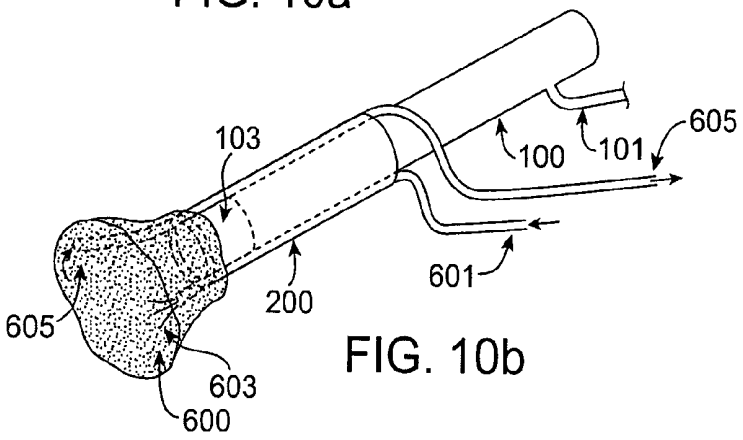

FIG. 10b

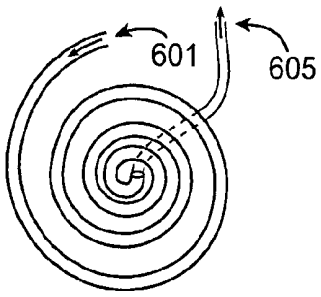

FIG. 10c

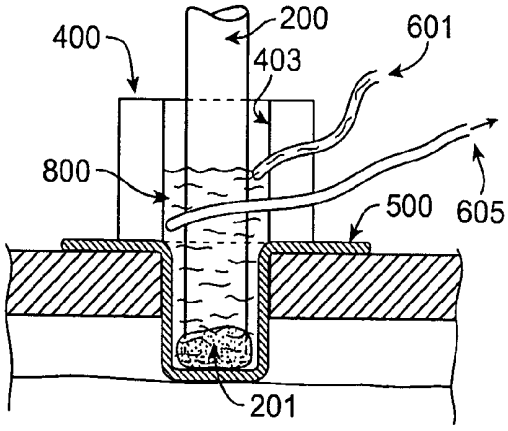

FIG. 10d

METHODS AND SYSTEMS FOR ULTRASOUND DELIVERY THROUGH A CRANIAL APERTURE

RELATED APPLICATION AND INCORPORATION BY REFERENCE

[0001] This is a continuation-in-part of the following co-pending U.S. patent application Ser. No. 11/165,872, filed on Jun. 24, 2005; U.S. Ser. No. 11/203,738, filed on Aug. 15, 2005; and U.S. Ser. No. 11/274,356, filed on Nov. 15, 2005, whose entire disclosures are incorporated by this reference as though set forth fully herein.

BACKGROUND OF THE INVENTION

[0002] 1. Field of the Invention

[0003] The present invention relates generally to medical methods and apparatus. More specifically, the invention relates to methods and apparatus for intracranial ultrasound delivery, which may include diagnostic ultrasound, therapeutic ultrasound, or both, delivered through an aperture or hole in the skull.

[0004] 2. Background Art

[0005] Stroke is characterized by the sudden loss of circulation to an area of the brain, resulting in a corresponding loss of neurological function. Also called cerebrovascular accident or stroke syndrome, stroke is a nonspecific term encompassing a heterogeneous group of pathophysiologic causes, including thrombosis, embolism, and hemorrhage. Strokes currently are classified as either hemorrhagic or ischemic. Acute ischemic stroke refers to strokes caused by thrombosis or embolism and accounts for 80% of all strokes.

[0006] More than 400,000 people per year in the U.S. have a first-time stroke. At current trends, this number is projected to increase to one million per year by the year 2050. Stroke is the third leading cause of death and the leading cause of disability in the U.S. Worldwide, cerebrovascular disease was the second leading cause of death in 1990, killing over 4.3 million people. Cerebrovascular disease was also the fifth leading cause of lost productivity, as measured by disability-adjusted life years (DALYs). In 1990, cerebrovascular disease caused 38.5 million DALYs throughout the world. And although stroke often is considered a disease of the elderly, 25% of strokes occur in persons younger than 65 years. When the direct costs (care and treatment) and the indirect costs (lost productivity) of strokes are considered together, strokes cost the American society $43.3 billion per year.

[0007] Until very recently, almost nothing could be done to help patients with acute stroke. Little treatment existed for ischemic stroke until 1995, when the National Institute of Neurologic Disorders and Stroke (NINDS) recombinant tissue-type plasminogen activator (rt-PA) stroke study group first reported that the early administration of rt-PA benefited some carefully selected patients with acute ischemic stroke. Encouraged by this breakthrough study and the subsequent approval of t-PA for use in acute ischemic stroke by the U.S. Food and Drug Administration, administration of t-PA has become increasingly more prevalent in stroke treatment. Treating patients early enough in the course of stroke, however, is an extremely challenging hurdle to effective treatment of stroke. Furthermore, t-PA for stroke treatment is much more effective if delivered locally at the site of blood vessel blockage, but such delivery requires a great deal of skill and training, which only a small handful of medical professionals possess.

[0008] One proposed enhancement for treatment of stroke is the administration of trans-cranial Doppler (TCD) at high frequencies (i.e., approximately 2 MHz) and low intensities, which is normally used for diagnostic functions. TCD has been shown not only to be effective in visualizing clots, but also to be effective in lysing clots in the middle cerebral arteries, in combination with lytic drugs such as t-PA and/or microbubbles. TCD has also been shown to be safe, with no clinically significant brain bleeding effects. (See, for example: A.V. Alexandrov et al., "Ultrasound-Enhanced Thrombolysis for Acute Ischemic Stroke," N. Engl. J. Med. 351;21, Nov. 18, 2004; and W. C. Culp and T. C McCowan, "Ultrasound Augmented Thrombolysis," Current Medical Imaging Reviews, 2005, 1, 5-12.) The primary challenge in using TCD to enhance stroke treatment, however, is that the skull attenuates the ultrasound signal to such a high degree that it is very difficult to deliver high-frequency, low-intensity signals through the skull. Using higher intensity ultrasound signals, in an attempt to better penetrate the skull, often causes unwanted bleeding of small intracranial blood vessels and/or heating and sometimes burning of the scalp. The only other option is to carefully aim a high-frequency, low-intensity TCD signal through a small window in the temporal bone of the skull to arrive at the middle cerebral artery, which is the technique described in the studies cited above and is the only technique studied thus far.

