US 20100179425A1

(19) United States
(12) Patent Application Publication
Zadicario
(10) Pub. No.: US 2010/0179425 A1
(43) Pub. Date: Jul. 15, 2010

(54) **SYSTEMS AND METHODS FOR CONTROLLING ULTRASOUND ENERGY TRANSMITTED THROUGH NON-UNIFORM TISSUE AND COOLING OF SAME**

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(21) Appl. No.: **12/352,932**

(22) Filed: **Jan. 13, 2009**

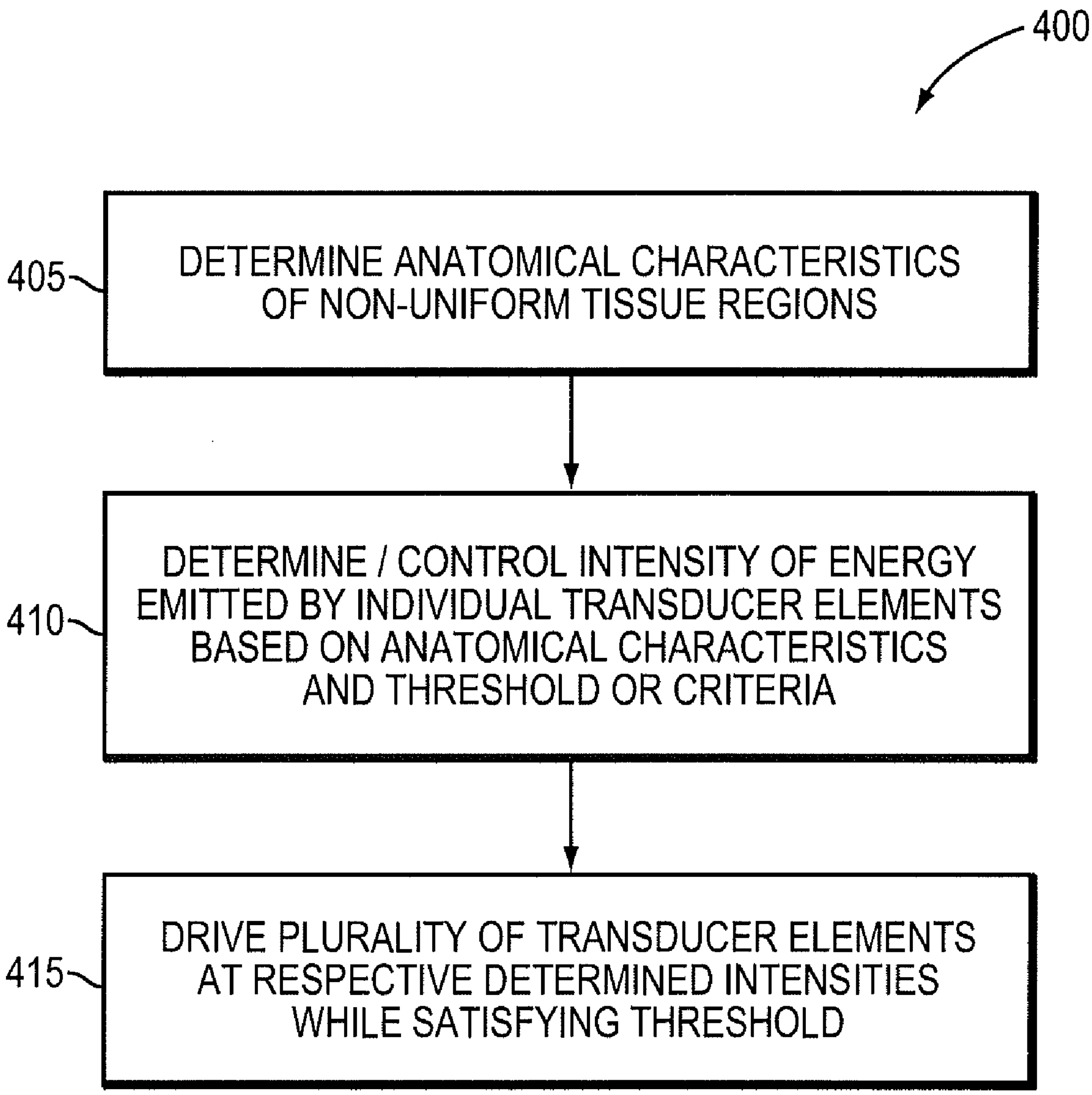
Publication Classification

(51) **Int. Cl.**
A61B 8/00 (2006.01)

(52) **U.S. Cl.** **600/438**

(57) **ABSTRACT**

The emission intensities of transducer elements of an ultrasound transducer array are controlled based on anatomical characteristics of non-uniform tissue regions, e.g., regions of a skull, and a pre-determined threshold.



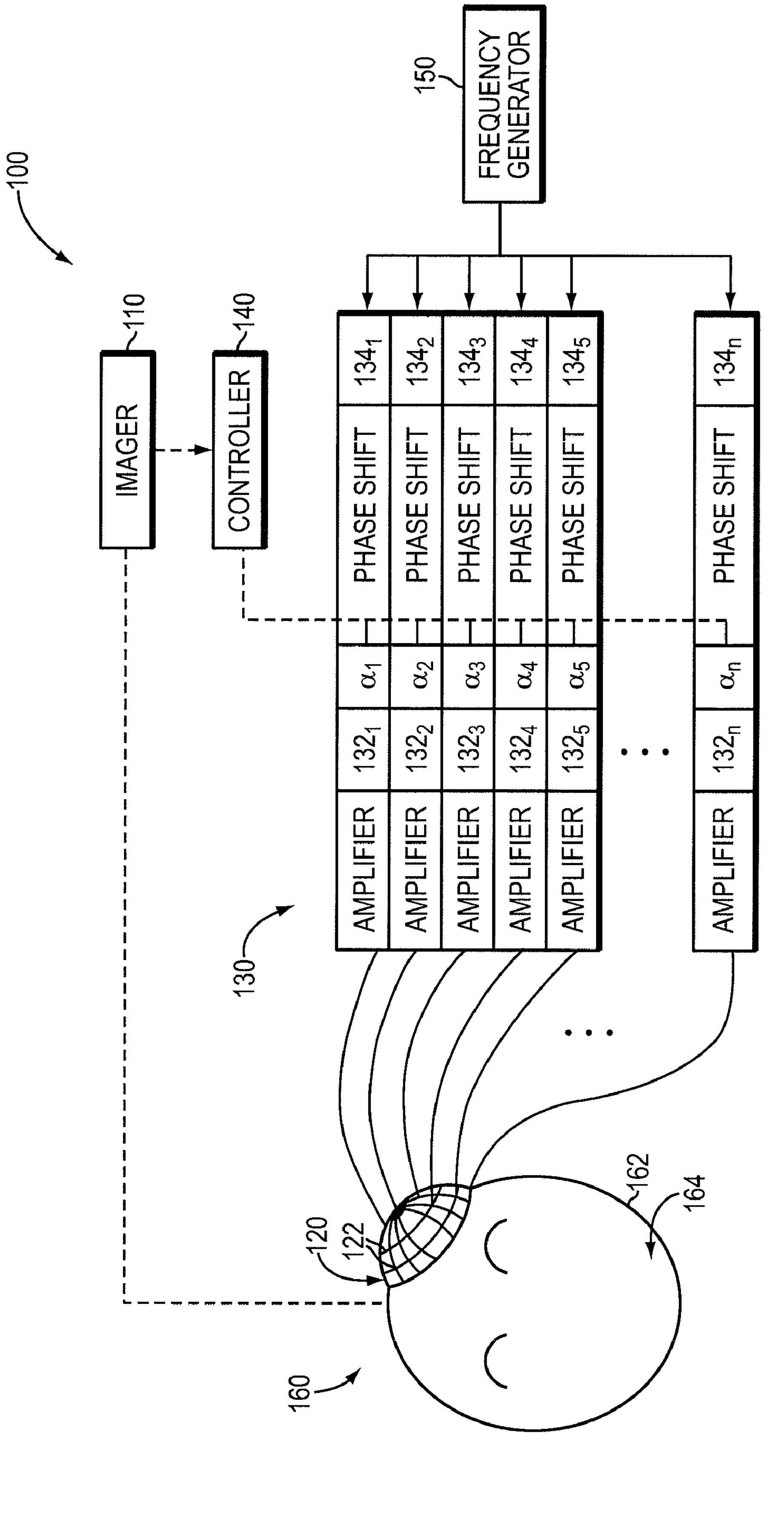


FIG. 1
(PRIOR ART)

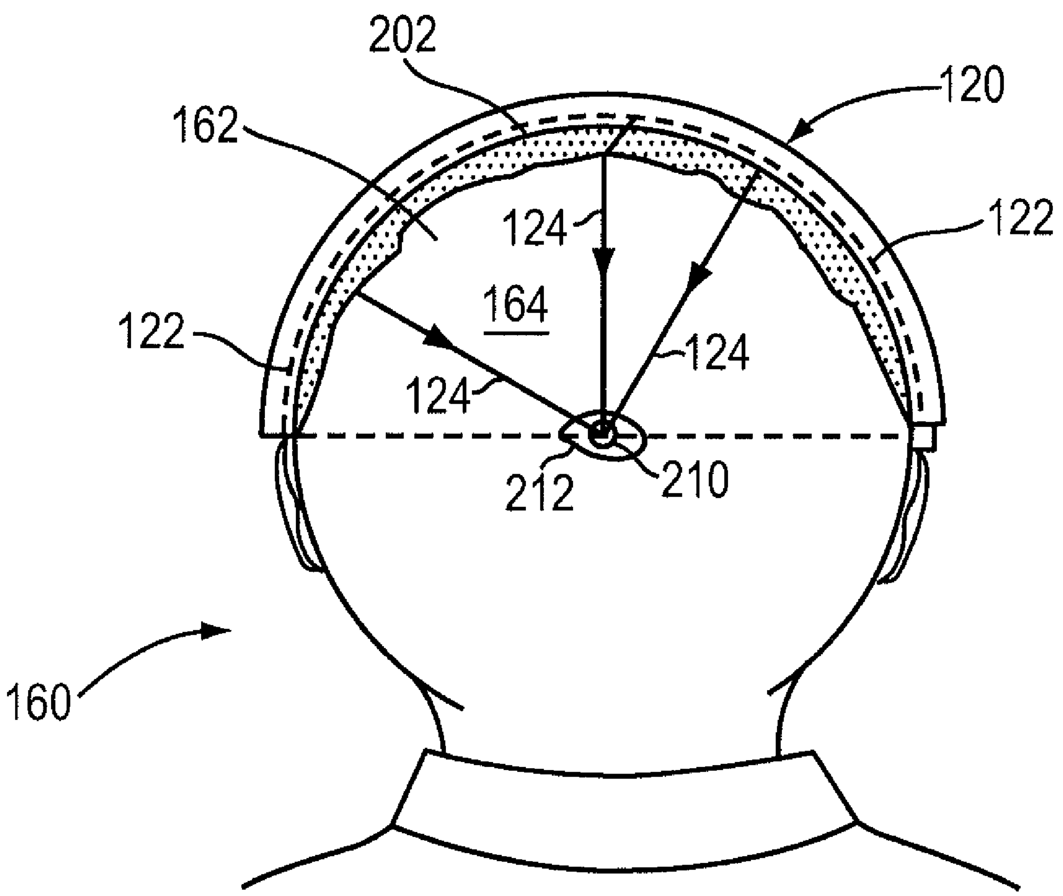


FIG. 2
(PRIOR ART)

