

(19)



(11)

**EP 2 051 777 B1**

(12)

**EUROPEAN PATENT SPECIFICATION**

(45) Date of publication and mention of the grant of the patent:

**16.01.2019 Bulletin 2019/03**

(51) Int Cl.:

**A61N 7/00** (2006.01)      **A61B 8/06** (2006.01)  
**A61B 8/00** (2006.01)      **A61B 5/026** (2006.01)  
**A61B 17/22** (2006.01)      **A61B 8/08** (2006.01)

(21) Application number: **07825989.2**

(86) International application number:

**PCT/IB2007/053073**

(22) Date of filing: **03.08.2007**

(87) International publication number:

**WO 2008/017997 (14.02.2008 Gazette 2008/07)**

**(54) ULTRASOUND SYSTEM FOR CEREBRAL BLOOD FLOW IMAGING AND MICROBUBBLE-ENHANCED BLOOD CLOT LYSIS**

ULTRASCHALLSYSTEM ZUR STRÖMUNGSABBILDUNG VON HIRNBLUT UND MIKROBLÄSCHEN-BLUTGERINNUNGSLYSE

SYSTÈME À ULTRASONNS POUR L'IMAGERIE DE LA CIRCULATION SANGUINE CÉRÉBRALE ET LA LYSE DE CAILLOT SANGUIN AU MOYEN DE MICROBULLES

(84) Designated Contracting States:

**AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IS IT LI LT LU LV MC MT NL PL PT RO SE SI SK TR**

(74) Representative: **de Haan, Poul Erik et al**

**Philips International B.V.  
Philips Intellectual Property & Standards  
High Tech Campus 5  
5656 AE Eindhoven (NL)**

(30) Priority: **11.08.2006 US 822106 P**

(56) References cited:

**EP-A- 1 591 073      US-A1- 2004 049 134  
US-A1- 2005 015 009**

(43) Date of publication of application:

**29.04.2009 Bulletin 2009/18**

(73) Proprietor: **Koninklijke Philips N.V.**

**5656 AE Eindhoven (NL)**

- "Ultraschallanwendung am Menschen - Empfehlung der Strahlenschutzkommission", , 19 April 2012 (2012-04-19), XP055089522, Retrieved from the Internet: URL:[http://www.ssk.de/SharedDocs/Beratungsergebnisse\\_PDF/2012/Ultraschall.pdf?\\_\\_blob=publicationFile](http://www.ssk.de/SharedDocs/Beratungsergebnisse_PDF/2012/Ultraschall.pdf?__blob=publicationFile) [retrieved on 2013-11-21]
- "The Safe Use of Ultrasound in Medical Diagnosis", , 1 January 2012 (2012-01-01), XP055089603, ISBN: 978-0-90-574979-2 Retrieved from the Internet: URL:[http://www.birjournals.org/site/books/Safe\\_Use\\_of\\_Ultrasound.pdf](http://www.birjournals.org/site/books/Safe_Use_of_Ultrasound.pdf) [retrieved on 2013-11-21]

(72) Inventors:

- **BROWNING, Edward, J.**  
**Bothell, Washington 98041-3003 (US)**
- **SHI, William**  
**Bothell, Washington 98041-3003 (US)**
- **POWERS, Jeffry, E.**  
**Bothell, Washington 98041-3003 (US)**
- **AVERKIOU, Michalakis**  
**Bothell, Washington 98041-3003 (US)**
- **GAUTHIER, Thomas**  
**Bothell, Washington 98041-3003 (US)**

**EP 2 051 777 B1**

Note: Within nine months of the publication of the mention of the grant of the European patent in the European Patent Bulletin, any person may give notice to the European Patent Office of opposition to that patent, in accordance with the Implementing Regulations. Notice of opposition shall not be deemed to have been filed until the opposition fee has been paid. (Art. 99(1) European Patent Convention).

## Description

**[0001]** This invention relates to medical diagnostic ultrasound systems and, in particular, to ultrasound systems which perform imaging and therapy for stroke victims.

**[0002]** Ischemic stroke is one of the most debilitating disorders known to medicine. The blockage of the flow of blood to the brain can rapidly result in paralysis or death. Attempts to achieve recanalization through thrombolytic drug therapy such as treatment with tissue plasminogen activator (tPA) has been reported to cause symptomatic intracerebral hemorrhage in a number of cases. Advances in the diagnosis and treatment of this crippling affliction are the subject of continuing medical research.

**[0003]** Transcranial Doppler ultrasound has been developed for use in monitoring and diagnosing stroke. A headset device manufactured by Spencer Technologies of Seattle, Washington, USA holds two transducers against the side of the skull, one on each temporal bone just in front of the ear. The transducers transmit ultrasonic waves through the temporal bone and the returning echo signals are Doppler processed and the phase shift information reproduced at audible frequencies. The audible Doppler identifies the presence or absence of blood flow inside the cranium as the clinician listens for characteristic sounds of blood flow velocities of specific arteries. The technique can also be augmented with a spectral Doppler display of the phase shift information, providing information on flow velocities inside the cranium. However, since there is no information concerning the anatomy inside the skull, the clinician must attempt to make a diagnosis on the basis of this limited information.

**[0004]** A system according to the preamble of claim 1 is known from EP 1 591 073 A1.

**[0005]** Recently Dr. Andrei Alexandrov of the University of Texas Medical School at Houston, Texas found that the application of ultrasound during tPA treatment improved the efficacy of tPA for stroke treatment. Dr. Alexandrov observed that the micro-vibrations of the ultrasonic waves work on the surface of the blood clot to open up a larger surface that the tPA can then bind to and penetrate. Dr. Alexandrov is now leading a research team which is investigating the added efficacy of adding ultrasonic contrast agent microbubbles to the tPA or using microbubbles and ultrasound alone to dissolve blood clots. It is also contemplated that microbubbles may be targeted to components in the blood clot such as fibrin and stick to the clot, increasing the concentration and effectiveness of the treatment. Targeted nanoparticles are another possibility for this procedure. It is thus believed by many that ultrasound together with thrombolytic drugs, microbubbles, or both can lead to significant improvement in stroke treatment.

**[0006]** In accordance with the principles of the present invention, a diagnostic ultrasound system is described which enables a clinician to transcranially visualize a re-

gion of the cerebral vasculature where blood clots may be present. A corresponding method is described, too, however, with no claim being directed at such method. Either two dimensional or three dimensional imaging may be employed. The imaging of the vasculature is preferably enhanced by the administration of microbubbles. If the flow conditions of the vasculature indicate the presence of a partial or complete occlusion, a focused or pencil beam is directed to the location of the blockage to break up the clot by the vibrations and/or rupturing of the microbubbles. In some instances the ruptured microbubbles may also release an encapsulated thrombolytic drug. In accordance with a further aspect of the present invention, the cranial vasculature may be monitored by ultrasonic imaging for changes which are indicative of the recurrence of an occlusion, and medical aid alerted to the condition.

**[0007]** In the drawings:

FIGURE 1 illustrates in block diagram form an ultrasonic diagnostic imaging system constructed in accordance with the principles of the present invention.

FIGURES 2a and 2b illustrate a safety helmet liner suitable for use in a transcranial imaging transducer headset.

FIGURE 3 illustrates a procedure for ultrasonically imaging the cranial vasculature and dissolving blood clots.

FIGURE 4 illustrates three dimensional transcranial imaging.

FIGURE 5 illustrates two dimensional transcranial imaging.

FIGURES 6a-6d illustrate treatment of a cranial occlusion.

FIGURE 7 illustrates a procedure for ultrasonically monitoring for cranial occlusions.

**[0008]** Referring first to FIGURE 1, an ultrasound system constructed in accordance with the principles of the present invention is shown in block diagram form. Two transducer arrays 10a and 10b are provided for transmitting ultrasonic waves and receiving echo information. In this example the arrays shown are two dimensional arrays of transducer elements capable of providing 3D image information although an implementation of the present invention may also use two dimensional arrays of transducer element which produce 2D (planar) images. The transducer arrays are coupled to microbeamformers 12a and 12b which control transmission and reception of signals by the array elements. Microbeamformers are also capable of at least partial beamforming of the signals received by groups or "patches" of trans-

ducer elements as described in US Pats. 5,997,479 (Savord et al.), 6,013,032 (Savord), and 6,623,432 (Powers et al.) Signals are routed to and from the microbeamformers by a multiplexer 14 by time-interleaving signals. The multiplexer is coupled to a transmit/receive (T/R) switch 16 which switches between transmission and reception and protects the main beamformer 20 from high energy transmit signals. The transmission of ultrasonic beams from the transducer arrays 10a and 10b under control of the microbeamformers 12a and 12b is directed by the transmit controller 18 coupled to the T/R switch, which received input from the user's operation of the user interface or control panel 38.

