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(54) **Ultrasonic apparatus for diagnosis and therapy**

Ultraschallgerät zur Diagnose und Therapie

Appareil à ultrasons pour ea diagnose et la thérapie

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• **SIMON C ET AL: "QUANTITATIVE ANALYSIS AND APPLICATIONS OF NON-INVASIVE TEMPERATURE ESTIMATION USING DIAGNOSTIC ULTRASOUND" PROCEEDINGS OF THE 1997 IEEE ULTRASONICS SYMPOSIUM. ONTARIO, CANADA, OCT. 5 - 8, 1997, IEEE ULTRASONICS SYMPOSIUM PROCEEDINGS, NEW YORK, NY : IEEE, US, vol. VOL. 2, 5 October 1997 (1997-10-05), pages 1319-1322, XP000800017 ISBN: 0-7803-4154-6**

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## Description

### BACKGROUND OF THE INVENTION

#### 1. FIELD OF THE INVENTION

**[0001]** The present invention relates to an apparatus for a diagnosis and therapy utilizing an ultrasound, and particularly, to the apparatus for the diagnosis and therapy utilizing the ultrasound used in combination with a phase-shift type ultrasound contrast agent.

#### 2. DESCRIPTION OF THE RELATED ART

**[0002]** It is a long time since image diagnostic modalities such as an X-ray CT (Computed Tomography) apparatus, an MRI (Magnetic Resonance Imaging) apparatus, and an apparatus for a diagnosis and therapy became an indispensable tool in clinical settings. These are something where differences of a CT value, a spin relaxation time, and an acoustic impedance within a living body are imaged, respectively, and are called "anatomical imaging" because the differences of these physical properties mainly reflect a living organism. On the other hand, something for imaging a target position of a functionally different state is called "functional imaging" even if it is a structurally same tissue.

**[0003]** Out of the functional imaging, for example, something for visualizing an existing state of a living body constitutional molecule such as a protein, an amino acid, and a nucleic acid is called "molecular imaging" in many cases. The molecular imaging is one of research areas that currently get most attention because an application to an elucidation of a life process such as a generation and differentiation and to a diagnosis and therapy of a disease is expected.

**[0004]** As image diagnostic modalities specialized in such the molecular imaging can be cited a PET (Positron Emission Tomography) apparatus and an optical imaging apparatus. The former is broadly used as a tool for classifying a clinical widening extent and proceeding stage of a tumor; the latter as a noninvasive analysis tool of a drug in such a drug development where a small animal is used.

**[0005]** In addition, also in modalities such as the MRI and the ultrasonic apparatus for the diagnosis and therapy where an application as the morph imaging is precedent, a research and development for utilizing them as the molecular imaging progresses.

**[0006]** Furthermore, the ultrasonic apparatus for the diagnosis and therapy is expected as a diagnosis and therapy integration tool usable other than in a big hospital because it has features, which other modalities do not have, such as being 1) excellent in real time property, 2) less in restriction with respect to a use within an operation room thanks to its smallness, and 3) also usable as a therapeutic tool as well as a diagnostic tool.

**[0007]** Here, a therapeutic method of using an ultra-

sound can be mainly classified into two. One is a thermal coagulation therapy that converges and exposes the ultrasound, heats up a target position not less than a protein denaturation temperature (about 65 degrees Celsius) in a short time of a few seconds, and thereby, treats the target position. Because the thermal coagulation therapy is a therapy of using a high intensity focused ultrasound (HIFU) not less than 1kW/cm<sup>2</sup>, it is called an "HIFU" therapy in many cases.

**[0008]** However, if because the HIFU therapy obtains an exposure positional selectivity only due to a convergence of an ultrasound, an aim is missed due to a body movement, there is a possibility that a high intensity ultrasound not less than 1kW/cm<sup>2</sup> is exposed on a target position other than a target position. Therefore, it is preferable that a therapeutic method has the positional selectivity other than the convergence of the ultrasound. Document US 2005/0038340 discloses an ultrasonic apparatus wherein the therapy transducer is used at a lower intensity in order to locate the treatment position.

**[0009]** Another therapeutic method for using an ultrasound is a therapy by (acoustic) cavitation action. A cavitation is basically a phenomenon that a bubble nucleus is produced by ultrasound, the bubble grows, and is collapsed. Because if the cavitation occurs, a high temperature of several thousand degrees and a high pressure of several hundreds occur at the collapse stage of a last bubble, it is enabled to treat a target position, utilizing this. Furthermore, it is enabled to more effectively treat the target position by a chemical substance called an acoustic chemical active substance activated by cavitation (for example, see a pamphlet of WO 98/01131).

**[0010]** In any one of the therapeutic methods for using an ultrasound, it is preferable to reduce an ultrasound exposure amount in order to alleviate a burden of an inspected body. Consequently, in order to restrict an exposure range, a method of properly identifying a tumor position is requested.

**[0011]** In general chemical and radio active therapy fields are disclosed methods of utilizing a "molecular probe" for selectively bonding a living body constitutional molecule such as an antibody and a ligand, detecting a tumor, and making the tumor a therapy target (for example, see pages 750-763 in Cancer 2 (Nature Rev. 2) by Allen (2002)). These tumor identification methods are also utilized for an ultrasonic contrast agent used for an ultrasonic apparatus for a diagnosis and therapy.

**[0012]** In addition, if there exist a micro bubble used as an ultrasonic contrast agent, it is well known in exposing an ultrasound that an apparent absorption coefficient becomes higher (for example, see pages 1399-1412, Ultrasound Med. Biol 27 by Holt et al. (2001)). Because if it is possible to restrict the micro bubble only to a target position, it is enabled to selectively heat up the target position with using the phenomenon, it is enabled to reduce an ultrasound exposure amount in a thermal coagulation therapy.

**[0013]** In addition, an existence of a micro bubble in

an ultrasound exposure position corresponds to a stage that the bubble on the way of a cavitation process has grown, and it is possible to omit one step of a nucleus production requested for a production of a cavitation by exposing an ultrasound at the stage. Therefore, it is well known that an acoustic intensity requested for the production of the cavitation is reduced by the existence of the micro bubble (for example, see pages 2059-2069 in J. Acoust. Soc. Am. 88 by Holland et al. (1990)). In other words, if it is possible to restrict a micro bubble to a target position, with using the phenomenon it is enabled to reduce an ultrasound exposure amount in a therapy by cavitation action.

**[0014]** However, because a micro bubble cannot exist only in a blood vessel due to a restriction of a size thereof, it is difficult to restrict the bubble to a specific position of a tissue.

**[0015]** Consequently, a phase-shift or phase transition type ultrasound contrast agent is disclosed that is a droplet of a nano size when dosed in a living body, produces a phase shift by ultrasound exposure, and thereby produces a micro bubble (for example, see Ultrasound Contrast Image 92 (Proc. 4th Intern Symp.) by Kawabata et al. (2004)). It is possible to move the droplet of the nano size if any to a tissue such as a tumor, and furthermore, it is possible to make the droplet have a tissue selectivity by adding the molecular probe. Ultrasound imaging higher in tissue selectivity is enabled by using such a phase-shift type ultrasound contrast agent.

**[0016]** Meanwhile, it is disclosed that in order to stably causing a phase shift of such a phase shift ultrasound contrast agent is requested a temporally averaged acoustic intensity surpassing  $0.72 \text{ W/cm}^2$  of an upper limit usable in a usual ultrasonic apparatus for a diagnosis and therapy (for example, see Ultrasound Contrast Image 92 (Proc. 4th Intern Symp.) by Kawabata et al. (2004)).