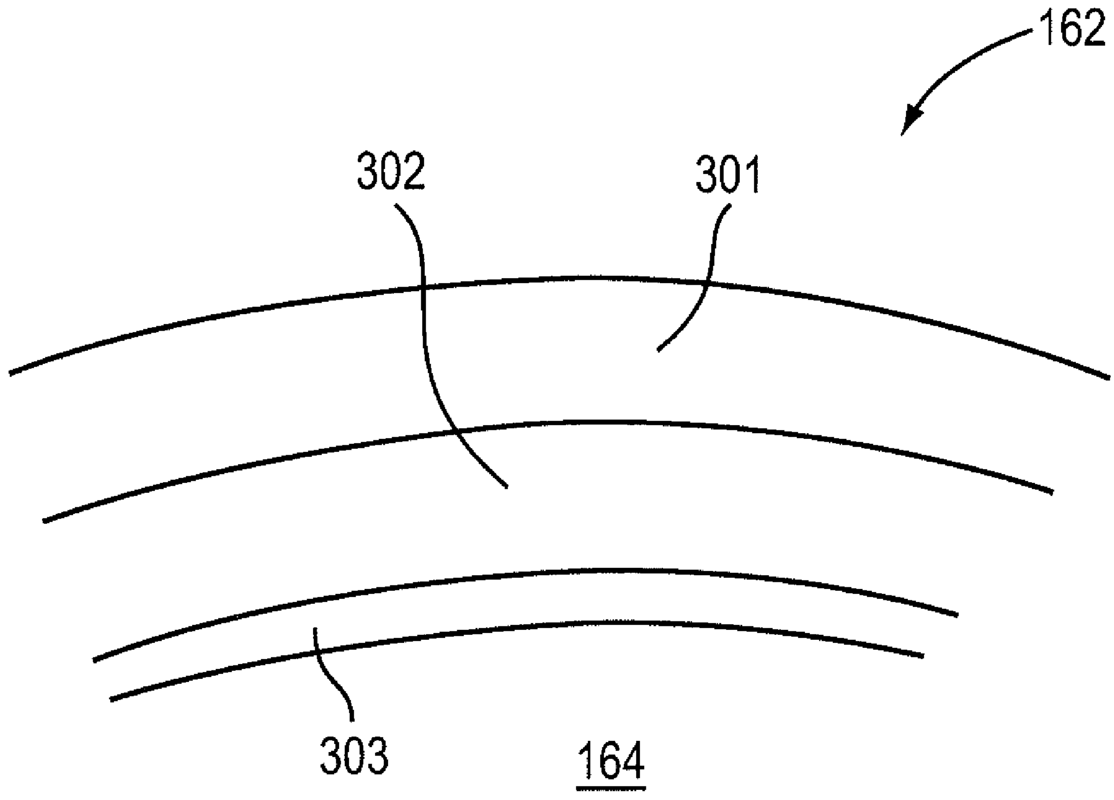


FIG. 3
(PRIOR ART)

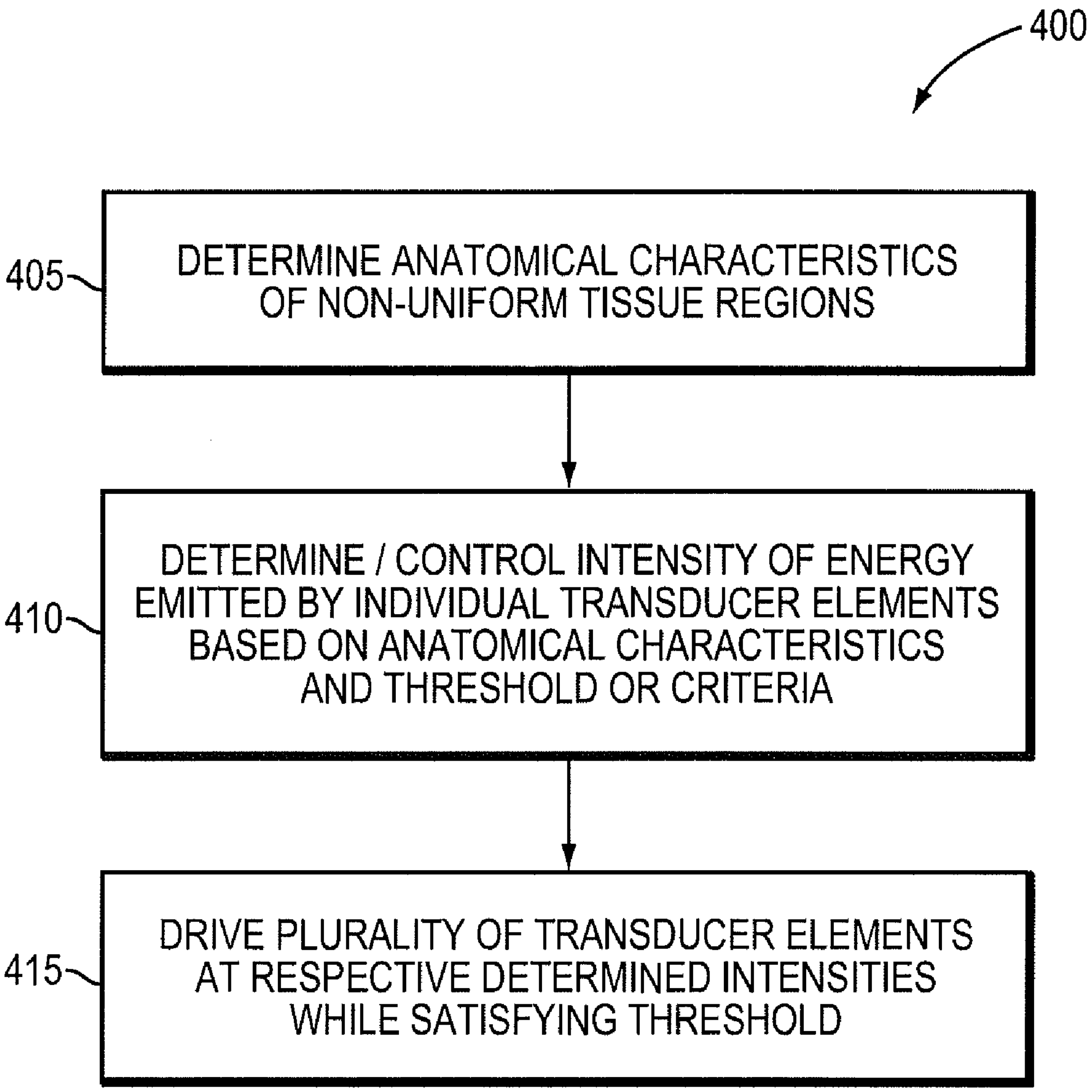

400
405
DETERMINE ANATOMICAL CHARACTERISTICS OF NON-UNIFORM TISSUE REGIONS
410
DETERMINE / CONTROL INTENSITY OF ENERGY EMITTED BY INDIVIDUAL TRANSDUCER ELEMENTS BASED ON ANATOMICAL CHARACTERISTICS AND THRESHOLD OR CRITERIA
415
DRIVE PLURALITY OF TRANSDUCER ELEMENTS AT RESPECTIVE DETERMINED INTENSITIES WHILE SATISFYING THRESHOLD

FIG. 4

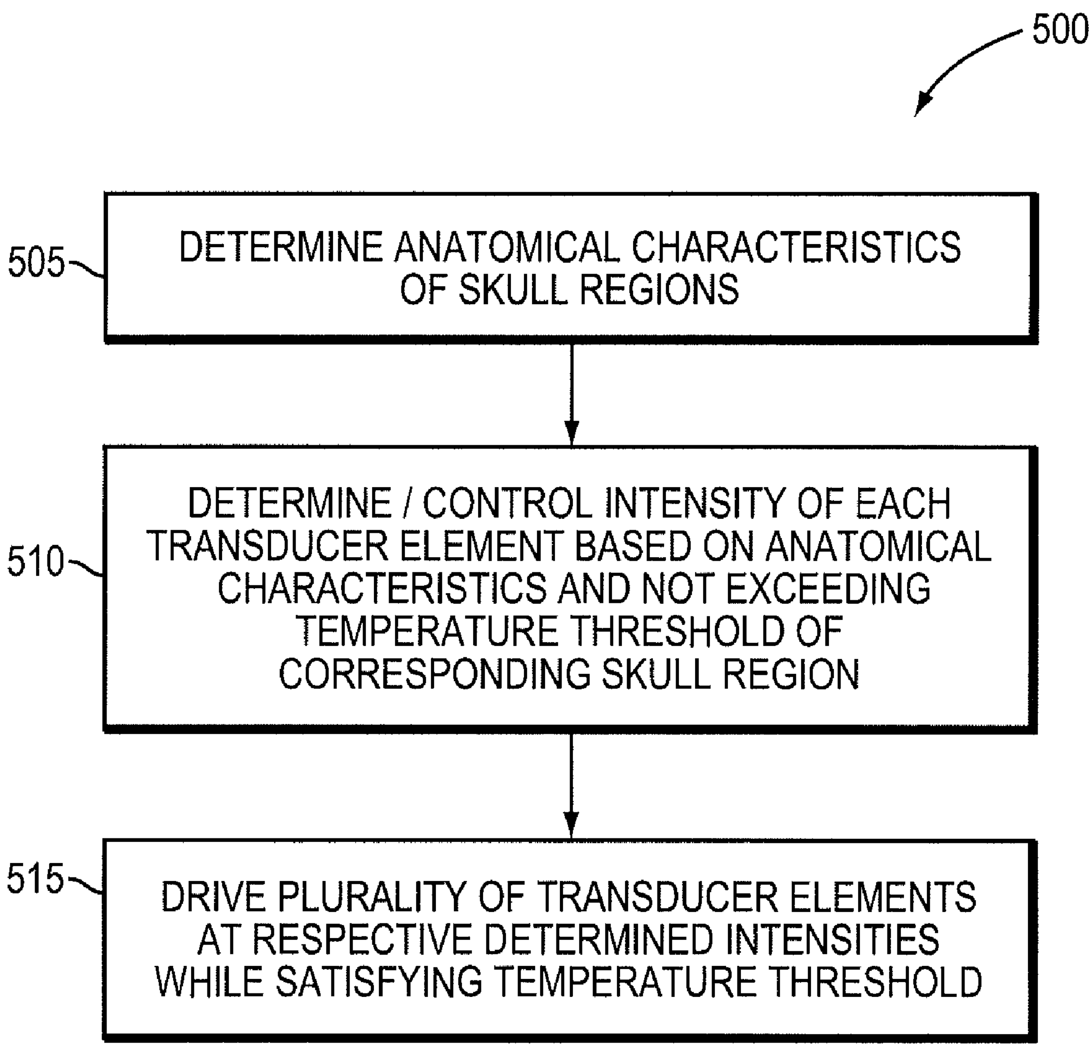

500
505
DETERMINE ANATOMICAL CHARACTERISTICS OF SKULL REGIONS
510
DETERMINE / CONTROL INTENSITY OF EACH TRANSDUCER ELEMENT BASED ON ANATOMICAL CHARACTERISTICS AND NOT EXCEEDING TEMPERATURE THRESHOLD OF CORRESPONDING SKULL REGION
515
DRIVE PLURALITY OF TRANSDUCER ELEMENTS AT RESPECTIVE DETERMINED INTENSITIES WHILE SATISFYING TEMPERATURE THRESHOLD