[0009] There are two main drawbacks to delivering high-frequency TCD through the temporal window. First, such delivery requires a high level of skill, and only a small handful of highly trained ultrasonographers are currently capable of performing this technique. Second, not all intracranial blood vessels are reachable with TCD via the temporal window. For example, although the temporal window approach may work well for addressing the middle cerebral artery, it may not work as well for reaching the anterior cerebral artery or various posterior intracranial arteries.

[0010] Assuming effective ultrasound delivery is achieved, in addition to enhancing treatment of acute thrombotic or embolic ischemic stroke, TCD may also enhance and/or facilitate treatment of other cerebral disorders. For example, recurrent lacunar strokes, dementia, head trauma patients with intracerebral blood clots or perfusion abnormalities, and even Alzheimer's patients may benefit from TCD. In any such disorders, administration of TCD may help restore normal blood flow to the brain, help disperse harmful blood clots inside or outside blood vessels, and/or cause hyper-perfusion in one or more areas of the brain, thus enhancing cerebral function. For example, ultrasound administration has been shown to enhance the production of nitric oxide in or nearby blood vessels, which may thus cause vasodilatation of nearby arteries and arterioles and enhance tissue perfusion. (See, for example, W. Steffen et al., "Catheter-Delivered High Intensity, Low Frequency Ultrasound Induces Vasodilation in Vivo," European Heart Journal (1994) 15, 369-376.) In any such treatments, however, use of TCD faces the same challenges in that it is very difficult to deliver at safe and effective frequencies to desired locations in the brain and thus can be performed only by a small handful of highly skilled technicians and can be directed only to a few areas in the brain. Also, the high

intensities required to transmit ultrasound through the skull in TCD make its utility for treating any chronic disorder impractical, since any implantable power source used with a chronic, implantable ultrasound delivery device would be depleted too quickly.

[0011] Acoustic properties of soft tissue typically change as the temperature of the tissue changes. This characteristic of soft tissue is of particular interest when delivering focused ultrasound energy through tissue to a target area located apart from the ultrasound source. Ultrasound energy propagation through soft tissue produces localized heating by ultrasound absorption and thus induces changes in acoustic properties of surrounding tissue, thereby increasing the risk of thermal injury to that surrounding tissue. This risk of tissue damage is especially important in ultrasound delivery to intracranial tissues, as damage to surrounding soft tissues may compromise the blood-brain barrier.

[0012] In addition to the risk of surrounding tissue damage, localized tissue heating during ultrasound treatment typically distorts the acoustic waves intended to treat the target tissue. Furthermore, nonlinear effects related to acoustic propagation through soft tissue can become significant when higher ultrasound intensities are required for therapeutic action, especially when the therapeutic target is located apart from the energy source and ultrasound energy needs to propagate through soft tissue to reach the target. Non-linear effects can produce unanticipated effects on soft tissue including unwanted damage to the tissue between the ultrasound source and targeted areas. In addition, the non-linear effects can limit the effectiveness of treatment, such as tissue lysis, directed at the target area.

[0013] Therefore, it would be desirable to have improved methods and apparatus for intracranial delivery of ultrasound energy for diagnostic ultrasound, therapeutic ultrasound, or both. Ideally, such techniques would be usable by a larger number of medical professionals than are currently qualified to administer TCD. Also ideally, such techniques would use ultrasound frequencies that do not cause unwanted bleeding in other blood vessels in the brain and that do not cause overheating or burning of the skin. In addition, it may be desirable to provide for intracranial delivery of ultrasound while minimizing or reducing non-linear acoustic effects on soft tissue. At least some of these objectives will be met by the present invention

BRIEF SUMMARY OF THE INVENTION

[0014] Methods and apparatus of the present invention generally involve delivering ultrasound energy to a patient's intracranial space for diagnostic purposes, therapeutic treatment, or both. The methods involve placing at least one access device on the scalp, skull, or partially through an aperture or hole in the skull, advancing at least one ultrasound delivery device partially through the access device, and transmitting ultrasound energy from the ultrasound delivery device(s) to the patient's intracranial space. When a hole in the skull is formed, the ultrasound delivery device can be placed over the hole, partially through the hole, or at the edge of the skull, and then used to transmit energy to the patient's intracranial space.

[0015] In some instances, such as in the treatment of ischemic stroke, ultrasound energy may be delivered to a target clot in a blood vessel. In other cases, such as in acute head trauma, ultrasound energy may be directed toward an extravascular blood clot in the brain. In other cases, energy may be delivered towards an area of blood vessels to cause vasodilatation and thus increase blood flow. Thus, the techniques and apparatus described herein may be used for a number of different applications and treatments.

[0016] In one aspect of the present invention, methods and devices provide intracranial ultrasound delivery while minimizing or reducing non-linear acoustic effects on soft tissue. In one embodiment, for example, non-linear effects are reduced by controlling the temperature of tissue between the ultrasound source and a target area. In some embodiments, targeted areas may include, for example, occluded intracranial blood vessels and/or blood clots in the intracranial space. The present invention provides methods to cool tissue exposed to ultrasound energy. In one embodiment, an acoustical medium used to improve ultrasound energy transmission from the ultrasound source to the tissue may also facilitate temperature modulation or cooling of the tissue. Alternatively, a separate element capable of cooling tissue may be delivered into a burr hole, through the dura, to a targeted location in the brain, penumbra, ventricle and/or along the epidural space to a secondary location on top of the dura mater. In some embodiments, the temperature of brain tissue may be reduced in combination with delivery of ultrasound energy into the intracranial space, which combination may significantly reduce metabolic needs of the affected brain tissue and reduce the severity and/or size of the stroke.

[0017] Further aspects and embodiments of the present invention are described in greater detail below, with reference to the attached drawing figures.

BRIEF DESCRIPTION OF THE DRAWINGS

[0018] FIG. **1** is an expanded sectional view of a portion of a human skull, showing a cross section of the skull, duramater, skull surface, epidural space, an access device with an introducer device and an ultrasound device together in place, in accordance with one embodiment of the present invention.

[0019] FIG. **2** is a perspective view of the ball used to modify the orientation of the ultrasound device or the introducer to the patient's skull, according to the present invention.

[0020] FIG. **3***a* is a top view of the access device of FIG. **1**.

[0021] FIG. **3***b* is a cross-sectional view of the access device with a thin film interface mounted to the skull with an acoustically conductive patient interface located within the burr hole according to the present invention.

[0022] FIG. **3***c* is a cross-sectional view of the access device mounted to the skull with an acoustically conductive patient interface located within the burr hole and an additional patient interface located between the introducer and the patient according to the present invention.