**[0017]** In addition, as a new diagnostic modality for using an ultrasound is disclosed radiation pressure imaging (for example, see pages 1087-1093 in Trans. IEEE Medical Imag. 23 by Alizards et al. (2004)). In the Medical Imag. 23 is proposed the diagnostic modality for performing a diagnosis, using an ultrasound not less than an acoustic intensity restricted in a conventional ultrasonic apparatus for a diagnosis and therapy.

**[0018]** By combining the phase-shift type ultrasound contrast agent and an ultrasound therapy, it is enabled to restrict a micro bubble to a target position and to reduce an ultrasound exposure amount in the ultrasound therapy.

**[0019]** As described above, because a micro bubble is produced in making an image, using the phase-shift type ultrasound contrast agent, it is enabled to apply the contrast agent to a therapy as well as a diagnosis.

**[0020]** However, because a conventional ultrasonic apparatus for a diagnosis and therapy cannot start a therapy in conjunction with the production of a micro bubble from the phase-shift type ultrasound contrast agent, there

is a problem that an ultrasound of a comparatively high intensity is requested to be exposed in producing the micro bubble from the contrast agent.

**[0021]** Consequently, an ultrasonic apparatus for a diagnosis and therapy is strongly requested that can perform the therapy in conjunction with making imaging by a phase-shift type ultrasound contrast agent.

## SUMMARY OF THE INVENTION

**[0022]** In order to solve the problem, an apparatus of the present invention is an ultrasonic apparatus for a diagnosis and therapy comprising: a first ultrasound probe for exposing an ultrasound for a phase shift; a second ultrasound probe for exposing an ultrasound for a diagnosis; an ultrasound exposure apparatus for exposing an ultrasound for a therapy; an echo detection device for detecting an ultrasound echo; a control part for the phase shift for causing the phase shift in an ultrasound contrast agent by exposing the ultrasound for the phase shift through the first ultrasound probe; a control part for the diagnosis for detecting the phase shift of the contrast agent, using the ultrasound echo detected by the echo detection device with corresponding to an exposure of the ultrasound for the diagnosis by the second ultrasound probe; a difference calculation device for calculating a difference over time of the phase shift detected by the control part for the diagnosis; a device for positioning for deciding a target position where the difference is produced; and a control part for the therapy for exposing the ultrasound for the therapy to the decided target position through the ultrasound exposure apparatus.

**[0023]** Thus configured, it is enabled to move an exposure of an ultrasound for a phase shift and that of an ultrasound for a diagnosis in conjunction with each other, and to reduce the exposure amount of the ultrasound.

## BRIEF DESCRIPTION OF THE DRAWINGS

**[0024]**

FIG. 1 is a block diagram showing a configuration of an ultrasonic apparatus for a diagnosis and therapy of an embodiment of the present invention.

FIGS. 2A and 2B are drawings respectively showing waveforms of ultrasonic pulses for a phase shift of the embodiment.

FIG. 3 is a flowchart explaining one example of a method of diagnosing and treating an inspected body, using an ultrasonic apparatus for a diagnosis and therapy of the embodiment.

FIGS. 4A to 4D are drawings respectively verifying phase shift differences of a contrast agent in cases that waveforms of ultrasonic pulses for a phase shift are changed.

FIG. 5 is a drawing in an example 2 showing one example of diagnostic images displayed in a display device.

FIG. 6 is a drawing showing a tumor segment after exposing an ultrasound for a therapy to it.

#### BEST MODE FOR CARRYING OUT THE INVENTION

**[0025]** Here will be described a best mode for carrying out the present invention (hereinafter referred to as "embodiment") in detail, referring to drawings as needed.

**[0026]** As shown in FIG. 1, an ultrasonic apparatus 1 for a diagnosis and therapy comprises a diagnostic probe 2, a phase shift probe 3, a therapeutic probe 4, and an apparatus body 5, and a display device 6.

**[0027]** In addition, it is assumed that a predetermined phase-shift type ultrasound contrast agent (hereinafter referred to as "contrast agent") has been dosed in an inspected body 7 containing a target position 8. The contrast agent is not specifically limited in its composition if a phase shift thereof occurs from a liquid to a gas at least in its part by exposing an ultrasound for a phase shift.

**[0028]** Meanwhile, if although an "inspected body" means an object for a diagnosis and therapy by the ultrasonic apparatus 1 of the embodiment, it has a constitution inside which a phase shift can occur, anything is available. For example, the inspected body 7 is such a living body tissue of any one of an animal (including a human) and a plant, and a solution held in a container.

#### <Diagnostic Probe>

**[0029]** The diagnostic probe 2 exposes an ultrasonic pulse for a diagnosis to the target position 8 of the inspected body 7, and receives an ultrasound echo corresponding to the ultrasonic pulse for the diagnosis.

**[0030]** The diagnostic probe 2 comprises a vibrator 2a for converting an electric signal to a vibration and vice versa. As the vibrator 2a can be utilized, for example, such a magnetic strain resonator and a piezoelectric resonator. In addition, in order to diagnose a predetermined range in the inspected body 7, it is preferable to be able to display a plurality of scan lines corresponding to each vibrator 2a by arraying a plurality of vibrators 2a. Meanwhile, it is preferable for the vibrators 2a to be arrayed in any one of a flat plane and a convex plane.

**[0031]** In addition, the diagnostic probe 2 is connected to the apparatus body 5.

#### <Phase Shift Probe>

**[0032]** The phase shift probe 3 exposes an ultrasonic pulse for a phase shift to the target position 8 of the inspected body 7 in order to cause a phase shift in a contrast agent dosed in the inspected body 7.

**[0033]** It is enabled to make a configuration of the phase shift probe 3 similar to that of the diagnostic probe 2. Meanwhile, it is preferable for a vibrator 3a to be arrayed in any one of a flat plane and a convex plane (in a case that the vibrator is one, to be formed in any one of a flat plane and a convex plane) in order to converge an

ultrasound.

**[0034]** In addition, the phase shift probe 3 is connected to the apparatus body 5.

#### 5 <Therapeutic Probe>

**[0035]** The therapeutic probe 4 exposes an ultrasound for a therapy for the target position 8 of the inspected body 7 in order to treat the inspected body 7.

10 **[0036]** It is also enabled to make a configuration of the therapeutic probe 4 similar to that of the diagnostic probe 2. Meanwhile, it is preferable for a vibrator 4a to be arrayed in any one of a flat plane and a convex plane (in a case that the vibrator is one, to be formed in any one of a flat plane and a convex plane) in order to converge an ultrasound.

15 **[0037]** In addition, the therapeutic probe 4 is connected to the apparatus body 5.

20 **[0038]** In addition, each of the probes 2 to 4 is usually installed at the inspected body 7 through an acoustic coupling 9 in order to sensitively send and receive an ultrasonic pulse.

#### <Apparatus Body>

25 **[0039]** The apparatus body 5 performs processing for an electric signal corresponding to an ultrasound echo collected from the inspected body 7, controls sending and receiving an ultrasound, controls an ultrasound image display, and the like.

30 **[0040]** As shown in FIG. 1, the apparatus body 5 comprises a control part 52 for a diagnosis, a control part 53 for a phase shift, a control part 54 for a therapy, and a data-process part 55.

