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## Declarations under Rule 4.17:

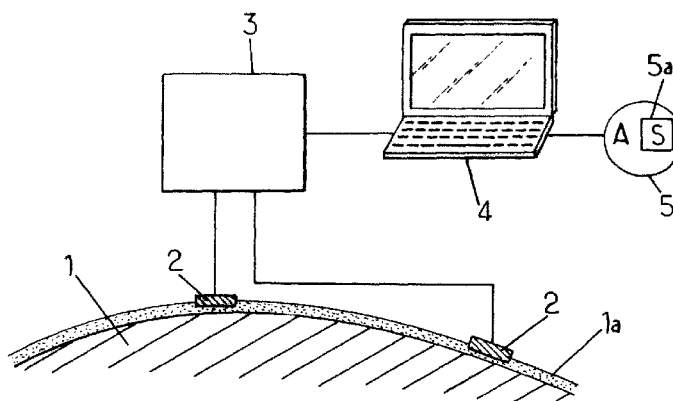
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(54) Title: METHOD FOR ULTRASOUND FUNCTIONAL IMAGING, MAN-MACHINE INTERFACE METHOD AND APPARATUS USING SUCH METHODS

FIG.1.



(57) Abstract: Method for ultrasound functional imaging including the following steps: (a) N successive imaging steps being realized at a minimum frame rate of 200 Hz, N being an integer and being at least 50; (b) a coherent addition step wherein the images  $I_i$  of each imaging step are coherently added to obtain a high signal-to-noise ratio; (c) an accumulation step wherein a motion parameter P related to local motion is computed based on the N successive images respectively obtained at step (a) as Formula (I), where  $K(I_n)$  is a non linear function;  $n=1$  (d) a repetition step for observing the temporal variations of the motion parameter P with time, wherein the accumulation step (c) is repeated  $N_t$  times,  $N_t$  being at least 2, with a repetition time comprised between 0 and 10 min.

**METHOD FOR ULTRASOUND FUNCTIONAL IMAGING, MAN-MACHINE  
INTERFACE METHOD AND APPARATUS USING SUCH METHODS.**

FIELD OF THE INVENTION

5           The invention relates to methods and apparatus for ultrasound functional imaging, to man-machine interface methods and to apparatuses using such methods.

BACKGROUND OF THE INVENTION

          A method for ultrasound brain functional imaging is  
10   disclosed in JP-A-2003079626, wherein the skull of a patient is partially removed and the velocity of bloodstream in tiny arteries of the brain is measured from the surface of the dura mater with an ultrasonic probe, by Doppler effect. Doppler sound data are turned into a  
15   waveform with a time-frequency analyzer, and peak values in all phases of the waveforms are traced. A plurality of results of task trials is added, percent changes of peak values at rest and at work are computed, and on the basis of data obtained, percent changes of bloodstream are  
20   plotted in color on a tomogram, and the tomogram is three-dimensionally reconstructed, using computer graphics software to obtain a functional image of the brain.

OBJECTS AND SUMMARY OF THE INVENTION

          However, this method is in fact unable to provide  
25   brain functional images, i.e. real time images of the activity of the brain, since the acquisition time of ultrasound images through a classical process leads to a very low sensibility.

          Further, ultrasound functional imaging of the brain  
30   is based on visualization of the blood flows in capillaries, since these blood flows are representative of the local activity of the brain, but the sensitivity of classical Doppler ultrasound imaging is too limited to visualize these blood flows in capillaries and therefore  
35   too limited obtain useful functional images of the brain.

One object of the present invention is to remedy these drawbacks.

To this end, according to an embodiment of the invention, a method for ultrasound functional (real time) imaging of the brain or spinal chord is provided, which includes at least the following steps:

(a) N successive imaging steps being realized at a minimum frame rate of 200 Hz, N being an integer and being at least 50, each imaging step i including the following substeps:

(a1) a transmission substep in which a plurality of ultrasonic waves  $e_i(x,t)$  are transmitted into an imaged region of the brain or spinal chord and a respective set of raw data  $r_i(x,t)$  is acquired by at least one array of transducers in response to each ultrasonic wave,  $x$  being a space variable representing a position on the array of transducers and  $t$  being time, each set of raw data  $r_i(x,t)$  representing the time signals received by the transducers in response to the corresponding ultrasonic wave  $e_i(x,t)$ , said plurality of ultrasonic waves being transmitted at a rate of at least 500 ultrasonic waves per second;