[0023] FIG. **3***d* is a cross-sectional view of an alternative to FIGS. **3***b* and **3***c*, where an acoustically conductive material is located within the burr hole between the introducer and the patient.

[0024] FIG. **4***a* illustrates the thin film that is positioned between the access device and the skull surface according to the present invention.

[0025] FIG. **4***b* is a cross-sectional view of the elements shown in FIG. **4***a*, and includes a conductive 'pack' integrated into the bottom side of the film.

[0026] FIG. **5***a* is a perspective view showing the ultrasound device of the present invention with an attached acoustically conductive patient interface inserted through the introducer.

[0027] FIG. **5***b* is a perspective view showing an ultrasound device of the present invention inserted through the introducer having an acoustically attached conductive material placed at the end of the ultrasound device inside the introducer, and an additional conductive material provided at the end of the introducer.

[0028] FIG. **6** shows an acoustically conductive media being attached to the ultrasound device within the introducer.

[0029] FIG. **7** is a cross-sectional view of a human skull and brain, showing the access device, the tubular introducer and the ultrasound device advanced in the skull and into a ventricle of the brain according to the present invention.

[0030] FIG. **8***a* is a cross-sectional view of a human skull, and brain, showing the access device and the ultrasound device directed to treat one portion of the clotted cerebral artery.

[0031] FIG. **8***b* is a similar view as FIG. **8***a*, showing the access device and the ultrasound device redirected to treat the second portion of the clotted cerebral artery.

[0032] FIG. **9** is a side view of a human head with three ultrasound devices coupled thereto, illustrating a triangulation technique for delivering ultrasound energy to a location in the brain, according to one embodiment of the present invention.

[0033] FIG. **10***a* is a cross-sectional view of an access device mounted to a skull with an acoustically conductive patient interface located within the burr hole, where the acoustically conductive patient interface has input and output ports allowing for fluid and/or gas exchange to enable cooling, according to one embodiment of the present invention.

[0034] FIG. **10***b* is a perspective view showing an ultrasound device inserted through an introducer and a conductive material provided at a distal end of the introducer with input and output ports allowing for fluid and/or gas exchange to enable cooling, according to one embodiment of the present invention.

[0035] FIG. **10***c* shows an acoustically conductive patient interface device having a spiral configuration and input and output ports to allow for fluid and/or gas exchange and enable cooling, according to one embodiment of the present invention.

[0036] FIG. **10***d* is a cross-sectional view showing an acoustically conductive material located within a burr hole between an introducer and a patient, and an access device with input and output ports to allow for fluid and/or gas exchange thereby enabling cooling of the brain, according to one embodiment of the present invention.

DETAILED DESCRIPTION OF THE INVENTION

[0037] In one aspect of the present invention, a method for delivering ultrasound energy to a patient's intracranial space involves fixing at least one access device to the patient's skull, advancing at least one ultrasound delivery device at least partway through the access device, and transmitting ultrasound energy from the ultrasound delivery device to the patient's intracranial space. The access device may be fixed in place with screws through the scalp and into the skull, or alternatively the scalp may be retracted so that the base of the access device is located directly on the skull. If the scalp is retracted, it may be advantageous to also drill a hole through the skull near the center location of the access device to provide a route for minimal attenuation of the signals delivered from the ultrasound device to the intracranial space. In some embodiments, one hole is placed in the skull, and one ultrasound delivery device is used. In alternative embodiments, multiple holes are formed in the skull, and at least one ultrasound delivery device is advanced through the access device and at least partway through each hole. In other alternative embodiments, one hole is formed in the skull, and multiple ultrasound delivery devices are advanced through the hole.

[0038] The hole (or holes) in the patient's skull may be formed using any suitable devices and methods. For example, in some embodiments, a hand or power drill or burr device may be used, such as those commonly known in the art for forming holes in the skull. Once a hole is formed in the skull, one or more ultrasound delivery devices may be placed above the hole, advanced partway or completely into the hole or through the hole. In one embodiment, for example, an ultrasound delivery device is placed above the hole, at the edge of the skull or into the hole so that a distal end of the device is inserted through the access device and into the skull. In other alternative embodiments, one or more ultrasound delivery devices are advanced through the hole(s) into the epidural space, one or more ventricles and/or an intracerebral space of the patient's brain. For the purposes of this application, "intracerebral space" means any location within brain tissue or parenchyma outside of blood vessels.

[0039] To facilitate the introduction of ultrasound delivery devices through one or more holes in the patient's skull, one or more introducer devices may optionally be used. For example, in one embodiment, an introducer device is placed through the access device and at least partway into a hole, and at least one ultrasound delivery device is advanced partway or all the way through the introducer device. In one alternative embodiment, the introducer device is advanced through the access device and through a hole and into the patient's epidural space, and one or more ultrasound devices are advanced into the epidural space. In other alternative embodiments, the introducer device may be advanced through the hole and into a ventricle or an intracerebral space of the patient's brain, and one or more ultrasound devices are then advanced into the ventricle or intracerebral space. The introducer may be made of polymer or metal or of a composite construction.

[0040] To support the placement of the ultrasound device, either with the introducer or without the introducer, an

access device may be used. The access device also has attributes that enable precise positioning and immobilization of the ultrasound device at a specific angle or range or angles with respect to the base or the access device and/or the skull. The access device can be a part of a stereotaxis frame, or it can be frameless and therefore directly secured to the skull. Examples of such frameless devices include the "Navigus System for Frameless Access" and the "Navigation" products made by Image-Guided Neurologics, Inc., located in Melbourne, Florida. Using either a stereotaxis frame or a frameless access device, the ultrasound device (with the introducer or without the introducer) may be placed on the scalp surface, on the skull surface, inside the skull, or positioned above the skull. The ultrasound device may also be directed to the treatment area and immobilized at a desired angle, thereby allowing longer therapy time without the risk of disengagement from the treatment target or misdirection by the ultrasound device. If the treatment area is of a larger size or length, the access device may allow re-positioning and can be used to immobilize the ultrasound device at various parts of the treatment area. For example, treatment of larger cerebrovascular clots may require that a proximal portion of the clot be targeted and treated first before repositioning the ultrasound device to target and treat a more distal portion of the clot. Alternatively, a large treatment area may be treated by either manually or automatically maneuvering the ultrasound device position through a range of angles with respect to the skull surface. Automatic maneuvering can be achieved by limiting the ultrasound device to a range of angles and then continuously powering the device through various angles by a power driven element (such as a motor). For example, in order to treat a cerebral clot which occludes several centimeters of the blood vessel it may be necessary to have the ultrasound device oscillate over a range of angles to treat the elongated clot. The angle between the ultrasound device and skull or base of the access device can range from 1 to 179 degrees, and more typically between 45 to 135 degrees. The ultrasound device can be limited to a specific range of angles through a plate having a slot placed about the ultrasound device, or around the ultrasound device and introducer. The plate can be fixed with respect to the base of the access device. The orientation and length of the slot would dictate the range of angles the ultrasound device could oscillate through.

