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(54) Title: CLOSED-LOOP CLOT LYSIS

(57) Abstract: The present invention provides procedures and systems that use a closed-loop approach for directing ultrasound energy at a clot while monitoring blood flow and/or liquification of the clot tissue so as to allow automated and/or manual adjustments to various treatment parameters.



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CLOSED-LOOP CLOT LYSIS

Cross-Reference to Related Applications

[0001] This application claims priority to and the benefits of U.S. provisional patent application serial number 61/116,111, filed November 19, 2008, the entire disclosure of which is incorporated by reference herein.

Technical Field

5 [0002] The present invention relates generally to systems and methods for performing noninvasive procedures using acoustic energy, and, more particularly, to systems and methods for focusing ultrasonic energy to treat thrombotic disease.

Background Information

[0003] Tissue, such as a benign or malignant tumor or blood clot within a skull or other
10 region of a patient's body may be treated invasively by surgically removing the tissue, or non-invasively by using effects of focused ultrasound. Both approaches may effectively treat certain localized conditions within the brain, but involve delicate procedures in which it is desired to avoid destroying or damaging otherwise healthy tissue. These treatments may not be appropriate for conditions in which diseased tissue is integrated into healthy tissue, unless
15 destroying the healthy tissue is unlikely to affect neurological function significantly.

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[0004] The application of ultrasound energy, has been investigated as a potential primary and adjunctive treatment for thrombotic disease. High-intensity focused ultrasound (HIFU) has been shown to enhance thrombolysis induced by tissue plasminogen activator (tPA) in-vitro and in-vivo.

5 **[0005]** Focused ultrasound, has particular appeal for treating tissue within the brain because it generally does not disturb intervening or surrounding healthy tissue. Focused ultrasound may also be attractive because acoustic energy generally penetrates well through soft tissues and ultrasonic energy, in particular, may be focused toward focal zones having a cross-section of only a few millimeters due to relatively short wavelengths (e.g., as small as 1.5 millimeters
10 (mm) in cross-section at one Megahertz (1 MHz)). Thus, ultrasonic energy may be focused at a small target in order to ablate the tissue without significantly damaging surrounding healthy tissue.

[0006] To focus ultrasonic energy toward a desired target, drive signals are sent to a piezoelectric transducer having a number of transducer elements such that constructive
15 interference occurs at a "focal zone." At the focal zone, sufficient acoustic energy may be delivered either to heat tissue until necrosis occurs, or mechanically disrupt its structure until the tissue is destroyed. Preferably, tissue along the path through which the acoustic energy passes (the "pass zone") outside the focal zone is heated only minimally, if at all, thereby minimizing damage to tissue outside the focal zone.

20 **[0007]** Stroke is the third leading cause of death in the United States and a leading cause of adult disability. In general, strokes can be classified as either ischemic or hemorrhagic. In ischemic strokes, the blockage of blood flow results from a clot in intracerebral vessels, whereas hemorrhagic strokes are caused by ruptured blood vessels. Several clinical trials were initiated to evaluate the safety and efficacy of ultrasound-assisted tPA approach to treat stroke

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patients. However, these trials were generally unsuccessful due to adverse events associated with bleeding that were triggered outside the target area.

[0008] Accordingly, there is a need for systems and methods for effectively focusing acoustic energy to treat clots in a manner that does not adversely affect surrounding tissue and
5 can be administered in a timely fashion.

Summary of the Invention

[0009] The present invention provides procedures and systems that facilitate non-invasive, focused clot lysis. In general, the technique uses a closed-loop approach such that immediate feedback is provided to an operator or to an automatic control system. One application directs
10 ultrasound energy at the clot so as to cause it to become smaller (typically through liquefaction) while sparing adjacent tissue. During the application of the ultrasound, blood flow is monitored in the vicinity of the blocked vessel, or, in the case of hemorrhagic stroke, the liquefaction of the clot is monitored. For example, in some embodiments, images are taken of the area surrounding the clot and displayed to an operator so as to provide a real-time indication of blood flow in
15 and/or around the affected blood vessel or the content of the hemorrhage (i.e., solid versus liquid). Based on the monitoring, alterations to the treatment regimen can be administered by increasing or decreasing the overall pressure, energy and changing temporal or spatial characteristics of the acoustic beam (i.e., on/off timing, location). For example the energy transmitted to the clot may be increased or decreased and/or the focus of the ultrasound
20 transducer may be adjusted by modifying various operational parameters of the individual transducer elements. In other embodiments, control is automated — that is, a controller responds to the measured blood flow (and changes therein), and/or the content of the hemorrhage and alters the intensity, pressure and/or direction of the ultrasound energy accordingly. As a result,

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victims of stroke and other clot-related conditions can be treated in a non-invasive, timely manner.