**[0009]** The partially beamformed signals produced by the microbeamformers 12a, 12b are coupled to a main beamformer 20 where partially beamformed signals from the individual patches of elements are combined into a fully beamformed signal. For example, the main beamformer 20 may have 128 channels, each of which receives a partially beamformed signal from a patch of 12 transducer elements. In this way the signals received by over 1500 transducer elements of a two dimensional array can contribute efficiently to a single beamformed signal.

**[0010]** The beamformed signals are coupled to a fundamental/harmonic signal separator 22. The separator 22 acts to separate linear and nonlinear signals so as to enable the identification of the strongly nonlinear echo signals returned from microbubbles. The separator 22 may operate in a variety of ways such as by bandpass filtering the received signals in fundamental frequency and harmonic frequency bands, or by a process known as pulse inversion harmonic separation. A suitable fundamental/harmonic signal separator is shown and described in international patent publication WO 2005/074805 (Bruce et al.) The separated signals are coupled to a signal processor 24 where they may undergo additional enhancement such as speckle removal, signal compounding, and noise elimination.

**[0011]** The processed signals are coupled to a B mode processor 26 and a Doppler processor 28. The B mode processor 26 employs amplitude detection for the imaging of structures in the body such as muscle, tissue, and blood cells. B mode images of structure of the body may be formed in either the harmonic mode or the fundamental mode. Tissues in the body and microbubbles both return both types of signals and the harmonic returns of microbubbles enable microbubbles to be clearly segmented in an image in most applications. The Doppler processor processes temporally distinct signals from tissue and blood flow for the detection of motion of substances in the image field including microbubbles. The structural and motion signals produced by these processors are coupled to a scan converter 32 and a volume renderer 34, which produce image data of tissue structure, flow, or a combined image of both characteristics. The scan converter will convert echo signals with polar coordinates into image signals of the desired image for-

mat such as a sector image in Cartesian coordinates. The volume renderer 34 will convert a 3D data set into a projected 3D image as viewed from a given reference point as described in US Pat. 6,530,885 (Entrekin et al.)

5 As described therein, when the reference point of the rendering is changed the 3D image can appear to rotate in what is known as kinetic parallax. This image manipulation is controlled by the user as indicated by the Display Control line between the user interface 38 and the volume renderer 34. Also described is the representation of a 3D volume by planar images of different image planes, a technique known as multiplanar reformatting. The volume renderer 34 can operate on image data in either rectilinear or polar coordinates as described in US  
10 Pat. 6,723,050 (Dow et al.) The 2D or 3D images are coupled from the scan converter and volume renderer to an image processor 30 for further enhancement, buffering and temporary storage for display on an image display 40.

20 **[0012]** A graphics processor 36 is also coupled to the image processor 30 which generates graphic overlays for displaying with the ultrasound images. These graphic overlays can contain standard identifying information such as patient name, date and time of the image, imaging parameters, and the like, and can also produce a graphic overlay of a beam vector steered by the user as described below. For this purpose the graphics processor received input from the user interface 38. The user interface is also coupled to the transmit controller 18 to control the generation of ultrasound signals from the transducer  
25 arrays 10a and 10b and hence the images produced by and therapy applied by the transducer arrays. The transmit parameters controlled in response to user adjustment include the MI (Mechanical Index) which controls the peak intensity of the transmitted waves, which is related to cavitation effects of the ultrasound, steering of the transmitted beams for image positioning and/or positioning (steering) of a therapy beam as discussed below.

30 **[0013]** The transducer arrays 10a and 10b transmit ultrasonic waves into the cranium of a patient from opposite sides of the head, although other locations may also or alternately be employed such as the front of the head or the sub-occipital acoustic window at the back of the skull. The sides of the head of most patients advantageously  
35 provide suitable acoustic windows for transcranial ultrasound at the temporal bones around and above the ears on either side of the head. In order to transmit and receive echoes through these acoustic windows the transducer arrays must be in good acoustic contact at these locations which may be done by holding the transducer arrays  
40 against the head with a headset. For instance, FIGURE 2a shows a conventional safety helmet 200 which is adjustably held on the wearer's head by a helmet liner 202 shown in the view of FIGURE 2b. The helmet liner wraps securely about the circumference of the wearer's head.  
45 Transducer arrays positioned inside the helmet liner on either side as indicated by the locations of circles 204,206 will be held securely against the skin of the temporal

bones of the wearer, enabling the helmet liner 202 to function as a transcranial ultrasound headset. The helmet liner headset is adjustably secured in place by an adjustment knob 208. An occipital transducer would be positioned at or below the location of adjustment knob 208. The headset has one or more straps 210 which pass over the top of the head for adjustment of the vertical position of the headset. These straps and other adjustable members of the headset can be elastic or adjustable through other means such as buckles or Velcro®. When properly adjusted the headset will hold the acoustic transducer arrays securely in good acoustic contact on the temples of the patient. Acoustic coupling may be aided by applying an acoustic coupling gel between the transducer and the skin.

**[0014]** A procedure which uses the ultrasound system and transcranial ultrasound headset just described is illustrated by the flowchart of FIGURE 3. In step 60 the headset is put on the patient with the transducer arrays in acoustic contact with the skin of the patient. The system is activated to image inside the cranium and in step 62 the headset is adjusted until flow inside the cranium can be seen in the ultrasound image of one or (when displayed in duplex) both of the transducer arrays. The colorflow imaging mode of the system is preferably used at this time to produce a two or three dimensional image of the bloodflow inside the cranium. If the cranial flow can be seen in colorflow, the other steps of this procedure can be expected to proceed as desired. When the flow is seen in the ultrasound images the headset is tightened in step 64 to secure the transducer array in their imaging positions. FIGURE 4 illustrates the situation at this point for 3D imaging. In this illustration the transducer arrays 10a,10b are held against the sides of the skull 100 and are imaging 3D image fields 102,104 inside the cranium. The user will see one or both of the 3D image fields 102,104 on the display of the ultrasound system in either a multiplanar or volume rendered 3D projection. The user can manipulate the kinetic parallax control to observe the volume rendered 3D image from different orientations. The user can adjust the relative opacity of the tissue and flow components of the 3D image to better visualize the vascular structure inside the brain tissue as described in US Pat. 5,720,291 (Schwartz) or can turn off the B mode (tissue) portion of the display entirely and just visualize the flow of the vascular structure inside the 3D image field 102,104.

**[0015]** When the cranium is being imaged successfully a microbubble contrast agent is introduced into the patient's bloodstream at step 66. In a short time the microbubbles in the bloodstream will be pumped through the carotid arteries and into the cranial vascular system and appear in the image. The clinician user is now able to begin a diagnostic search for blood clots occluding blood vessels in the brain, looking for branches of the vasculature which terminate or are only dimly lighted by echo returns from microbubbles due to a partial occlusion. When a dual display from both transducer arrays is

present the clinician is also able to compare the relative symmetry of the two displayed regions, looking for signs of asymmetry. If the clinician finds no signs of occlusion in the vasculature presently being viewed by the image fields 102,104, the clinician can steer the image field to other regions of the anatomy as indicated by step 68. Steering the image field can be done mechanically by physically adjusting the position of a transducer array to aim its image field through different anatomy of the brain. Preferably, the clinician is able to adjust the steering of the beams from the transducer array with a control on the user interface. By adjusting this control (the Beam Steer control line to the transmit controller 18), the clinician is able to electronically steer the image field around inside the skull without disturbing the acoustic coupling of the array against the head of the patient.