[0041] Any suitable ultrasound delivery device may be used in implementing various embodiments of the present invention. For example, in one embodiment, the device may include an ultrasound device transducer. In another embodiment, the device may include a transducer-tipped ultrasound catheter. In either case, the ultrasound transducers may be formed from piezoelectric crystal or from silicon-based ultrasonic transducer technology.

[0042] In many embodiments, the ultrasound energy is transmitted acutely, such as in treatment of ischemic stroke or acute head trauma. In alternative embodiments, the ultrasound energy may be transmitted chronically, such as in treatment of chronic brain perfusion disorders or stroke rehabilitation. In some cases, a device or part of a device may be implanted in the patient for chronic treatment. In various embodiments, any of a number of different conditions may be treated or ameliorated according to the methods of the invention. For example, the ultrasound energy may be transmitted to a blood clot, either within or outside of a blood vessel, to help disrupt the clot. In another embodiment, the energy may be transmitted to a blood vessel to treat atherosclerosis of the vessel. In other embodiments, the energy may be transmitted to one or more blood vessels in the brain to help treat any of a number of blood perfusion abnormalities.

[0043] Optionally, the method may further include providing one or more pharmacologic agents to the patient, in conjunction with the delivered ultrasound energy. Examples of such agents include, but are not limited to, tissue plasminogen activator and other blood clot reducing agents, such as rTPA, Urokinease, Streptase (Streptokinase) Actiase (Alteplase) and Desmoteplase. Other agents which may be used include antiplatelet agents such as aspirin, Plavix (clopidorgel) and Ticlid (Ticclopidine), and GP IIb/IIIa inhibitors, such as Reopro (abciximab), Aggrestat (Tirofiban) and Integrilin (eptifibatide). Such a pharmacologic agent may be delivered intravenously, arterially, via intramuscular injection, or orally. Alternative methods involve delivering microbubbles or nanobubbles into the patient's bloodstream, in conjunction with the delivered ultrasound energy. Such microbubbles may be delivered intravenously or arterially. In some embodiments, both microbubbles and a pharmacologic agent(s) may be delivered to the patient along with the ultrasound energy. In some embodiments, pharmaceutical agent(s) may be delivered first, followed with delivery of microbubbles along with ultrasound energy. In other embodiments, microbubbles may be delivered first, followed by the delivery of pharmaceutical agent(s) along with ultrasound energy. Microbubbles may also be administered to the patient in a mixture with a pharmaceutical agent(s). In one such mixture, the majority of the pharmaceutical agent(s) may be present outside of microbubbles. In another mixture, the majority of the pharmaceutical agent(s) may be attached to microbubbles. Microbubbles and pharmaceutical agent(s) may also be administered simultaneously, through such means as through a single syringe or through more than one syringe. Ultrasound energy can be delivered to the patient prior to, during, or after, the delivery of a pharmaceutical agent(s) or microbubbles or both.

[0044] In one embodiment, one or more access devices are located on the scalp, skull, or partially through the skull, and ultrasound energy may be transmitted from any of several locations about the head and in any number of different pulsing sequences. For example, in one embodiment, access devices are located in several locations on the head, and ultrasound energy is simultaneously transmitted from multiple ultrasound devices at multiple locations. Such a delivery pattern of ultrasound about the head may be advantageous, for example, in triangulating the ultrasound transmissions towards the same target. In an alternative embodiment, ultrasound energy is delivered sequentially from multiple delivery devices. In some cases, the ultrasound energy is transmitted from multiple delivery devices with the same frequency and intensity. Alternatively, the ultrasound energy may be transmitted from multiple delivery devices with different frequencies, different intensities and/or different modes. Ultrasound energy may be transmitted at any desired frequency, although in preferred embodiments the energy has a frequency between about 10 KHz and about 20 MHz, and more preferably between about 20 KHz and about 10 MHz. According to different embodiments, the

ultrasound energy may be transmitted in continuous mode or pulse mode, or may be modulated.

[0045] At any point during or after advancement of the access device, introducer or ultrasound device, the location of the apparatus may be monitored via any suitable visualization tools. For example, radiographic, computed tomography (CT) or magnetic resonance imaging (MRI) technologies may be used to help facilitate placement of an ultrasound delivery device in a desired location. In some embodiments, radiographs, CT images and/or MRI images may be used before device placement to determine an ideal location for the device. In some embodiments, during ultrasound energy delivery to the target site in the brain, patient recovery status may be monitored using a diagnostic ultrasound or one or more sensing methods, such as but not limited to the monitoring of oxygen levels or saturation, the rate of carbon dioxide production, heart rate, intracranial pressure and/or blood pressure. Also, the sensing element's measurements can be used to modulate the intensity, frequency and/or duty cycle of the ultrasonic device(s). Such a feedback process is also known as a closed loop control system.

[0046] Another aspect of the present invention includes the provision of a sterile or non-sterile acoustically conductive medium to facilitate ultrasound energy transmission to the targeted site. The acoustically conductive medium is positioned between the ultrasound transducer and the patient. The acoustically conductive medium may include a condense gel, diluted gel, oil, saline or any other semi-solid, fluid or gaseous material that conducts ultrasonic energy. The acoustically conductive medium may also be embodied in the form of a compliant pack which contains any of the above-identified acoustically conductive media inside the pack. In one embodiment, the pack has a thin conductive shell designed to contain the acoustically conductive medium. The compliant pack may be located within the hole in the skull, on the skull surface, on the scalp surface, at the tip of the introducer, at the tip of the ultrasound device, or inside or under the access device. The acoustically conductive medium may be delivered through the transducer or around the transducer, through the introducer or around the introducer, or through the access devices intermittently or continuously during the procedure. Low viscosity fluids may be preferred for this approach and may also assist in cooling of the ultrasound device and/or adjacent tissues (such as the scalp, skull or brain).

