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(71) Applicant (for all designated States except US): **COM-PUMEDICS MEDICAL INNOVATIONS PTY LTD**  
[AU/AU]; 30-40 Flockhart Street, Abbotsford, Victoria  
3067 (AU).

(72) Inventor; and

(75) Inventor/Applicant (for US only): **BURTON, David**  
[AU/AU]; 30-40 Flockhart Street, Abbotsford, Victoria  
3067 (AU).

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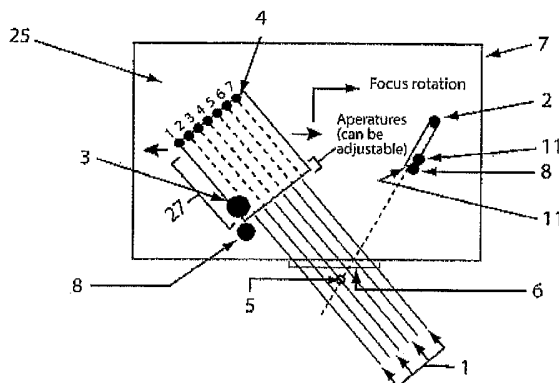
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(54) Title: **ULTRASOUND DIAGNOSIS AND TREATMENT APPARATUS**



(57) Abstract: The invention provides apparatus and methods for semi-automatic or automatic imaging or treatment of occlusions in vessels using pulsed or unpulsed focussed sound waves, preferably ultrasound, in Doppler technology. The apparatus comprises at least one sound transducer member including at least one sound-emitting element for producing at least one sound wave beam; means to adjust the parameters of said at least one sound wave beam; means to spatially locate said at least one sound-emitting element; means to move said at least one transducer member; means to control movement of said at least one transducer member automatically or semi- automatically; means to automatically or semi-automatically focus sound waves generated by said at least one sound-emitting element into a beam; and means to accept sound signals from sound-emitting element or elements. The invention provides method for semi-automatically or automatically locating an occlusion in a vessel, including the steps of identifying regions of a body in which emboli might be found are identified; selecting a region of interest for sonication; sonicating the region of interest with at least one sound wave beam by moving said sound beam across the region of interest; receiving reflected sound signals from the region of interest; and calculating the Doppler effect parameters of flow and turbulence from said reflected sound signals.



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**Title of the Invention**

Ultrasound Diagnosis and Treatment Apparatus

**5 Field of the Invention**

This invention relates to apparatus for the generation of sound waves, in particular to apparatus for transcranial Doppler sound devices for medical treatment of patients suffering from blood vessel occlusions or restriction in the brain characteristic of a stroke.

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**Background**

Blood circulation through the body is essential for maintenance and growth of cells and tissues. Any condition that restricts blood flow can have mild to disastrous consequences. For example, when blood flow in the brain is impeded, stroke can result. Stroke is a medical affliction that has severe consequences for most people who suffer it. Stroke is classified into four types, two of which are caused by blood clots (ischaemic stroke) and two of which are caused by haemorrhage (haemorrhagic stroke). Cerebral thrombosis and cerebral embolism account for up to 80 per cent of all strokes.

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Treatment options for stroke are limited. For example, only tissue plasminogen activator (tPA) has been approved by the United States Food and Drug Administration as a pharmaceutical therapeutic treatment for ischaemic stroke.

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It has been shown that the use of ultrasound waves and the Doppler frequency shift can be used to monitor the flow of blood through vessels (eg. Tegeler and Ratanakorn, 1999). Apparatus have been developed to exploit the potential of ultrasound to locate the interface between tissue types in the body, in particular, in the head, using transcranial Doppler ultrasound technology (TCD). US patent no. 4,817,621 described apparatus to locate reliably blood vessels in the brain and to determine blood flow through vessels in the head using TCD. The apparatus relied on the combination of two parallelogram-like linkage systems to support and locate an ultrasound

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transducer near the head of a patient to locate occluded blood vessels in the brain using TCD. More recently, it has been shown that monitoring of patients with TCD, in addition to treatment with tPA may increase the effectiveness of tPA in the treatment of ischaemic stroke (Alexandrov et al. 2004), using  
5 commonly available TCD devices and operators skilled in using the devices to locate occlusions.

Transcranial Doppler technology has been shown to be useful in the identification and treatment of small vessel knock (WO2004/103184)  
10 associated with small vessel occlusion leading to stroke. The treatment taught in WO2004/103184 requires significant effort by an operator to find and diagnose the occluded blood vessels characteristic of stroke. While it has been shown that currently available ultrasound transducers and systems may be used for monitoring occluded blood vessels in stroke might also be a  
15 beneficial treatment method alleviating the symptoms of stroke, the ability to use TCD as a therapeutic treatment is currently constrained by the ease of use of said currently available systems. Clinicians who have used currently available TCD systems have noted that vascular tests that require the use of said TCD systems are among the most difficult to perform (Alexandrov et al.,  
20 2004). The ability of clinicians to diagnose and treat stroke with the promising TCD ultrasound technology may be limited by the apparatus with which to diagnose and treat the condition. For example, the current method of identifying the presence of occlusions in brain blood vessels is a manual grading system, known as the thrombolysis in brain ischaemia (TIBI) flow  
25 grading system. One of the problems with a head cap or band mounted or any other body or head mounted automatic diagnostic or treatment ultrasound device is that stability of movement of the sensor with patient movement or simply device attachment slippage can affect measures and data integrity.

30 What is needed is an apparatus and method to more efficiently locate occluded blood vessels or vessels having restriction in the brain characteristic of stroke and to treat the occlusions or restrictions to alleviate the stroke symptoms.

In this document the words "including" and "comprising" are used interchangeably and with the same meaning, which is intended to indicate non-limiting incorporation of elements.

## 5    **Brief Description of the Figures**

Figure 1 shows an embodiment of an ultrasound transducer useful in the invention.

Figure 2a shows a table of data providing near-field lengths and far-field divergence of ultrasound waves generated by typical ultrasound transducers.

10    Figure 2b shows a table of data showing the variation in velocity of ultrasound waves through selected materials found in living organisms.

Figure 3a shows an embodiment of multiple ultrasound transducers focussed electronically.

15    Figure 3b shows an embodiment of a concave lens being used to focus a linear array of ultrasound transducers.

Figure 4 shows embodiments of arrays of transducers, including curved and linear arrays.

Figure 5 shows embodiments of phased arrays of transducers which can be steered and focussed electronically.

20    Figure 6 shows an embodiment of the invention as an adjustable servo-array of ultrasound transducers.

Figure 7 shows an embodiment of invention in a sequence of operation of a phased array of ultrasound transducers.

Figure 8a shows an example of electric focussing of an ultrasound transducer.