[0010] In a first aspect, a system for delivering acoustic energy to a clot within a blood vessel or a hemorrhage includes a high-intensity focused ultrasound phased-array transducer, means for monitoring blood flow (such as a visual display providing magnetic resonance images, computer tomography images and/or ultrasound images) in the vicinity of the blood vessel as ultrasound energy is directed at the blood vessel, and a controller for operating the transducer and adjusting transducer operation based on the monitored blood flow.

[0011] In some embodiments, the system also includes a processor for generating correction factors based on the monitored blood flow, and the controller responds to the processor by implementing the correction factors (and, based thereon, adjusting the application of the acoustic energy). A beam former may also be used to drive the transducer elements according to the correction factors. In certain cases, the controller may also allow an operator to manually override the correction factors. The phased-array transducer may include numerous transducer elements, each of which can deliver ultrasound energy independent of the others. The images may, in some cases, provide an indication of blood flow and/or oxygen level in blood vessels about the clot, and in certain within the specific blood vessel containing the clot. In other instances, the focal quality of the images being used to monitor the blood flow may be used to determine one or more adjustments.

[0012] The correction factors may include phase correction factors for each (or a group of) transducer elements. In such cases, the controller may also include a phase adjuster for adjusting the excitation signals provided to the transducer elements based on the correction factors. The controller may include amplifiers coupled to the phase adjuster for amplifying the excitation signals provided to respective transducer elements based upon amplitude and/or

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phase correction factors. In some embodiments, the processor constructs an acoustic transmission regime that includes a series of treatment parameters optimized to perform clot lysis. In such cases, the correction factors influence the treatment parameters, thereby adjusting the delivery of ultrasound energy to the clot.

5 **[0013]** In another aspect of the invention, a system for treating a clot within a blood vessel includes a focused ultrasound energy transducer, means for monitoring the liquid content of the blood vessel as energy is delivered to the clot (by an operator using a visual display, for example), and a controller for adjusting the transducer operation based on the monitored liquid content.

10 **[0014]** In some case cases, the system also includes a processor for generating correction factors based on the liquefaction information. In such cases, the controller is responsive to the processor and implements the correction factors, thereby influencing the application of acoustic energy to the clot.

15 **[0015]** In another aspect of the invention, a method for treating a clot within a blood vessel includes applying focused ultrasound energy to the blood vessel using a focused ultrasound phased-array transducer, monitoring blood flow in a vicinity of the blood vessel, and operating the transducer including adjusting the transducer operation based on the monitored blood flow.

20 **[0016]** In some embodiments, the method also includes obtaining subsequent images (e.g., magnetic resonance images, computer tomography images and/or ultrasound images) of the blood vessel during the application of the ultrasound energy and generating correction factors based on the images for transducer elements that comprise the transducer array. In some cases, the focal quality of the images used to monitor the blood flow may also be used to determine or influence the correction factors.

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[0017] The correction factors are then used to create excitation signals based upon the correction factors to focus acoustic energy from the transducer elements at the clot. In some implementations, the above technique may be repeated until the clot is substantially liquefied. The correction factors may include phase correction factors for each (or a group of) transducer elements. In such cases, the excitation signals may be adjusted based on the correction factors, and may further be amplified prior to being provided to respective transducer elements based upon amplitude correction factors. In some embodiments, an acoustic transmission regime that includes a series of treatment parameters optimized to perform clot lysis may be provided. In such cases, the correction factors influence the treatment parameters, thereby adjusting the delivery of ultrasound energy to the clot.

[0018] In another aspect, a method for treating a clot within a blood vessel includes applying focused ultrasound energy to the blood vessel using a focused ultrasound phased-array transducer, monitoring liquid content of the clot in a vicinity of the blood vessel, and operating the transducer including adjusting the transducer operation based on the monitored liquid content.