[0047] In one embodiment, a cooled acoustically conductive medium may be introduced to the intracranial space to contact brain tissue and at least partially surround or touch the ultrasound energy source. The cooled conductive medium may enable or facilitate localized tissue temperature control. In one embodiment, for example, a cooled conductive medium may be housed in a compliant pack. In alternative embodiments, such a medium may either be cooled outside the body or cooled in situ. Optionally, such a complaint pack may also include inlet and outlet ports enabling fluid exchange to maintain appropriate temperature inside the compliant pack or the tissue. In one embodiment, a thermocouple or another feedback method(s) may be used to control the compliant pack temperature and/or tissue temperature. For example, one or more thermocouples may be placed on a surface of the brain, a surface of the dura, in the complaint pack, deep in the brain penumbra and/or in the brain ventricles. Temperature information may be transmitted from the thermocouple(s) to a control system, which may modulate temperature of the cooling medium, such as by adding or withdrawing medium. Such a control system may also, in some embodiments, modulate the intensity, frequency and/or other parameters of an ultrasound generator, based on the tissue temperature information transmitted from the thermocouple. For example, as brain tissues cools, it may be safe to increase the ultrasound power level without risk of damaging brain tissue as result of thermal effects.

[0048] In alternative embodiments, cooled acoustically conductive medium may be delivered through an ultrasound transducer, around the transducer, through an introducer device, around the introducer, or through one or more access devices intermittently or continuously during a procedure. The cooled conductive medium temperature may be cooled prior to and/or during use, in various embodiments. In various other alternative embodiments, one or more acoustically conductive media may be located within a burr hole in the skull, on the skull surface, on the scalp surface, inside the access device and/or inside the introducer device. In other alternative embodiments, an acoustic medium may be placed through a separate element extending through the dura and into the brain penumbra or brain ventricles or along the epidural space to an alternative site. In yet another embodiment, a cooling medium may be used along with a separate acoustically conductive medium. For example, in one embodiment, an acoustically conductive gel pack may be used, and additionally, the gel pack may be exposed in situ to a cooling medium and/or cooling element. In some embodiments, one or more secondary areas of brain tissue, away from a target area and a path through tissue to the target area, may also be cooled, such as via separate access ports or burr holes, in order to minimize adverse thermal effects associated with the ultrasound energy delivery or adverse effects of brain ischemia. In any of the various embodiments described above, an acoustically conductive medium may be cooled to any suitable temperature. For example, in various embodiments, the temperature of an acoustically conductive medium may be adjusted to approximately room temperature, to below room temperature, to below body temperature, or the like.

[0049] In another aspect of the present invention, the access device has a base which includes a distal part and a proximal part, with a positioning movable member located between the distal and proximal parts. The distal part is attached to the skull and has a nest to receive a movable positioning member. The proximal part is attached to the distal part of the base and also has a nest to receive the movable positioning member. The proximal part of the base has a stabilizing element. The access device has a longitudinal aperture to receive the ultrasound device or other surgical or diagnostic tool therein. The distal part of the base is operable to be placed and affixed to the skull. In one embodiment, the positioning member includes a ball with a through-hole. The ball is movable within the nest between the distal and proximal parts of the base. The distal and proximal parts of the base may be attached using conventional methods such as bonding, frictional interface, fusing, welding, or screw(s). In one embodiment, the positioning ball can be made of a rigid material, and the size of its through-hole can be provided to match the size of the ultrasound device or other surgical tool to be used. In another embodiment, the positioning ball can be made of

elastic material so that when the distal and proximal part of the base are tightened together, the size of the through-hole of the positioning ball is also tightened to immobilize the ultrasound device or other surgical tool received therein. In one embodiment, the stabilizing member includes at least two screws which are placed in the proximal part of the base, and which function to grip the ultrasound device, the introducer device or other surgical instruments at a fixed position and at a specific angle, as determined by the positioning ball.

[0050] In another aspect of the present invention, a thin film or a liner can be positioned between the access device and the skull, and/or between the ultrasound device and the skull. The film serves as a sterility barrier between the patient's inner tissue (epidural space) and the access device or the ultrasound device. The film can also serve as an acoustically conductive medium to facilitate ultrasound energy transmission. Also, the film may aid in the sealing of the burr hole to prevent bleeding of the skull. The film may have thrombogenic properties on its surfaces to enhance thrombosis of the scalp and/or skull bleeding. The film may be attached to the scalp, the skull, the access device, the introducer or the transducer device. The film can be composed of organic or synthetic polymers. The polymer material can be coated or impregnated with oil, gels, saline or other fluids to enhance its acoustically conductive properties. Alternatively, the film surfaces can be hydrophilic, thereby attracting fluid and/or ions that would also enhance its conductive properties.

[0051] In another aspect of the present invention, a method for delivering ultrasound energy to the patient's intracranial space involves positioning the ultrasound device at least partially through the access device and either locating the device juxtaposition to the scalp, skull or through a hole in the skull, at the edge of the hole in the skull or above the hole in the skull, and positioning the ultrasound device at the treatment target and immobilizing the ultrasound device. The ultrasound device may perform diagnostic functions, therapeutic functions or both functions.

[0052] According to another embodiment, the introducer may be placed between the access device and the ultrasound device. The introducer may be advanced through the access device and the ultrasound device may be placed through the introducer. A treatment target may be identified and located using diagnostic ultrasound techniques. Then, the introducer may be immobilized at the target treatment direction and exchanged for the therapeutic device. Ultrasound energy is then transmitted to the localized target in the patient intracranial space.

[0053] According to another embodiment, the introducer device may be placed through an access device located about a hole in the skull, and the ultrasound device may be advanced through an introducer and positioned in the patient's epidural space, intracerebral space or patient's ventricle, and ultrasound energy is transmitted into the patient intracranial space. A diagnostic ultrasound device may be used to locate the treatment side and a second ultrasound device may be used for therapy, or one ultrasound device may be used for both diagnostics and therapy. Such a method may further involve forming the hole(s) in the patient's skull.

[0054] Delivery of ultrasound energy through the scalp, the skull, a hole in the skull to the patient intracranial space either from above the hole or within the hole, from the epidural space, from the intracerebral space, or from the patient's ventricle, may be used for treatment of any of a number of conditions, such as acute clot outside of blood vessels caused by brain trauma, or ischemic stroke caused by a clot within a vessel. In various embodiments, ultrasound may be combined with delivery of a pharmacological agent(s) and microbubbles/nanobubbles. Ultrasound, with or without additional agents, may be delivered until the patient's symptoms improve and/or until a brain imaging study (e.g. MR, CT, PET, SPECT) demonstrate that the adverse "mass effects" of a clot are significantly reduced (e.g., <10% in size). For treatment of clot inside a vessel, as in ischemic stroke patients, the ultrasound delivery device may be placed near or directly adjacent to the clotted blood vessel.