25    Figure 8b shows an example of a phased array of ultrasound transducers.

Figure 9a shows an example of the pulse rate of an ultrasound transducer.

Figure 9b shows an example of depth resolution of an ultrasound transducer.

## **Summary of the Invention**

30    In one aspect the invention provides apparatus for imaging or treatment of restrictions or occlusions in vessels using sound waves, comprising at least one sound transducer member including at least one sound-emitting element for producing at least one sound-wave beam; means to adjust the parameters of said at least one sound-wave beam; means to spatially locate said at least

one sound-emitting element; means to automatically or semi-automatically focus sound waves generated by said at least one sound-emitting element into a beam; and means to accept sound signals from sound-emitting element or elements. Preferably the apparatus includes means to move said at least one transducer member and means to control movement of said at least one transducer member automatically or semi-automatically. Preferably the sound-emitting element and the means to accept sound signals are the same. Preferably the at least one sound-wave beam is pulsed. Preferably the at least one sound-wave beam is focussed electronically. The invention may include two or more sound-emitting elements forming an array and the array may be curved. The at least one sound-wave beam may incorporate a plurality of frequencies of sound waves in combinations of concurrent frequencies generated by the sound-emitting elements in the array or in a series of frequencies over time. The array may be comprised of sound-emitting elements in any of fixed position, adjustable position, or scanning position. The apparatus may include fiducial registration means and communication mean for communicating the position of the at least one sound-emitting element and maintaining the at least one sound-emitting element in optimal positioning during sonication.

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In another aspect, the invention provides apparatus for imaging or treatment of restrictions or occlusions in vessels using sound waves, comprising at least one sound-wave transducer member including at least one sound-emitting element for producing at least one sound-wave beam; means to adjust the parameters of said at least one sound-wave beam; means to orient said at least one transducer member; means to focus sound waves generated by said sound-emitting element into a beam; and means to accept sound signals from sound-emitting element or elements. The sound-emitting elements may be moveable singly or in a coordinated manner, including simultaneously.

The sound-emitting elements may be servo-controlled, including feedback control. The servo-control means may be self-tracking and include means for determining out-of-range positioning of said at least one sound-emitting element. The feedback control may incorporate a signal characteristic of an occlusion in a fluid flow. The apparatus may include a plurality of sound-

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- emitting elements in at least two layers of at least two arrays. Preferably each transducer member is operable to enable a continuously adjustable focus point comprising of two or more sound beams emitted by at least two sound-emitting elements. Preferably the apparatus includes means to transform
- 5 sound signals from analogue to digital forms or digital to analogue forms. Preferably the apparatus includes means to store transformed digital data. Preferably the apparatus includes means to display analogue or digital data. Preferably the apparatus includes video display means for displaying data. The apparatus may include voice coil control means. Preferably the
- 10 apparatus is operable in real-time or near real time. Preferably the apparatus includes fiducial registration means for maintaining targeted sonication. Preferably the apparatus is used for detecting and sonicating vessels in the brain of a being. Preferably the sound waves are ultrasound waves.
- 15 In another aspect, the invention provides a method for locating an occlusion or restriction in a vessel, including the steps of identifying regions of a body in which an occlusion or restriction in a vessel might be found; selecting a region of interest for sonication; sonicating the region of interest with at least one sound-wave beam by moving said at least one sound-wave beam across the
- 20 region of interest; receiving reflected sound signals from the region of interest; and calculating the Doppler effect parameters of flow and turbulence from said reflected sound signals.
- In another aspect, the invention provides a method for distinguishing
- 25 anatomical features of an organism including the steps of sonicating a region of interest in a subject with at least one sound-wave beam, whereby the frequency of said at least one sound-wave beam is suitable for determining a particular tissue type, receiving reflected sound signals from said region of interest, calculating the Doppler effect parameters of said reflected sound
- 30 signals and characterising said Doppler effect parameters according to parameters associated with known tissue types.

The method of the invention may include the step of modifying the characteristics of the at least one sound-wave beam to target a region of

interest wherein the Doppler effect parameters are indicative of reduced flow attributable to an occlusion or a restriction. The method may include the step of sonicating the region of interest thereby causing agitation or dissipation of the occlusion by prolonged sonication or recanalisation of a restriction. The

5 method may include the step of automatically or semi-automatically evaluating and optimising the effect of sonication on an occlusion for feedback modification of said at least one sound-wave beam, said evaluating and optimising including tissue safety guidelines. The method may include that the step of automatically or semi-automatically evaluating and optimising the

10 effect of sonication includes maintaining a fiducial registration between sound waves beams and a registration signal. The method may include the step of calculating and displaying any one or a combination of an index, measure, or marker or suitable representation indicating the progress of dissipation of an occlusion in a vessel or recanalisation of a vessel having an occlusion or

15 restriction. The method may be carried out automatically or semi-automatically substantially without human control. The method may be carried out wherein the region of the body is the head. Preferably the region of the head is the circle of Willis. The method may include the two or more sound-wave beams moving across said region of interest in either a

20 simultaneous or sequential manner. The method may include having the at least one sound-wave beam pulsed. The method may include the parameters calculated from said reflected sound signals being any one or a combination of power, spectral, amplitude, phase coupling or frequency characteristics characteristic of a spatial representation of anatomical features in said region

25 of interest or occlusive material. Preferably the power or amplitude spectral analysis are carried out using Fast Fourier Transform techniques. Preferably the at least one sound-wave beam is continuous. The method may include the at least one sound-wave beam being initially transmitted with a first frequency or amplitude and subsequently with periodic changes resulting a

30 second and further frequency or frequencies or amplitude(s) relative to the first beam frequency so that the mark-to-space ratio of the apparent changing and pulse formation is continuous. Preferably the sound-wave beam is comprised of ultrasound waves. The method may include the step of conducting a spatial voxelated analysis of received signals.

### Detailed Description of the Drawings and Preferred Embodiments

It is an object of the present invention to provide an apparatus that reduces  
5 the need for significant operator interaction with a sound-wave generating  
device used in the identification and treatment of embolism or stenosis. It is a  
further object of the invention to provide a method of semi-automatic or  
automatic location of embolism or stenosis using sound waves. It is a further  
10 object of the invention to provide an apparatus for the automatic or semi-  
automatic location of blood vessel emboli or stenosis in the brain. It is a  
further object of the invention to provide a means to semi-automatically or  
automatically locate an occlusion or restriction in a blood vessel. It is a further  
object of the invention to provide a means to semi-automatically or  
15 automatically treat said emboli or occlusion or restriction with sound waves. It  
is a further object of the invention to provide an apparatus to utilise the energy  
of transcranial Doppler ultrasonography in thrombolysis and recanalisation of  
blood vessels in the brain.