(a2) a beamforming substep in which, for each set of raw data  $r_i(x,t)$ , an image  $I_i(x,y)$  is computed in a set of pixels  $(x,y)$ ;

(b) a coherent addition step in which the images  $I_i(x,y)$  of each imaging step are coherently added to obtain a high signal-to-noise ratio;

(c) an accumulation step wherein a motion parameter  $P(x,y)$  related to local motion is computed based on the N successive images respectively obtained at step (a) as

$$P(x,y) = \sum_{n=1}^N K(I_n(x,y)), \text{ where } K(I_n) \text{ is a non linear function;}$$

(d) a repetition step for observing the temporal variations of the motion parameter  $P(x,y)$  with time,

wherein the accumulation step (c) is repeated  $N_t$  times,  $N_t$  being at least 2, with a repetition time between successive accumulation steps (c) being comprised between 0 and 10 min.

5           Thanks to these dispositions, it is possible to obtain a functional image of the brain or of part of it, with an excellent spatial resolution.

          Further, since hemodynamic changes in the brain are a relatively slow process (with time constants of about 0.5  
10 to 1 s), the present inventors had the idea to use the available time between two functional brain images, to perform the above-mentioned accumulation and repetition steps. One can thus obtain an outstanding sensitivity (high signal-noise ratio) of the image.

15           In various embodiments of the method for ultrasound imaging according to the above embodiment of the invention, one may possibly have recourse in addition to one and/or other of the following arrangements:

          - the plurality of emitted waves  $e_i(x,t)$  are plane  
20 waves;

          - the plurality of emitted waves  $e_i(x,t)$  are cylindrical or spherical waves;

          - the plurality of emitted waves  $e_i(x,t)$  are a plurality of focused waves;

25           - where the parameter  $P(x,y)$  is a Power Doppler image obtained by using a function  $K(\ln(x,y)) = (h(t) * \ln(x,y))^2$  where  $h$  is a high pass filter;

          - the motion parameter  $P(x,y)$  is a motion image obtained by using a function  $K = |(h(t) * \ln(x,y))|$  where  $h$  is  
30 a high pass filter;

          - the repetition step is carried out at time intervals longer than 50 ms, and more preferably around 100 ms.

          Another object of the present invention is a man-  
35 machine interface method comprising the following steps:

(A) collecting a neural signal directly from the brain of a subject through at least one Doppler image of the brain obtained by a method as defined above;

(B) extracting a motor command from said neural  
5 signal;

(C) controlling an actuator based on said motor command.

The man-machine interface method may further include the following steps after step (C):

10 (D) acquiring sensory feedback information from said actuator;

(E) interpreting said sensory feedback information to form interpreted sensory feedback information;

(F) and, between two imaging steps (a),  
15 transmitting, through said array of transducers, at least one focussed ultrasonic wave in an area of the brain or spinal chord adapted to neurostimulate or neuromodulate the brain or spinal chord and thus give the brain or spinal chord a sensory feedback corresponding to said interpreted  
20 sensory feedback information.

Another object of the present invention is an apparatus for ultrasound functional (real time) imaging which includes at least the following means:

(a) imaging means specially adapted to perform N  
25 successive imaging steps being realized at a minimum frame rate of 200 Hz, N being an integer and being at least 50, said compound imaging means including:

(a1) means for transmitting a plurality of ultrasonic waves  $e_i(x, t)$  into an imaged region of the  
30 brain or spinal chord and acquiring a respective set of raw data  $r_i(x, t)$  by an array of transducers in response to each ultrasonic wave,  $x$  being a space variable representing a position on the array of transducers and  $t$  being time, each set of raw data  
35  $r_i(x, t)$  representing the time signals received by the

transducers in response to the corresponding ultrasonic wave  $e_i(x,t)$ , said plurality of ultrasonic waves being transmitted at a rate of at least 500 ultrasonic waves per second;

5 (a2) beamforming means for computing an image  $I_i(x,y)$  for each set of raw data  $r_i(x,t)$ , in a set of pixels  $(x,y)$ ;

(b) means for coherently adding the images  $I_i(x,y)$  of each imaging step to obtain a high signal-to-noise  
10 ratio;

(c) means for carrying out an accumulation step for computing a motion parameter  $P(x,y)$  related to local motion, based on the  $N$  successive images respectively obtained at step (a) as  $P(x,y) = \sum_{n=1}^N K(I_n(x,y))$ , where  $K(I_n)$  is a  
15 non linear function;

(d) means for carrying out a repetition step for observing the temporal variations of the motion parameter  $P(x,y)$  with time, wherein the accumulation step is repeated  $N_t$  times,  $N_t$  being at least 2, with a repetition time  
20 between successive accumulation steps (c) being comprised between 0 and 10 min.