[0019] In some case cases, images may be used to monitor the liquid content of the clot, and correction factors may be determined based on the liquefaction information as provided in the images.

[0020] The foregoing and other objects, features and advantages of the present invention disclosed herein, as well as the invention itself, will be more fully understood from the following description of preferred embodiments and claims, when read together with the accompanying drawings.

Brief Description of the Drawings

[0021] In the drawings, like reference characters generally refer to the same parts throughout the different views. Also, the drawings are not necessarily to scale, emphasis instead generally being placed upon illustrating the principles of the invention.

5 Fig. 1 schematically illustrates a system for monitoring physiological effects of ultrasound treatment in accordance with various embodiments of the invention.

Fig. 2 is a flow chart illustrating a method for administering ultrasound therapy in accordance with various embodiments of the invention.

Detailed Description

10 [0022] In accordance with the present invention and referring to FIG. 1, a system for quickly treating a patient **P** suffering from a stroke and/or an intracranial clot **C** includes a high-intensity focused-ultrasound phased-array transducer **105** (which is driven by one or more drivers **110**), a controller **120**, and one or more imagers **130** for monitoring clinical parameters related to the clot **C**. The parameters are detectable via the imaging apparatus **130** and can be
15 used to monitor the successful liquefaction of the clot **C**. Examples of such parameters include blood flow in the vicinity of a blood vessel being treated and/or liquification of the clot **C**. In various implementations, the system may also include a processor **140** and a display **150**. Optionally, the system may also include a user interface **160**, such as a touch screen, a keyboard, and/or a mouse. Preferably, the system is configured for delivering ultrasonic energy
20 between ten kilohertz (0.01 MHz) and ten Megahertz (10 MHz) to tissue within the skull or other anatomical regions. Such a system may be used to treat blood clots lodged within blood vessels of a patient or a clot outside blood vessels (generated by ruptured blood vessels) by delivering acoustic energy to the clot. In some cases, the clot may be partially or completely

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blocking a blood vessel in the patient's cranium, or applying intra cranial pressure in case of hemorrhagic clot and causing life-threatening conditions such as a stroke. During delivery of the ultrasonic energy, blood flow (as well as other clinical parameters) in and/or around the affected blood vessel is monitored, and adjustments made to one or more treatment parameters
5 based thereon. The adjustments may be automatic or manual. For example, various images of the patient's anatomy surrounding the clot may be viewed on a display, and adjustments made based on automated or human analysis of the images.

[0023] The transducer **105** may include "n" (where $n > 1$) transducer elements, thereby providing a multiple-element transducer array. The transducer **105** may include a flexible or
10 semi-rigid base or panel conforming to the shape of patient's anatomy, such as the skull if being used to treat cranial blood clots. The transducer **105** may be pre-curved (e.g. biased to a spherical or other concave shape), such that the transducer may be placed on or near a portion of a skull. Alternatively, the transducer **105** may be planar, parabolic, or any other suitable shape, e.g., circular, elliptical, and the like.

15 [0024] Suitable HIFU phased-array transducers are known in the art. *See, e.g.*, co-pending, commonly-owned U.S. Patent Application Serial No. 10/328,584, entitled "Tissue Aberration Corrections in Ultrasound Therapy."

[0025] The system may obtain, process and present images of the interior anatomy of the patient **P**, including the area surrounding the clot **C**. For example, the images may be taken
20 using a magnetic resonance imaging (MRI) device, a computer tomography (CT) device, or an ultrasound imaging device. The images processed by the processor **140** and presented on the display **150** indicate the state of blood flow and/or liquification of tissue about the clot **C**, either within the specific blood vessel in which the clot is lodged, or, in some cases, in blood vessels surrounding the clot or a general measure of perfusion surrounding the clot **C** or within the

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hemorrhagic clot. As ultrasound energy is applied to the clot, an operator views the images in real-time or pseudo-real time (e.g., a delay of less than five seconds), and thus is able to see the effects of the ultrasound on the clot and the resulting improvement of blood flow or perfusion. The effects of reflow or liquefaction may be also assessed directly or by other bio-imaging parameters.