The following description refers to the preferred embodiment of the invention  
20 using ultrasound waves. It will be understood that sound waves of other  
frequencies than ultrasound are suitable for other embodiments within the  
scope of the invention. For example, in another embodiment, the invention  
includes apparatus that utilises low-frequency pulsatile sound waves that may  
be focussed to achieve similar results as the preferred ultrasound waves. In  
25 this document, the word, "occlusion", includes any one of, or a combination of,  
an embolism, thrombus, or other biological matter, non-biological matter,  
including gases, from whatever source. In this document, the word,  
"stenosis", includes any restriction in a fluid-containing vessel.

30 An example transducer member 24 comprising a single ultrasound-emitting  
element is illustrated in Figure 1, the ultrasound-emitting element includes a  
piezoelectric element 21, backing material 22, and electrodes 23. The  
ultrasound-emitting element converts electric voltage applied across the  
ultrasound-emitting element into ultrasonic sound-wave energy. When a



beam of ultrasonic sound-wave energy is directed toward heterogeneous biological material of interest, the ultrasonic sound-wave energy is reflected at the interfaces of biological structures within the biological material. The reflected energy causes an ultrasound-receiving element to vibrate and to  
5 produce a voltage signal which can be processed to decipher the reflective properties of the biological material. It will be understood by persons skilled in the art that a single ultrasound element may function either as an ultrasound-emitting element, an ultrasound-receiving element, or both an ultrasound-emitting and an ultrasound-receiving element. An ultrasound beam produced  
10 by an ultrasound-emitting element may be pulsed or unpulsed in duration. A pulsed beam is pulsed at a rate required for the biological material of interest as illustrated in Figure 9a. Figure 9b shows the time sequence of an ultrasound beam resolving two surfaces. It will be understood that axial or depth resolution is the ability to determine the axial resolution of two objects  
15 located tandem to the ultrasonic beam. The axial resolution is determined by the spatial pulse length.

The transducer diameter can be selected to suit various depth ranges required for different treatment applications. Figure 2a shows the properties  
20 of a range of depths of commercially available ultrasound transducers and Figure 2b shows the variability of velocity of ultrasound beams in different biological materials, which is exploited in the invention. The velocity of the ultrasound signal depends on the constitution of the material through which the signal travels, the velocity being directly proportional to the density  
25 through which the ultrasound is transmitted. The transmission through tissue is  $1540 \text{ m sec}^{-1}$  or, alternatively, a 1 cm transmission depth requires 13  $\mu\text{sec}$  to be traversed by an ultrasound wave.

The ultrasonic beams generated by a transducer can be focussed with  
30 focussing means. Preferably the lateral and depth positioning of the ultrasonic beam focus point can be adjusted by way of electronic focussing, illustrated in Figure 8a. An embodiment of a focussed transducer member 25 with an ultrasound-emitting element, shown in Figure 3a, can provide improved lateral resolution at depth. Focussing types can include curved

mirrors, acoustic crystals, acoustic lens, or phased array (employing electronic focussing). The operation of ultrasound-emitting elements in a phased array is shown in Figure 8b.

- 5 The ultrasound-emitting elements may be positioned in an array within a transducer member 25 and may take alternative forms. Figure 4 shows that such forms may include curved arrays 26 and linear arrays 27. The application of voltage to an array of ultrasound-emitting elements of a transducer member may be pulsed out-of-phase to achieve steering and  
10 focussing of an ultrasound beam as illustrated in Figure 5. The invention includes that each of said at least one transducer members 25 may be comprised of any combination of ultrasound-emitting and receiving elements.

- Illustrated in Figure 6 is an embodiment of the invention. It will be understood  
15 that a particular embodiment will incorporate a selection of features to achieve the objects of the invention and that the embodiment in Figure 6 is illustrative only. A sensor enabling said ultrasonic-beam transmission and/or handling may be comprised of piezo or PVD material, or other suitable material or a suitable sensor capable of generating and/or receiving ultrasonic beam  
20 signals. Said at least one transducer member may include a combination of one or more members in fixed-position array, adjustable-position array 1, scanning-position single-member 2 or multiple-element transducer members, fixed-position single-member or multiple-element transducer members.

- 25 The focussing point 5 of an ultrasonic beam can be achieved through any combination of servo-driven control of an adjustable-position array-transducer member 3, servo-driven control of the scanning-position single-member 2 or multiple-element transducer member 4, the switching combination of fixed-array beams 6 or any combination thereof. Preferably the location of  
30 ultrasound transducers is achieved through servo-movement.

Said ultrasonic beams can be accurately positioned via ultrasonic grid arrays or reference markers located on a device case or housing 7 or at any point within said beams as a measure of final beam-positioning feedback for high

resolution and focus accuracy for said converging ultrasonic beams. The beam-positioning feedback enables the servo-control position circuitry 8, in turn, to reflect the positional requirement for said ultrasonic beams, either in accordance with an operator's remote selection, by way of communication means, or locally selected by way of direct communication, input into said

5 servo-control position circuitry through manipulation of ultrasonic beams 1 and focal point 5. Transducer members 4 may be adjusted so that the direction of the ultrasonic beams 1 can be oriented either two-dimensionally or three-dimensionally according to the positioning of at least one servo-adjust spigot

10 3. A secondary ultrasound member comprising a single transducer member, or alternatively at least two transducer elements, may comprise of either a single ultrasonic beam 2 or multi-array ultrasonic beams 4. Furthermore, multi-layer, multi-array ultrasonic beams may be used where a singular or group of three-dimensional (in space) positioning ultrasonic beam focus

15 capability by way of aperture adjustment 11, such as piezo-aperture control.

As stated, the scope of the invention includes alternative embodiments to that herein illustrated and may include embodiments wherein the sound transducers are arranged in arrays and in multiple layers of arrays.

20 Embodiments include those where the sound transducers are arranged in a single array, the sound beams generated by a plurality of transducers in an array focussed at a single target. The transducers in an array may be in fixed position or moveable.

25 The apparatus may include a fiducial registration means (not shown) for maintaining the optimal positioning of sound-emitting elements for continued sonication when the subject moves, for example. Preferably said fiducial registration means are additional sensors attached to ultrasonic transducers and transceiver devices attached to a subject. Communication between

30 fiducial registration means may be through wire connectors or wireless communication means. Said fiducial registration means includes means for attachment to the subject and means for communicating between the subject and the servo-control means 8. The control means includes means to measure the correct registration of signals from the fiducial registration

means. The fiducial registration means is placed in fixed position at the commencement of sonication with a suitable adhesive material such as self-adhesive locators attached to a subject. When the communication between the fiducial registration means and the control means indicate a departure  
5 from the initial optimal signal registration, the control system may prompt the operator by way of a prompting means that the sound-emitting means is out of alignment. Said prompting may occur automatically. Such a method and device enhances the ultrasonic beam targeting method, where for example, a subject ultrasonic transducer attachment device, such as one located on  
10 glasses or a headcap, moves during automatic or remote-controlled recanalisation or sonication of the subject.