FIG. 5

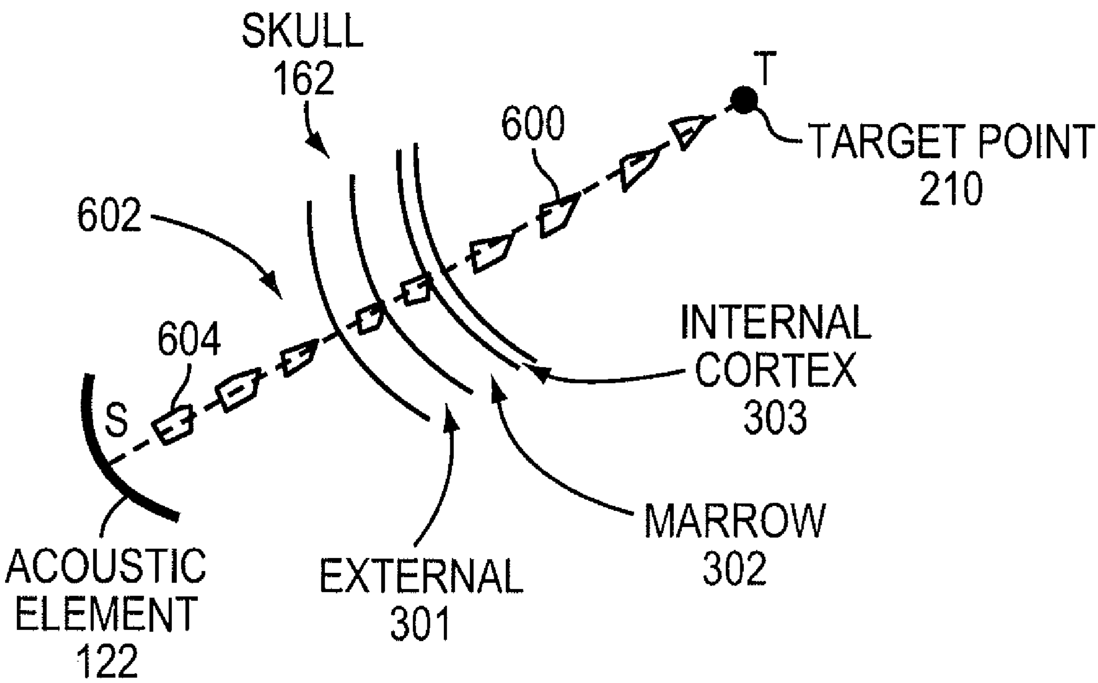

SKULL
162
T
600
TARGET POINT
210
602
INTERNAL
CORTEX
303
604
S
MARROW
302
ACOUSTIC
ELEMENT
122
EXTERNAL
301

FIG. 6

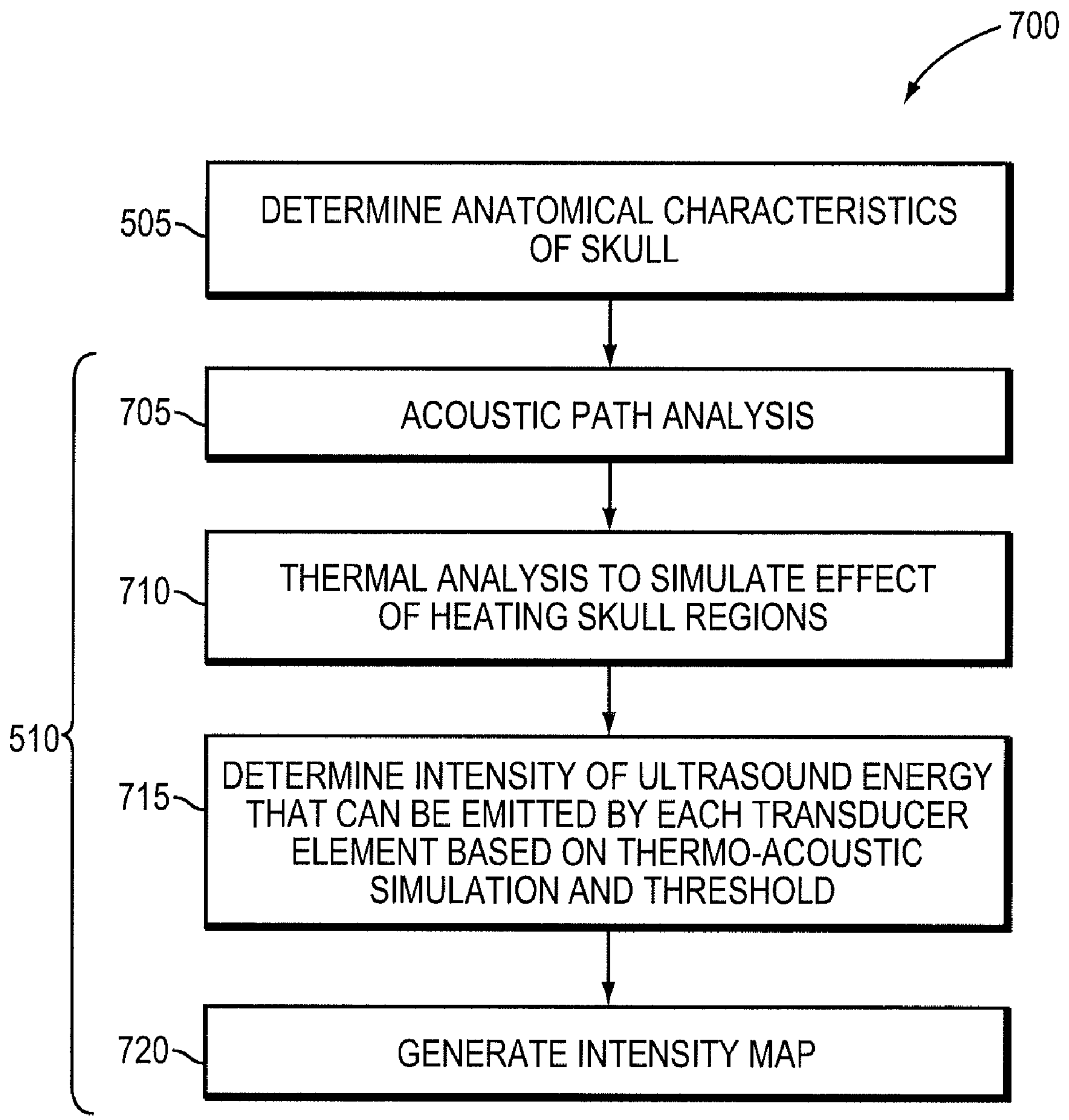

700
505
DETERMINE ANATOMICAL CHARACTERISTICS OF SKULL
705
ACOUSTIC PATH ANALYSIS
710
THERMAL ANALYSIS TO SIMULATE EFFECT OF HEATING SKULL REGIONS
510
715
DETERMINE INTENSITY OF ULTRASOUND ENERGY THAT CAN BE EMITTED BY EACH TRANSDUCER ELEMENT BASED ON THERMO-ACOUSTIC SIMULATION AND THRESHOLD
720
GENERATE INTENSITY MAP