[0026] Based on the observed and/or detected blood flow or liquid content of the hemorrhage, a processor **140** may generate correction factors to be applied to the signals that drive the transducers **105**. The processor **140** may, for example, determine the correction factors by automatically analyzing images and estimating blood flow or liquid content (and, in some embodiments, identifying tissue characteristics of interest) from the images. Sufficient information is provided by the images (or other monitoring modality) to facilitate determination of the correction factors. Alternatively, a user may manually analyze the images and observe blood flow or liquid content and identify tissue characteristics, or a combination of automatic and manual analysis may be used. In some instances, the focal quality of the images themselves may be determined and used to influence the correction factors. For example, if a particular image is known to be of poor quality, its contribution to the correction factor(s) may be down-weighted.

[0027] The processor **140** may, for example, receive instructions as input by the operator, or, in some cases, automatically recognize an increase in blood flow, perfusion (or lack thereof), and/or liquid content based, for example, on the images. The correction factors can be applied to treatment parameters that govern the application of HIFU energy, thereby influencing subsequent ultrasound applications. In some implementations, the processor **140** includes a number of amplifiers and/or phase shifters that are coupled in respective sets. The amplifiers provide amplified excitation signals to the transducer elements **105**, e.g., via coaxial

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cables or other connections, which may individually connect the amplifiers and respective transducer elements.

[0028] Among other effects, the correction factors allow the acoustic energy transmitted by the transducer elements to be steered such that the “focal zone” (the region in space toward
5 which the acoustic energy is focused) can be moved, along the z axis (i.e., an axis extending orthogonally from the transmission surface of the transducer into the skull) and/or along the x or y axes. The component of each phase-shift factor associated with steering may be computed using known techniques, e.g., using the average speed of sound in the body (possibly adjusted for different tissue types) and the distance from each transducer element to a target site of
10 interest (the intended focal zone within a tissue region).

[0029] In addition, in cranial applications, the correction factors may also compensate for phase distortion of the ultrasonic energy transmitted by each transducer element that occurs when the acoustic energy passes through the skull. The component of each correction factor associated with phase distortion may compensate for perturbations and distortions introduced
15 by the bone of the skull, the skin/skull interface, the dura matter/skull interface, by variations in skull thickness or density, and/or by structural considerations such as air-filled or liquid-filled pockets in the skull. The two components that make up the phase-shift factors, i.e., the steering components and the phase-distortion components, are summed to determine the composite phase-shift factors for the respective channels in order to focus ultrasonic energy at a desired
20 location.

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[0030] In some cases, the processor **140** or the operator may also construct an initial treatment regime describing various treatment parameters (e.g., pressure, temporal structure, frequency, energy, etc.) that creates a sharp focus (e.g., less than 5 mm) of the ultrasound energy, thereby facilitating clot lysis in a targeted manner. In such cases, the correction factors
5 determined during treatment may be applied to the treatment regime in real-time.

[0031] The phase-shift factors may, in some cases, be determined by the processor **140** and/ or the system image and display computer, which may be coupled to the controller **120** and to an imager **130**. Alternatively, the controller **120** itself may include all necessary hardware components and/or software modules to determine the correction factors instead of
10 requiring a separate computer. The system may include one or more software modules, hardware components, firmware, hardwiring, or any combinations of these. For example, the processor may be a general or special purpose digital data processor programmed with software to generate the phase shift factors, which may be transferred to the controller for subsequent transfer to the phase shifters or directly to the phase shifters based upon images shown on the
15 display.

[0032] In addition to providing a system for using high-intensity ultrasound to treat transcranial clots, various embodiments of the invention provide methods for treating stroke victims using such a system as described below and illustrated in FIG. 2.

[0033] Upon initial examination, an imager is used to acquire one or more images (**STEP**
20 **205**) of a clot area within a patient's brain. As explained above, the imager may be any of a variety of imaging devices, such as an MRI device, a CT device, or an ultrasound device or a combination/fusion of images.

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[0034] Data representing the images are transferred to a processor (**STEP 210**), and presented on a display (**STEP 215**). In implementations in which the patient is being treated for a stroke, the transfer of image data may occur immediately upon acquiring the images from the patient in order to provide treatment quickly. The transfer may be completed automatically
5 or may occur only upon instruction from a physician or other operator.

[0035] Based on the image data, correction factors and other potential adjustments may be determined (**STEP 220**) for treatment of the clot. As described above, the correction factors may account for different speeds of sound that are encountered as the acoustic energy passes through different tissue types in respective segmented tissue regions. In addition or
10 alternatively, the correction factors may account for aberrations generated by the skull or at boundaries of the segmented tissue regions, as explained further below.