Still another object of the present invention is a man -machine interface apparatus including an apparatus for ultrasound functional (real time) imaging as defined above  
25 and:

(A) collecting means for collecting a neural signal directly from the brain or spinal chord of a subject through at least one functional image of the brain or spinal chord obtained by said apparatus for ultrasound  
30 functional imaging;

(B) means for extracting a command from said neural signal;

(C) means for controlling an actuator based on said command.

## BRIEF DESCRIPTION OF THE DRAWINGS

Other features and advantages of the invention appear from the following detailed description of one embodiment thereof, given by way of non-limiting example, and with reference to the accompanying drawings.

In the drawings:

- Figure 1 is a schematic drawing showing a synthetic ultrasound imaging apparatus according to one embodiment of the invention;
- 10       - Figure 2 is a block diagram showing part of the apparatus of Figure 1; and
- Figures 3 and 4 are images of the same rat brain, obtained respectively through the method according to the present invention and through conventional Doppler  
15       imaging.

## MORE DETAILED DESCRIPTION

In the Figures, the same references denote identical or similar elements.

The apparatus shown on Figure 1 is adapted for functional ultrasound imaging of a region 1, for instance at least part of the brain or spinal chord of a patient. The apparatus may include for instance:

- at least one ultrasound transducer array 2 and preferably at least two ultrasound transducer arrays 2  
25       disposed on different portions of the skull 1a of the patient (each array may be positioned either outside the skull, or in a groove which has been previously machined in the skull on purpose, as shown in Figure 1); each array 2 may be for instance a linear array typically including a  
30       few tens of transducers (for instance 100 to 300) juxtaposed along an axis X as already known in usual echographic probes (each array 2 is then adapted to perform a bidimensional (2D) imaging of the region 1, but the array 2 could also be a bidimensional array adapted to perform a  
35       3D imaging of the region 1);

- an electronic bay 3 controlling the transducer arrays 2 and acquiring signals therefrom;

- a computer 4 for controlling the electronic bay 3 and viewing ultrasound images obtained from the electronic bay (in a variant, a single electronic device could fulfill all the functionalities of the electronic bay 3 and of the microcomputer 4),

- optionally, one or several actuators 5 (A), each actuator 5 itself optionally including a feedback sensor 5a (S).

As shown on Figure 2, the electronic bay 3 may include for instance:

- for each array of transducers 2, n analog/digital converters 5 ( $A/D_1$ - $A/D_n$ ) individually connected to the n transducers ( $T_1$ - $T_n$ ) of the transducer array 2;

- n buffer memories 6 ( $B_1$ - $B_n$ ) respectively connected to the n analog/digital converters 5 for each array of transducers 2;

- a central processing unit 8 (CPU) communicating with the buffer memories 6 and the microcomputer 4;

- a memory 9 (MEM) connected to the central processing unit 8;

- a digital signal processor 10 (DSP) connected to the central processing unit 8.

The above apparatus may implement a method for ultrasound functional imaging of the brain or spinal cord, including at least the following steps:

(a) N successive imaging steps being realized at a minimum frame rate of 200 Hz, N being an integer and being at least 50, each imaging step i including the following substeps:

(a1) a transmission substep in which a plurality of ultrasonic waves  $e_i(x,t)$  are transmitted by the arrays of transducers 2 into the imaged region

of the brain or spinal chord and a respective set of raw data  $r_i(x,t)$  is acquired by the arrays of transducers 2 in response to each ultrasonic wave,  $x$  being a space variable representing a position on the array of transducers and  $t$  being time, each set of raw data  $r_i(x,t)$  representing the time signals received by the transducers in response to the corresponding ultrasonic wave  $e_i(x,t)$ , said plurality of ultrasonic waves being transmitted at a rate of at least 500 ultrasonic waves per second;

(a2) a beamforming substep in which, for each set of raw data  $r_i(x,t)$ , an image  $I_i(x,y)$  is computed by the electronic bay 3 or computer 4 in a set of pixels  $(x,y)$ ;