FIG. 7

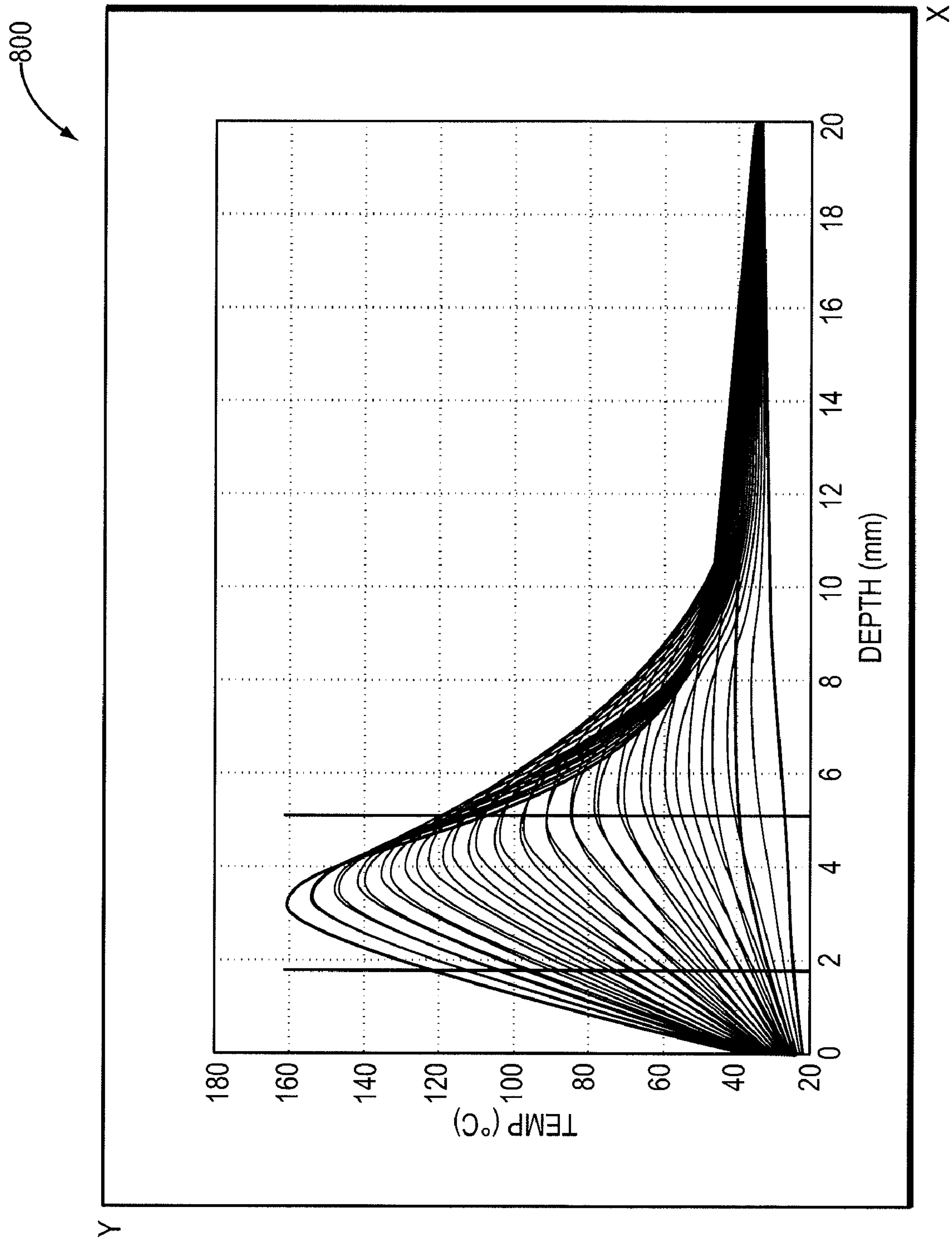

800
X
Y
TEMP (°C)
180
160
140
120
100
80
60
40
20
DEPTH (mm)
0
2
4
6
8
10
12
14
16
18
20

FIG. 8

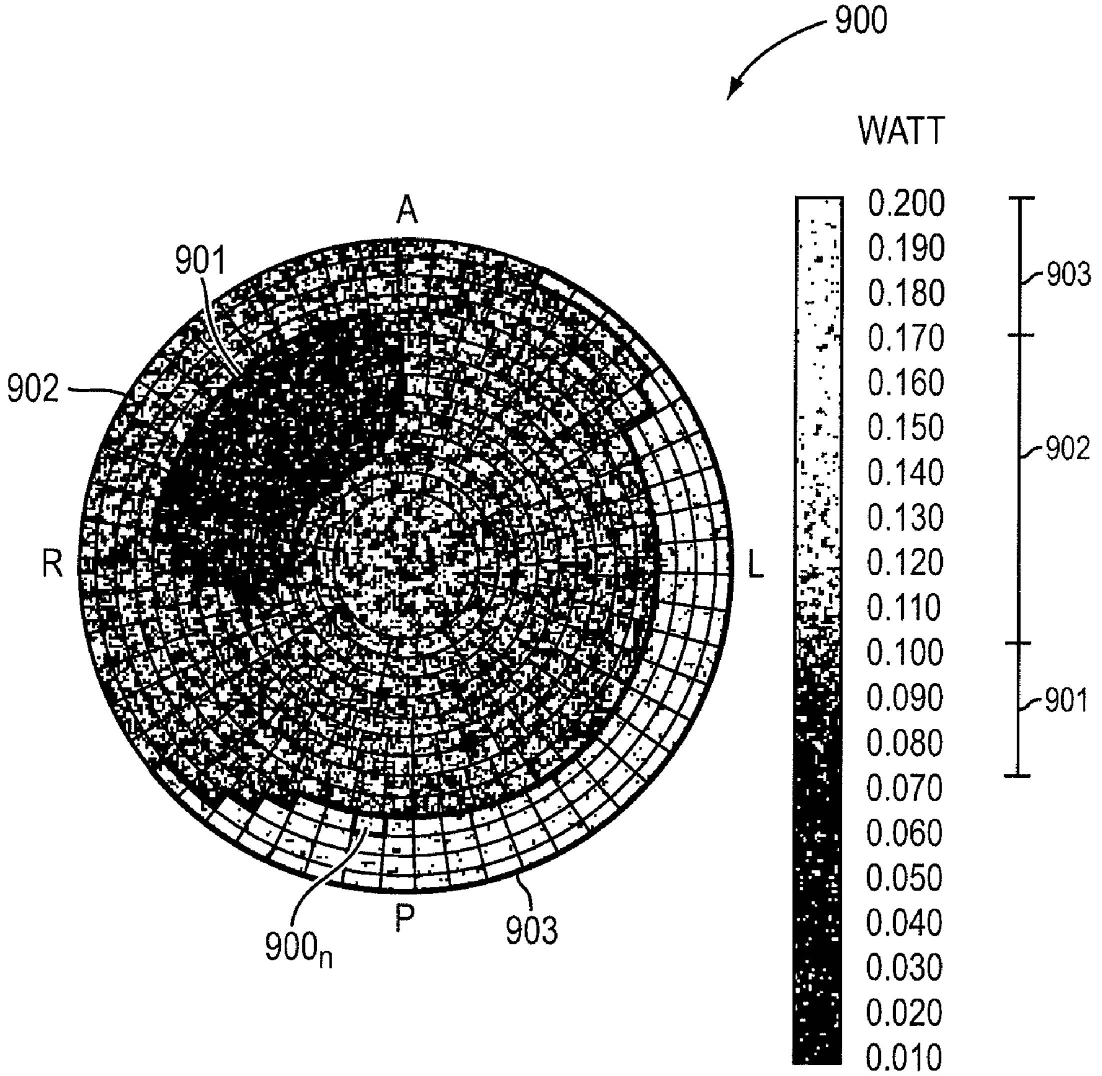

900
WATT
A
901
902
R
L
P
900n
903
0.200
0.190
0.180
0.170
0.160
0.150
0.140
0.130
0.120
0.110
0.100
0.090
0.080
0.070
0.060
0.050
0.040
0.030
0.020
0.010
903
902
901

FIG. 9

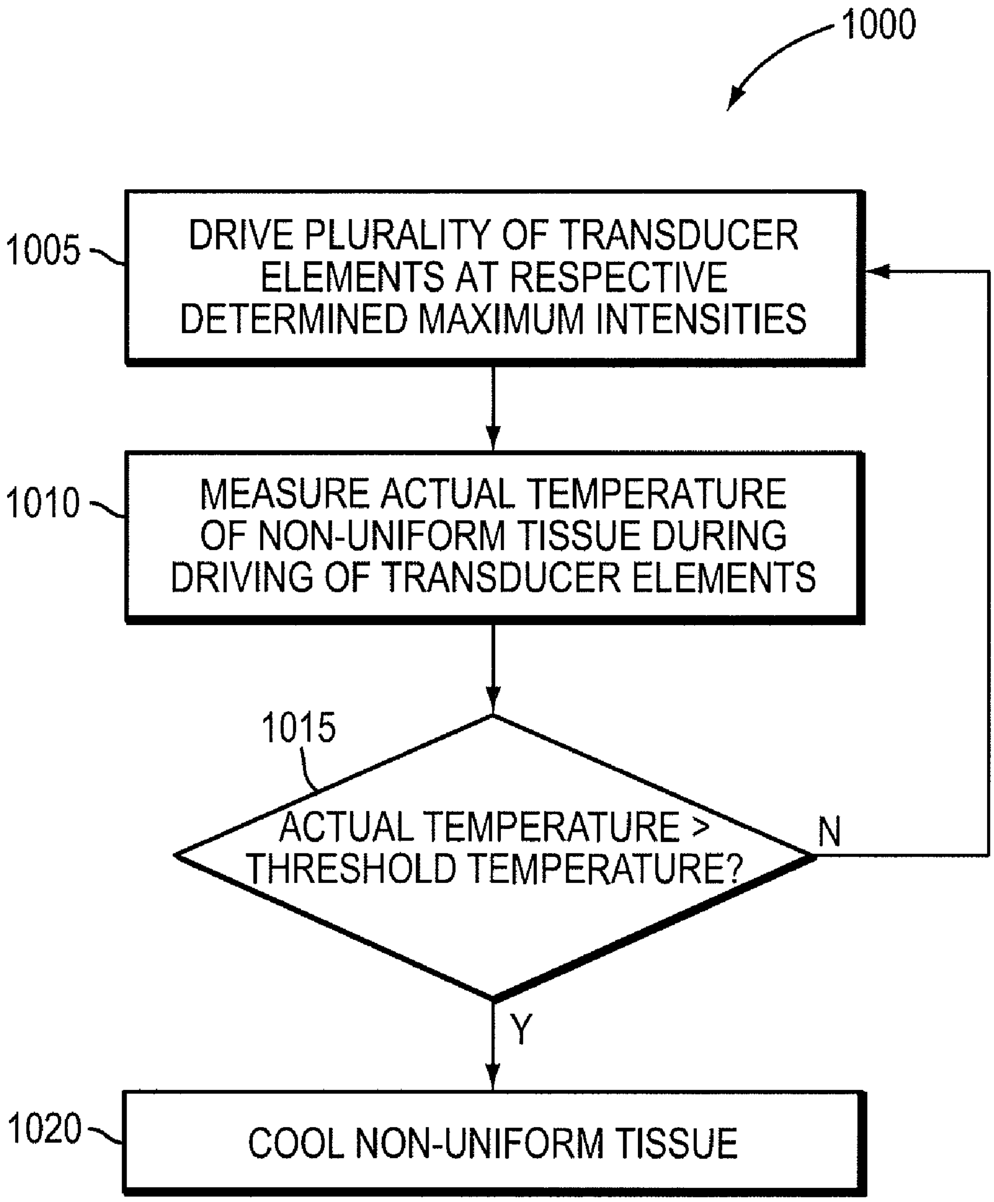

1000
1005
DRIVE PLURALITY OF TRANSDUCER ELEMENTS AT RESPECTIVE DETERMINED MAXIMUM INTENSITIES
1010
MEASURE ACTUAL TEMPERATURE OF NON-UNIFORM TISSUE DURING DRIVING OF TRANSDUCER ELEMENTS
1015
ACTUAL TEMPERATURE > THRESHOLD TEMPERATURE?
N
Y
1020
COOL NON-UNIFORM TISSUE

FIG. 10

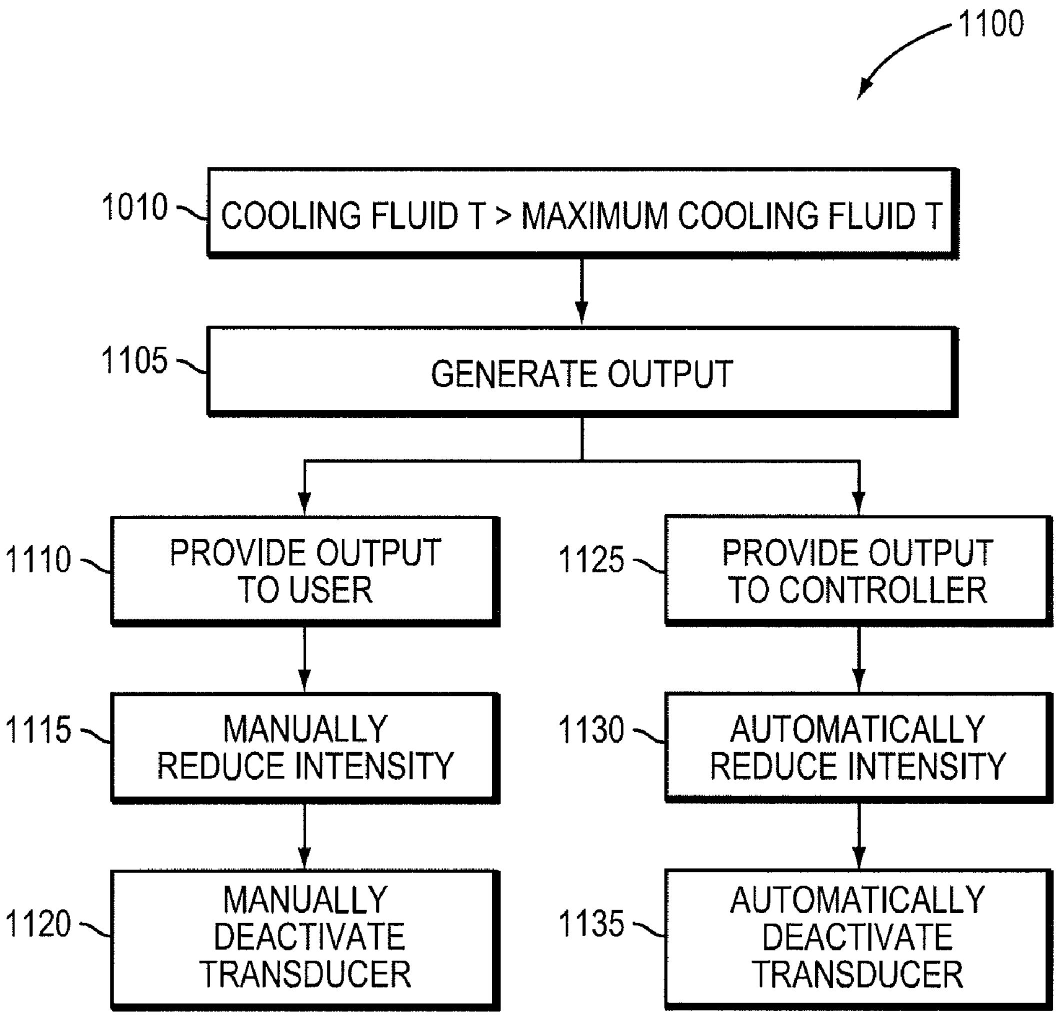

1100
1010
COOLING FLUID T > MAXIMUM COOLING FLUID T
1105
GENERATE OUTPUT
1110
PROVIDE OUTPUT TO USER
1125
PROVIDE OUTPUT TO CONTROLLER
1115
MANUALLY REDUCE INTENSITY
1130
AUTOMATICALLY REDUCE INTENSITY
1120
MANUALLY DEACTIVATE TRANSDUCER
1135
AUTOMATICALLY DEACTIVATE TRANSDUCER