**[0016]** At each position of the image field 102,104 the clinician can look for obstructions of the blood flow in the real time images on the display, or can capture (freeze) an image or map of the cranial vasculature as indicated in step 70. When the vascular map is acquired and held statically, the image can undergo enhanced processing (e.g., compounding, signal averaging) to improve the resolution or scale of the image and can be manipulated on the screen and examined carefully at different points and from different views in a precise search for blood vessel occlusions. In this way the clinician can diagnose for stenoses as indicated at step 72. If the clinician examines a vascular map and finds no evidence of obstruction in the blood flow paths, the clinician can steer the image field to another region of the cranium and examine the vascular map of another image field. The clinician can use the Doppler data of the vascular map or the spectral Doppler function of the ultrasound system to take flow velocity measurements at specific points in the cranial vasculature, then use the report generation capabilities of the ultrasound system to record the measurements and prepare a report of his diagnosis.

**[0017]** Examples of vascular maps are shown in FIGURES 6a-6c. FIGURE 6a illustrates a vascular network 300 of blood vessels. When only flow imaging is performed and the flow image is displayed in the absence of any surrounding B mode tissue structure, as described in US Pat. 5,474,073 (Schwartz et al.), only the flow of the vasculature is shown without any obscuring surrounding structure as FIGURE 6a illustrates. The vascular network 300 may be displayed in two dimensions, three dimensions, and by various Doppler techniques such as colorflow (velocity) Doppler or power (intensity) Doppler. In the absence of stenoses the flow network will appear continuous and with velocities and intensities proportionate to vessel size. But if a branch 302 of the vascular network is obstructed, the flow will appear different, e.g., higher velocity and/or intensity, and, if completely obstructed, will disappear entirely in the Doppler flow map as shown in FIGURE 6c. By discerning characteristics such as these, the clinician can diagnose a stenosis, then direct a therapeutic beam 110 to the suspected

location of the obstruction of the vessel as shown in FIGURE 6d.

**[0018]** If the clinician discovers a stenosis, therapy can be applied by agitating or breaking microbubbles at the site of the stenosis in an effort to dissolve the blood clot. The clinician activate the "therapy" mode, and a graphic 110,112 appears in the image field 102,104, depicting the vector path of a therapeutic ultrasound beam. The therapeutic ultrasound beam is manipulated by a control on the user interface 38 until the vector graphic 110,112 is focused at the site of the blockage, as indicated by step 74. The therapeutic beam can be a tightly focused, convergent beam or a beam with a relatively long focal length known as a pencil beam. The energy produced for the therapeutic beam can be in excess of the ultrasound levels permitted for diagnostic ultrasound, in which case the microbubbles at the site of the blood clot will be sharply broken. The energy of the resulting microbubble ruptures will strongly agitate the blood clot, tending to break up the clot and dissolve it in the bloodstream. However in some instances insonification of the microbubbles at diagnostic energy levels may be sufficient to dissolve the clot. Rather than breaking in a single event, the microbubbles may be vibrated and oscillated, and the energy from such extended oscillation prior to dissolution of the microbubbles can be sufficient to break up the clot, as indicated at step 76.

**[0019]** A particularly effective way to insonify the microbubbles is known as "flash" transmission. In flash transmission, insonification is halted to allow the flow of blood to deliver a substantial volume of microbubbles to the site of the blockage. At the end of this pause, a rapid series of high MI pulses are transmitted to rapidly and energetically rupture the microbubbles, which releases energy at the site of the blockage. The gas from the ruptured microbubbles dissolves in the bloodstream. Another pause period commences to allow the buildup of a fresh supply of microbubbles and the process continues. See US Pats. 5,560,364 (Porter) and 5,685,310 (Porter). The flash technique was improved with the discovery that imaging can be performed at low MI levels as the microbubbles accumulate, enabling the clinician to visually monitor the buildup of microbubbles and determine the optimal time to administer the high MI flash. See US Pat. 6,171,246 (Averkiou et al.)

**[0020]** It has been found that a low duty cycle flash will create rapid microbubble destruction within the energy limits of diagnostic ultrasound. There is thus no need to expose the patient to possibly harmful therapeutic exposure levels. In this technique, the flash pulses are delivered within the MI (instantaneous pressure) limits of diagnostic ultrasound. Another energy limit parameter for ultrasound is the spatial peak temporal average (SPTA), which is a measure of the average energy delivered over time and is related to temperature rise. It has been discovered that a series of high MI pulses (within diagnostic limits) will cause the targeted microbubbles to break up and dissolve in the bloodstream in 100-300 milliseconds.

Thus, continued insonification is of no effect, for virtually no microbubbles remain after this period. In the inventive technique, the high MI pulse period has a duty cycle of 50% or less. For instance, the high MI pulses may be delivered for 200ms, after which high MI pulses are inhibited for the following 800msec. The duty cycle of the high MI pulse delivery period is thus only 20%. Needless high MI pulses are inhibited and the time averaged energy delivered over the one second interval is within the temporal average limits of the SPTA parameter. Furthermore, new microbubbles are allowed to reinfuse the blood clot site as soon as the high MI transmission has ceased. Moreover, longer pulse lengths may be employed during the high MI portion of the duty cycle, which have been found to be very effective for microbubble disruption.

**[0021]** The type of stroke suffered by a patient can be either hemorrhagic stroke or ischemic stroke. Hemorrhagic stroke, which may for instance be caused by a ruptured aneurism, results in blood flow outside of blood vessels and will not be improved by treatment with microbubbles and ultrasound. Furthermore, a hemorrhagic condition is often worsened by the application of tPA. Ischemic stroke caused by a stenosis such as a blood clot is the type of stroke that an embodiment of the present invention is designed to treat. Accordingly it is desirable to initially determine whether the stroke condition is hemorrhagic or ischemic. One way this may be done is by looking for a blood pool outside the vasculature, which is indicative of a hemorrhagic condition. A blood pool will appear black in the standard ultrasound image since blood is not a strong reflector of ultrasonic waves. The blood pool may also exhibit a lower rate of flow (Doppler velocity) than the flow of blood in a containing blood vessel. After the contrast agent is introduced, the perfusion of the contrast agent into the microvasculature of surrounding tissue can create a slight halo effect of brighter contrast about the darkened blood pool in an ultrasound image. It is characteristics such as these which can be used to identify whether the stroke is hemorrhagic or ischemic in origin.

**[0022]** In the depiction of FIGURE 4, each image field 102, 104 is seen to extend almost halfway across the cranium, which is a balance between the size of the image field and the acoustic penetration and attenuation which may be expected through the bone at the acoustic window. For some patients, low attenuation effects may enable an image field to extend fully across the cranium, allowing the clinician to examine the vascular structure near the skull bone on the opposite side of the cranium. By alternately examining image fields of both transducer arrays, the vasculature across the full cranium may be effectively examined. It is possible to acquire extended image fields which cover the same central region of the cranium but image from opposite sides of the head. These images can be correlated and compounded together, forming a fused image that may reveal additional characteristics of the brain. The therapeutic beam can

also be transmitted from both sides of the head, enabling breakup of a clot at both sides of the clot. Rather than be limited to reflective ultrasound imaging, through-transmission imaging can be performed by transmitting ultrasound from one transducer array and receiving the remaining unabsorbed ultrasonic energy at the other transducer array, which may reveal yet other characteristics of the brain tissue.

**[0023]** FIGURE 5 illustrates a two dimensional imaging example. In this example the transducer array 122 is a one dimensional array which performed 2D imaging. The array is configured as a circular phased array transducer as described in US Pat. 5,226,422. This transducer array, like the other arrays described herein, is covered with a lens 124 which electrically insulates the patient from the transducer array and in the case of a one dimensional array may also provide focusing in the elevation (out-of-plane) dimension. The transducer array 122 is backed with acoustic damping material 126 which attenuates acoustic waves emanating from the back of the array to prevent their reflection back into the transducer elements. Behind this transducer stack is a device 130 for rotating the image plane 140 of the array. The device 130 may be a simple knob or tab which may be grasped by the clinician to manually rotate the circular array transducer in its rotatable transducer mount (not shown). The device 130 may also be a motor which is energized through a conductor 132 to mechanically rotate the transducer as discussed in US Pat. 5,181,514 (Solomon et al.) Rotating the one dimensional array transducer 122 as indicated by arrow 144 will cause its image plane 140 to pivot around its central axis, enabling the repositioning of the image plane for full examination of the vasculature in front of the transducer array. As discussed in the '514 patent, the planes acquired during at least a 180o rotation of the array will occupy a conical volume in front of the transducer array, which may be rendered into a 3D image of that volumetric region. Other planes outside this volumetric region may be imaged by repositioning, rocking or tilting the transducer array in its headset in relation to the skull 100. If a stenosis is found in the image of the plane being imaged, the therapeutic beam vector graphic 142 can be steered by the clinician to aim the beam at the stenosis and therapeutic pulses applied to disrupt the microbubbles at the site of the stenosis.