(b) a coherent addition step in which the images  $I_i(x,y)$  of each imaging step are coherently added by computer 4 to obtain a high signal-to-noise ratio;

(c) an accumulation step wherein a motion parameter  $P(x,y)$  related to local motion is computed by computer 4 based on the  $N$  successive images respectively obtained at step (a) as  $P(x,y) = \sum_{n=1}^N K(I_n(x,y))$ , where  $K(I_n)$  is a non linear function;

(d) a repetition step for observing the temporal variations of the motion parameter  $P(x,y)$  with time, wherein the accumulation step (c) is repeated  $N_t$  times,  $N_t$  being at least 2, with a repetition time between successive accumulation steps (c) being comprised between 0 and 10 min.

The plurality of emitted waves  $e_i(x,t)$  may be plane waves, cylindrical or spherical waves, or focused waves.

The motion parameter  $P(x,y)$  may be :

- a Power Doppler image obtained by using a function  $K(I_n(x,y)) = (h(t) * I_n(x,y))^2$  where  $h$  is a high pass filter, or

- a motion image obtained by using a function  $K=|(h(t)*\text{In}(x,y))|$  where  $h$  is a high pass filter.

The repetition step may be carried out at time intervals longer than 50 ms, and more preferably around 100 ms.

Figures 3 and 4 show a comparative example of a blood flow image of a rat brain obtained respectively through a power Doppler image realized according to the invention (Figure 3) and through a conventional Doppler method using focused waves (Figure 4). The image of Figure 3 is of much higher quality in terms of sensitivity and spatial resolution. The functional image of the rat brain may be obtained from the variations of the blood flow image in time.

As it is known *per se*, it is possible to use the functional images of the brain or spinal chord to control an actuator according to the patient's will, and optionally to stimulate or modulate brain neurons with a feedback signal (see in particular: *Lebedev et al.* [Trends in neurosciences, vol. 29, N°9, pp 537-546, Elsevier 2006], *Tufail et al.* [Neuron 66, pp681-694, June 10 2010, Elsevier], US7209788, US7283861).

Thus, the above apparatus may also perform a man-machine interface method comprising the following steps:

(A) collecting a neural signal directly from the brain or spinal chord of a subject through at least one functional image of the brain or spinal chord obtained by a method as described above;

(B) extracting a command from said neural signal;

(C) controlling an actuator 5 (A) based on said command.

The man-machine interface method may further include the following steps after step (C):

(D) acquiring sensory feedback information from the sensor 5a (S) said actuator 5;

(E) interpreting said sensory feedback information to form interpreted sensory feedback information;

(F) and, between two imaging steps (a), transmitting, through the arrays of transducers 2, at least  
5 one focussed ultrasonic wave in an area of the brain or spinal chord adapted to neurostimulate or neuromodulate the brain or spinal chord and thus give the brain or spinal chord a sensory feedback corresponding to said interpreted sensory feedback information.

**CLAIMS:**

1. Method for ultrasound functional imaging of the brain or spinal cord, including at least the following steps:

5 (a) N successive imaging steps being realized at a minimum frame rate of 200 Hz, N being an integer and being at least 50, each imaging step i including the following substeps:

10 (a1) a transmission substep in which a plurality of ultrasonic waves  $e_i(x,t)$  are transmitted into an imaged region of the brain or spinal chord and a respective set of raw data  $r_i(x,t)$  is acquired by at least one array of transducers in response to each ultrasonic wave, x being a space variable representing  
 15 a position on the array of transducers and t being time, each set of raw data  $r_i(x,t)$  representing the time signals received by the transducers in response to the corresponding ultrasonic wave  $e_i(x,t)$ , said plurality of ultrasonic waves being transmitted at a  
 20 rate of at least 500 ultrasonic waves per second;

(a2) a beamforming substep in which, for each set of raw data  $r_i(x,t)$ , an image  $I_i(x,y)$  is computed in a set of pixels (x,y);

25 (b) a coherent addition step in which the images  $I_i(x,y)$  of each imaging step are coherently added to obtain a high signal-to-noise ratio;

(c) an accumulation step wherein a motion parameter  $P(x,y)$  related to local motion is computed based on the N successive images respectively obtained at step (a) as

30  $P(x,y) = \sum_{n=1}^N K(I_n(x,y))$ , where  $K(I_n)$  is a non linear function;

(d) a repetition step for observing the temporal variations of the motion parameter  $P(x,y)$  with time, wherein the accumulation step (c) is repeated  $N_t$  times,  $N_t$  being at least 2, with a repetition time between successive

accumulation steps (c) being comprised between 0 and 10 min.