FIG. 11

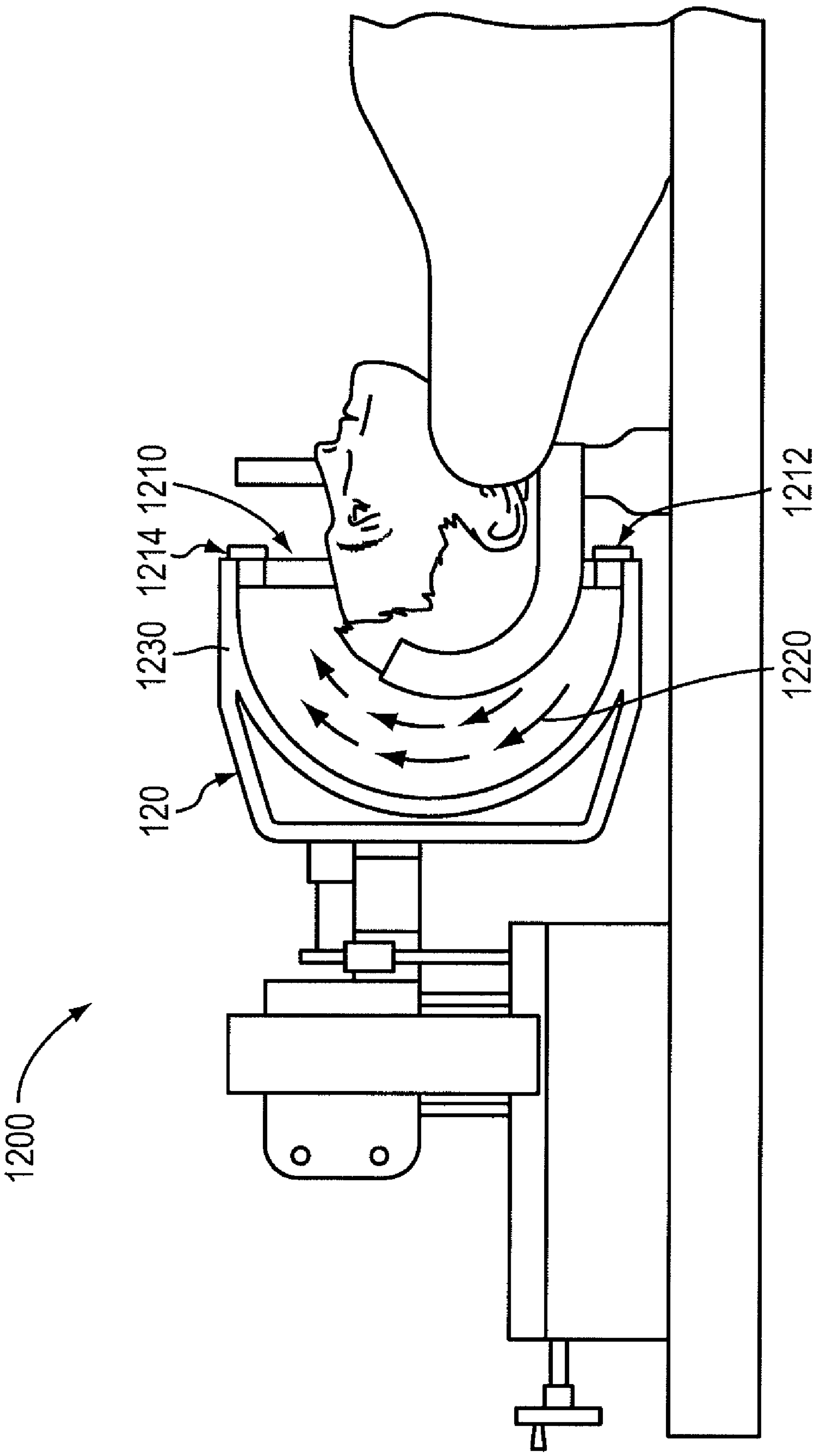


FIG. 12

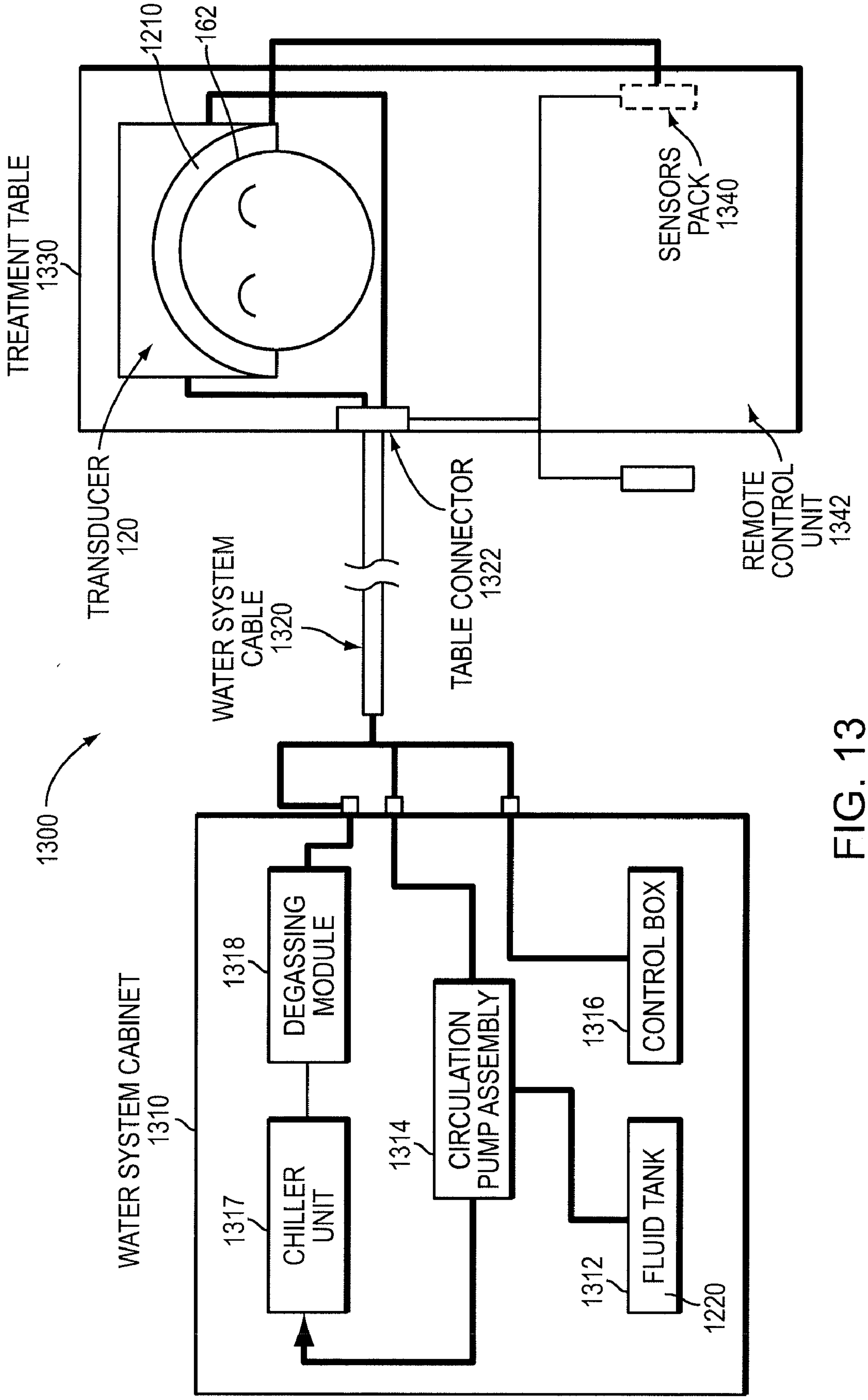

1300
TREATMENT TABLE
1330
1210
162
TRANSDUCER
120
SENSORS
PACK
1340
REMOTE
CONTROL
UNIT
1342
TABLE CONNECTOR
1322
WATER SYSTEM
CABLE
1320
WATER SYSTEM CABINET
1310
1318
DEGASSING
MODULE
1317
CHILLER
UNIT
1314
CIRCULATION
PUMP ASSEMBLY
1316
CONTROL BOX
1312
FLUID TANK
1220

FIG. 13

SYSTEMS AND METHODS FOR CONTROLLING ULTRASOUND ENERGY TRANSMITTED THROUGH NON-UNIFORM TISSUE AND COOLING OF SAME

FIELD OF THE INVENTION

[0001] The field of the invention relates generally to thermal energy treatment systems and, more particularly, to systems and methods for controlling the intensity of acoustic energy transmitted through a non-uniform tissue, such as the skull, and cooling such tissue.

BACKGROUND

[0002] High-intensity focused acoustic waves, such as ultrasound or acoustic waves at a frequency greater than about 20 kilohertz, may be used to therapeutically treat internal tissue regions within a patient. For example, ultrasound waves may be used in applications involving ablation of tumors, thereby eliminating the need for invasive surgery, targeted drug delivery, control of the blood-brain barrier, lysing of clots, and other surgical procedures.

[0003] Focused ultrasound systems typically include piezoelectric transducers that are driven by electric signals to produce ultrasound energy. In such systems, a transducer may be geometrically shaped and positioned such that ultrasound energy emitted by an array of transducers collectively forms a focused beam at a "focal zone" corresponding to the target tissue region. As used herein, the terms "beam," "energy beam," or "acoustic energy beam" refer generally to the sum of the waves emitted by the various transmitting elements of a focused ultrasound system.

[0004] When using a focused ultrasound "energy beam" to thermally treat a certain area of the body, e.g., to ablate a tumor, the beam must be precisely focused to the target location to avoid damage to healthy tissue surrounding the target region. For this purpose, the transducer may be sequentially focused and activated at a number of focal zones in close proximity to one another. For example, this series of "sonications" may be used to cause necrosis of a tissue structure of a desired size and shape.

[0005] FIGS. **1** and **2** illustrate a known ultrasound system **100** that may be used for these purposes. The illustrated system **100** includes an imager **110** for determining characteristics of a skull **162** of a patient **160**, a phased array **120** of n transducer elements **122**, which may be in the form of a spherical cap (as shown in FIG. **2**), a controller **140** operably coupled to the imager **110**, a signal adjuster **130** operably coupled to the controller **140**, and a frequency generator or energy source **150**, such as a radio frequency (RF) generator, operably coupled to the signal adjuster **130**.

[0006] The transducer elements **122** are piezoelectric transducer elements, e.g., piezoelectric ceramic pieces. The signal adjuster **130** includes phase adjustment elements $\mathbf{132}_{1-n}$ (generally **132**) and associated amplifiers $\mathbf{134}_{1-n}$ (generally **134**). The frequency generator **150** provides a RF signal as an input to the signal adjuster **130**. The RF generator **150** and signal adjuster **130** are configured to drive individual transducer elements **122** of the transducer array **120** at the same frequency, but at different phases. These controls are utilized to transmit ultrasound energy through the patient's skull **162** and to focus the energy at a selected target region within the brain **164**. An acoustically conductive fluid or gel **202** is preferably introduced between the inner face of the transducer array **120** and the exterior of the patient's skull **162** in order to prevent any acoustically reflecting air gaps that may reduce the effectiveness of the applied energy.

[0007] In the illustrated system **100**, n input signals based on the RF generator **150** output are provided to the signal adjuster **130**. Coupled to receive each of the n input signals are n pairs of amplifiers $\mathbf{132}_1$-$\mathbf{132}_n$, and associated phase shifters $\mathbf{134}_1$-$\mathbf{134}_n$. Each amplifier **132**-phase shifter **134** pair represents a channel of the signal adjuster **130**. Phase shifters **134** are configured to provide n independent output signals to the amplifiers **132** by altering or adjusting incoming signals from the RF generator **150** by respective phase shift factors **134**. The amplifier **132** outputs drive transducer elements **122**, and the collective energy **124** emitted by the transducer elements **122** forms a focused beam of ultrasound energy that traverses the skull **162** and is focused at a target region **210** within the brain **164**. Further aspects of known systems **100** and spherical cap transducers are described in U.S. Pat. Nos. 6,612,988 and 6,666,833, the contents of which are incorporated herein by reference as though set forth in full.