The invention includes that the variability of velocity of ultrasound waves in different tissues may be exploited to characterise the tissues in a region of  
15 interest in a subject where it is suspected that there might be an occlusion or a restriction in fluid flow, for example, blood flow. Sonication of a region of interest with multiple frequencies of sound-wave beams, each selected frequency being associated with a tissue type as indicated in Figure 2b, wherein the multiple frequencies are generated by any of at least one sound-emitting element at spaced intervals or two or more sound-emitting elements  
20 concurrently or in a pre-determined series of frequencies allows the characterisation of an occlusion or restriction in fluid flow as being attributable to a cause such as a gas bubble or bubbles, solid material, blood, tissue, vessel, skin, organs or other material.

25

The invention includes an apparatus having an arrangement of ultrasound transducers that enables the automatic mapping or visualisation of the progress of the dissolution of the target embolus.

30 The invention includes means capable of servo-feedback to ultrasonic turbulence (such as fast Fourier transformation) representation of the turbulence associated with blood vessel occlusion. Preferably the servo-feedback is optimised for the most effective vessel recanalisation.

The invention advantageously utilises sound waves produced by an ultrasound transducer to locate blood vessels that might show embolism. One embodiment of the invention includes a method for identifying an embolism or stenosis. In a first step of said method, regions of the body in which emboli  
5 might be found are identified. Preferably the region of the body is the head. More preferably the region of the body is the circle of Willis in the head. In a second step, a particular region of interest is selected. In a third step parameters of flow and turbulence are calculated for subsequent automatic ultrasound beam localisation in a fourth step, said parameters including the  
10 spectral power or amplitude or phase coupling or frequency segmented characteristics of flow and turbulence of flow blood.

In said first step of identifying regions of the body in which emboli might be found, at least one ultrasound transducer generates an ultrasound beam  
15 which is moved across the surface of the region of the body in a scanning motion. Said ultrasound transducer or transducers may be fixed in an array in space relatively to one another or moveable in space relative to one another. Alternatively, said transducers may be fixed in arrays in layers. Said beams from said ultrasound transducers in said scanning motion may be operated in  
20 said scanning motion either simultaneously or sequentially across said body regions.

In the second step the Doppler effect on echo beams received by the transducers is calculated. The analysis characterises the flow characteristics  
25 associated with the variation in frequency detected from the original ultrasonic transmission beam frequency. The analysis incorporates referencing and compensating for beam signals associated with normal echo beams such as flows associated with heart pumping or respiration and distinguishes such echo beams from beam signals of interest. The analysis further incorporates  
30 compensating for beam signals such as those associated with flow artefacts associated with ghost echoes, and those attributable to partial flows around occlusions and/or locally enhanced flows near occlusions.

Said ultrasound transducers generating the pulsed or unpulsed ultrasound beams may also receive the transmitted return echoes of transmitted beams. Where ultrasound beams are transmitted from a transducer in a continuous, i.e. unpulsed wave, a beam is initially transmitted with a first frequency or amplitude and subsequently with periodic changes resulting a second and further frequency or frequencies or amplitude(s) relative to the first beam frequency so that the mark-to-space ratio of the changing (apparent) pulse formation (but continuous) enables the computation of distance by decoding and determining the received (apparent) pulse from the last or a specific transmission pulse (known from the changes amplitude, frequency, phase or any combination thereof characteristics in the second and later characteristics of the continuous beam, known receive time and known speed of beam enables distance calculation related to reflected beam and Doppler shifted return pulse, for example).

The changes in frequency based upon the principles of Doppler frequency modification provide a composited signal comprised of various blood flow characteristics associated with said scanning beam. Contained within said composited signal is a range of data which may be extracted by means of frequency power and frequency segment characterisation.

Preferably the sound waves generated by an ultrasound-emitting element are within the ultrasound frequency range. It will be understood that the invention is not restricted to an apparatus or method comprising ultrasound waves, but that an apparatus or method according to the invention can accommodate frequency bands other than those within the ultrasound frequency band.

Frequency power or amplitude spectral analysis can be conducted using same or similar means to Fast Fourier Transform, whereupon various components of the flow and flow turbulence signals associated with said ultrasound beam are represented in terms of power or amplitude of each respective frequency or range of frequencies of said beams. The frequencies or range of frequencies in turn represent the various changes or modifications through the Doppler principle of the original transmission ultrasonic beam. In

turn the combination or characteristic "fingerprint" of the combinations of frequency power and absolute frequencies present provide an indication of Suspicious Regions of Interest (SROI) wherein an embolism might be located.

- 5 For the desirable target scanning and detection of SROI certain properties will be detected in a sequence of more and more sensitive scans, conducted in a spatial voxelated (3D spatial biological substance segmented into triangular voxels each associated to a mathematical matrix to enable recall with spatial localisation of x, y, z coordinates) visualisation (means to represent said  
10 voxels into an image or image view or travel path through said biological subject) until the most sensitive scan sequence is conducted and the subsequent SROI also marked.

- The properties of the characteristics or "finger-prints" and the sequence of  
15 progressively more sensitive scans will determine the sensitivity and specificity of the present device and method for detection SROI in relation in particular to vessel occlusions.

- The invention includes that the unique combination of blood flow or absolute  
20 and specific frequency of the blood and the spectral power enables a determination of the location of a specific occlusion and a determination of the nature of the material causing the occlusion.

- The invention includes a method that utilises such characteristics and  
25 associated determinations to firstly, detect the spatial location of such occlusions and, secondly, determine the specific location of the occluding material in order to determine where to direct the ultrasonic beam to assist with the agitation or dissipation of such an occlusion to advantageously be most effective in eliminating or reducing the occlusions. Similarly, the beams  
30 can be directed in such a manner that the paths or trajectory of the beams provide minimal power and energy transfer to healthy cells but the focus or combined beams enhance the ability to diffuse or break-up such blockage material, in the fastest but safe manner.

The invention includes apparatus and methods for focussing a plurality of beams of ultrasound waves with the concentration of said beams causing the agitation or dissipation of an occlusion in a blood vessel.

- 5 The invention includes apparatus that generates ultrasound waves and measures the Doppler effect on reflected waves in a stable manner. In operation the apparatus scans the target areas of the body for known spatial flow characteristics of relatively strong and distinct blood vessels. The locational map of the spatial characteristics or a simplified syntactic  
10 representation of the blood vessel spatial characteristics are stored in memory, in particular, specific coordinates that respond to certain known vessel location properties.