2. Method according to claim 1 where the plurality of emitted waves  $e_i(x,t)$  are plane waves.

5           3. Method according to claim 1, wherein the plurality of emitted waves  $e_i(x,t)$  are cylindrical or spherical waves.

          4. Method according to claim 1, wherein the plurality of emitted waves  $e_i(x,t)$  are a plurality of  
10 focused waves.

          5. Method according to claim 1, wherein the parameter  $P(x,y)$  is a Power Doppler image obtained by using a function  $K(In(x,y)) = (h(t) * In(x,y))^2$  where  $h$  is a high pass filter.

15           6. Method according to anyone of the preceding claims, wherein the motion parameter  $P(x,y)$  is a motion image obtained by using a function  $K = |(h(t) * In(x,y))|$  where  $h$  is a high pass filter.

          7. Method according to anyone of the preceding  
20 claims, wherein the repetition step is carried out at time intervals longer than 50 ms, and more preferably around 100 ms.

          8. A man-machine interface method including the following steps:

25           (A) collecting a neural signal directly from the brain or spinal chord of a subject through at least one functional image of the brain or spinal chord obtained by a method as claimed in anyone of claims 1-7;

          (B) extracting a command from said neural signal;

30           (C) controlling an actuator based on said command.

          9. A man-machine interface method according to claim 8, further comprising the following steps after step (C):

          (D) acquiring sensory feedback information from  
35 said actuator;

(E) interpreting said sensory feedback information to form interpreted sensory feedback information;

(F) and, between two imaging steps (a), transmitting, through said at least one array of transducers (2), at least one focussed ultrasonic wave in an area of the brain or spinal chord adapted to neurostimulate or neuromodulate the brain or spinal chord and thus give the brain or spinal chord a sensory feedback corresponding to said interpreted sensory feedback information.

10. Apparatus for ultrasound functional imaging of the brain or spinal cord, including at least the following means:

(a) imaging means specially adapted to perform N successive imaging steps being realized at a minimum frame rate of 200 Hz, N being an integer and being at least 50, said compound imaging means including:

(a1) means for transmitting a plurality of ultrasonic waves  $e_i(x,t)$  into an imaged region of the brain or spinal chord and acquiring a respective set of raw data  $r_i(x,t)$  by at least one array of transducers (2) in response to each ultrasonic wave,  $x$  being a space variable representing a position on the array of transducers and  $t$  being time, each set of raw data  $r_i(x,t)$  representing the time signals received by the transducers in response to the corresponding ultrasonic wave  $e_i(x,t)$ , said plurality of ultrasonic waves being transmitted at a rate of at least 500 ultrasonic waves per second;

(a2) beamforming means for computing an image  $I_i(x,y)$  for each set of raw data  $r_i(x,t)$ , in a set of pixels  $(x,y)$ ;

(b) means for coherently adding the images  $I_i(x,y)$  of each imaging step to obtain a high signal-to-noise ratio;

(c) means for carrying out an accumulation step for computing a motion parameter  $P(x,y)$  related to local motion, based on the  $N$  successive images respectively obtained at step (a) as  $P(x,y) = \sum_{n=1}^N K(\ln(x,y))$ , where  $K(\ln)$  is a

5 non linear function;

(d) means for carrying out a repetition step for observing the temporal variations of the motion parameter  $P(x,y)$  with time, wherein the accumulation step is repeated  $N_t$  times,  $N_t$  being at least 2, with a repetition time  
10 between successive accumulation steps (c) being comprised between 0 and 10 min.