35 **[0041]** Meanwhile, each of the parts 52 to 55 comprises a memory consisting of such a CPU (Central Processing Unit), a ROM (Read Only Memory), and a RAM (Random Access Memory); a hard disk; and the like. Each of the parts 52 to 55 within the apparatus body 5 corresponds to a program or data stored in the memory or the hard disk. Then it is assumed that the CPU reads the program into the memory, performs calculation processing, and thereby, each processing is realized.

40 **[0042]** In addition, each of the parts 52 to 54 further comprises such an amplifier circuit and an A/D converter circuit not shown.

45 **[0043]** The control part 52 for the diagnosis is electrically connected to the diagnostic probe 2 and controls sending and receiving an ultrasound for a diagnosis.

50 **[0044]** In addition, the control part 52 for the diagnosis is configured to be able to send and receive an ultrasound of a frequency of roughly an extent of 2 to 10 MHz and a temporally averaged acoustic intensity not more than 0.72 W/cm<sup>2</sup> usable in a usual ultrasound diagnostic apparatus.

55 **[0045]** Here will be described a procedure of controlling sending and receiving the ultrasound for the diagnosis.

**[0046]** Firstly, the control part 52 for the diagnosis produces an electric signal (appropriately called "pulse signal") and sends it to the diagnostic probe 2.

**[0047]** Specifically in a case of a pulse inversion mode, the control part 52 produces the pulse signal so as to expose a predetermined basic wave and a reverse phase basic wave to one scan line, and sends them to the diagnostic probe 2.

**[0048]** Then, the control part 52 receives an echo signal from the diagnostic probe 2.

**[0049]** Specifically in a case of the pulse inversion mode, a basic wave is cancelled by a reverse phase basic wave out of the basic wave and a higher harmonic wave contained in an ultrasound echo, and thereby, mainly the higher harmonic wave results in being received by the diagnostic probe 2. The higher harmonic wave tends to occur if a larger component of a volume change is contained in the inspected body 7. Accordingly, the pulse inversion mode is suitable for detecting a gas inside the inspected body 7, compared to a B mode generally used in an ultrasound diagnosis. Meanwhile; the control part 52 of the embodiment is not limited to the pulse inversion mode if it can detect a phase shift.

**[0050]** In addition, in the control part 52 of the embodiment there is a fear that an accuracy of a diagnostic image is degraded by receiving not only an echo signal corresponding to the ultrasonic pulse for the diagnosis but also echo signals corresponding to ultrasonic pulses for a phase shift and a therapy. Consequently, it may be configured that, for example, a filter for restricting a frequency and a voltage out of a predetermined bandwidth is provided in the control part 52.

**[0051]** Then the control part 52 amplifies the received echo signal by the amplifier circuit not shown, samples it by a sampling frequency suitable for signal processing by the A/D converter circuit, and converts it to a digital signal.

**[0052]** Then the digital signal corresponding to the echo signal is output to the data-process part 55.

**[0053]** The control part 53 for the phase shift is electrically connected to the phase shift probe 3, and controls sending an ultrasound for a phase shift. The control part 53 is configured to be able to expose an ultrasound in a range of 0.5 to 10 W/cm<sup>2</sup> in temporally averaged acoustic intensity, wherein the ultrasound is any one of a single frequency selected from a range of 0.5 to 10 MHz and a frequency where on a basic frequency selected from a range of 0.5 to 5 MHz is superposed a double frequency of the basic frequency.

**[0054]** The control part 53 produces an electric signal corresponding to the ultrasonic pulse for the phase shift, and sends it to the phase shift probe 3.

**[0055]** If the ultrasonic pulse for the phase shift is exposed to a contrast agent dosed in the inspected body 7, in the contrast agent the phase shift occurs from a liquid to a gas. Such the phase shift of the contrast agent can be detected more clearly in a case that the control part 52 for the diagnosis is the pulse inversion mode.

**[0056]** Meanwhile, it is preferable that the ultrasonic pulse for the phase shift is weak as much as possible in acoustic intensity in a range of being able to cause the phase shift in the contrast agent in order to prevent an excessive ultrasound exposure to the inspected body 7.

**[0057]** In addition, although a larger energy is requested to produce a cavitation caused by phase shift, the inventors et al. have proved that such the energy as in producing the cavitation is not needed to maintain the cavitation once caused. If it is enabled to lessen an energy for maintaining the cavitation, it is enabled to reduce an ultrasound exposure amount to the inspected body 7, and to alleviate a burden of the inspected body 7.

**[0058]** FIGS. 2A and 2B are drawings respectively showing waveforms of ultrasonic pulses for a phase shift of the embodiment; FIG. 2A is a drawing explaining waveforms of ultrasonic pulses; and FIG. 2B is a schematic drawing explaining continuous ultrasonic pulses. In FIGS. 2A and 2B a horizontal axis is a time; a vertical axis is an acoustic intensity of an ultrasonic pulse. As shown in FIG. 2A, the ultrasonic pulses for the phase shift are configured with a first wave and a second wave. The first wave causes a phase shift of a contrast agent; the second wave maintains the caused phase shift of the contrast agent. In addition, as shown in FIG. 2B, it is preferable to provide an interval of 50 ms for an ultrasound of 10 ms in order to more effectively cause the phase shift of the contrast agent.

**[0059]** Here, although an acoustic intensity requested is preferably not less than 0.72 W/cm<sup>2</sup> in order to stably cause a phase shift as shown in Ultrasound Contrast Image 92 (Proc. 4<sup>th</sup> Intern Symp.) by Kawabata et al. (2004) described before, the phase shift can be caused if the acoustic intensity is at least 0.1 W/cm<sup>2</sup>.

**[0060]** In addition, an acoustic intensity requested for maintaining the phase shift is preferably in a range of one fourth to one fold of the first wave. The acoustic intensity of the second wave is prescribed in an example 1 described later.

**[0061]** In addition, returning to FIG. 1, the control part 53 for the phase shift comprises an ultrasonic pulse scan device not shown for scanning the ultrasonic pulse for the phase shift (specifically its focus). The ultrasonic pulse scan device may also be any configuration of, for example, mechanically moving the phase shift probe 3 and of controlling only a direction of an ultrasound beam exposed by controlling a pulse signal.

**[0062]** The control part 54 for the therapy is electrically connected to the therapeutic probe 4 and controls sending an ultrasound pulse for a therapy.

**[0063]** The control part 54 produces an electric signal corresponding to the ultrasonic pulse for the therapy and sends it to the therapeutic probe 4. The control part 54 is configured to be able to expose any one of an ultrasound selected from a range of 0.5 to 10 MHz and a frequency where on a basic frequency selected from a range of 0.5 to 5 MHz is superposed a double frequency of the basic frequency; and an acoustic intensity can be

made an arbitrary value selected from a range of 1 to 1000 W/cm<sup>2</sup>.

**[0064]** As described before, the therapeutic methods by ultrasound are mainly classified into the thermal coagulation therapy and the therapy by cavitation action. In accordance with the control part 54 of the embodiment, in any case can be supplied an electric signal for exposing an ultrasonic pulse of a proper acoustic intensity.

**[0065]** Generally, although the stronger the acoustic intensity, the more effective the ultrasound of the thermal coagulation therapy is, the embodiment obtains a sufficient effect because of utilizing a micro bubble even if, for example, the acoustic intensity of the ultrasound is not more than 1000 W/cm<sup>2</sup>.