- By utilising a biological referencing system said apparatus or method can  
15 periodically check the movement of the apparatus against said biological reference point and appropriately adjust the display or data coordinates in accordance to the compensation of such detected movement. This enables an operator to continue to read and view relatively stable readings, data or image display. Also the servo mechanisms of the apparatus can compensate  
20 for the movement of the apparatus during operation and continue to treat or diagnose the selected areas or regions of interest.

- The method includes the use of Doppler signal data to calculate parameters associated with fluid flow, including the speed, volume, and intensity of flow.  
25 This includes the ability to determine the rate of change in any parameter over time. By calculating these parameters at spaced intervals and calculating the differences in the parameters over the intervals the progress of dissipation of an occlusion or recanalisation of a restriction may be conveniently measured. The changes in the parameters can be conveniently used to determine the  
30 effectiveness of the sonication procedure, in particular, that the procedure has effectively dissipated an occlusion or recanalised a restriction so that the cause of the reduced fluid flow has been removed substantially from the vessel. In particular, the rate of change of any parameter may be included in



the calculation of any index, marker, measure, or representation of the progress of the sonication.

Figure 7 shows a typical sequence of operation of an embodiment of the invention in apparatus and method for identifying and sonication a thrombosis in the following sequence of steps, wherein the number of the step below is indicated at its corresponding place in Figure 7.

1. Start ultra-sound occlusion-related detection and target treatment;
- 10 2. Ultrasonic Beam Focus Control.
3. Scan for Suspicious Region Of interest (SROI). The Doppler stroke-treatment ultrasound phased-array transducers can be steered across larger regions to enable a means to scan for SROI.
- 15 4. Once the SROI candidate(s) are detected the finer resolution focus mode can be applied to determine the Region Of Interest (ROI). The ROI as with SROI can be subjected to further FFT or acoustic footprint analysis, characterisation and comparison (with deviation consideration) and final operator verification.
- 20 5. Scan for ROI comprising finer beam focus and ultrasonic spectral (FFT), phase, amplitude or any combinational analysis thereof. FFT spectral "foot-print" or acoustic characteristic footprint, associated with occlusion blood flow can be detected firstly on the course scan and detect mode [SROI] Acquire ultrasonic data for archive, analysis, retrieval, remote view, remote control purposes.
- 25 6. Transform ultrasonic return echo data into frequency spectral (FFT), phase and/or amplitude characteristics. ROI can be detected by way of computing the acoustic or FFT foot print across a region using sweep mode and then utilisation representing characteristic of blood turbulence or flow characteristics associated with vascular partial or
- 30 total occlusion.
7. Compare acquisitioned ultrasonic acoustic echo data characteristics with those of reference fingerprints for likely acoustic characteristic representing stroke-related occlusion acoustic flow related turbulence.

8. Reference data base presenting FFT characteristics and ultrasonic characteristics or footprint associated with SROI or ROI detection determination.
9. Deviation Characteristics- being the allowable detection tolerances against the data base of acoustic "occlusion" "fingerprint" data base comparison events.
10. Using any combination of neural network, artificial intelligence, or other analysis methods compare reference data base of typical "finger-prints" of stroke-related occlusions; along with acceptable deviation characteristics, in order to compute valid detection of occlusion and co-ordinates for optimal treatment focus and targets.
11. Co-ordinate data associated with ROI and assonating target data available for phase array or other type of ultrasonic transducer focussing control.
12. Ultrasonically enhanced Thrombosis Treatment Operator validation and Focus Treatment Focus Targeting.
13. Once operator verification is acknowledged user can select to automatically lock in ultrasonic-enhanced thrombosis mode, where upon phase array multiple beam focus treatment can be applied.
14. User display and user interface allowing manual, automatic or computer assisted ultrasound stroke-related occlusion detection and/or treatment.
15. Knowledge decision base option for artificial intelligent occlusion detection and ultrasonic control analysis option. Artificial Intelligence reference to support neural network processing decision matrix. Can be updated by system expert users or remote intelligence base. Current system can be designated as expert user to enable artificial intelligence supporting increased accuracy in detection and control of stroke-related occlusion (emboli).
16. Spatial cycling or "massaging" modes possible with variation of frequency or sequences of treatment frequencies as well as variation of spatial positioning to enable optimal working at the edges and/or solid occluding material in order to control optimal diffusion and safe

agitation or dissipation of dissolving of material (minimise further occlusion with risk of large break-away material).

17. Treatment temporal analysis and progress tracking in order to enable adjustment for intensity or and power of ultrasonic treatment from most gentle and safest treatment to most aggressive and rapid emergency treatment modes.

18. Screen shows treatment target display marking of SROI and also audible or other local or remote system alert.

19. Screen target display marking of ROI and also audible or other local or remote system alert.

20. Screen target display marking of ROI and SROI and also audible or other local or remote system alert.

The invention includes apparatus having remote video capabilities for observing the output of ultrasound beams generated from an ultrasound transducer at a location remote to the subject on which the beams are focussed.

The apparatus include the possibility of remote manual adjustment to the control on ultrasound beam parameters.

The apparatus may include a three-dimensional bio-optical means wherein the ultrasound signal received by an ultrasound transducer is transformed into computer graphics for easy viewing and interpretation by an operator.

The apparatus may include a method for transforming TCD output signals into graphical representations for a computer or other viewing screen. It will be understood that the screen may be any screen capable of displaying a digital or analogue signal.

The invention includes an array of ultrasound-emitting elements wherein each element of said array is capable of focussing ultrasound waves at a focal point. The invention includes ultrasound elements that are piezo-electric crystals in an ultrasound transducer.

The invention may include apparatus operable with voice coil technology for the positioning of ultrasound transducers on a patient's head.

- 5 The invention includes an apparatus for TCD ultrasound that automatically or semi-automatically scans and maps the location of blood vessel occlusions, using the methods described herein. Said automatic or semi-automatic mapping is effected by the use of means, such as a computer database and program or programs in which normalative sound-wave data is stored for
- 10 automatic comparison with sound-wave data acquired from the sonication of an SROI or ROI according to the procedure illustrated in Figure 7. Said database may contain data representative of a two-dimensional or three-dimensional map for the SROI or ROI in a subject or a representative normalised subject. Said means may further include computer program or
- 15 programs for displaying representations of the acquired data in comparison with normalative data, such as on a video display unit. Said computer program or programs may suitable processing techniques for reflected ultrasound waves such as fast Fourier transformation techniques, and determining the most likely regions for occlusions by comparing fast Fourier outputs for free-
- 20 flowing or occluded vessels. Said video display unit may show a representation of the region being sonicated, preferably in real-time according to the information stored in the database. Said computer program may further display acquired sonication data on said video display unit to indicate the position of sonication in two-dimensional or three-dimensional space in
- 25 relation to known anatomical characteristics of a subject.