[0036] The resulting correction factors, e.g., phase-shift factors and/or amplitude factors, may be used to assist a particular course of treatment, preferably focusing acoustic energy at the clot. Once determined, the correction factors may be provided to the controller which, in
15 turn, provides excitation signals (**STEP 225**) to the transducer array. The focused ultrasound system uses the correction factors to control a beam former or signal adjuster which delivers excitation or drive signals to the transducer based upon the correction factors for application of the ultrasound treatment (**STEP 230**). For example, one or more base signals may be supplied to a signal adjuster and split into a plurality of channels, preferably into individual channels
20 corresponding to respective transducer elements or transducer element groupings of the transducer array. The phase of the signals for the respective channels may be adjusted by the signal adjuster according to phase correction factors received by the controller. For example, the phases may be adjusted to compensate for acoustic energy from respective transducer elements passing through different tissue types and/or encountering one or more tissue

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boundaries. In one particular case, the amplitude adjustments may be done to compensate for a known or calculated skull temperature or to generate desired skull temperature. Such an approach may be implemented a priori based, for example, on an acoustic-bio-heat simulation or based on actual skull temperature measurements. In some cases, the system may assume an
5 even temperature distribution on the skull.

[0037] This may be in addition to other phase adjustments that focus the acoustic energy at a particular location or in a particular shape or to compensate for transducer element variations, as is known to those skilled in the art. The phase-adjusted signals may be amplified based upon amplitude correction factors, e.g., by amplifiers, which may amplify the excitation signals.
10 Alternatively, the signals for the respective channels may be amplified before they are phase-adjusted.

[0038] The amplified and phase-adjusted excitation signals may be delivered to the transducer to drive the respective transducer elements. The transducer elements convert the excitation signals into acoustic energy that is transmitted from the respective transducer
15 elements of the transducer into the blood vessel containing the clot or hemorrhage inside the brain (or its general area) through any intervening tissue and/or bone, such as the skull.

[0039] During the treatment, additional images may be acquired (**STEP 235**) using the same or a different imager than used to acquire reference image data to monitor the progress of the treatment. For example, the images may be transferred to the processor and/or rendered on
20 a display for real-time or nearly real-time monitoring. In some implementations, the images acquired during treatment may be compared with the previously acquired reference images to determine if, for example, the blood flow within the blood vessel has improved or the hemorrhage has been liquefied. This comparison may be made by the operator or in an automated fashion using image-analysis software configured to recognize fluid flow through or

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liquid content of a clot. If necessary, the treatment parameters may be adjusted, e.g., by providing further amplitude and/or phase correction factors, to modify the energy delivered to the tissue region and reflect events as they unfold, e.g., to increase monitored blood flow or liquid content. Treatment is thereby delivered in a controlled, closed-loop manner that
5 considers how the treatment is affecting the physiological characteristics of the clot and/or the treatment zone surrounding the clot.

[0040] In another mode of implementation the phase settings are adjusted based on the quality of the focus. The focal quality may be sensed using regular imaging or, in some cases, unique modes of imaging tailored to assess focus quality such as acoustic radiation force
10 imaging. In these implementations, the phases are dithered to identify optimal focus that defines the phase setting.

[0041] While the invention has been particularly shown and described with reference to specific embodiments, it should be understood by those skilled in the area that various changes in form and detail may be made therein without departing from the spirit and scope of the
15 invention as defined by the appended claims. The scope of the invention is thus indicated by the appended claims and all changes which come within the meaning and range of equivalency of the claims are therefore intended to be embraced.

[0042] What is claimed is:

CLAIMS

- 1 1. A system for delivering acoustic energy to a clot within a blood vessel, the system
2 comprising:
 - 3 a. a focused-ultrasound phased-array transducer;
 - 4 b. means for monitoring blood flow in a vicinity of the blood vessel as ultrasound
5 energy is directed at the blood vessel; and
 - 6 c. a controller for operating the transducer and adjusting transducer operation
7 based on the monitored blood flow.
- 1 2. The system of claim 1 wherein the means for monitoring blood flow comprises a visual
2 display.
- 1 3. The system of claim 1 further comprising a beam former for driving the transducer
2 elements based on the monitored blood flow.
- 1 4. The system of claim 1 further comprising a processor for generating correction factors
2 based on the monitored blood flow and wherein the controller is responsive to the processor,
3 thereby implementing the correction factors and influencing the application of acoustic energy
4 to the clot.
- 1 5. The system of claim 2 wherein the controller further assesses a focal quality of images
2 used to monitor the blood flow applying phase correction factors to adjust alter the focus.
- 1 6. The system of claim 1 wherein the treatment effect is monitored based on an oxygen
2 level within the vicinity of the blood vessel blood.
- 1 7. The system of claim 4 wherein the controller permits a user to override one or more of
2 the correction factors.