**[0066]** In addition, although a cavitation can be produced enough by an ultrasound consisting of one frequency, it is well known that an ultrasound where two frequencies are superposed can more efficiently produce the cavitation as indicated by a pamphlet of WO 94/06380. Because the embodiment is the configuration of being able to exposing an ultrasound where two frequencies are superposed, it obtains a sufficient therapeutic effect even in an ultrasound of a lower acoustic intensity.

**[0067]** In addition, the control part 54 for the therapy comprises an ultrasonic pulse movement device not shown for moving the ultrasonic pulse for the therapy (specifically its focus). The ultrasonic pulse movement device may be any configuration of, for example, mechanically moving the therapeutic probe 4, and of controlling only a direction of an ultrasound beam exposed by controlling a pulse signal.

**[0068]** The data-process part 55 processes digital data based on an echo signal acquired by the control part 52 for the diagnosis, and supplies control information to the control part 53 for the phase shift and the control part 54 for the therapy.

**[0069]** The data-process part 55 comprises, for example, a device 551 for forming diagnostic images, a device 552 for calculating differences between data, and a device 553 for positioning.

**[0070]** The device 551 for forming diagnostic images processes to produce a diagnostic image such as a pulse inversion mode tomogram from a digital signal based on an echo signal. The production processing of the diagnostic image by the device 551 can be performed in a field of an ultrasound image diagnosis by a conventional well known method.

**[0071]** Then the diagnostic image produced by the device 551 is output to the device 552 for calculating differences between data.

**[0072]** The device 552 digitalizes brightness in diagnostic images before an ultrasonic pulse for a phase shift and after an exposure, respectively, and calculates their difference.

**[0073]** Then the difference calculated by the device 552 is output to the device 553 for positioning.

**[0074]** The device 553 decides a target position where

a phase shift is produced by comparing the difference calculated by the device 552 with a predetermined threshold. To be more precise, in a case that the difference exceeds the predetermined threshold, the device 553 decides the target position, assuming that the phase shift is produced; in a case that the difference does not exceed the predetermined threshold, the device 553 assumes that the phase shift is not produced.

**[0075]** Then information of the target position decided by the device 553 is output to the display device 6 and the control parts 53 and 54.

<Ultrasonic Method for Diagnosis and Therapy>

**[0076]** Next will be described one example of a method for diagnosing and treating the inspected body 7 by using the ultrasonic apparatus 1, referring to FIG. 3.

**[0077]** Firstly, the control part 52 of the ultrasonic apparatus 1 acquires an electric signal of an ultrasound echo corresponding to an ultrasonic pulse for a diagnosis with respect to the target position 8 (diagnosis region) of the inspected body 7, and converts it to a digital signal (step S01).

**[0078]** Next, the data-process part 55 of the ultrasonic apparatus 1 makes a diagnostic image (before a phase shift) of the target position 8 by the device 551, based on the digital signal, and notifies (step S02) the control part 53 of having made the diagnostic image (before the phase shift).

**[0079]** Then if the control part 53 of the ultrasonic apparatus 1 receives the notification of having made the diagnostic image (before the phase shift), it starts to scan (step S03) the ultrasonic pulse for the phase shift in the target position 8.

**[0080]** Meanwhile, scanning the ultrasonic pulse for the phase shift is performed, including a region where the diagnostic image is formed.

**[0081]** Then the data-process part 55 of the ultrasonic apparatus 1 makes (step S04) a diagnostic image (after the phase shift) for every scan (every movement of a focus) of the ultrasonic pulse for the phase shift by the device 551.

**[0082]** Then the data-process part 55 of the ultrasonic apparatus 1 calculates (step S05) a difference of brightness by the device 552, comparing the diagnostic images before and after the phase shift for every scan.

**[0083]** Then the data-process part 55 of the ultrasonic apparatus 1 compares (step S06) the difference of the brightness with a threshold by the device 553.

**[0084]** In a case that the difference of the brightness does not exceed the threshold (No in the step S06), the control part 53 of the ultrasonic apparatus 1 moves (step S10) the focus of the ultrasonic pulse for the therapy to a target position where the pulse is not yet exposed.

**[0085]** In a case that the difference of the brightness exceeds the threshold (Yes in the step S06), the control part 53 of the ultrasonic apparatus 1 lowers (step S07) the acoustic intensity of the ultrasonic pulse for the phase

shift to one fourth to one fold thereof.

**[0086]** Then the data-process part 55 of the ultrasonic apparatus 1 decides (step S08) a target position (which matches the focus of the ultrasonic pulse for the phase shift during exposure in many cases) by the device 553 where the difference of the brightness has exceeded the threshold.

**[0087]** Then the control part 54 of the ultrasonic apparatus 1 exposes (step S09) the ultrasonic pulse for the therapy to the decided target position.

**[0088]** Then the control part 53 of the ultrasonic apparatus 1 moves (step S10) the focus of the ultrasonic pulse for the therapy to a target position where the pulse is not yet exposed.

**[0089]** Thus the following effects can be obtained in the embodiment:

Because it is configured that exposing an ultrasonic pulse for a phase shift and that for a diagnosis are made to move in conjunction with each other, it is enabled to reduce an exposure amount of the ultrasounds.

**[0090]** In addition, by configuring the ultrasonic pulse for the phase shift with the first wave and the second wave lower in acoustic intensity than the first wave, it is enabled to confirm the target position 8 while suppressing an excess exposure of the ultrasounds to the inspected body 7 and to perform a therapy.

**[0091]** Meanwhile, the present invention is not limited to the embodiment, and various variations are available without departing from the spirit and scope of the invention.

**[0092]** For example, in the embodiment, although the exposure position of the ultrasonic pulse for the therapy is decided by calculating the difference of brightness of the diagnostic images before and after exposing the ultrasonic pulse for the phase shift, a method for deciding the exposure position of the ultrasonic pulse for the therapy is not limited thereto described above. For example, the exposure position may be decided by calculating a difference between levels of the echo signals. Or else the exposure position may be decided by calculating a difference of the digital signals corresponding to the echo signals. In addition, it is preferable to compare each even harmonic wave component of central frequencies of ultrasonic pulses for the diagnosis before and after the exposures of ultrasonic pulses for the phase shift.

**[0093]** Meanwhile, In any case it is enabled to image a target position where a difference of the signals is produced and to display it in the display device 6.

**[0094]** In addition, the diagnostic probe 2, the phase shift probe 3, and the therapeutic probe 4 can also be combined without being made independent configurations, respectively. In this case it is enabled to achieve to image the target position by controlling each sending timing of pulse signals sent from the control parts 52 to 54 corresponding to the probes 2 to 4.

<Example 1>

**[0095]** In an example 1 is verified a phase-shift type ultrasound contrast agent in a case that a waveform of an ultrasonic pulse for a phase shift is changed. In the example 1, as the contrast agent was used an emulsion type agent disclosed in Ultrasound Contrast Image 92 (Proc. 4th Intern Symp.) by Kawabata et al. (2004) described before.

**[0096]** FIGS. 4A to 4D are drawings respectively verifying phase shift differences of a contrast agent in cases that waveforms of ultrasonic pulses for a phase shift are changed. Although in FIGS. 4A to 4D an acoustic intensity of a first wave is 4 W/cm<sup>2</sup> (temporal averaged) in common, a second wave is changed to a predetermined acoustic intensity. Meanwhile, an ultrasound frequency is 3.4 MHz in both of the first and second waves.