- The method of the invention includes a diagnostic capability to detect an occlusion either by way of the measurement of fluid flow in a ROI or turbulence in the vicinity of an occlusion. Said diagnostic capability may
- 30 include a comparison of sound-wave data indicating the presence of fluid spurts within a vessel or fluid flow rates associated with recanalisation of stenosis in such a way as to enable the distinction between the presence of an occlusion or a stenosis. Said diagnostic capability includes the calculation of fluid flow and turbulence in the region of the occlusion or stenosis by way of

using sound-wave data for measurement of any of fluid flow rate, fluid flow quantity, fluid turbulence, or intensity.

The apparatus or method further includes displaying an index, measure, 5  
marker, or series of markers or other suitable representation characteristic of  
the progress of recanalisation of a vessel during any or both of diagnosis or  
treatment on said video display unit. The apparatus or method further may  
include the incorporation of said index, measure, or series of markers into a  
means, such as a computer program, for optimising the at least one sound-  
10 wave beam incorporating at least one frequency in order to provide better  
control over the rate of recanalisation and sonication power.

The invention includes many embodiments. For example, the invention  
includes apparatus wherein a first ultrasound transducer is fixed in relation to  
15 a target occlusion characteristic of embolism in a blood vessel. A second  
ultrasound transducer is positioned in relation to said first transducer such that  
both transducers focus the emitted beams of ultrasound waves onto an  
occlusion in said blood vessel. The second transducer may be positioned  
using a servo device. It will be apparent to those skilled in the art that more  
20 than two ultrasound transducers may be included in the invention and that  
each transducer may be positioned relative to the others so that the target  
occlusion is located at a common focal point for the beams of ultrasound  
waves. Preferably the invention includes an array of transducers. Preferably  
the array is a structured array. The advantageous effect of the multiple  
25 ultrasound transducers with a common focal point will be to focus the  
maximum ultrasound energy on the occlusion and result in the most effective  
embolism dispersing treatment.

The invention provides a method to optimise the focus of the ultrasound beam  
30 or beams using servo-movement. One or more servo mechanisms and/or  
ultrasonic phased array transducer control systems can be deployed to enable  
a continuously variable positioning of focus point in order to enable optimal  
energy focus of one or more beams. The said energy focus is able to be  
divided at one or more precise locations with high spatial resolution in order to

focus energy away from healthy tissue (is desirable and as desirable), where at the same time focussing energy of a set of beams at the location of vascular occluding material, in order to disintegrate or diffuse or disperse said occluding material in an optimal and safe treatment manner.

5 Furthermore, the at least one treatment beam of ultrasonic frequency can comprise one or more frequencies optimized for functions enabling any sequence or simultaneous combination of optimal a) gaseous partial or total occlusive material detection; b) solid material partial or total occlusive material  
10 detection; or c) gaseous partial or total thrombolysis and recanalisation of partial or fully occluded blood vessels.

The invention provides an apparatus and method to facilitate the safe dispersion or dissolving of an occlusion (thrombolysis or recanalisation of  
15 blood vessel). One of the risks associated with ultrasonically enhanced thrombolysis is the risk that dislodged occluding material can "break away" or disintegrate in large and unsafe particle sizes, which in turn can cause further occlusion or risks of occlusion or partial vessel blockages. In particular, vessel blockages such as within the legs or lower body may be recanalised  
20 and cause particles to travel higher in the circulatory system such as in the brain. In these regions the vessels can be smaller and lead to further blockages and more serious consequences such as ischaemic stroke.

The invention provides an apparatus and method for simultaneous diagnosis  
25 and treatment to regulate towards safe thrombolysis and recanalisation of blood vessels. The present invention includes the diagnosis or identification of a particle or total occlusion of a vessel while at the same time or separately providing ultrasonically enhanced thrombolysis or vessel recanalisation.

30 The focus adjustment and targeting of the at least one ultrasonic beam, along with accurate spatial resolution and power control (of targeted ultrasound treatment) enables a controlled dispersion of occluding material in a vessel by allowing different patterns or massaging (movement of beam focus around, over and near occluding material) and different ultrasonic frequencies or  
35 combination or sequences of frequencies (different frequencies effect different

material types and also effect the dispersion rate and size of dispersed occluding material particles) or any combination thereof to be applied to the region of vessel occlusion or partial occlusion. The treatment of an occluded vessel can thus be controlled, targeted and regulated in order to minimize the particle dispersion size and risk for further occlusion.

The present invention enables one or more ultrasonic frequencies either sequentially or simultaneously to be generated as a means to both enhance diagnosis and imaging and also enhance ultrasonic vessel recanalisation treatment.

The present invention includes a three-dimensional mapping capability and tracking of the maximum power generation by the at least one ultrasound transducer. This enables a register or matrix representing the computation of ultrasonic power generation at any point in time and any spatial location under scan. Said "matrix or register" computes the probable power dissipation of ultrasound scan beams based on the beam dispersion characteristics. Furthermore, the intersection of beams along with the focus characteristics are computed and provide a resulting reference data set to enable or to ensure that maximal safe power thresholds are achieved at all locations and that the additional ultrasonic power required to rapidly diffuse vessel occlusion is only directed specifically where required and where safe, i.e., targeted at surrounding healthy tissues.

The present invention provides the capability to enable ultrasonically-enhanced thrombolysis and vessel recanalisation to be moderated in treatment intensity (power) in accordance with or in harmony with "clot-busting drug" characteristics of action. This consideration can minimize risk of side effects of each said treatment, such as haemorrhage risk with "clot-busting drug" treatment, or excessive ultrasound power and cell harm with ultrasound treatment.

The present invention provides that data such as the drug administration rate, drug composition or type, and patient risk category to haemorrhage, such as

haemophiliacs, can be entered into a clot drug-profusion device and also ultrasound power and focus control, for example.

The present invention most advantageously enables the intravenous or  
5 manual administration of clot-busting drugs to be regulated or monitored in  
such a manner as to regulate the balance between the strength of the clot  
balanced or administration optimized to minimize the risk of side effects the  
occluding material and minimally targeted clot-busting drug administration,  
with risks of haemorrhage side effects, with the aggressive or high powered  
10 application of ultrasonically enhanced thrombolysis treatment, with the risk of  
healthy cell harm and also dispersion of further clot-causing material.

The present invention enables the ultrasonic control and the "clot-busting  
drug" administration to be servo-controlled in such a manner that optimal  
15 speed of thrombolysis and recanalisation of the vessel(s) and also optimal  
safety or mitigation to patient risks are possible.