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- 1 8. The system of claim 1 wherein the phased-array transducer comprises a plurality of
2 transducer elements, each element configured to deliver ultrasound energy independently of the
3 others.
- 1 9. The system of claim 1 wherein the images comprise one or more of a magnetic
2 resonance image, a computer tomography image, and an ultrasound image.
- 1 10. The system of claim 1 wherein the images provide an indication of blood flow about the
2 blood vessel.
- 1 11. The system of claim 10 wherein the monitored blood flow includes blood flow through
2 the blood vessel containing the clot.
- 1 12. The system of claim 1 wherein the controller comprises a phase adjuster for adjusting
2 phases of excitation signals provided to transducer elements based upon phase correction
3 factors for respective transducer elements.
- 1 13. The system of claim 12, wherein the controller comprises one or more amplifiers
2 coupled to the phase adjuster for amplifying the excitation signals provided to the respective
3 transducer elements based upon amplitude correction factors.
- 1 14. The system of claim 13 where the amplitude adjustments result in a uniform
2 temperature distribution about the patient's skull.
- 1 15. The system of claim 13 where the amplitude adjustments are determined at least in part
2 on a predefined temperature map.
- 1 16. The system of claim 1 wherein the processor constructs an acoustic transmission regime
2 comprising a plurality of treatment parameters optimized to perform clot lysis, the correction
3 factors influencing one or more of the treatment parameters.

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1 17. A system for delivering acoustic energy to a clot within a blood vessel, the system
2 comprising:

- 3 a. a focused-ultrasound phased-array transducer;
- 4 b. means for monitoring liquid content of the clot as ultrasound energy is directed
5 at the clot; and
- 6 c. a controller for operating the transducer and adjusting transducer operation
7 based on the monitored liquid content.

1 18. The system of claim 17 wherein the means for monitoring liquefaction comprise a
2 visual display.

1 19. The system of claim 17 further comprising a processor for generating correction factors
2 based on the liquefaction information and wherein the controller is responsive to the processor,
3 thereby implementing the correction factors and influencing the application of acoustic energy
4 to the clot.

1 20. A method for treating a clot within a blood vessel, the method comprising the steps of:

- 2 a. applying focused ultrasound energy to the blood vessel using a focused-
3 ultrasound phased-array transducer;
- 4 b. monitoring blood flow in a vicinity of the blood vessel as ultrasound energy is
5 directed at the blood vessel; and
- 6 c. operating the transducer including adjusting transducer operation based on the
7 monitored blood flow.

1 21. The method of claim 20 further comprising obtaining subsequent images of the cranial
2 blood vessel during the application of the ultrasound energy.

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- 1 22. The method of claim 20 further comprising
2 (d) assessing a focal quality in situ and applying phase correction factors to adjust alter
3 the focus.
- 1 23. The method of claim 22 further comprising:
2 (e) generating respective correction factors for one or more transducer elements of the
3 transducer array based on the images.
- 1 24. The method of claim 20 wherein the images comprise at least one of a magnetic
2 resonance image, a computer tomography image, and an ultrasound image.
- 1 25. The method of claim 20 wherein the indication of blood flow indicates blood flow
2 through the blood vessel in which the clot lies.
- 1 26. The method of claim 23 wherein the correction factors comprise phase correction
2 factors associated with respective transducer elements, and further comprising adjusting phases
3 of excitation signals provided to the transducer based upon the phase correction factors.
- 1 27. The method of claim 23 further comprising driving the phased-array transducer with
2 excitation signals based upon the correction factors to focus acoustic energy from the
3 transducer elements at the clot.
- 1 28. The method of claim 26, wherein the excitation factors comprise amplitude correction
2 factors associated with respective transducer elements, and further comprising amplifying the
3 excitation signals provided to the respective transducer elements based upon the amplitude
4 correction factors.