[0055] FIG. **1** is a cross-sectional view of a portion of a human head showing with an ultrasound assembly attached to the skull, and identifying the skull Sk, the skull's top surface SKTS, the skull's bottom surface SKBS, the scalp S, the pia matter P, the dura matter D, the epidural space ES, and the brain tissue B. An access device **400** is attached to the skull through the use of screw(s), pin(s) or adhesives (not shown). Through holes **406** can be used to enable the fixation of the access device **400** to the skull. The access device **400** can be used for placing an ultrasound device **100** or other surgical tools through the skull S with the ability to adjust the trajectory path of the ultrasound device **100** or surgical tool. The ultrasound device **100** can include electrical cables **101**, and a conductive medium **102** provided at its distal end. The access device **400** has a base which includes a distal part **401** and a proximal part **402**. Each part **401** and **402** defines a nest **404***a* and **404***b* respectively, therebetween that is size and configured to receive a movable positioning member **300**. The access device **400** has a longitudinal aperture **403** which receives the introducer **200**, the ultrasound device **100** or other surgical or diagnostic tools. The positioning member **300** of the access device **400** is positioned between the distal part **401** of the access device **400** and the proximal part **402** of the access device **400**. The positioning member **300** has a ball with a through-hole **301** extending therethrough, as best shown in FIG. **2**. The ball **300** is movable within the nest **404***a* and **404***b* between the distal part **401** and the proximal part **402**. The distal part **401** of the access device **400** and the proximal part **402** of the access device **400** are attached together.

[0056] Stabilizing members **405** are provided within the proximal part **402** of the access device **400**. The stabilizing members can be embodied in the form of at least two screws **405** which are placed in the proximal part **402** of the access device **400**, and which function to grip the ultrasound device **100**, introducer **200** or other surgical instruments, at a fixed position and at a specific angle, as determined by the positioning ball **300**. The positioning ball **300** can be made of a rigid material and its through-hole **301** can be sized and configured to match the size of the introducer **200**, the ultrasound device **100** or other surgical tool. Also, the positioning ball **300** can be made of elastic material so that when the distal part **401** and the proximal part **402** of the base **400** are tightened together, the size of the through-hole **301** of the positioning ball **300** can also be tightened, thereby immobilizing the ultrasound device or other surgical tool received therein.

[0057] The ball **300** enables the introducer **200** to be adjusted to a variety of angles with respect to the skull. Once the desired introducer angle or range of angles are identified by the user, the introducer **200** that is positioned through the pivoting ball **300** can be immobilized using the stabilizing members **405**. Alternatively, the positioning ball does not need to be a separate element, but instead can be integrated with the distal end of the introducer **200** or the ultrasound device **100**.

[0058] Also shown in FIG. **1**, an acoustically conductive film **500** can optionally be positioned between the access device **400** and the skull prior to fixation of the access device **400** to the skull. A portion of the film **500** can be located on the skull's top surface SKTS, or alternatively the film **500** can be located on top of the scalp S (not shown).

[0059] To deliver ultrasound energy to the targeted intracranial site, the ultrasound device **100** can be delivered through the introducer **200** as shown in FIG. **1**, or alternatively, the ultrasound device **100** can be used with the access device **400** without the introducer **200**. The access device **400** is used to support the placement of the ultrasound device **100** in the skull, either with the introducer **200** or without the introducer **200**. The access device **400** may be fixed in place with screws inserted through the scalp S and into the skull SK, or alternatively the scalp S may be retracted so that the distal part **401** of the access device **400** is positioned directly on the skull's top surface SKTS. If the scalp S is retracted, it may be advantageous to also drill a burr hole BR through the skull S, near the center location of the access device **400**, to minimize related attenuation of the ultrasonic signals associated with transmitting through bone. To secure the film **500** in place, the same screws located in the holes **406** that are used to fix the access device **400** to the skull S can also be passed through the film **500**. The screws can be coated, impregnated, covered, or constructed of a substance that minimizes bleeding at the entry sites of the screws. Alternatively, the screws can expand in situ to aid in hemostasis of the entry site.

[0060] The access device **400** may be a part of a stereotaxis frame, or it may be frameless and therefore directly secured to the skull. Using a stereotaxis frame or a frameless access device, the ultrasound device **100** (with the introducer **200** or without the introducer **200**) may be placed on the scalp surface S, on the skull's top surface SKTS, inside the skull S, or positioned above the skull S. It may be directed to the treatment area and immobilized at a desired angle, thereby allowing longer therapy time without the risk of disengagement from the treatment target or misdirection by the ultrasound device.

[0061] FIGS. **3***a*, **3***b*, **3***c* and **3***d* illustrate an access device **400** positioned on top of a hole in the skull. FIG. **3***a* is a top view of an access device **400** showing an aperture **403** and an acoustically conductive film **500** located under access device **400**. FIG. **3***b* shows a cross section of FIG. **3***a* with a burr hole BR drilled through the skull SK, and with an access device **400** and a film **500** provided on the skull's top surface SKTS and about the burr hole BR. Acoustically conductive medium **600** can be provided in the burr hole BR. This acoustically conductive medium **600** can be sterile or not sterile, and is intended to facilitate ultrasound energy transmission from the ultrasound transducer **100** to the patient.

[0062] The acoustically conductive medium according to the present invention may include a condense gel, diluted gel, oil, saline or any other semi-solid, fluid or gaseous material that conducts ultrasonic energy. The acoustically conductive medium **600** may also be embodied in the form of a compliant pack which contains a gel, oil, saline or other acoustic conductive media contained inside the pack. The compliant pack can be positioned between the film **500** and duramater D, but may also be located within the hole in the skull, on the skull's top surface SKTS, on the scalp surface S, at the tip of the introducer **200**, at the tip of the ultrasound device **100** or inside or under the access device **400**. Alternatively, the acoustically conductive medium **600** may be delivered through the ultrasound device **100** or around the ultrasound device **100**, or through the introducer **200** or around the introducer **200**, through the access device **400** either intermittently or continuously during the procedure. This media could also serve a second function by cooling the distal end of the ultrasound device and/or adjacent tissue.

[0063] FIG. **3***c* shows an alternative cross section of FIG. **3***a*. FIG. **3***c* provides a film **500** and an acoustically conductive media **600** that are integrated into a pack **501**. Integrating these two elements into one member makes it easier for the user to assemble in situ. FIG. **3***c* also shows an alternative conductive media **201** located between the introducer **200** and the film **500**. This alternative conductive media **201** enhances the transmission of ultrasound energy from the ultrasound device **100** to the patient's intracranial space.