[0008] While focused ultrasound systems and spherical cap transducers shown in FIGS. **1** and **2** have been used effectively in the past, they can be improved, particularly in procedures involving non-uniform tissue such as the skull. As generally illustrated in FIG. **3**, a typical human skull **162** includes multiple tissue layers including an external layer **301**, a bone marrow layer **302**, and an internal layer or cortex **303**, which may be highly irregular in shape. Cortex **303** irregularities may cause certain sections of the skull **162** to be more susceptible to excessive heating when exposed to ultrasound energy. Further, attempts to focus energy at the focal regions **210** may result in excessive heating of certain sections of the skull **162** which, in turn, damages adjacent healthy tissue. Accordingly, by "non-uniform" is meant varying in tissue type, shape and/or conformation so as to respond differently to ultrasound energy.

[0009] Known ultrasound therapy systems may operate by focusing an ultrasound beam at a desired focal region **210** with the goal of precisely ablating target tissue. While this avoids ablation of tissue surrounding the target region **212**, once again the skull **162** may absorb substantial energy and become heated excessively, resulting in damage to adjacent tissue. One type of injury, in other words, is merely exchanged for another.

SUMMARY

[0010] Embodiments of the invention are directed toward application of focused ultrasound to non-uniform tissue in a manner that avoids harm to healthy anatomy outside the target zone.

[0011] In a first aspect, a method for controlling intensities in a transducer array having multiple transducer elements, each being primarily associated with a corresponding tissue region, includes determining anatomical characteristics of non-uniform tissue regions (e.g., the skull) to be traversed when the transducer array delivers focused ultrasound to a target region. For each of the transducer elements, a preferred intensity of ultrasound energy is determined based on the anatomical characteristics of the corresponding non-uniform tissue region and pre-determined energy thresholds (e.g., a maximum temperature) associated with the region. The individual transducer elements are then driven at their respective preferred intensities, thereby directing ultrasound energy through the non-uniform tissue. As a result, the directed ultrasound energy emitted by the transducer array is non-uniform across the transducer array and maximized while satisfying the pre-determined thresholds.

[0012] In certain embodiments of the invention, the anatomical characteristics may include the thickness of the non-uniform tissue, the density of the non-uniform tissue, an entrance point of a ray emitted by a transducer element into the non-uniform tissue, and/or an exit point of a ray emitted by a transducer element from the non-uniform tissue. Further, the intensity of the emitted ultrasound energy may also be influenced by an increase in temperature of the non-uniform tissue. In various implementations of the invention, the intensity of ultrasound energy emitted by individual transducer elements may range from 0 Watt to about 10 Watts. The difference between minimum intensity and maximum intensity levels of ultrasound energy emitted by individual transducer elements can vary from 0.0 Watt to about 10 Watts.

[0013] In some cases, an actual temperature of the non-uniform tissue is measured (using, for example, magnetic resonance thermometry) and compared to a maximum temperature, and if the measured temperature exceeds the maximum, the non-uniform tissue is cooled. In some instances, the ultrasound transducer may be deactivated.

[0014] The cooling process may include circulating a cooling fluid within an interface between the ultrasound transducer and the non-uniform tissue, measuring the temperature of the cooling fluid, comparing the measured temperature to a maximum temperature. An output signal indicating the results of the comparison may be generated and displayed to an operator.

[0015] In another aspect, a method for controlling the intensity of ultrasound energy emitted by a transducer array having multiple transducer elements includes determining anatomical characteristics of regions of a non-uniform tissue (such as a skull), simulating, for each transducer element, the effect of heating a corresponding non-uniform tissue region with ultrasound energy using an intensity based on the anatomical characteristics, and determining a maximum intensity of ultrasound energy for each transducer element based on the simulation and a pre-determined threshold (e.g., a maximum temperature).

[0016] In some embodiments, an intensity map may be generated based on the simulation that includes ultrasound energy intensity values for each transducer element such that ultrasound energy emitted by the transducer array is maximized and non-uniform across the transducer array while satisfying the pre-determined threshold. The transducer elements may be driven based on the intensity values in order to direct a beam of ultrasound energy through the non-uniform tissue region (e.g., to a target region beyond the non-uniform tissue).

[0017] In some cases, the actual temperature of the non-uniform tissue is measured (using, for example, magnetic resonance thermometry) and compared to a maximum temperature, and if the measured temperature exceeds the maximum, the non-uniform tissue is cooled. In some instances, the ultrasound transducer may be deactivated.

[0018] The cooling process may include circulating a cooling fluid within an interface between the ultrasound transducer and the non-uniform tissue, measuring the temperature of the cooling fluid, and comparing the measured temperature to a maximum temperature. An output signal indicating the results of the comparison may be generated and displayed to an operator.

[0019] In various implementations, the intensity of ultrasound energy emitted by individual transducer elements may range from about 0.0 Watt to about 10 Watts.

[0020] In another aspect, a system for controlling an intensity of a transducer array having multiple transducer elements includes an imaging system, a controller and drive circuitry. The imaging system is configured to determine anatomical characteristics of non-uniform tissue regions (e.g., a skull), while the controller is configured to determine a maximum allowable intensity of ultrasound energy emitted by each transducer element into (and through) a corresponding non-uniform tissue region based the determined anatomical characteristics and a pre-determined threshold (such as a maximum temperature) associated with the tissue regions. The drive circuitry drives the transducer elements to emit ultrasound energy at the determined maximum intensities through the non-uniform tissue.

[0021] In various embodiments a computed tomography (CT) imaging system may be used to determine the anatomical characteristics of the non-uniform tissue and a magnetic resonance imaging (MRI) system may be used in conjunction with the CT imaging system to localize the transducer elements relative to the non-uniform tissue regions. In certain cases, the MRI system determines an actual temperature of the non-uniform tissue while the transducer elements are being driven, and the controller is further configured to generate an output signal indicating when the measured temperature exceeds the maximum temperature. In some implementations, the individual transducers are independently controllable such that the temperature of each non-uniform tissue region does not exceed the maximum temperature for that region.

[0022] The system may also include a fluid interface integrated with the transducer and coupled to the controller such that it is positionable around the non-uniform tissue region and further facilitates the circulation of cooling fluid about the tissue, either periodically or continuously. In some instances, a temperature sensor may be positioned within the interface to allow for the measurement of the cooling fluid and communication of the measured temperature to the controller.

[0023] In another aspect, a system for controlling the intensity of a transducer array comprising multiple transducer elements includes an imaging system, a controller and drive circuitry. The imaging system is configured to determine anatomical characteristics of non-uniform tissue regions, and the controller simulates, for each transducer element, the effects of heating corresponding non-uniform tissue regions based at least in part on the determined anatomical characteristics. The controller further determines a maximum allowable intensity of ultrasound energy emitted by each transducer element based on the simulation and a pre-determined threshold, such as a maximum allowable temperature. The drive circuitry causes the transducer elements to emit ultrasound energy at the determined maximum intensities.

[0024] In some embodiments, the controller generates an intensity map of ultrasound energy intensity values for each transducer based on the simulation. The system may also include an MRI system that measures the temperature of the non-uniform tissue and based on the temperature, and, if above a maximum temperature, causes the controller to generate an output signal that indicating as such. In some cases, individual transducer elements are independently configurable to ensure that the temperature of each tissue regions does not exceed the maximum temperature.

[0025] The system may also include a fluid interface integrated with the transducer and coupled to the controller such that it is positionable around the non-uniform tissue region and further facilitates the circulation of cooling fluid about the tissue, either periodically or continuously. In some instances, a temperature sensor may be positioned within the interface to allow for the measurement of the cooling fluid and communication of the measured temperature to the controller.

[0026] In yet another aspect, a method for cooling skull tissue during delivery of ultrasound energy thereto includes positioning the head of a patient within an ultrasound transducer such that a fluid interface integral with the ultrasound transducer is positioned about skull tissue of the patient and between an inner surface of the ultrasound transducer and the skull tissue. Transducer elements are driven in such a manner as to direct a beam of ultrasound energy through the skull tissue, thereby heating the skull tissue, and a cooling fluid is circulated (either periodically or continuously) within the fluid interface to cool the skull. In some cases, the fluid may be circulated prior to delivery of ultrasound energy.

[0027] The temperature and/or pressure of the fluid circulating within the interface may be monitored (using, for example, a temperature sensor within the interface) and an output signal indicated whether the fluid has exceeded a maximum temperature may be generated. The signal may be displayed to a user, thereby allowing the user to interrupt the delivery of ultrasound energy to the skull.

[0028] In another aspect of the invention, a system for cooling skull tissue of a patient during application of ultrasound energy through the skull tissue includes an ultrasound transducer having multiple transducer elements and a fluid interface. The transducer is positionable about the skull tissue and emits ultrasound energy through the skull tissue. The fluid interface is integral with the ultrasound transducer and positionable between the ultrasound transducer and the skull tissue, and facilitates continuous circulation of cooling fluid about the skull tissue.

BRIEF DESCRIPTION OF THE DRAWINGS

[0029] Referring now to the drawings in which like reference numbers represent corresponding parts throughout and in which:

[0030] FIG. **1** is a schematic diagram of an example of a known ultrasound therapy system;

[0031] FIG. **2** is a schematic diagram of a known spherical cap transducer that may be used with the ultrasound therapy system shown in FIG. **1**;

[0032] FIG. **3** generally illustrates tissue layers of a human skull;

[0033] FIG. **4** is a flow chart illustrating a method for controlling the intensity of energy emitted by transducer array elements during therapy involving a non-uniform tissue according to one embodiment of the invention;

[0034] FIG. **5** is a flow chart illustrating a method for controlling the intensity of energy emitted by transducer array element during therapy of brain tissue while the temperature of skull tissue remains less than a maximum or threshold temperature according to one embodiment;

[0035] FIG. **6** illustrates ray analysis used in embodiments to determine geometric attributes of a skull region;

[0036] FIG. **7** is a flow chart illustrating a method of determining intensities involving heating simulations and generation of an intensity map according to one embodiment;

[0037] FIG. **8** is a graph illustrating one example of results of thermal simulation conducted according to one embodiment;

[0038] FIG. **9** illustrates one example of an intensity map generated according to one embodiment;

[0039] FIG. **10** is a flow chart of a method of cooling non-uniform tissue according to one embodiment;

[0040] FIG. **11** is a flow chart of a method of cooling non-uniform tissue according to another embodiment in which cooling adjustments are implemented manually or by a controller;

[0041] FIG. **12** illustrates a cooling interface constructed according to one embodiment that is integral with an ultrasound transducer and provides for continuous flow of cooling fluid; and

[0042] FIG. **13** schematically illustrates a cooling system constructed according to one embodiment that may be utilized with the cooling interface shown in FIG. **12**.

DETAILED DESCRIPTION OF ILLUSTRATED EMBODIMENTS

[0043] Embodiments of the invention advantageously control and optimize energy emitted by a transducer array to effectively focus energy at a focal zone while maintaining the temperature of non-uniform tissue, such as the skull, at acceptable and safe levels. In particular, embodiments of the invention are capable of precisely focusing an energy beam at a target region to avoid damage to healthy tissue surrounding the target region while also reducing or preventing heating of the skull, thereby also preventing or reducing damage to tissue adjacent to the skull. These significant advantages are achieved by controlling the intensities of energy emitted by individual transducer elements to satisfy skull temperature criteria or thresholds. The expected collective energy may be maximized at the focus, while temperature thresholds or criteria outside the target area are satisfied locally, on an element-by-element basis, and/or globally. A cooling system integral with the transducer may be utilized to monitor the skull tissue temperature and cool the skull tissue as necessary. The cooling system may be used to cool the skull in the event that during therapy, the skull is heated to such a degree such that the skull temperature exceeds a desired or threshold temperature or other safety criterion. Further aspects of embodiments of the invention are described with reference to FIGS. **4-13**.