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1 29. The method of claim 23 further comprising constructing an acoustic transmission
2 regime comprising a plurality of treatment parameters optimized to perform clot lysis and
3 wherein the correction factors influence one or more of the treatment parameters.

1 30. The method of claim 23 further comprising repeating steps (b) – (e) until the clot is
2 substantially ablated.

1 31. A method for treating a clot within a blood vessel, the method comprising the steps of:

2 a. applying focused ultrasound energy to the clot using a focused-ultrasound
3 phased-array transducer;

4 b. monitoring liquid content of the clot as ultrasound energy is directed at the
5 blood vessel; and

6 c. operating the transducer including adjusting transducer operation based on the
7 monitored liquid content.

1 32. The method of claim 31 further comprising obtaining subsequent images of the clot
2 during the application of the ultrasound energy.

1 33. The method of claim 32 further comprising generating respective correction factors for
2 each transducer element of the transducer array based on the images.

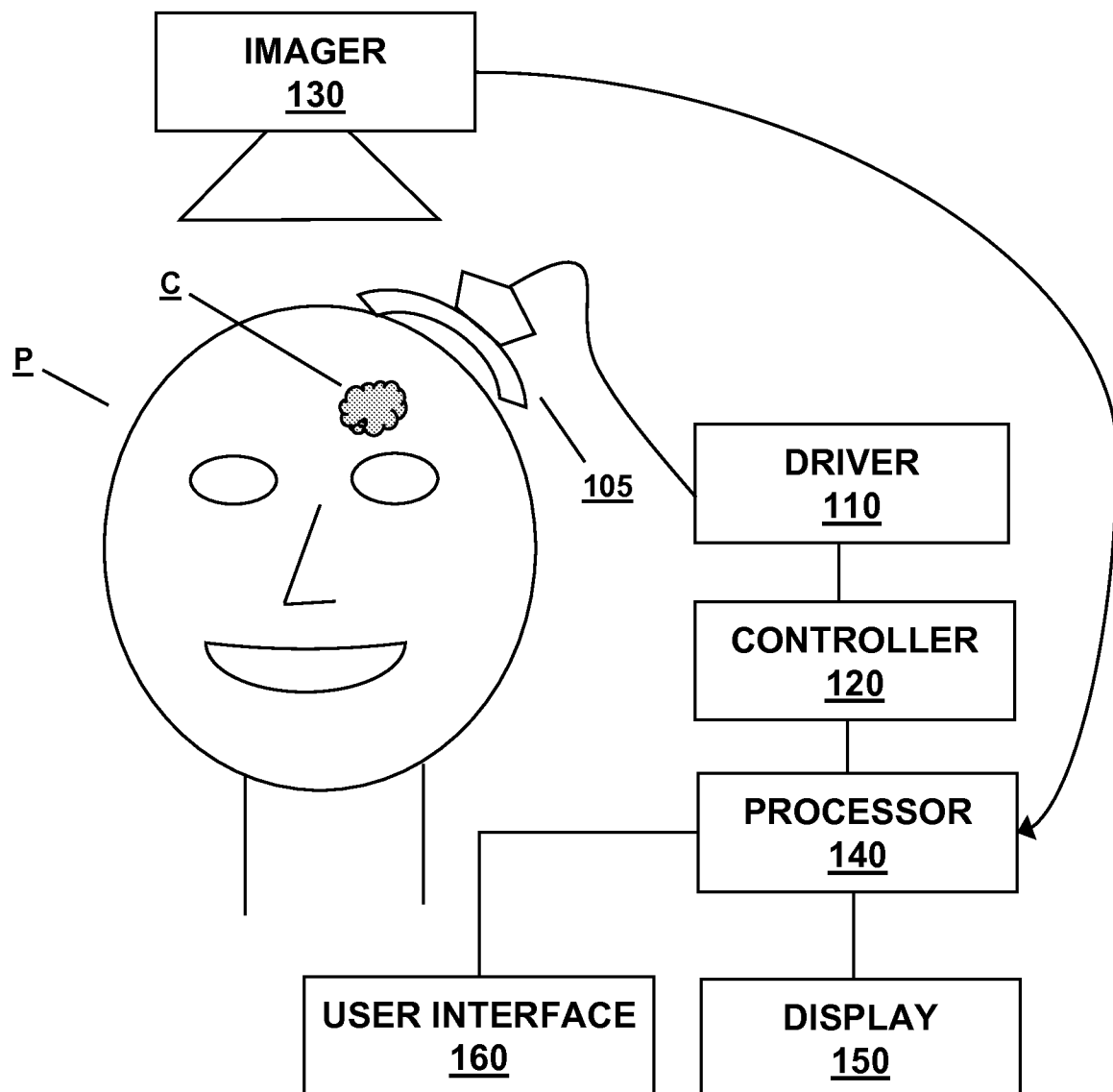
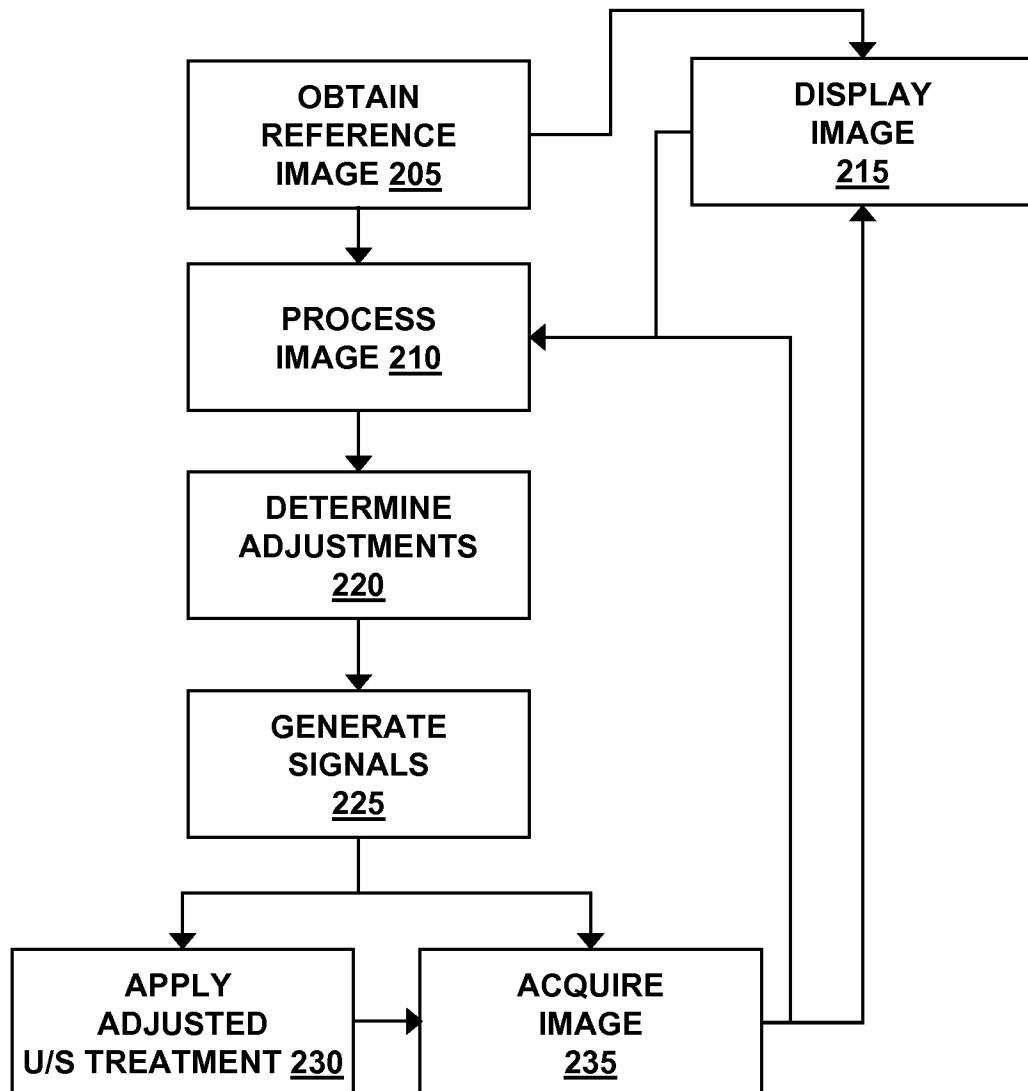


FIG. 1

**FIG. 2**