**[0097]** As shown in FIGS. 4A to 4C, in cases that the second wave is not less than 1 W/cm<sup>2</sup> with respect to 4 W/cm<sup>2</sup> of the first wave, it was enabled to detect the phase shift even if the acoustic intensity of the second wave is made lower than that of the first wave. On the other hand, as shown in FIG. 4D, in a case that the second wave is 0.5 W/cm<sup>2</sup> with respect to 4 W/cm<sup>2</sup> of the first wave, it was not enabled to detect the phase shift.

**[0098]** In other words, in accordance with the example 1 was indicated that a phase shift state of the contrast agent is maintained in a range of the acoustic intensity of the second wave being one fourth to one fold of that of the first wave.

<Example 2>

**[0099]** In an example 2 was practically performed a diagnosis and therapy, using the ultrasonic apparatus 1 of the embodiment. An object for the diagnosis and therapy is colon 26 tumor subdermally implanted in a mouse.

**[0100]** As a contrast agent was used the emulsion type agent disclosed in Ultrasound Contrast Image 92 (Proc. 4th Intern Symp.) by Kawabata et al. (2004) described above.

**[0101]** In addition, for the diagnosis was used an ultrasonic pulse of 7.5 MHz; for the phase shift, an ultrasonic pulse of 3.4 MHz and 4 W/cm<sup>2</sup> (temporal averaged) (10 ms ON, 50 ms OFF); and for the therapy, an ultrasonic pulse of 3.4 MHz and 50 W/cm<sup>2</sup> (temporal averaged) (10 ms ON, 50 ms OFF). Meanwhile, in the example 2 was not scanned the ultrasound for the phase shift.

**[0102]** FIG. 5 is a drawing in the example 2 showing one example of diagnostic images displayed in a display device; (B1) and (B4) are diagnostic images of a B mode used in a general ultrasound diagnosis; and (P1), (P2), (P3), and (P4) are diagnostic images of the pulse inversion mode of the embodiment.

**[0103]** In addition, in FIG. 5 each region indicated by an outline square on a black background is a target position where the phase shift of the contrast agent is observed by exposing the ultrasonic pulse for the phase

shift.

**[0104]** The (B1) and (P1) at respective first stages are diagnostic images after 15 minutes of a dose of the contrast agent and before exposing the ultrasonic pulse for the phase shift.

**[0105]** The (P2) at the second stage is a diagnostic image during exposing the ultrasonic pulse for the phase shift. Brightness of an exposure position surrounded by the outline square on the black background of the (P2) results in being higher than that of the (P1).

**[0106]** The (P3) at the third stage is a diagnostic image during exposing the ultrasonic pulse for the therapy. Meanwhile, as soon as the ultrasonic pulse for the phase shift is stopped after three seconds from its start, the ultrasonic pulse for the therapy is started to expose the same position.

**[0107]** Brightness of an exposure position of the (P3) results in being more remarkable than that of the (P2). This is because even if a micro bubble is collapsed by the ultrasonic pulse for the therapy, a signal in its collapse is detected in the diagnostic image.

**[0108]** The (B4) and the (P4) at respective fourth stages are diagnostic images when the ultrasonic pulse for the therapy is stopped after exposing the ultrasonic pulse for the diagnosis for 60 seconds.

**[0109]** Comparing the (B4) with the (B1), an obvious tissue change is observable on the diagnostic images by exposing the ultrasonic pulse for the therapy.

**[0110]** FIG. 6 is a drawing showing a tumor segment after exposing an ultrasonic pulse for a therapy. At a brightness change position of the (P4) of FIG. 5 is observed a tumor necrosis.

**[0111]** Meanwhile, although not shown, as a result of having performed a study similar to the example 2 by frequencies of 0.5 and 1.0 MHz (each acoustic intensity, 10 W/cm<sup>2</sup>), a tumor necrosis effect equivalent to that of the example 2 was obtained.

## Claims

1. An ultrasonic apparatus (1) for a diagnosis and therapy comprising:

- a first ultrasound probe (3) for phase shifting ultrasound exposure;
- a second ultrasound probe (2) for diagnostic ultrasound exposure;
- an ultrasound exposure apparatus (4) for therapeutic ultrasound exposure;
- an echo detection device (2) for detecting an ultrasound echo;
- a phase shift control part (53) for causing the phase shift in an ultrasound contrast agent by said phase shifting ultrasound exposure through said first ultrasound probe;
- a diagnosis control part (52) for detecting the phase shift of said ultrasound contrast agent,

using said ultrasound echo detected by said echo detection device corresponding to said diagnostic ultrasound exposure by said second ultrasound probe;

a difference calculation device (552) for calculating a difference over time of said phase shift detected by said diagnosis control part;

a position device (553) for deciding a target position where said difference is produced; and

a therapy control part (54) for said therapeutic ultrasound exposure of said decided target position through said ultrasound exposure apparatus .

2. The ultrasonic apparatus of claim 1, wherein said first ultrasound probe is configured for exposure by at least two kinds of ultrasound different in acoustic intensity.
3. The ultrasonic apparatus of claim 2, wherein said at least two kinds of ultrasound comprise a first wave and a second wave, and said second wave has not less than one fourth and not more than one times the acoustic intensity of said first wave.
4. The ultrasonic apparatus of claim 1, wherein the frequency of said phase shifting ultrasound controlled by said phase shift control part is not less than 0.5 MHz and not more than 10 MHz.
5. The ultrasonic apparatus of claim 1, wherein the frequency of said diagnostic ultrasound controlled by said diagnosis control part is not less than 0.5 MHz and not more than 10 MHz.
6. The ultrasonic apparatus of claim 5, wherein the acoustic intensity of said therapeutic ultrasound controlled by said therapy control part is not less than 1 W/cm<sup>2</sup> and not more than 1000 W/cm<sup>2</sup>.

## Patentansprüche

1. Ultraschallvorrichtung (1) zur Diagnose und Therapie, aufweisend:

- eine erste Ultraschallsonde (3) zur phasenändernden Ultraschallbestrahlung,
- eine zweite Ultraschallsonde (2) zur diagnostischen Ultraschallbestrahlung,
- eine Ultraschallbestrahlungsvorrichtung (4) zur therapeutischen Ultraschallbestrahlung,
- eine Echoerfassungseinrichtung (2) zur Erfassung eines Ultraschallechos,
- eine Phasenänderungs-Steuereinheit (53), um mittels der phasenändernden Ultraschallbestrahlung durch die erste Ultraschallsonde eine Phasenänderung in einem Ultraschall-Kontrast-