**[0024]** It is common in the case of stroke that the affliction will not manifest itself in a single episode, but in repeated episodes as a blood clot or obstruction in the heart, lungs, or blood vessel breaks up gradually, releasing small clots which successively make their way to the vascular system of the brain over time. Thus, a patient who survives an initial stroke event, may be at risk for other events in the near future. Accordingly, it is desirable to monitor these patients for some time after an initial stroke event so that recurrences can be treated immediately. An embodiment of the invention may be used for the monitoring of stroke victims for recurrent events. The transducer arrays 10a,10b, microbeamformers 12a,12b,

and multiplexer 14 can be efficiently packaged in a flip-chip configuration as part of the headset. These components can be battery powered and the output of the multiplexer connected to an r.f transmitter. A fixed image field 102,104 is continually imaged as shown in FIGURE 4; it is not necessary to be able to steer or reposition the image field in this embodiment. The image data produced by the microbeamformers 12a,12b is wirelessly transmitted to a base unit as described in US Pat. 6,113,547 (Catallo et al.) At the base station additional beamforming can be performed if necessary as well as the image processing and display functions of the system of FIGURE 1. If a patient is not ambulatory a wireless connection may not be necessary and a wired connection to the base station may be employed. The wireless connection is also useful when the headset is being applied by individuals having minimal experience with the device. For example, a first responder may be unsure that the headset is applied properly and is acquiring a satisfactory image data set of the patient's vasculature. In that case the images can be transmitted to a base station, hospital or other location where experienced personnel can view the images in real time and talk the first responder through a successful application of the headset on the patient.

**[0025]** In the present example, image display is not necessary for the monitoring application. As successive images of the vasculature are formed at the base station they are stored in an image store 52, and temporally different images are compared to detect changes in flow of the vasculature by operation of flow change detector 50. The flow change detector operates by comparing the identical nature of the temporally different images, similar to the image data correlation techniques used to identify motion by image processing as described in US Pat. 6,442,289 (Olsson et al.) As long as successive images and images separated by greater time intervals appear substantially the same in their flow characteristics, e.g., there is no localized change in the flow characteristics of a particular section of the vasculature and no section of the vasculature has ceased to return a Doppler signal indicating the continuation of flow, the flow change detector 50 will continue its monitoring of the vasculature with no change. For example, the vasculature may appear as the vascular network 300 of FIGURE 6a for an extended period, and suddenly a section of the flow may cease to be detected as illustrated by the absence of vessels 302 in FIGURE 6c. If a flow change such as one of those indicated above is detected by the flow change detector 50, an alarm is activated such as an audible alarm 42 at a nurse's station. Medical assistance can then be brought immediately to the patient. In addition, the images stored in the image store at the time of the detected flow change can be examined by medical personnel to discern exactly where in the vasculature the detected obstruction occurred. Therapy can then be directed specifically to the site of the obstruction without the need to closely examine a series of vascular maps.

**[0026]** Since this is a monitoring application, image ac-

quisition does not have to be performed at the high rates necessary for real time imaging. A new image could be acquired every second, for example, or at greater intervals between image acquisitions. The lower acquisition rate is helpful for conserving battery power in an ambulatory implementation with an r.f. link. The lower image rate also permits images from multiple patients to be processed in a time-interleaved manner by the same system, which is useful for a nurse's station which needs to monitor multiple patients.

**[0027]** During long term monitoring or monitoring of ambulatory patients it is possible that the headset may move relative to the head of the patient, causing a difference between successive images from a transducer 10a, 10b which has moved. Such movement can also cause a specific anatomical region being monitored to move outside of the image field of the transducer array 10a or 10b. While the flow change detector 50 can be designed to be immune to such global changes and look only for localized changes in flow, it may be desirable to alert medical personnel to readjust the headset or to reacquire target anatomy in the image field. This is done in the embodiment of FIGURE 1 by means of an image field controller 54, which performs image analysis of temporally different images to detect changes in global alignment of the image data. If the headset has not moved between successive images, for example, the successive images of each transducer array will be the same and the image data of the images will exhibit a high degree of correlation. The image analysis techniques used to measure image alignment in US Pats. 5,556,674 (Weng), 6,572,549 (Jong et al.) or 6,589,176 (Jago et al.) and others may be used to perform the image comparison, for instance. Movement of the headset will result in a global change in correlation, which can alert medical personnel to adjust the headset. A local change in correlation may be a localized flow change that should be detected by the flow change detector 50 or the local decorrelation can be used to alert medical personnel to check the patient's condition. Another possibility is to use the global correlation vector as an indication of image-to-image motion. The motional change is then used by the transmit controller 18 to adjust the steering of beams of the image field 102, 104, 140 to relocate the anatomy in the same position in the newly acquired image field, as in the manner of image stabilization discussed in the aforementioned US Pat. 6,589,176. This will enable the anatomy initially monitored by the system to remain in view and in the image data set despite small changes in the headset positioning. If the target anatomy moves beyond the range of beam steering reacquisition, an alert can be issued for medical personnel to reposition the headset. Such restearing correction in the presence of motion can similarly be used to keep the therapeutic pencil beam 110, 112 constantly directed at a targeted blood clot being treated.

**[0028]** A typical sequence for a monitoring implementation is illustrated by the flowchart of FIGURE 7. The

headset with the array transducers is put on the patient at step 60 and images are initially displayed and reviewed until the headset is adjusted so that flow is observed in the images in step 62. When it is determined that images of cranial flow are being acquired, image display is no longer necessary and the headset is tightened in place on the patient at step 64. Periodically image data is acquired from the image field of the arrays and transmitted to the monitoring unit at step 80. At the monitoring unit the image data may be further processed as desired at step 82, then the new image is compared to one or more previously acquired images at step 84. If the flow characteristics of the images are unchanged, periodic transmission, reception, and comparison of image data continues. But if the new image is different in a predetermined flow characteristic, the flow change is detected at 86 and an alert issued at 88 for medical attention.

**[0029]** While the monitoring implementation can be performed with 2D (planar) imaging, it is preferred that 3D imaging be used so that a larger volumetric region can be monitored. Monitoring can be performed with only one transducer array, but a greater number of arrays likewise provides monitoring of a larger region of the cranium.

## Claims

1. A stroke therapy system for treating cranial vascular obstructions comprising:

a transducer array headset (200) which maintains an ultrasonic transducer array (10a, 10b, 122) in acoustic contact with the head of a subject;

an image processor (26, 28, 30, 32, 34), coupled to the ultrasonic transducer array, which produces images of blood flow in the cranium of the subject in an imaging mode of the ultrasonic transducer array;

an image display (40), coupled to the image processor, which produces an image of the cranial vasculature;

**characterized in that:**

the ultrasonic transducer array is operable in a therapy mode to direct a therapeutic beam at an obstruction site (302) in the cranium of the subject, said therapeutic beam being capable of breaking up microbubbles, introduced to the subject's bloodstream, at the obstruction site and comprising a series of ultrasonic beam pulses having a duty cycle of 50% or less,

wherein, in the therapy mode, the ultrasonic therapeutic beam is iteratively:

delivered to the obstruction site for a

period of 100-300 milliseconds, to thereby break up substantially all of the microbubbles at the obstruction site; and

subsequently inhibited, to allow new microbubbles to reinfuse the obstruction site.