[0064] FIG. **3***d* shows another alternative to FIG. **3***b* with the film **500** being flexible enough or pre-shaped to recess into or through the burr hole BR, and acoustically conductive media **201** being located between the introducer **200** and the flexible film **500**. The thin film **500** or a liner may be located between the access device **400** and the skull S, or between the ultrasound device **100** and the skull S. The film **500** can serve as a sterility barrier between the epidural space or skull, and the access device **400** or the ultrasound device **100**. The film **500** can also serve as an acoustically conductive medium to facilitate ultrasound energy transmission. Also, the film **500** can provide a sealing of the burr hole BR to prevent bleeding of the skull or scalp. The film surface can be provided with thrombogenic properties to enhance thrombosis of bleeding at the scalp S or the skull's top surface SKTS. The film **500** may be attached to the scalp S, the skull SK, the access device **400**, the introducer **200** or the transducer device **100**.

[0065] The film **500** can be composed of organic or synthetic polymers. The polymer material can be coated or impregnated with oil, gels, saline or other fluids to enhance its acoustically conductive properties. Alternatively, the film **500** can have hydrophilic properties so that upon attracting fluid and ions it would also enhance its conductive properties. The film **500** may be embodied in the form of one homogenous layer as shown in FIGS. **1**, **3***a* and **3***d*, or it can be embodied as two sections, with an outer ring **504** and an inner ring **503** as shown in FIGS. **4***a* and **4***b*. The inner ring **503** is constructed of a material whose primary purpose is that of transmitting ultrasound energy. The outer ring **504** is constructed of a material whose primary purpose is helping promote hemostasis of any bleeding at the surgery site. Some examples of materials that can aid in promoting hemostasis include thrombin, cotton, adhesives, gel foam,

cellulose, activated cellulose (such as thrombin impregnated or coated cellulose), Surgicel or Avitene. Alternatively, radio frequency energy and/or bipolar devices can be used to minimize bleeding about the surgical area. Also, bone wax could be used to line the burr hole BR to promote hemostasis. Referring also to FIG. **4***b*, the bottom surface of the film **500** can include a compliant ultrasonically conductive pack that can be constructed of a thin shell material **505** and a liquid or semi-liquid filler material **506**. The material **506** can include materials such as oil, gels or saline.

[**0066**] FIG. **5***a* shows ultrasonically conductive medium in form of a compliant pack **102** attached to the distal end of the ultrasound device **100**. Alternatively, in FIG. **5***b*, a compliant pack **201** is attached to the distal end of the introducer **200** and additional conductive media **103** is provided inside the introducer **200** at the end of the ultrasound device **100**.

[**0067**] FIG. **6** shows ultrasonically conductive medium in a different form of compliant pack **104** located inside the introducer **200** at the end of the ultrasound device **100**.

[**0068**] FIG. **7** shows a cross-sectional view of a human skull and brain. The access device **400** is placed on the skull, and the tubular introducer **200** (with acoustically conductive medium **201**) is advanced in the skull and into a ventricle of the brain. The ultrasound device **100** (with acoustically conductive medium **102**) may to be introduced through the introducer **200** and advanced into a ventricle of the brain. An acoustically conductive thin film **500** or a liner is provided between the access device **400** and the skull.

[**0069**] FIG. **8***a* is a cross-sectional view of a human skull, and brain, showing the access device **400** and the ultrasound device **100** targeting one portion of the clotted cerebral artery, treatment area A. Acoustically conductive medium **102** is positioned at the end of the ultrasound device **100** between the ultrasound device **100** and the patient. Stabilizing members **405** surround the ultrasound device **100** to immobilize the ultrasound device **100** with respect to the base of the access device **400** and with respect to the skull and the treatment area A.

[**0070**] FIG. **8***b* shows the access device **400** and the ultrasound device **100** of FIG. **8***a* redirected to treat a second portion of the clotted cerebral artery, treatment area B. Stabilizing members **405** are repositioned and immobilize the ultrasound device **100** within the access device **400** with respect to the skull and the treatment area B.

[**0071**] FIG. **9** shows the access devices **400** located in several locations on the head with ultrasound energy simultaneously transmitted from multiple ultrasound delivery devices **100** at multiple locations towards the treatment area C. Acoustically conductive medium **600** is located between each ultrasound device **100** and the patient. Such a delivery pattern may be advantageous, for example, in triangulating the ultrasound transmissions toward the same target to facilitate therapy process.

[**0072**] FIG. **10***a* shows an alternative embodiment, in which an acoustically conductive medium **600** may be actively cooled or heated through fluid or gas exchange through an input port **601** and an output port **605**. In one embodiment, an optional nozzle member **700** may be disposed at the distal end **603** of input port **601**, to facilitate the expansion of a liquid into a gas and thus help drive temperature reduction inside acoustically conductive cooling medium **600**. In various embodiments, any suitable acoustically conductive cooling medium **600** may be used, such as but not limited to water, saline, CO2 and/or nitrogen. Additionally, acoustically conductive cooling medium **600** may be delivered under any of a number of suitable pressures or temperatures, according to various embodiments. In one embodiment, an optional vacuum member **701** may be located at the proximal end of output port **605**, to facilitate circulation of acoustically conductive cooling medium **600** through the distal end **604** of the output port **605**. Additionally, in some embodiments, a temperature of acoustically conductive cooling medium **600** may be measured via a thermocouple **608** located inside, outside, or on the surface of acoustically cooling medium **600**. One or more leads **609** of thermocouple **608** would interface with a control box. Some embodiments may further include an optional mixing member **607**, disposed inside of interface **600**, to enhance mixing of acoustically conductive cooling medium **600**.

[**0073**] FIG. **10***b* shows an alternative embodiment, in which an ultrasound device **100** is inserted through an introducer **200** and acoustically conductive cooling medium **600** is provided at the end of introducer **200**, which has an input port **601** and output port **605** allowing for fluid and/or gas exchange to enable cooling. In and alternative embodiment, input port **601** and output port line **605** may be integrated into introducer **200**, which would allow fluid or gas communication with acoustically conductive cooling medium **600** allowing cooling of this element.

[**0074**] FIG. **10***c* shows an alternative embodiment of an acoustically conductive cooling medium **600** having a spiral configuration providing an input port **601** and an output port **605** to allow for fluid and/or gas exchange and enable cooling.

[**0075**] FIG. **10***d* shows a cross-sectional view of an alternative embodiment, in which an access device **400** has an input port **601** and output port **605** to allow for fluid and/or gas exchange inside of the access device **403** to enable cooling the acoustically conductive medium **201**. The acoustically conductive medium **201** may be exposed to the temperature modulation of the cooling fluid **800**.