- mittel zu bewirken,  
 eine Diagnosesteuereinheit (52), um unter Verwendung des von der Echoerfassungseinrichtung erfassten Ultraschallechos, das der diagnostischen Ultraschallbestrahlung durch die zweite Ultraschallsonde entspricht, die Phasenänderung des Ultraschallkontrastmittels zu erfassen,  
 eine Differenzberechnungseinrichtung (552), um eine zeitliche Differenz der von der Diagnosesteuereinheit erfassten Phasenänderung zu berechnen,  
 eine Positionseinrichtung (553), um eine Zielposition zu bestimmen, an der die Differenz bewirkt wird, und  
 eine Therapiesteuereinheit (54) für die therapeutische Ultraschallbestrahlung der bestimmten Zielposition durch die Ultraschallbestrahlungsvorrichtung.
2. Vorrichtung nach Anspruch 1, wobei die erste Ultraschallsonde zur Bestrahlung mittels mindestens zweier Arten Ultraschall eingerichtet ist, die sich in der akustischen Intensität unterscheiden.
3. Vorrichtung nach Anspruch 2, wobei die mindestens zwei Arten Ultraschall eine erste Welle und eine zweite Welle umfassen, von denen die zweite Welle nicht weniger als ein Viertel und nicht mehr als ein Mal die akustische Intensität der ersten Welle aufweist.
4. Vorrichtung nach Anspruch 1, wobei die Frequenz des von der phasenändernden Steuereinheit gesteuerten phasenändernden Ultraschalls nicht weniger als 0,5 MHz und nicht mehr als 10 MHz beträgt.
5. Vorrichtung nach Anspruch 1, wobei die Frequenz des von der Diagnosesteuereinheit gesteuerten diagnostischen Ultraschalls nicht weniger als 0,5 MHz und nicht mehr als 10 MHz beträgt.
6. Vorrichtung nach Anspruch 5, wobei die akustische Intensität des von der Therapiesteuereinheit gesteuerten therapeutischen Ultraschalls nicht weniger als 1 W/cm<sup>2</sup> und nicht mehr als 1000 W/cm<sup>2</sup> beträgt.
- Revendications**
1. Appareil à ultrasons (1) pour diagnostic et thérapie comprenant :
- une première sonde à ultrasons (3) pour exposition à des ultrasons de déphasage ;  
 une seconde sonde à ultrasons (2) pour exposition à des ultrasons de diagnostic ;  
 un appareil d'exposition aux ultrasons (4) pour exposition à des ultrasons thérapeutiques ;  
 un dispositif de détection d'écho (2) pour détecter un écho ultrasonore ;  
 une partie de contrôle de déphasage (53) pour provoquer le déphasage dans un agent de contraste ultrasonore grâce à ladite exposition aux ultrasons de déphasage par le biais de ladite première sonde à ultrasons ;  
 une partie de contrôle de diagnostic (52) pour détecter le déphasage dudit agent de contraste ultrasonore, en utilisant ledit écho ultrasonore détecté par ledit dispositif de détection d'écho correspondant à ladite exposition aux ultrasons de diagnostic grâce à ladite seconde sonde à ultrasons ;  
 un dispositif de calcul de différence (552) pour calculer une différence au fil du temps dudit déphasage détecté par ladite partie de contrôle de diagnostic ;  
 un dispositif de position (553) pour décider d'une position cible où ladite différence est produite ;  
 et  
 une partie de contrôle de thérapie (54) pour ladite exposition aux ultrasons thérapeutiques de ladite position cible décidée par le biais dudit appareil d'exposition aux ultrasons.
2. Appareil à ultrasons selon la revendication 1, dans lequel ladite première sonde à ultrasons est configurée pour une exposition par au moins deux sortes d'ultrasons d'intensité acoustique différente.
3. Appareil à ultrasons selon la revendication 2, dans lequel lesdites au moins deux sortes d'ultrasons comprennent une première onde et une seconde onde, et ladite seconde onde n'a pas moins d'un quart et pas plus d'une fois l'intensité acoustique de ladite première onde.
4. Appareil à ultrasons selon la revendication 1, dans lequel la fréquence dudit ultrason de déphasage contrôlée par ladite partie de contrôle de déphasage n'est pas inférieure à 0,5 MHz et pas supérieure à 10 MHz.
5. Appareil à ultrasons selon la revendication 1, dans lequel la fréquence dudit ultrason de diagnostic contrôlée par ladite partie de contrôle de diagnostic n'est pas inférieure à 0,5 MHz et pas supérieure à 10 MHz.
6. Appareil à ultrasons selon la revendication 5, dans lequel l'intensité acoustique dudit ultrason thérapeutique contrôlée par ladite partie de contrôle de thérapie n'est pas inférieure à 1 w/cm<sup>2</sup> et pas supérieure à 1000 w/cm<sup>2</sup>.