11. Man-machine interface apparatus including an apparatus for ultrasound functional imaging as claimed in claim 10 and:

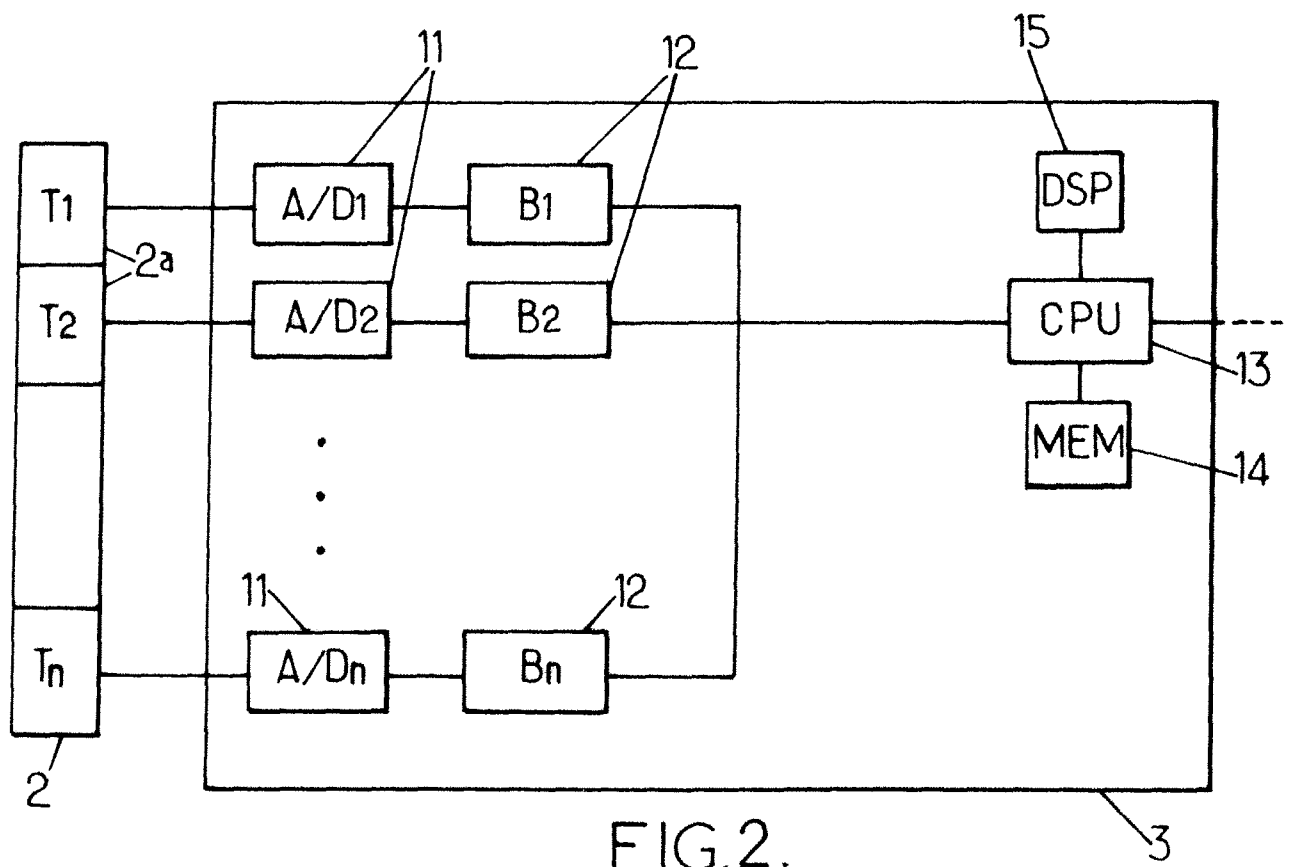
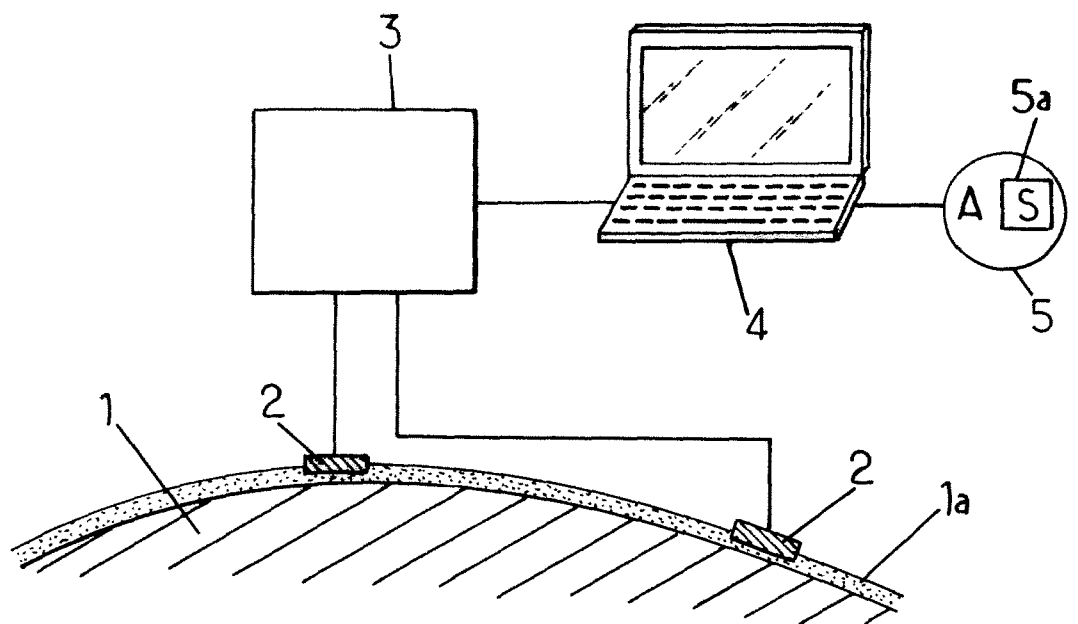
15 (A) collecting means for collecting a neural signal directly from the brain or spinal chord of a subject through at least one functional image of the brain or spinal chord obtained by said apparatus for ultrasound functional imaging;