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**Claims**

1. Apparatus for imaging or treatment of occlusions or restrictions in vessels using sound waves, comprising:  
5       at least one sound transducer member including at least one sound-emitting element for producing at least one sound wave beam;  
      means to adjust the parameters of said at least one sound wave beam;  
      means to spatially locate said at least one sound-emitting element;  
      means to automatically or semi-automatically focus sound waves  
10       generated by said at least one sound-emitting element into a beam;  
      and  
      means to accept sound signals from sound-emitting element or elements.
- 15   2. Apparatus according to claim 1 including means to move said at least one transducer member.
3. Apparatus according to claim 2 including means to control movement of said at least one transducer member automatically or semi-  
20       automatically.
4. Apparatus according to any one of claims 1 to 3 wherein the sound-emitting element and the means to accept sound signals are the same.
- 25   5. Apparatus according to any one of claims 1 to 4 wherein the at least one sound beam is pulsed.
6. Apparatus according to any one of claims 1 to 5 wherein the at least one sound wave beam is focussed electronically.
- 30   7. Apparatus according to any of claims 1 to 6 wherein two or more sound-emitting elements form an array.
8. Apparatus according to claim 7 wherein the array is curved.

- 5 9. Apparatus according to claim 7 or claim 8 wherein the at least one sound beam incorporates a plurality of frequencies of sound waves in combinations of concurrent frequencies generated by the sound-emitting elements in the array or in series of frequencies over time.
- 10 10. Apparatus according to any one of claims 7 to 9 wherein the array is of sound-emitting elements is any of fixed position, adjustable position, or scanning position.
11. Apparatus for imaging or treatment of occlusions or restrictions in vessels using sound waves, comprising:  
at least one sound transducer member including at least one sound-emitting element for producing at least one sound wave beam;  
15 means to adjust the parameters of said at least one sound wave beam;  
means to orient said at least one transducer member;  
means to focus sound waves generated by said sound-emitting element into a beam; and  
means to accept sound signals from sound-emitting element or  
20 elements.
- 25 12. Apparatus according to any of claims 1 to 10 wherein the sound-emitting elements are moveable singly or in coordinated manner including simultaneously.
13. Apparatus according to any of claims 1 to 10 or claim 12 wherein at least one sound transducer member is servo-controlled.
- 30 14. Apparatus according to claim 13 wherein the means for servo-control includes feedback control.
15. Apparatus according to any one of claims 13 or 14 wherein the servo-control means is self-tracking and including means for determining out-of-range positioning of said at least one sound-emitting element.

16. Apparatus according to claim 15 wherein the feedback control incorporates a signal characteristic any one or a combination of an occlusion in a fluid flow or a restriction in a fluid flow.
- 5 17. Apparatus according to any one of claims 7 to 10 further including a plurality of sound-emitting elements in at least two layers of at least two arrays.
- 10 18. Apparatus according to any one of claims 11 to 13 wherein each transducer member is operable to enable a continuously adjustable focus point comprising of two or more sound beams emitted by at least two sound-emitting elements.
- 15 19. Apparatus according to any one of claims 1 to 18 including means to transform a sound signal from analogue to digital forms or digital to analogue forms.
- 20 20. Apparatus according to any one of claims 1 to 19 including means to store transformed digital data.
21. Apparatus according to any one of claims 1 to 20 including means to display analogue or digital data.
- 25 22. Apparatus according to claim 20 including video display means for displaying data or indicating to an operator of the status of the sonication.
- 30 23. Apparatus according to any one of claims 1 to claim 22 including voice coil control means.
24. Apparatus according to any one of claims 1 to 23 wherein said apparatus is operable in real-time or near real-time.

25. Apparatus according to any one of claims 1 to 24 including fiducial registration means for maintaining targeted sonication and communication means for communicating between fiducial registration means and servo-control means.
- 5
26. Apparatus according to claim 25 including means for prompting an operator when said apparatus is out of registration.
27. Apparatus according to claim 25 wherein the communication means
- 10 includes wireless communication capacity.
28. Apparatus according to any one of claims 1 to 27 for use in detecting and sonicating vessels in the brain of a being.
- 15
29. Apparatus according to any one of claims 1 to 28 wherein the sound waves are ultrasound waves.
30. Method for locating an occlusion in a vessel or a restriction in a vessel, including the steps of:
- 20 identifying regions of a body in which an occlusion or restriction might be found;
- selecting a region of interest for sonication with sound waves;
- sonicating the region of interest with at least one sound-wave beam by moving said sound-wave beam across said region of interest;
- 25 receiving reflected sound signals from said region of interest; and
- calculating the Doppler effect parameters of flow and turbulence from said reflected sound signals.
31. Method for distinguishing anatomical features of an organism including
- 30 the steps of:
- sonicating a region of interest in a subject with at least one sound-wave beam;
- whereby the frequency of said at least one sound-wave beam is suitable for determining a particular tissue type;

receiving reflected sound signals from said region of interest;  
calculating the Doppler effect parameters of said reflected sound  
signals; and  
characterising said Doppler effect parameters according to parameters  
associated with known tissue types.

5

32. The method according to claim 31 whereby a sound-wave frequency  
suitable for a particular tissue type is generated by at spaced intervals  
with a different frequency suitable for a different tissue type.

10

33. The method according to claim 31 whereby at least two frequencies  
suitable for at least two tissue types are generated simultaneously.

15

34. The method according to any one of claims 30 to 33 including the step  
of modifying the characteristics of the at least one sound-wave beam to  
target a region of interest wherein the Doppler effect parameters are  
indicative of reduced flow attributable to an occlusion or a vessel  
restriction.

20

35. The method according to any one of claims 31 to 34 including the step  
of calculating any one or a combination of fluid flow rate, fluid flow  
quantity, or turbulence from said Doppler effect parameters.

25

36. The method according to claim 35 including the step of sonicating the  
region of interest thereby causing agitation or dissipation of the  
occlusion by prolonged sonication or recanalisation of a vessel  
restriction.

30

37. The method according to claim 36 including the step of automatically or  
semi-automatically evaluating and optimising the effect of sonication for  
feedback modification of said at least one sound-wave beam  
incorporating tissue safety guidelines.