[**0076**] Although the invention has been described fully above, a number of variations and alterations could be made within the scope of the present invention. For example, in alternative embodiments, steps in the various described methods may be carried out in different orders or skipped altogether, and in other embodiments, additional optional steps may be added or one or more steps may be altered. Therefore, the foregoing description of exemplary embodiments should not be interpreted to limit the scope of the invention described by the following claims.

I claim:

1. A system for delivering ultrasound energy to an intracranial space of a patient, the system comprising:

an access device having an aperture and configured to be applied to a patient's skull;

an ultrasound device coupled with and extending at least partially through the access device, the ultrasound device including proximal and distal ends;

at least one acoustically conductive medium juxtaposed at the distal end of the ultrasound device; and

means for cooling the acoustically conductive medium to a temperature below at least one of room temperature and body temperature.

2. The system of claim 1, wherein the access device includes a movable positioning member that is coupled to the ultrasound device.

3. The system of claim 1, further comprising a tubular introducer member disposed at least partially within the access device, wherein the ultrasound device is disposed at least partially through the introducer member.

4. The system of claim 3, wherein the introducer member is adapted to allow delivery of the cooled acoustically conductive medium to the brain tissue and around the distal end of the ultrasound device.

5. The system of claim 1, further comprising a tubular introducer member disposed along at least a portion of the ultrasound device to facilitate delivery of the cooled acoustically conductive medium to the brain tissue and around the distal end of the ultrasound device.

6. The system of claim 1, wherein the acoustically conductive medium comprises a fluid that conducts ultrasonic energy.

7. The system of claim 1, further comprising a compliant pack, wherein the acoustically conductive medium is retained within the compliant pack.

8. The system of claim 7, wherein the compliant pack includes a thermal element for changing the temperature of the conductive medium.

9. The system of claim 7, wherein the compliant pack includes at least one of an input port and an output port to facilitate exchange of fluid(s) into and/or out of the pack.

10. The system of claim 7, further comprising at least one thermocouple coupled with the compliant pack.

11. The system of claim 1, wherein the ultrasound device is selected from the group consisting of an ultrasound transducer and a transducer-tipped ultrasound catheter.

12. The system of claim 1, wherein the ultrasound device comprises a diagnostic ultrasound device.

13. The system of claim 1, wherein the ultrasound device comprises a therapeutic ultrasound device.

14. The system of claim 1, wherein the ultrasound device comprises a dual-purpose diagnostic and therapeutic ultrasound device.

15. The system of claim 1, wherein the at least one conductive medium is selected from the group consisting of a condensed gel, a diluted gel, saline, and oil.

16. A method for delivering ultrasound energy to a patient's intracranial space, the method comprising:

forming at least one aperture in the patient's skull;

introducing at least one acoustically conductive medium into the intracranial space to contact brain tissue of the patient;

advancing an ultrasound device at least partially through the aperture in the skull;

cooling the acoustically conductive medium; and

transmitting ultrasound energy to the intracranial space, using the ultrasound device.

17. The method of claim 16, further comprising adjusting the orientation of the ultrasound device with respect to the aperture in the skull.

18. The method of claim 16, further comprising passing a tubular introducer at least partially through the aperture, wherein the ultrasound device is advanced at least partially through the introducer.

19. The method of claim 16, wherein advancing the ultrasound device comprises positioning a distal portion of the ultrasound device such that at least part of the distal portion is surrounded by the acoustically conductive medium.

20. The method of claim 16, wherein introducing the at least one conductive medium comprises introducing the medium intermittently during an intracranial procedure.

21. The method of claim 16, wherein introducing the at least one conductive medium comprises introducing at least a portion of the medium in the epidural space.

22. The method of claim 16, wherein introducing the at least one conductive medium comprises introducing at least a portion of the medium in the aperture.

23. The method of claim 16, wherein introducing the at least one conductive medium comprises introducing at least one material selected from the group consisting of a condensed gel, a diluted gel, saline, and oil.

24. The method of claim 16, further comprising delivering at least one pharmacologic agent to the patient.

25. The method of claim 24, wherein the agent is selected from the group consisting of tissue plasminogen activator, rTPA, Urokinease, Streptokinase, Alteplase, Desmoteplase, aspirin, Clopidorgel, Ticclopidine, Abciximab, Tirofiban and Eptifibatide.

26. The method of claim 24, wherein delivering the agent comprises using a method selected from the group consisting of intravenous, arterial and oral delivery.

27. The method of claim 16, further comprising delivering microbubbles or nanobubbles into the patient's bloodstream.

28. The method of claim 16, further comprising providing a mixture of microbubbles and at least one pharmacological agent to the patient.

29. The method of claim 16, wherein advancing the ultrasound device comprises advancing the device to a location selected from the group consisting of above the aperture, within the aperture, at the edge of the aperture into the patient's epidural space, and into an intracerebral space of the patient's brain.

30. The method of claim 16, wherein introducing the conductive medium comprises introducing the medium to a location selected from the group consisting of above the aperture, within the aperture, at the edge of the aperture, in the patient's epidural space, and in an intracerebral space of the patient's brain.

31. A method for delivering ultrasound energy to a patient's intracranial space and cooling a patient's brain tissue, the method comprising:

forming at least one aperture in the patient's skull;

introducing at least one acoustically conductive medium into the intracranial space to contact brain tissue of the patient;

advancing an ultrasound device at least partially through the aperture in the skull;

cooling at least a portion of the patient's brain tissue; and

transmitting ultrasound energy to the intracranial space, using the ultrasound device.

32. The method of claim 31, wherein cooling the brain tissue comprises cooling the acoustically conductive medium.

33. The method of claim 31, further comprising passing a tubular introducer at least partially through the aperture, wherein the ultrasound device is advanced at least partially through the introducer.

34. The method of claim 33, wherein cooling the brain tissue comprises cooling the tip of the introducer.

35. The method of claim 31, wherein cooling the brain tissue comprises cooling a distal end of the ultrasound transducer.

36. The method of claim 31, wherein cooling the brain tissue comprises cooling the tissue while the ultrasound device is not delivering ultrasound energy.

37. The method of claim 31, further comprising adjusting the orientation of the ultrasound device with respect to the aperture in the skull.

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专利名称(译)	用于通过颅孔进行超声输送的方法和系统		
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申请(专利权)人(译)	NITA HENRY		
当前申请(专利权)人(译)	半影区，INC.		
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摘要(译)

一种用于将超声能量传递到患者的颅内空间的方法包括在患者颅骨中形成至少一个孔，将至少一个声学传导介质引入颅内空间以接触患者的脑组织，使超声装置至少部分地前进通过颅骨中的孔径，并使用超声装置将超声能量传输到颅内空间。在一些实施例中，可以冷却声学传导介质以帮助调节患者脑组织的温度。