2. The stroke therapy system of Claim 1, wherein the system further comprises a user interface (38) comprising a control adapted to, in the therapy mode, be manipulated by a user to steer a therapeutic beam vector graphic (110, 112, 142) on the image display (40) to direct the therapeutic beam at the obstruction site (302).
3. The stroke therapy system of Claim 1, wherein the therapeutic beam is a pencil beam.
4. The stroke therapy system of Claim 1, wherein the image processor comprises a Doppler processor, wherein the Doppler processor (28) produces at least one of velocity Doppler images or power Doppler images.
5. The stroke therapy system of Claim 1, wherein the transducer array headset maintains a first ultrasonic transducer array (10a) in acoustic contact with one side (204) of the head (100); and further comprising a second transducer array (10b) maintained in acoustic contact with the other side (206) of the head by the headset (200).
6. The stroke therapy system of Claim 1, wherein the system further comprises a transmitter, coupled to the transducer array, which acts to cause the ultrasonic transducer array to transmit said therapeutic beam, wherein imaging and delivery of the therapeutic beam are done by the ultrasonic transducer array.
7. The stroke therapy system of Claim 6, wherein the transmitter further acts to cause the ultrasonic transducer array to transmit beams for at least one of Doppler or B mode imaging.
8. The stroke therapy system of Claim 6, wherein the transmitter further acts to transmit beams for imaging over an image field exhibiting a given lateral dimension in the cranium, wherein the therapeutic beam exhibits a lateral dimension which is less than the given lateral dimension.
9. The stroke therapy system of Claim 6, wherein the transmitter further acts to transmit image beams over an image field occupying a given spatial region in the cranium, wherein the therapeutic beam is transmitted over a portion of the given spatial region.

10. The stroke therapy system of Claim 9, wherein the ultrasonic transducer array comprises a two dimensional array of transducer elements, wherein the given spatial region is a volumetric region.

11. The stroke therapy system of Claim 10, wherein the two dimensional array is maintained in acoustic contact with one side of the head; the stroke therapy system further comprising a second two dimensional array maintained in acoustic contact by the headset with the other side of the head.

12. The stroke therapy system of Claim 11, wherein:

the first two dimensional array scans imaging beams over a majority of the cranial distance between the left side of the head and the center of the cranium; and

the second two dimensional array scans imaging beams over a majority of the cranial distance between the right side of the head and the center of the cranium.

## Patentansprüche

1. Schlaganfalltherapiesystem zur Behandlung der Obstruktion kranialer Gefäße, umfassend:

ein Wandlerarray-Headset (200), das ein Ultraschallwandlerarray (10a, 10b, 122) in akustischem Kontakt mit dem Kopf eines Patienten hält;

einen Bildprozessor (26, 28, 30, 32, 34), der mit dem Ultraschallwandlerarray gekoppelt ist und in einem Bildgebungsmodus des Ultraschallwandlerarrays Bilder der Blutströmung im Kraniaum des Patienten erzeugt;

eine Bildanzeige (40), die mit dem Bildprozessor gekoppelt ist und ein Bild der kranialen Gefäße erzeugt;

**dadurch gekennzeichnet, dass**

das Ultraschallwandlerarray in einem Therapiemodus betrieben werden kann, um ein therapeutisches Strahlenbündel auf einen Obstruktionsort (302) im Kraniaum des Patienten zu richten, wobei das therapeutische Strahlenbündel in der Lage ist, in den Blutstrom des Patienten eingeführte Mikrobläschen am Obstruktionsort aufzubrechen, und eine Serie von Ultraschallstrahlenbündelimpulsen mit einem Tastverhältnis von 50 % oder weniger umfasst, wobei das therapeutische Ultraschallstrahlenbündel im Therapiemodus iterativ:

für eine Zeitdauer von 100 - 300 Millisekunden an den Obstruktionsort abgegeben

- wird, um dadurch im Wesentlichen alle Mikrobäschen am Obstruktionsort aufzubrechen; und anschließend unterdrückt wird, damit neue Mikrobäschen den Obstruktionsort reinfundieren können.
2. Schlaganfalltherapiesystem nach Anspruch 1, wobei das System ferner eine Benutzerschnittstelle (38) umfassend eine Steuerung umfasst, die dafür ausgelegt ist, im Therapiemodus durch einen Benutzer manipuliert zu werden, um eine Vektorgrafik (110, 112, 142) für das therapeutische Strahlenbündel auf der Bildanzeige (40) so zu lenken, dass das therapeutische Strahlenbündel auf den Obstruktionsort (302) gerichtet wird.
  3. Schlaganfalltherapiesystem nach Anspruch 1, wobei das therapeutische Strahlenbündel ein Schmalbündel ist.
  4. Schlaganfalltherapiesystem nach Anspruch 1, wobei der Bildprozessor einen Doppler-Prozessor umfasst, wobei der Doppler-Prozessor (28) mindestens eines von Geschwindigkeits-Doppler-Bildern oder Leistungs-Doppler-Bildern erzeugt.
  5. Schlaganfalltherapiesystem nach Anspruch 1, wobei das Wandlerarray-Headset ein erstes Ultraschallwandlerarray (10a) in akustischem Kontakt mit einer Seite (204) des Kopfs (100) hält; und ferner umfassend ein zweites Wandlerarray (10b), das durch das Headset (200) in akustischem Kontakt mit der anderen Seite (206) des Kopfs gehalten wird.
  6. Schlaganfalltherapiesystem nach Anspruch 1, wobei das System ferner einen Sender umfasst, der mit dem Wandlerarray gekoppelt ist und wirkt, um das Ultraschallwandlerarray zu veranlassen, das genannte therapeutische Strahlenbündel auszusenden, wobei Bildgebung und Abgabe des therapeutischen Strahlenbündels durch das Ultraschallwandlerarray erfolgen.
  7. Schlaganfalltherapiesystem nach Anspruch 6, wobei der Sender ferner wirkt, um das Ultraschallwandlerarray zu veranlassen, Strahlenbündel für mindestens eine von Doppler- oder B-Mode-Bildgebung auszusenden.
  8. Schlaganfalltherapiesystem nach Anspruch 6, wobei der Sender ferner wirkt, um Strahlenbündel zur Bildgebung über ein Bildfeld auszusenden, das eine gegebene laterale Dimension im Kraniaum aufweist, wobei das therapeutische Strahlenbündel eine laterale Dimension aufweist, die kleiner als die gegebene laterale Dimension ist.
  9. Schlaganfalltherapiesystem nach Anspruch 6, wobei der Sender ferner wirkt, um Bildstrahlenbündel über ein Bildfeld auszusenden, das eine gegebene räumliche Region im Kraniaum einnimmt, wobei das therapeutische Strahlenbündel über einen Teil der gegebenen räumlichen Region ausgesendet wird.
  10. Schlaganfalltherapiesystem nach Anspruch 9, wobei das Ultraschallwandlerarray ein zweidimensionales Array von Wandlerelementen umfasst, wobei die gegebene räumliche Region eine volumetrische Region ist.
  11. Schlaganfalltherapiesystem nach Anspruch 10, wobei das zweidimensionale Array in akustischem Kontakt mit einer Seite des Kopfs gehalten wird; wobei das Schlaganfalltherapiesystem ferner ein zweites zweidimensionales Array umfasst, das durch das Headset mit der anderen Seite des Kopfs in akustischem Kontakt gehalten wird.
  12. Schlaganfalltherapiesystem nach Anspruch 11, wobei:
 

das erste zweidimensionale Array mit bildgebenden Strahlenbündeln einen Großteil des kranialen Abstands zwischen der linken Seite des Kopfs und der Mitte des Kraniaums abtastet; und das zweite zweidimensionale Array mit bildgebenden Strahlenbündeln einen Großteil des kranialen Abstands zwischen der rechten Seite des Kopfs und der Mitte des Kraniaums abtastet.
- 35 **Revendications**
1. Système de thérapie d'accident vasculaire cérébral pour traiter des obstructions vasculaires crâniennes comprenant :
 

un casque à réseau de transducteurs (200) qui maintient un réseau de transducteurs à ultrasons (10a, 10b, 122) en contact acoustique avec la tête d'un sujet ;

un processeur d'image (26, 28, 30, 32, 34), couplé au réseau de transducteurs à ultrasons, qui produit des images de circulation sanguine dans le crâne du sujet dans un mode d'imagerie du réseau de transducteurs à ultrasons ;

un affichage d'image (40), couplé au processeur d'image, qui produit une image de la vascularisation crânienne ;

**caractérisé en ce que :**

le réseau de transducteurs à ultrasons peut être utilisé en mode de thérapie pour diriger un faisceau thérapeutique au niveau d'un site d'obstruction (302) dans le crâne du su-

jet, ledit faisceau thérapeutique étant capable de briser des microbulles, introduites dans le flux sanguin du sujet, au niveau du site d'obstruction et comprenant une série d'impulsions de faisceau ultrasonore ayant un cycle de service égal ou inférieur à 50 %, dans lequel, dans le mode de thérapie, le faisceau thérapeutique ultrasonore est, de manière itérative :

délicé au site d'obstruction pendant une période de 100 à 300 millisecondes, afin de briser ainsi la quasi-totalité des microbulles au niveau du site d'obstruction ; et

ensuite inhibé, pour permettre à de nouvelles microbulles d'être réintroduites au niveau site d'obstruction.