FIG. 1

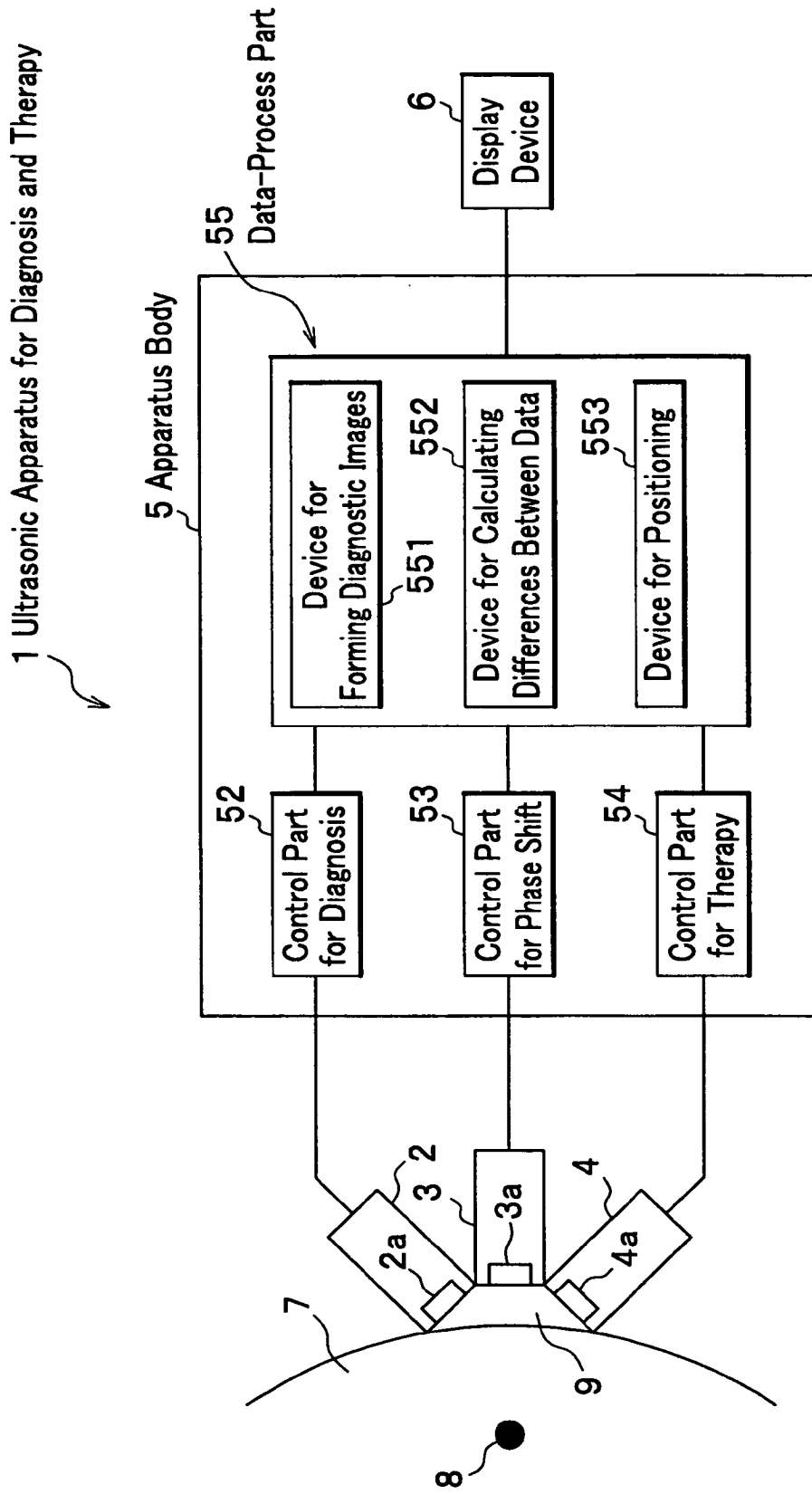


FIG.2A

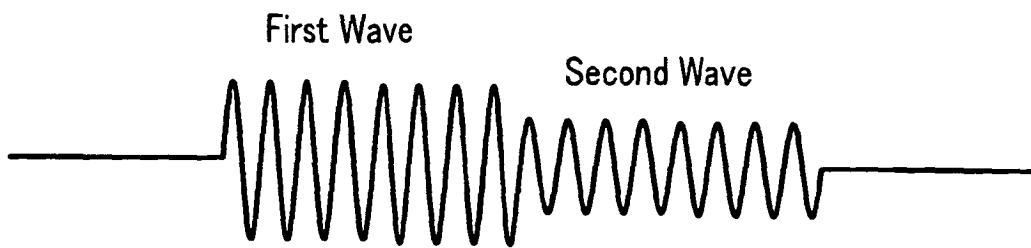


FIG.2B

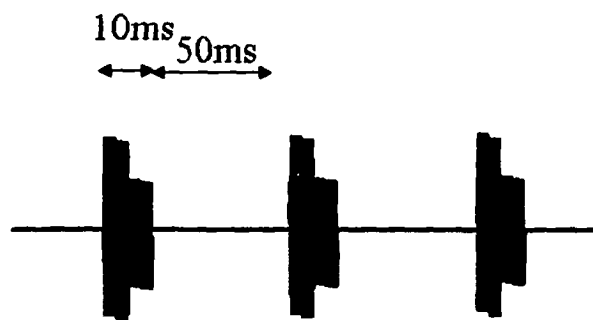


FIG.3

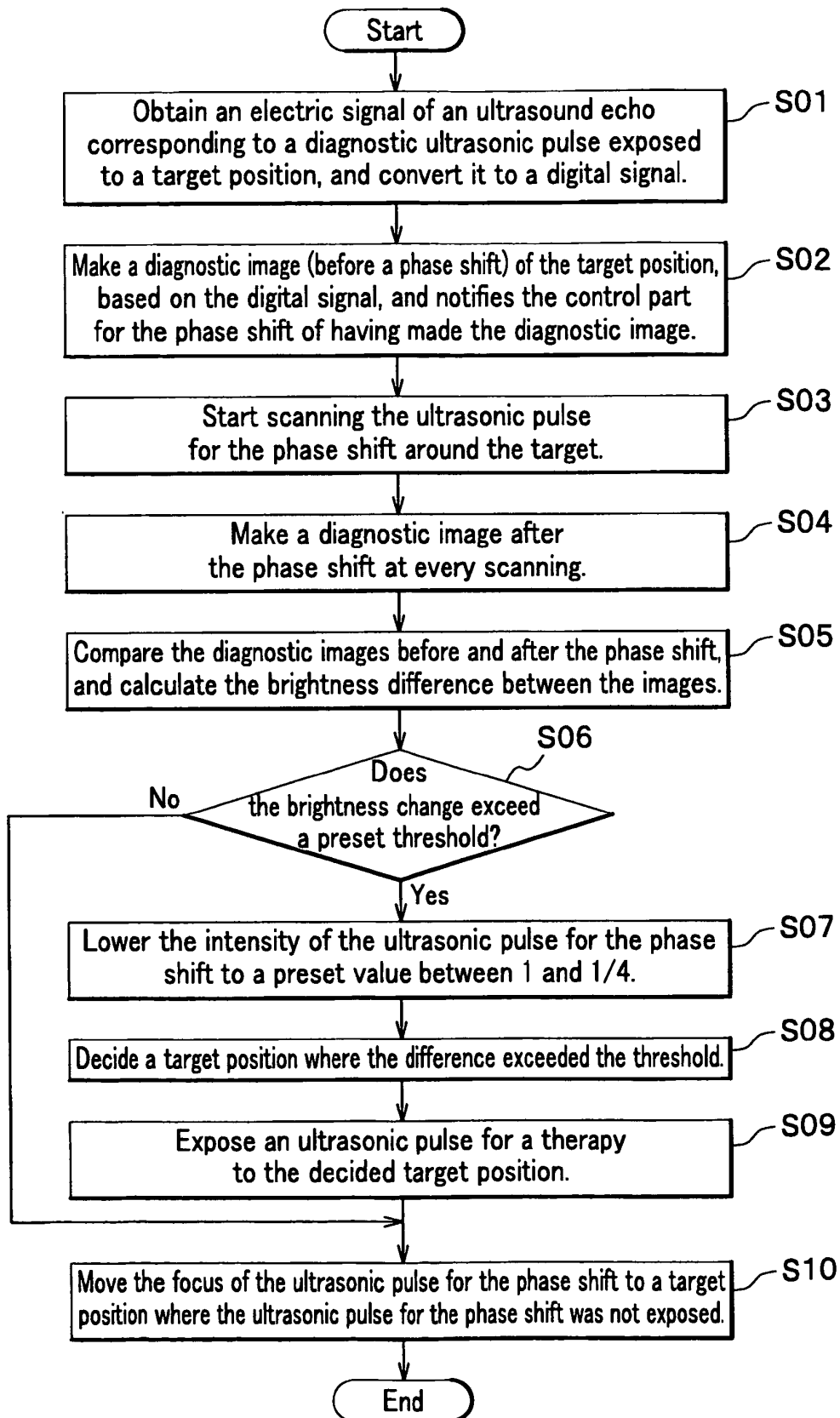
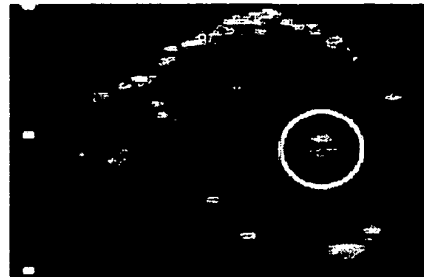