20 (B) means for extracting a command from said neural signal;

(C) means for controlling an actuator (5) based on said command.

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FIG.1.



2/2



FIG. 4.

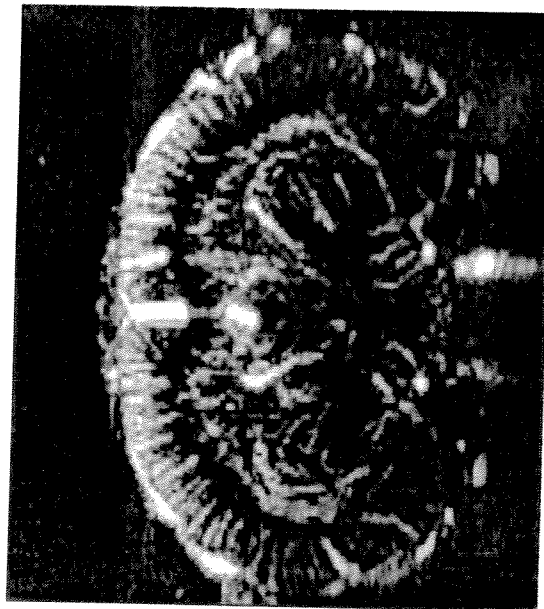


FIG. 3.

# INTERNATIONAL SEARCH REPORT

International application No  
PCT/IB2011/000934

## A. CLASSIFICATION OF SUBJECT MATTER

INV. A61B8/06 A61B8/08 G01S7/52 G01S15/89 G06F3/01  
A61F2/68 A61N7/00 A61B8/14 G06T5/50

ADD.

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

A61B G01S G06T G06F A61F A61N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EP0-Internal, WPI Data

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

| Category* | Citation of document, with indication, where appropriate, of the relevant passages                                                                                                                                                                              | Relevant to claim No. |
|-----------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------|
| X         | EMILIE MACE ET AL: "High sensitivity brain angiography using Ultrafast Doppler",<br>ULTRASONICS SYMPOSIUM (IUS), 2010 IEEE, IEEE,<br>11 October 2010 (2010-10-11), pages 1194-1197, XP031952945,<br>DOI: 10.1109/ULTSYM.2010.5935810<br>ISBN: 978-1-4577-0382-9 | 1-7,10                |
| Y         | the whole document<br>-----<br>-/--                                                                                                                                                                                                                             | 8,9,11                |



Further documents are listed in the continuation of Box C.



See patent family annex.

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Date of the actual completion of the international search

11 January 2012

Date of mailing of the international search report

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Name and mailing address of the ISA/

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# INTERNATIONAL SEARCH REPORT

International application No  
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| Category* | Citation of document, with indication, where appropriate, of the relevant passages                                                                                                                                                                                                                                                             | Relevant to claim No. |
|-----------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------|
| Y         | <p>LEBEDEV M A ET AL: "Brain-machine interfaces: past, present and future", TRENDS IN NEUROSCIENCE, ELSEVIER, AMSTERDAM, NL, vol. 29, no. 9, 1 September 2006 (2006-09-01), pages 536-546, XP025031271, ISSN: 0166-2236, DOI: 10.1016/J.TINS.2006.07.004 [retrieved on 2006-09-01] cited in the application abstract figure 2</p> <p>-----</p> | 8,9,11                |