2. Système de thérapie d'accident vasculaire cérébral selon la revendication 1, dans lequel le système comprend en outre une interface utilisateur (38) comprenant une commande adaptée pour, dans le mode de thérapie, être manipulée par un utilisateur pour diriger un graphique vectoriel de faisceau thérapeutique (110, 112, 142) sur l'affichage d'image (40) afin de diriger le faisceau thérapeutique au niveau du site d'obstruction (302).
3. Système de thérapie d'accident vasculaire cérébral selon la revendication 1, dans lequel le faisceau thérapeutique est un faisceau-crayon.
4. Système de thérapie d'accident vasculaire cérébral selon la revendication 1, dans lequel le processeur d'image comprend un processeur Doppler, dans lequel le processeur Doppler (28) produit au moins une d'images Doppler de vitesse ou des images Doppler de puissance.
5. Système de thérapie d'accident vasculaire cérébral selon la revendication 1, dans lequel le casque à réseau de transducteurs maintient un premier réseau de transducteurs à ultrasons (10a) en contact acoustique avec un côté (204) de la tête (100) ; et comprenant en outre un second réseau de transducteurs (10b) maintenu en contact acoustique avec l'autre côté (206) de la tête par le casque (200).
6. Système de thérapie d'accident vasculaire cérébral selon la revendication 1, dans lequel le système comprend en outre un émetteur, couplé au réseau de transducteurs, qui agit pour amener le réseau de transducteurs à ultrasons à transmettre ledit faisceau thérapeutique, dans lequel l'imagerie et la délivrance du faisceau thérapeutique sont effectuées par le réseau de transducteurs à ultrasons.
7. Système de thérapie d'accident vasculaire cérébral selon la revendication 6, dans lequel l'émetteur agit en outre pour amener le réseau de transducteurs à ultrasons à transmettre des faisceaux pour au moins une imagerie en mode Doppler ou en mode B.
8. Système de thérapie d'accident vasculaire cérébral selon la revendication 6, dans lequel l'émetteur agit en outre pour transmettre des faisceaux pour une imagerie sur un champ d'image présentant une dimension latérale donnée dans le crâne, dans lequel le faisceau thérapeutique présente une dimension latérale qui est inférieure à la dimension latérale donnée.
9. Système de thérapie d'accident vasculaire cérébral selon la revendication 6, dans lequel l'émetteur agit en outre pour transmettre des faisceaux d'image sur un champ d'image occupant une zone spatiale donnée dans le crâne, dans lequel le faisceau thérapeutique est transmis sur une partie de la zone spatiale donnée.
10. Système de thérapie d'accident vasculaire cérébral selon la revendication 9, dans lequel le réseau de transducteurs à ultrasons comprend un réseau bidimensionnel d'éléments transducteurs, dans lequel la zone spatiale donnée est une zone volumétrique.
11. Système de thérapie d'accident vasculaire cérébral selon la revendication 10, dans lequel le réseau bidimensionnel est maintenu en contact acoustique avec un côté de la tête ; le système de thérapie d'accident vasculaire cérébral comprenant en outre un second réseau bidimensionnel maintenu par l'intermédiaire du casque en contact acoustique avec l'autre côté de la tête.
12. Système de thérapie d'accident vasculaire cérébral selon la revendication 11, dans lequel :
  - le premier réseau bidimensionnel balaie des faisceaux d'imagerie sur une majorité de la distance crânienne entre le côté gauche de la tête et le centre du crâne ; et
  - le second réseau bidimensionnel balaye des faisceaux d'imagerie sur une majorité de la distance crânienne entre le côté droit de la tête et le centre du crâne.