[0044] Referring to FIG. **4**, a method **400** for controlling the intensity of a transducer array **120** according to one embodiment includes determining anatomical characteristics of non-uniform tissue regions (step **405**) using the imager **110** shown in FIG. **1**. At step **410**, the intensities of individual transducer elements **122** are controlled based on information received from the imager **110**, and also, if desired, based on certain pre-determined thresholds or criteria, such as a maximum allowable intensity or other safety criteria. In so doing, the energy intensities **124** emitted by individual transducer elements **122** may be determined and controlled on an element-by-element basis. At step **415**, the transducer elements **122** are driven at the respective determined intensities, resulting in a non-uniform intensity distribution across the transducer array **120** and across the non-uniform tissue.

[0045] In some embodiments, the transducer elements **122** are driven to generate ultrasound energy **124** at their respective determined intensities while ensuring that the total amount of ultrasound energy delivered collectively satisfies the pre-determined threshold. In particular, the total amount of energy **124** emitted by a transducer array **120** may be selected or maximized by locally maximizing the acoustic energy **124** passing through different skull **162** regions while simultaneously satisfying both the pre-determined threshold on an element-by-element basis and globally across the transducer array **120**. As a result, the total ultrasound energy **124** is maximized, focused at the target region **210**, and has a non-uniform temperature profile or distribution that satisfies both local (e.g., with respect to individual elements or small groups of elements driven by a single signal) and global thresholds or criteria.

[0046] According to one embodiment, the pre-determined threshold is a maximum tissue temperature, and the non-uniform tissue is a skull **162**. The skull **162** can be defined as more than one region, each of which may be related to or correspond to a particular transducer element **122** or grouping of elements. Referring specifically to FIG. **5**, a method **500** for controlling intensity of energy **124** emitted by a transducer array **120** includes determining anatomical characteristics of multiple regions of a skull **162** (step **505**) using imager **110**.

[0047] In various embodiments (e.g., step **405** of method **400** and/or step **505** of method **500**), the imaging system **110** includes computed tomography (CT) imaging and/or magnetic resonance imaging (MRI) elements. CT imaging may be used, for example, to extract anatomical characteristics of the skull **162**, such as the skull thickness, local bone densities and/or directional or geometrical features including a normal relative to a surface region of the skull **162**. MRI imaging may be used to localize the plurality of transducer elements **122** relative to the skull **162** and/or for purposes of therapy planning. CT and MRI data for a given skull **162** may be combined using multi-modal registration or other similar techniques.

[0048] FIG. **6** illustrates a single ray **600** traveling through a voxel of a CT-generated volume representing skull region **602**, following placement of transducer elements **122** relative to the skull **162** and target region **210**. In some embodiments, a set of x-rays **600** is projected through the CT volume set representing multiple skull regions **602**. Pixel values **604** along a ray **600** and extending through each volume or skull region **602** may be determined and arranged to form a CT intensity profile for each skull region **602**. The pixel values may represent, for example, the absorption of the x-rays in the skull region **602** (typically measured in "Hounsfield numbers" or "CT numbers"). In some implementations, such information can be used to relate x-ray absorption coefficients with ultrasound absorption coefficients. The CT intensity of bone or skull tissue along each ray **600** is known, and various geometric attributes of a skull region **602** and corresponding rays **600** passing therethrough may be determined based on the CT intensity profile. Examples of such geometric attributes include the entrance point of the ray **600** to the skull region **602**, the exit point of the ray **600** from the skull region **602**, thicknesses of different skull tissue layers **301**-**303**, and/or an average local density of a CT region **602** in CT units. Data acquired during ray analysis may then be used to construct internal and external surfaces of the skull **162** to create a local geometric characteristic mapping of the skull.

[0049] Referring again to FIG. **5**, at step **510**, the intensity of ultrasound energy **124** emitted by each transducer element **122** may be determined or controlled based on the previously determined anatomical characteristics (step **505**) and a maximum or threshold skull or skull region temperature. According to one embodiment, and with further reference to FIG. **7**, step **510** may also include a thermo-acoustic simulation. In such cases, the thermo-acoustic simulation can involve analyzing an acoustic path through a skull region **602** (step **705**), performing thermal simulations to estimate how different skull regions **602** absorb different quantities of energy and have different heating profiles (step **710**), determining the optimal intensity of energy to be emitted by each transducer element **122** (step **715**), and generating an intensity map corresponding to transducer elements **122** (step **720**). The resulting intensity map includes optimal intensity values of energy emitted by respective individual transducer elements **122**, which collectively optimize the energy delivered to a target region **210** while satisfying one or more temperature thresholds or safety criteria as described above.

[0050] According to one embodiment, steps **705** and **710** may be performed on an element-by-element basis to estimate how different skull tissue regions **602** will be heated as ultrasound energy **124** traverses the skull **160**. For this purpose, the local skull tissue geometry (determined at step **505** and discussed above) and the speed of sound through the skull **600** may be utilized to analyze the acoustic path of ray **600** through skull region **602**, and to predict how the skull region **602** will be heated as a result (based on the previously determined anatomical characteristics). In some instances, the speed of sound through the skull region **602** may be determined by utilizing an empirical model that correlates CT density to the speed of sound, or in accordance with other known techniques. A heat equation or model for each skull region **620** may then be solved or applied to predict how a given skull region **602** will be heated by ultrasound energy **124** emitted by a corresponding transducer element **122** or groupings of transducer elements **122**.

[0051] For example, angles of incidence between a ray **600** and skull **160** surfaces may be analyzed using Snell's law to estimate the path of an acoustic ray **600** emitted by a particular transducer element **122**, which traverses the skull region **602** and is directed to a target region **210** in the brain **164**. Energy reflected from the skull **160** surface and attenuation and absorption of energy within a skull region **602** can also be estimated utilizing the acoustic path analysis. This analysis may be repeated for each skull region **602** in order to acquire a complete picture of estimated energy reflection, absorption and attenuation for multiple skull regions **602**.

[0052] Referring again to FIG. **7**, acoustic path information (acquired at step **705**) is used to simulate how an individual skull region, characterized by the previously performed acoustic path analysis, is heated over time, for each point or pixel **604** along a ray **600** traversing the skull region **602** (step **710**). This information may then be used to estimate the amount of energy reflected from the skull **600** and the amount of energy absorbed by the skull, thus impacting heating of the skull region **602**.

[0053] For this purpose, thermal simulations may assume a steady-state temperature profile based on a thermal gradient between the external side **301** of the skull **162**, which is cooled by water at a temperature of about 10° C.-20° C., and the tissue distant from the surface at body temperature. A heat expression or model may then be used to iteratively solve heating effects for each skull region. One example of a suitable heat model that may be used for this purpose is a linear heat equation solved numerically with appropriate boundary constraints. The result of thermal simulation for a particular skull region **602** may be expressed as a heat simulation graph **800** (FIG. **8**), having skull tissue depth (mm) plotted along the x-axis and simulated temperature increases along the y-axis. The thermal simulation analysis may be conducted for each transducer element **122** (or groupings thereof) and each corresponding skull region **602**, thus resulting in a global thermal simulation across the skull **162**, and an estimate of the thermal rise of each skull region **602** when exposed to ultrasound energy.

[0054] Referring again to FIG. **7**, and with further reference to FIG. **9**, the optimal or maximum intensity of ultrasound energy **124** to be emitted by each transducer element **122** is determined based on the skull region **602** characteristics and temperature simulation (step **720**). According to one embodiment, each skull region **602** may be analyzed to determine the maximum intensity of ultrasound energy **124** that can be absorbed such that the expected temperature rise of the skull region **602** is below a threshold or acceptable maximum temperature. In the illustrated embodiment, the determined or maximum intensity values are collectively represented in the form of an intensity map **900**. Each segment **900***n* of the map **900** represents a transducer element **122** of the transducer array **120**, which may be in the form of a spherical cap as represented in FIGS. **2** and **9**.

[0055] As shown FIG. **9**, the intensity values across the transducer array **200** may vary from element to element and are therefore typically non-uniform. For example, regions **901** have a higher heat sensitivity than regions **902** and **903**, and region **903** has the lowest heat sensitivity. Different intensity levels may be assigned to certain transducer elements **122** to avoid excessive skull heating. For example, the intensity map **900** dictates that transducer elements **122** corresponding to map section **901** will emit energy **124** at low levels since the corresponding skull regions **602** have the highest heat sensitivity. In contrast, higher intensity ultrasound energy **124** may be applied to other skull regions **602**, e.g., skull regions corresponding to map region **903**, since these regions are less sensitive to heat generated by ultrasound energy. It should be understood that the identified regions **901-903** are provided for purposes of illustration, and that the change in intensity levels between regions (including neighboring regions) may be gradual or sharp depending on the anatomical structure of corresponding skull regions **602**. Moreover, it should be understood that FIG. **9** illustrates one example of an intensity map **900**, and that the intensity map **900** may vary depending on different skull structures.

[0056] In the illustrated example, transducer elements **122** associated with region **901** are controlled to emit ultrasound energy **124** at about 0.07 to about 0.10 Watt, transducer elements **122** associated with region **902** are controlled to emit ultrasound energy **124** at about 0.10 Watt to about 0.17 Watt, and transducer elements **122** associated with region **903** are controlled to emit ultrasound energy **124** at about 0.17 Watt to about 0.20 Watt. Thus, the power levels range from a minimum value of about 0.07 Watt to a maximum value of about 0.2 Watt, and the difference between minimum and maximum power levels is about 0.13 Watt. In other examples this difference can range from zero to 10 Watts per transducer element.

[0057] The intensity of ultrasound energy **124** is selected such that it accommodates the non-uniform tissue structure across skull **162** and forms an optimized, non-uniform intensity distribution, which achieves application of the highest possible level of ultrasound energy to a target region **210** by summation of local energy maxima emitted by individual transducer elements **122** while simultaneously complying with safety criteria such as the temperature of the skull **162** at different regions depending on the underlying characteristics of such skull regions.

[0058] By maximizing the overall energy and staying within acceptable energy thresholds, the ultrasound energy **124** actually reaching the focal zone **210** in order to treat the lesion, tumor or clot is also maximized. In this manner, the technique and system facilitate the application of effective therapy by generating a focused beam while at the same time preventing damage to tissue surrounding the target region **21**. In cases in which the energy is being directed inside the skull, skull tissue temperature is controlled both locally (based on analysis of tissue non-uniformities), and globally (based on summation of individual elements **122**) to satisfy skull temperature thresholds and safety criteria while the collective energy **124** emitted by the plurality of elements **122** is focused.

[0059] Thus, embodiments of the present invention function in a novel manner. For example, in typical systems, the intensity of ultrasound energy **124** emitted by transducer elements **122** is adjusted to improve focusing at the target region **210**. If a skull region absorbs a substantial amount of energy, resulting in attenuation, such systems may be configured to apply ultrasound energy at even higher intensities to compensate for attenuation in order to maintain or improve focusing. These known control mechanisms, while providing effective focus, may result in further heating of already overheated skull regions **602**, thereby causing even more damage to adjacent tissue. In contrast, embodiments of the invention locally control transducer elements **122** such that they apply ultrasound energy **124** to these selected skull regions **602** at lower intensity levels while achieving sufficient focus, thus prioritizing safety over focusing to protect critical or thermally sensitive skull regions **602**.