FIG.4A

First Wave

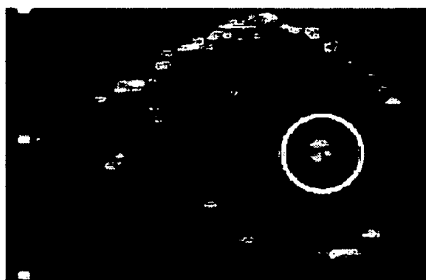
Second Wave



$4W/cm^2$

$4W/cm^2$

FIG.4B



$4W/cm^2$

$2W/cm^2$

FIG.4C



$4W/cm^2$

$1W/cm^2$

FIG.4D



$4W/cm^2$

$0.5W/cm^2$

**FIG.5**

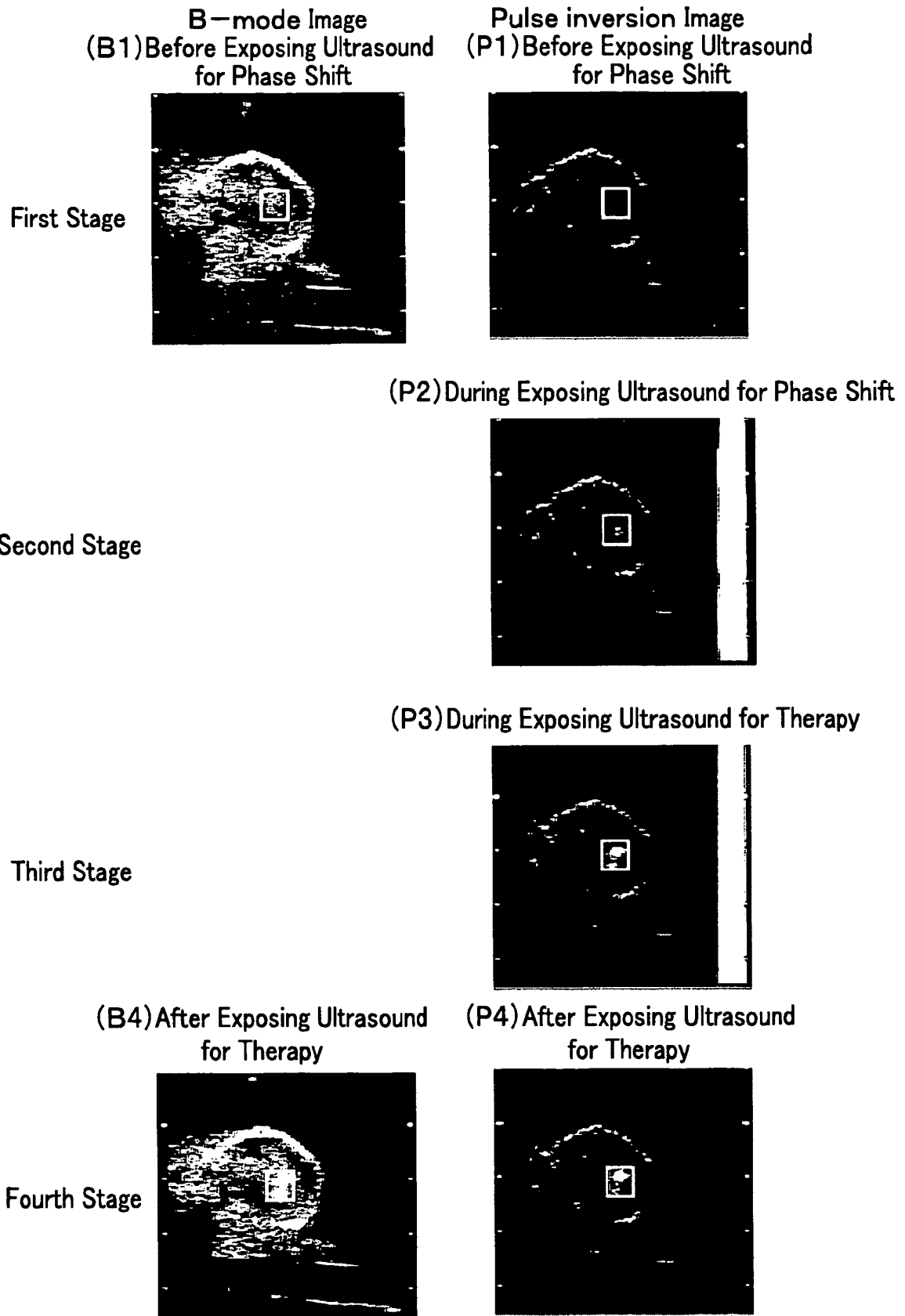
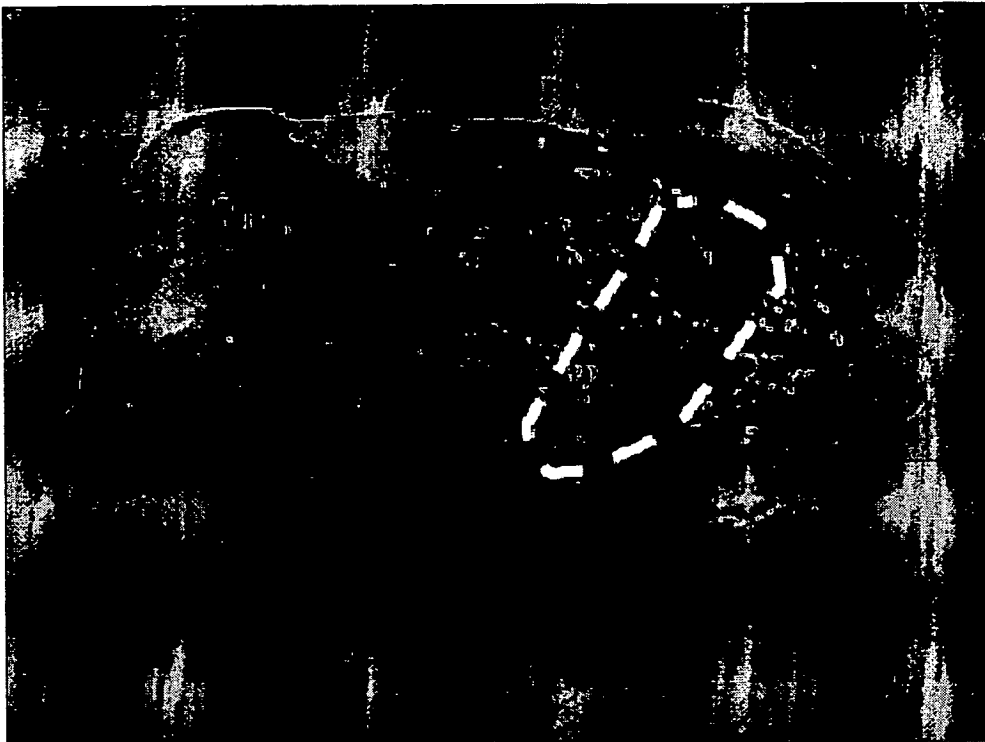


FIG.6



**REFERENCES CITED IN THE DESCRIPTION**

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专利名称(译)	用于诊断和治疗的超声波设备		
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摘要(译)

用于诊断和治疗的超声设备 (1) 包括：第一超声探头 (2)，第二超声探头 (3) 和超声曝光设备 (4)，用于分别通过超声波进行相变，诊断和治疗。；用于检测超声回波的回声检测装置 (2)；控制部分 (53,52) 用于相变，用于通过超声波曝光引起超声造影剂的转变以通过第一探头过渡，并通过检测试剂的转变进行诊断，使用检测装置，对应于超声波曝光，用于第二探头的诊断；差分计算装置 (552)，用于计算由控制部分检测到的用于诊断的转变随时间的差异；位置装置 (553)，用于判定产生差异的目标位置；治疗控制部分 (54)，用于通过用于治疗的超声波暴露于通过曝光设备到所确定的目标位置。

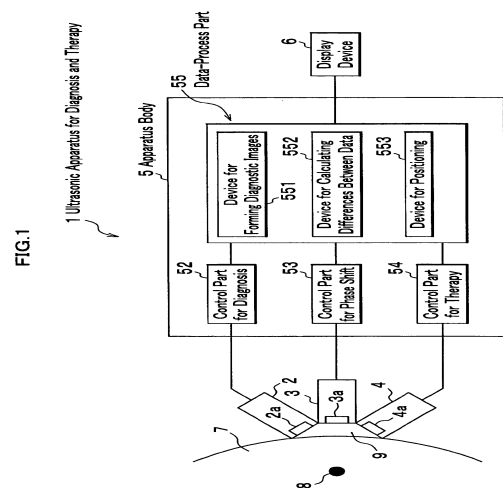


FIG.1