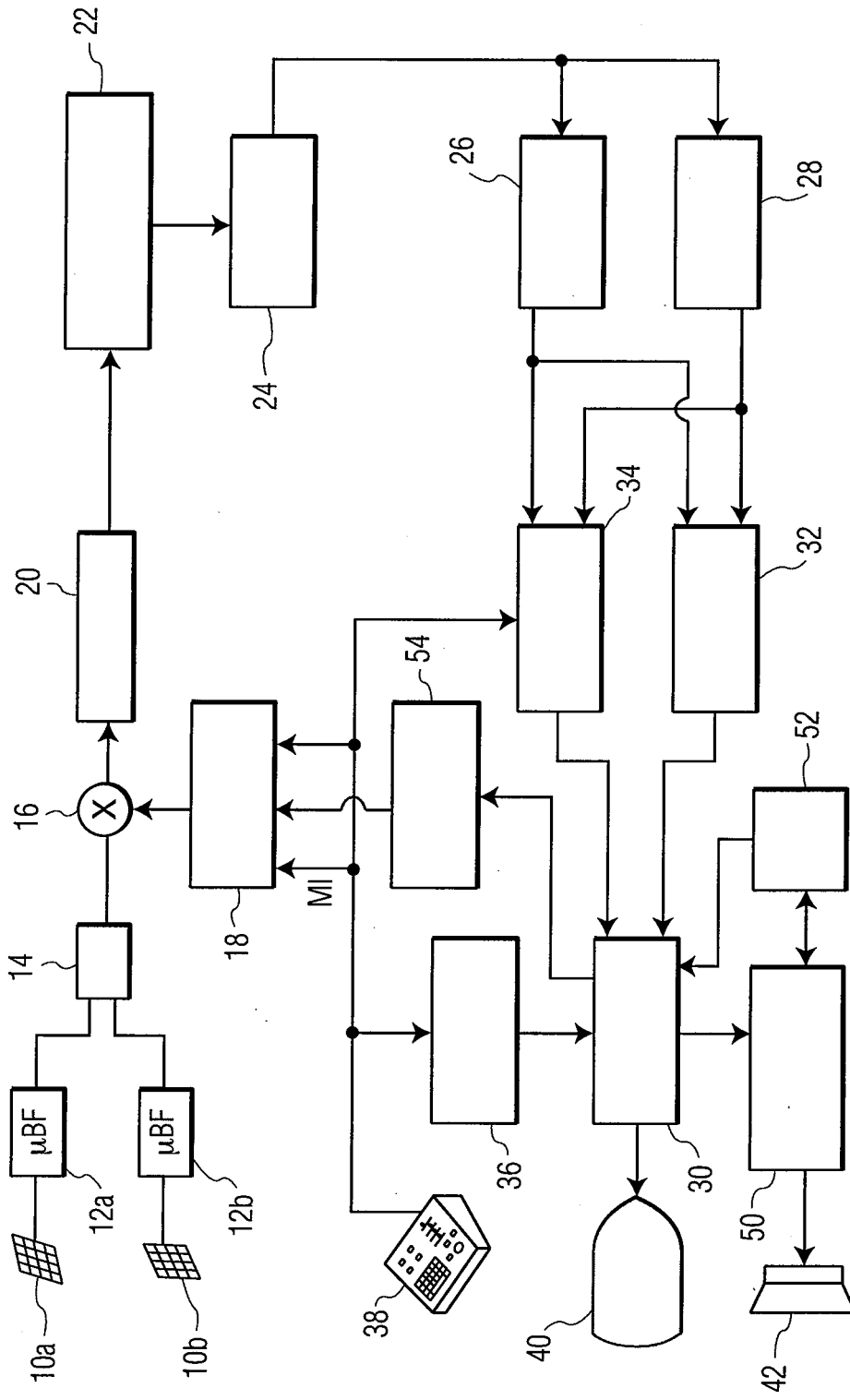


FIG. 1

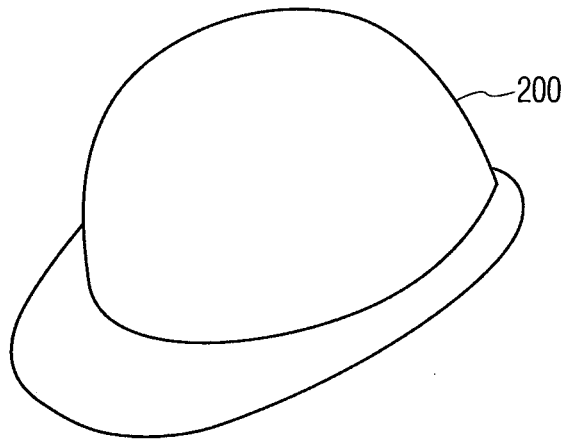


FIG. 2A

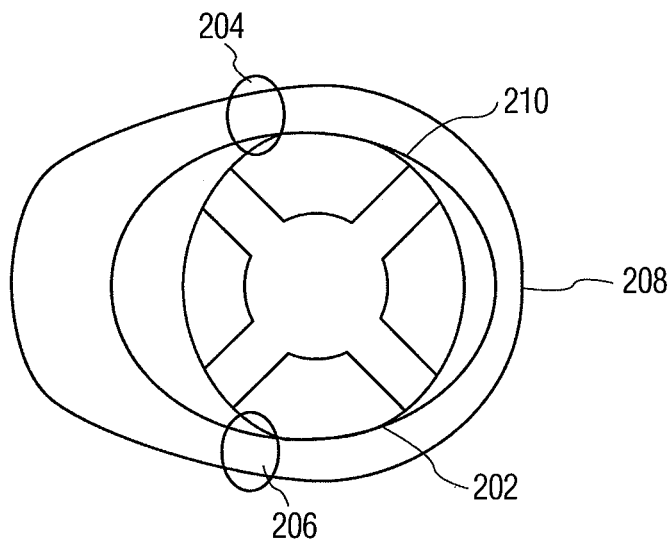


FIG. 2B

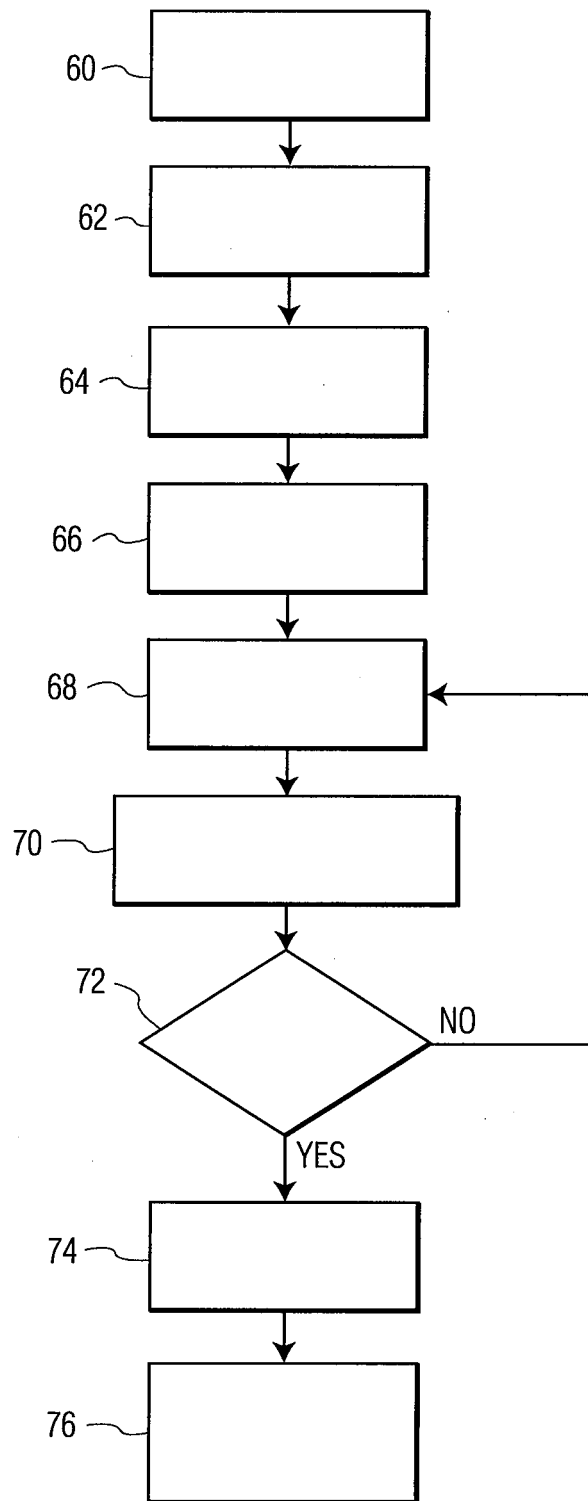


FIG. 3

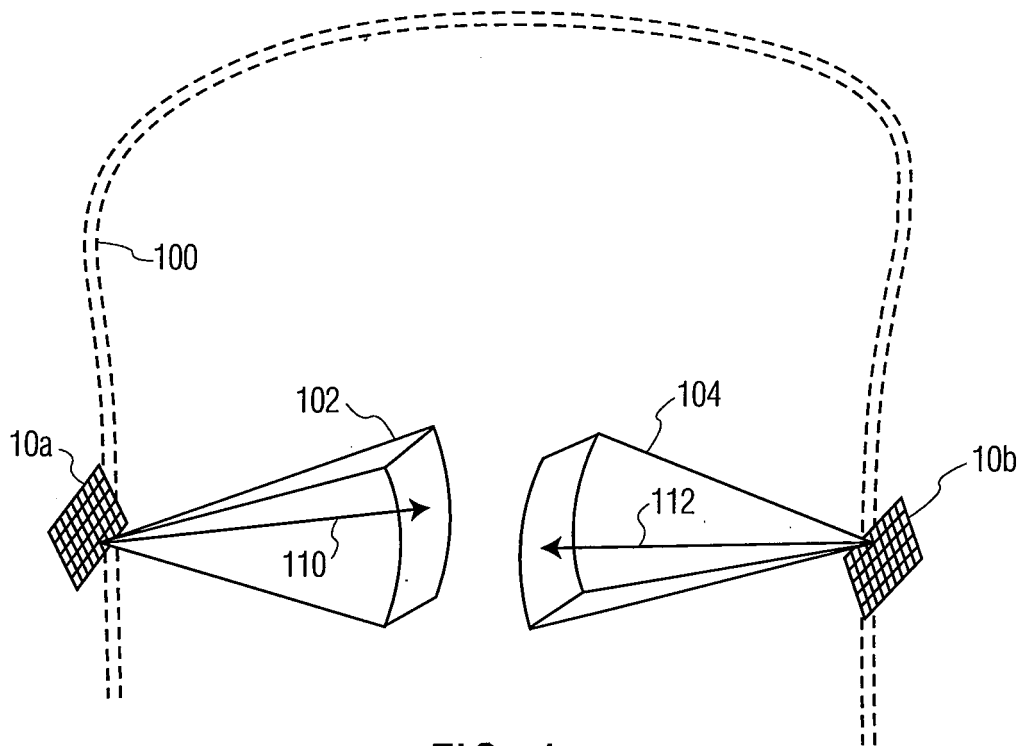


FIG. 4

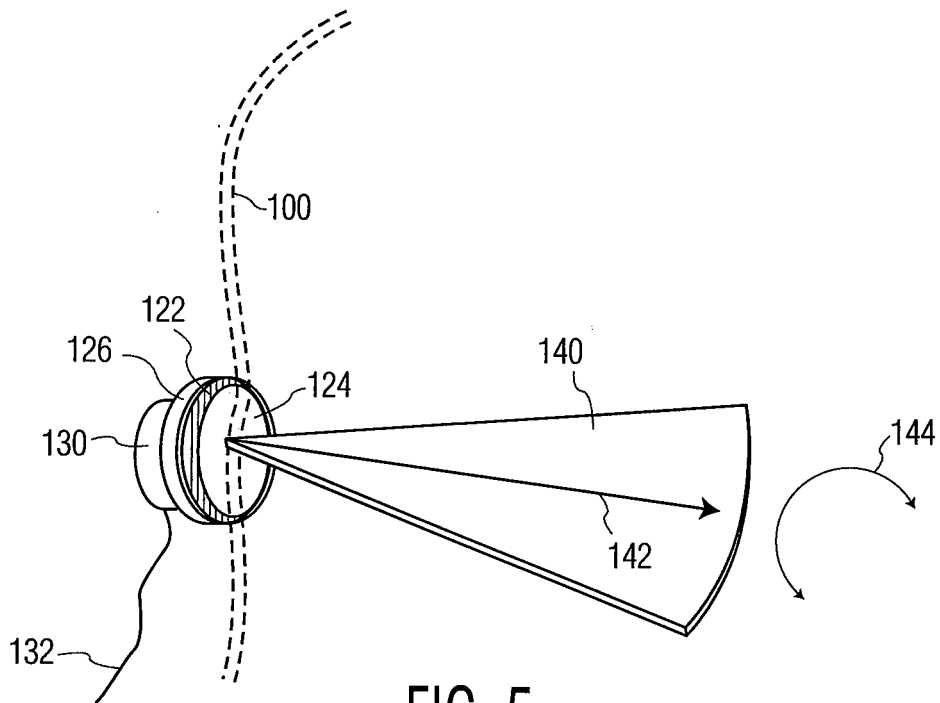


FIG. 5

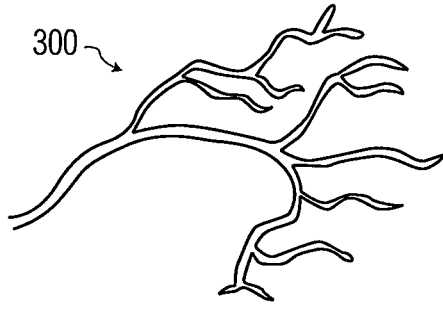


FIG. 6A

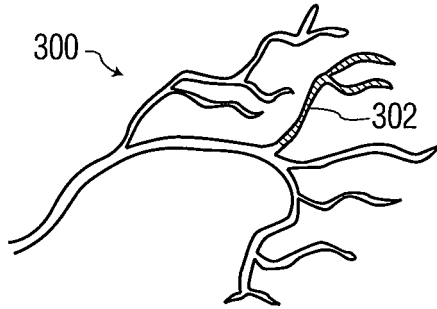


FIG. 6B

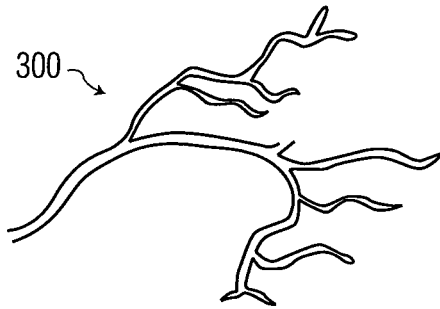


FIG. 6C

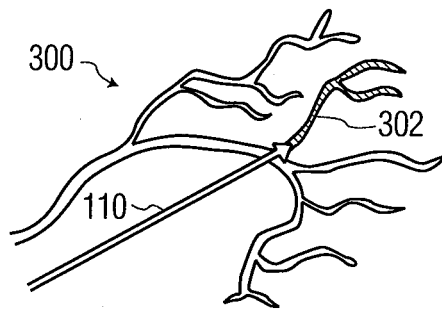


FIG. 6D

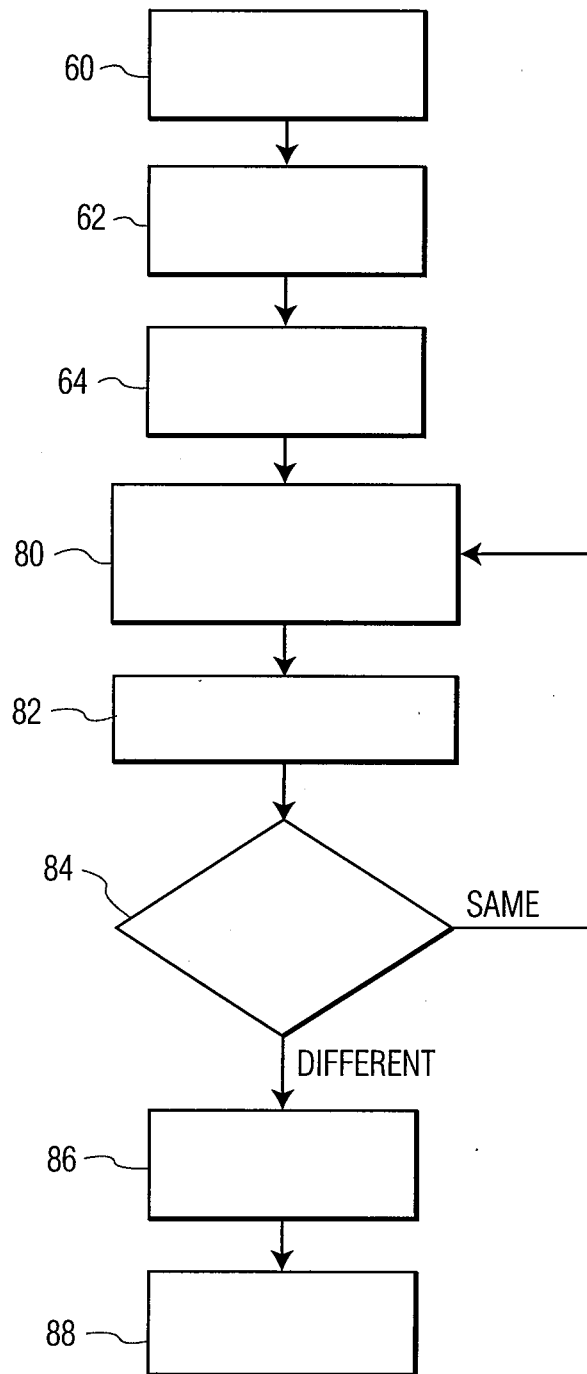


FIG. 7

**REFERENCES CITED IN THE DESCRIPTION**

*This list of references cited by the applicant is for the reader's convenience only. It does not form part of the European patent document. Even though great care has been taken in compiling the references, errors or omissions cannot be excluded and the EPO disclaims all liability in this regard.*

**Patent documents cited in the description**

- EP 1591073 A1 [0004]
- US 5997479 A, Savord [0008]
- US 6013032 A, Savord [0008]
- US 6623432 B, Powers [0008]
- WO 2005074805 A, Bruce [0010]
- US 6530885 B, Entrekim [0011]
- US 6723050 B, Dow [0011]
- US 5720291 A, Schwartz [0014]
- US 5474073 A, Schwartz [0017]