[0060] Other embodiments of the invention involve monitoring and controlling the temperatures of skull regions **602** heated by ultrasound energy **124** emitted by transducer elements **122** as described above. While the monitoring and controlling techniques described below may be employed independently of managing the energy emission, the two techniques may also be used in conjunction with each other.

[0061] Referring to FIG. **10**, a method **1000** of monitoring and controlling a temperature of a skull **162** during ultrasound therapy (step **1005**) includes monitoring the actual temperature of the surfaces of one or more skull regions **602** (or, in some cases, the entire skull **162**) (step **1010**). Step **1005** may, for example be performed while driving the transducer elements **122** according to intensity map **900**. In one embodiment, the skull temperature is monitored using magnetic resonance thermometry. The actual temperature of the skull **162** may then be compared to the pre-determined maximum or acceptable temperature (step **1015**). According to one embodiment, the maximum temperature of a skull **162** during ultrasound therapy is approximately 107° F., or 42° C. If the actual temperature is below the threshold, therapy can proceed according to the intensity map **900**. However, if the actual temperature exceeds the threshold temperature, the skull **162** may be cooled to a safe temperature (step **1020**). In addition, the actual temperature readings can be used to calibrate the relationship between applied energy and the resulting tissue temperature, e.g., in creating the intensity map depicted in FIG. **9**.

[0062] Referring to FIG. **11**, according to another embodiment, skull cooling may be implemented by generating an output signal (step **1105**) when the temperature of a cooling fluid applied to the skull reaches or exceeds a safety threshold. The output signal may be a visual and/or audible indicator that is provided to an operator via a speaker, display or other device (step **1110**). In response to the output signal, the operator may manually reduce the intensity of ultrasound energy **124** (step **1115**), by, for example, reducing the intensity of the entire transducer array **120** (and therefore the energy **124** emitted by each transducer element) and/or to only those transducer elements corresponding to thermally sensitive or critical skull regions **620**, thereby only affecting the temperatures at these regions. According to another embodiment, the operator may manually deactivate the transducer array **120** (step **1120**) to halt sonication altogether. In another embodiment, the generated output is provided to a controller (step **1125**), such as a processor, computer or other control element, which may then initiate an automatic reduction in the intensity of ultrasound energy **124** when the temperature of the cooling fluid reaches or exceeds the threshold. Such reductions may include reducing the energy emitted by all of the transducer elements, thereby ensuring reduction in the intensity of energy **124** reaching thermally sensitive or critical skull regions **602**, and/or automatically deactivating the transducer array **120** altogether to halt sonication.

[0063] Skull cooling may be achieved by employing a cooling element integral with the ultrasound transducer array **120**. The cooling element may be manually or automatically controlled. Referring to FIGS. **12** and **13**, the integrated cooling element **1200** may include a fluid interface **1202** that is integral with, or attached to, the ultrasound transducer array **120** and positioned between the transducer array **120** and the patient's skull **162**. The interface **1202** is preferably made of a compliant and flexible material to facilitate positioning around the skull and adjustment as necessary to provide a tight interface. Cooling fluid **1220** continuously circulates within or flows through the interface **1210** via a fluid inlet **1212**, exiting the interface **1210** via a fluid outlet **1214** or re-circulating as desired. By continuously circulating cooling fluid **1220** through the interface **1202**, the skull (or other tissue) can be kept below a ceiling temperature during administration of ultrasound.

[0064] According to one embodiment, the cooling interface **1210** is controlled based on the temperature of the skull **162**, which may be determined by an external sensor or device, including, for example, magnetic resonance thermometry as described above. According to another embodiment, the temperature of the cooling fluid rather than the skull is measured from within the interface **1210**, e.g., using an internal temperature sensor **1230** positioned inside the interface **1210** and within the flow path of the fluid **1220** such that fluid **1220** flows through or about the temperature sensor **1230**. The temperature of the cooling fluid **1220** may be monitored to determine if a pre-determined threshold or maximum fluid **1220** temperature has been reached, indicating that the skull temperature is too high. Appropriate action may then be taken in response to these elevated temperatures, including supplying additional cooling fluid **1220**, reducing the temperature of the cooling fluid **1220**, and/or increasing the flow rate of cooling fluid **1220**.

[0065] FIG. **13** illustrates one example of a cooling system **1300** that may be used for circulation or flow of cooling fluid **1220** through an integrated cooling element or interface **1210** as shown in FIG. **12**. The illustrated system **1300** includes a cabinet **1310** having a source of fluid **1312**, which supplies cooling fluid **1220** to a circulation pump **1314**. A controller **1316** controls the pump **1314** to circulate fluid **1220** through a chiller unit **1317**, and chilled fluid **1220** is degassed **1318** and provided to the inlet **1212** of the integrated cooling element **1210** through a suitable conduit **1320** and connector **1322** that interfaces with the transducer array **120** and treatment table **1330**. One or more sensors **1340**, whether external sensors on the patient's skull or internal sensors positioned within the cooling interface **1210**, are provided to monitor, determine or estimate the temperature of the skull **162**. Temperature data can be transmitted to a controller **1316** wirelessly or via a remote control unit **1342** (or other suitable device operably connected to or in communication with the controller **1316**), and the controller **1316** may implement appropriate adjustments to the output of transducer array **120** as necessary to achieve or maintain a target skull temperature.

[0066] Although particular embodiments have been shown and described, it should be understood that the above description is not intended to limit the scope of embodiments since various changes and modifications may be made without departing from the scope of the claims. It should be understood that embodiments directed to controlling the intensity of energy emitted by a transducer on an element-by-element or local basis may be utilized independently of or in conjunction with other embodiments. Further, although embodiments are described in applications involving transmission of ultrasound energy through skull tissue, embodiments may also be applicable in other treatments involving other non-uniform types of tissue. Moreover, although the advantages of embodiments are most readily realized by controlling the intensity of energy on an element-by-element basis, embodiments may also be configured in other ways that achieve similar results. For example, embodiments may be configured for control of intensity of energy emitted by pairs or other groupings of multiple ultrasound elements. Further, although certain figures illustrate one examples of an intensity map that may be used with one particular skull, it should be understood that the distribution, intensity levels and intensity difference may vary depending on, for example, the configuration of a subject skull. Thus, embodiments are intended to cover alternatives, modifications, and equivalents that fall within the scope of the claims.

What is claimed is:

1. A method for controlling intensities in a transducer array comprising a plurality of transducer elements, the method comprising:

determining anatomical characteristics of non-uniform tissue regions to be traversed using focused ultrasound, each of the transducer elements being primarily associated with a corresponding tissue region;

determining, for each of the transducer elements, a preferred intensity of ultrasound energy at a target region, the intensity being based on anatomical characteristics of the corresponding non-uniform tissue region and a pre-determined energy threshold associated therewith; and

driving the transducer elements at their respective preferred intensities, thereby directing ultrasound energy through the non-uniform tissue to the focus, the directed ultrasound energy emitted by the transducer array being non-uniform across the transducer array and maximized while satisfying the pre-determined thresholds.

2. The method of claim **1**, wherein the anatomical characteristics comprise at least one of a thickness of the non-uniform tissue, a density of the non-uniform tissue, a density distribution, an entrance point of a ray emitted by a transducer element into the non-uniform tissue, or an exit point of a ray emitted by the transducer element from the non-uniform tissue.

3. The method of claim **1**, wherein the pre-determined threshold is a maximum temperature.

4. The method of claim **3**, wherein the intensity of ultrasound energy emitted by the plurality of transducer elements is further based at least in part on an increase in temperature of the non-uniform tissue region.

5. The method of claim **3**, further comprising:

determining an actual temperature of the non-uniform tissue during driving of the transducer array;

comparing the actual temperature to the maximum temperature; and

cooling the non-uniform tissue if the actual temperature is greater than the maximum temperature.

6. The method of claim **5**, wherein the actual temperature is determined by magnetic resonance thermometry, and further comprising deactivating the ultrasound transducer if the actual temperature is greater than the maximum temperature.

7. The method of claim **3**, further comprising

circulating a cooling fluid within a fluid interface integral with the ultrasound transducer and positioned between the ultrasound transducer and the non-uniform tissue;

measuring a temperature of the cooling fluid;

comparing the measured temperature to a maximum cooling fluid temperature; and

generating an output signal representing the results of the comparison.

8. The method of claim **1** wherein the non-uniform tissue comprises skull tissue.

9. The method of claim **7**, wherein the output signal is displayed to an operator of the transducer array.

10. The method of claim **7**, wherein the cooling fluid circulates within the interface.

11. The method of claim **1**, wherein the intensity of ultrasound energy emitted by individual transducer elements ranges from about 0.0 Watt to about 10 Watts.

12. The method of claim **1**, wherein a difference between a minimum intensity and a maximum intensity of ultrasound energy emitted by individual transducer elements varies by about 0.0 Watt to about 10 Watts.

13. A system for controlling an intensity of a transducer array having a plurality of transducer elements, the system comprising:

an imaging system configured to determine anatomical characteristics of non-uniform tissue regions;

a controller operably, coupled to the imaging system, for determining a maximum allowable intensity of ultrasound energy emitted by each transducer element into a corresponding non-uniform tissue region based the determined anatomical characteristics and a pre-determined threshold associated with the tissue regions; and

drive circuitry for driving the transducer elements to emit ultrasound energy at the determined maximum intensities through the non-uniform tissue.

14. The system of claim **13** further comprising a computed tomography imaging system for determining the anatomical characteristics of the non-uniform tissue regions.

15. The system of claim **14** further comprising a magnetic resonance imaging system, associated with the computed tomography system, for localizing the plurality of transducer elements relative to the non-uniform tissue regions.

16. The system of claim **13**, wherein the predetermined threshold is a maximum temperature of a non-uniform tissue region.

17. The system if claim **13** wherein the non-uniform tissue regions comprise skull tissue.

18. The system of claim **16**, wherein the magnetic resonance imaging system is configured to determine an actual temperature of the non-uniform tissue during driving of the plurality of transducer elements, the controller being configured to generate an output indicating when the actual temperature of the non-uniform tissue is greater than the maximum temperature.

19. The system of claim **16**, wherein individual transducer elements are independently controllable such that the temperature of each non-uniform tissue region does not exceed the maximum temperature.

20. The system of claim **13**, further comprising a fluid interface integral with the ultrasound transducer and operably coupled to the controller, wherein the fluid interface is positionable around the non-uniform tissue region and configured to facilitate circulation of cooling fluid about the non-uniform tissue.

21. The system of claim **20**, further comprising a temperature sensor positioned within the fluid interface and in communication with the controller, the temperature sensor being configured to measure a temperature of the cooling fluid circulating within the fluid interface.

22. The system of claim **21**, wherein the fluid circulates within the interface in a continuous fashion.

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专利名称(译)	用于控制通过非均匀组织传输的超声能量及其冷却的系统和方法		
公开(公告)号	US20100179425A1	公开(公告)日	2010-07-15
申请号	US12/352932	申请日	2009-01-13
[标]申请(专利权)人(译)	ZADICARIO EYAL		
申请(专利权)人(译)	ZADICARIO EYAL		
当前申请(专利权)人(译)	InSightec的有限公司.		
[标]发明人	ZADICARIO EYAL		
发明人	ZADICARIO, EYAL		
IPC分类号	A61B8/00		
CPC分类号	A61B2018/00023 A61B2019/5236 A61B2019/524 A61B8/585 A61N2007/0078 A61B8/0816 A61N7/02 A61B2090/374 A61B2090/3762		
外部链接	Espacenet USPTO		

摘要(译)

基于非均匀组织区域（例如，颅骨区域）和预定阈值的解剖学特征来控制超声换能器阵列的换能器元件的发射强度。