- US 6171246 B, Averkiou [0019]
- US 5226422 A [0023]
- US 5181514 A, Solomon [0023]
- US 6113547 A, Catallo [0024]
- US 6442289 B, Olsson [0025]
- US 5556674 A, Weng [0027]
- US 6572549 B, Jong [0027]
- US 6589176 B, Jago [0027]

专利名称(译)	超声系统用于脑血流成像和微泡增强血凝块溶解		
公开(公告)号	<a href="#">EP2051777A2</a>	公开(公告)日	2009-04-29
申请号	EP2007825989	申请日	2007-08-03
[标]申请(专利权)人(译)	皇家飞利浦电子股份有限公司		
申请(专利权)人(译)	皇家飞利浦电子N.V.		
当前申请(专利权)人(译)	皇家飞利浦N.V.		
[标]发明人	BROWNING EDWARD J SHI WILLIAM POWERS JEFFRY E AVERKIOU MICHALAKIS GAUTHIER THOMAS		
发明人	BROWNING, EDWARD, J. SHI, WILLIAM POWERS, JEFFRY, E. AVERKIOU, MICHALAKIS GAUTHIER, THOMAS		
IPC分类号	A61N7/00 A61B8/06 A61B8/00 A61B5/026 A61B17/22 A61B8/08 A61B19/00		
CPC分类号	A61B8/0816 A61B5/02007 A61B5/6814 A61B8/06 A61B8/08 A61B8/0808 A61B8/085 A61B8/13 A61B8/4227 A61B8/4281 A61B8/481 A61B8/483 A61B8/488 A61B17/22004 A61B2017/22014 A61B2090/502 A61N7/00 A61N2007/0021 A61N2007/0039 A61N2007/0078 A61N2007/0082 A61N2007/0095 G01S7/52041 G01S15/8981		
优先权	60/822106 2006-08-11 US		
其他公开文献	EP2051777B1		
外部链接	<a href="#">Espacenet</a>		

#### 摘要(译)

描述了一种超声诊断成像系统，其利用固定在患者头部的一个或多个换能器阵列来诊断和治疗中风患者。换能器头戴式耳机产生颅内脉管系统的二维或三维图像，优选地由微泡造影剂辅助。系统产生血管流动图，可以诊断出血栓的迹象。如果检测到血凝块，则在存在造影剂的同时传输治疗束以通过破坏微泡来破坏血凝块。耳机还可以用于监测应用中以检测中风受害者中血凝块的复发。