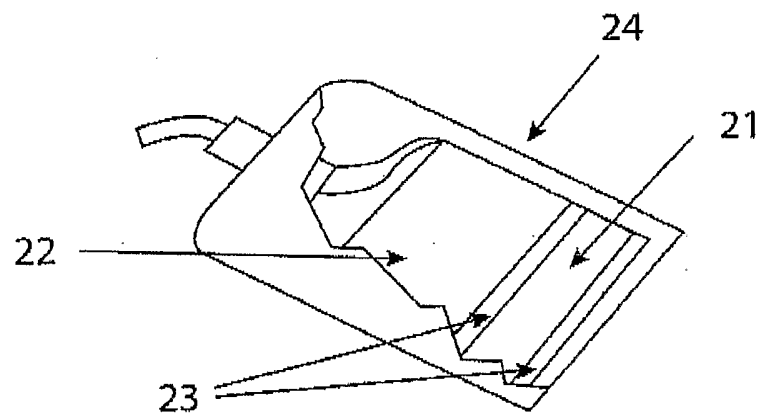
38. The method according to any one of claims 36 or 37 including the step of calculating and displaying any one or a combination of an index, measure, or marker or suitable representation indicating the progress of dissipation of an occlusion in a vessel or recanalisation of a vessel having an occlusion or restriction using said Doppler effect parameters.
39. The method according to claim 38 including carrying out calculating and displaying the result of any calculation at spaced intervals.
40. The method according to claim 39 wherein the step of automatically or semi-automatically evaluating and optimising the effect of sonication includes maintaining a fiducial registration between sound-wave beams and a registration signal.
41. The method according to claim 40 including the step of indicating when the sound-wave beams are out of registration.
42. The method according to any of claims 30 to 41 wherein the region of the body is the head.
43. The method according to claim 42 wherein the region of the head is the circle of Willis.
44. The method according to any of claims 30 to 43 wherein two or more sound-wave beams are moved across said region of interest in either a simultaneous or sequential manner.
45. The method according to any of claims 30 to 43 wherein the at least one sound-wave beam is pulsed.
46. The method according to any of claims 30 to 39 wherein the parameters calculated from said reflected sound signals are any one or a combination of power, spectral, amplitude, phase coupling or

frequency characteristics characteristic of a spatial representation of anatomical features in said region of interest or occlusive material.

- 5 47. The method according to claim 46 wherein the power or amplitude spectral analysis are carried out using Fast Fourier Transform techniques.
- 10 48. The method according to any one of claims 46 or 47 including the step of comparing calculated parameters with known parameters of anatomical features in said region of interest.
- 15 49. The method according to any one of claims 30 to 48 wherein the at least one sound wave beam is continuous.
- 20 50. The method according to claim 49 wherein the at least one sound wave beam is initially transmitted with a first frequency or amplitude and subsequently with periodic changes resulting a second and further frequency or frequencies or amplitude(s) relative to the first beam frequency maintaining the mark-to-space ratio of the apparent changing and pulse formation.
- 25 51. The method according to any one of claims 30 to 50 wherein the sound-wave beam is comprised of ultrasound waves.
- 30 52. The method according to any one of claims 30 to 50 including the step of conducting a spatial voxelated analysis of received signals.
53. The method according to any one of claims 30 to 52 wherein the steps are carried out automatically or semi-automatically substantially without human control.

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Figure 1





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Figure 2a

Near-field lengths and far-field divergence  
of commercially available transducers

Transducer diameter (mm)	Frequency (MHz)	Near-field length (cm)	Far-field divergence
8	10	10.4	1"21'
8	5	5.2	4"25'
12	2.5	1.1	1"48'
12	5.0	11.7	1"48'
15	1.0	9.1	2"52'
20	1.0	6.5	5"23'

Figure 2b

Approximate Velocities of  
Ultrasound In Selected Material

Material	Velocity (m/sec)
Fat	1.475
Brain	1.560
Liver	1.570
kidney	1.560
Spleen	1.570
Blood	1.570
Muscle	1.580
Lens of Eye	1.620
Skull Bone	3.360
Soft Tissue (Mean Value)	1.540
Air	331

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Figure 3a

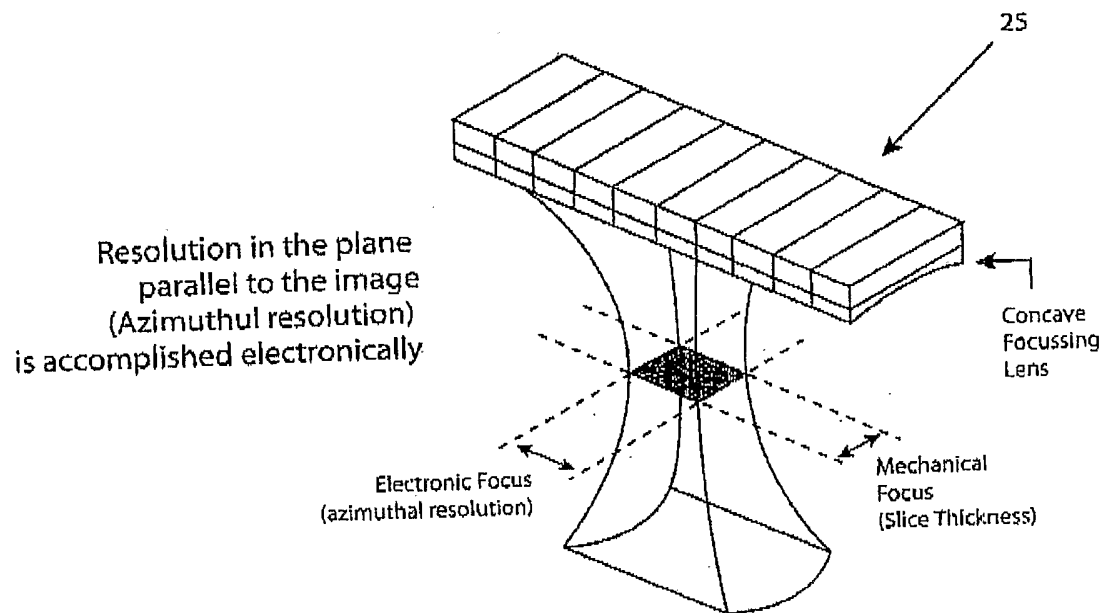
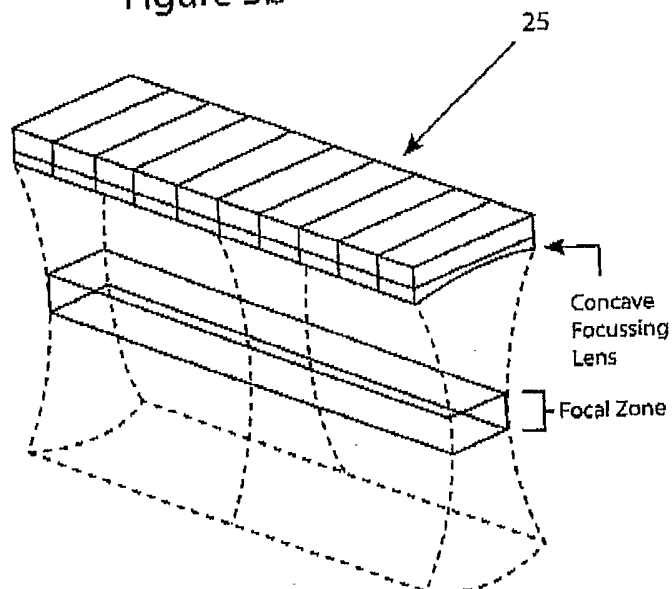


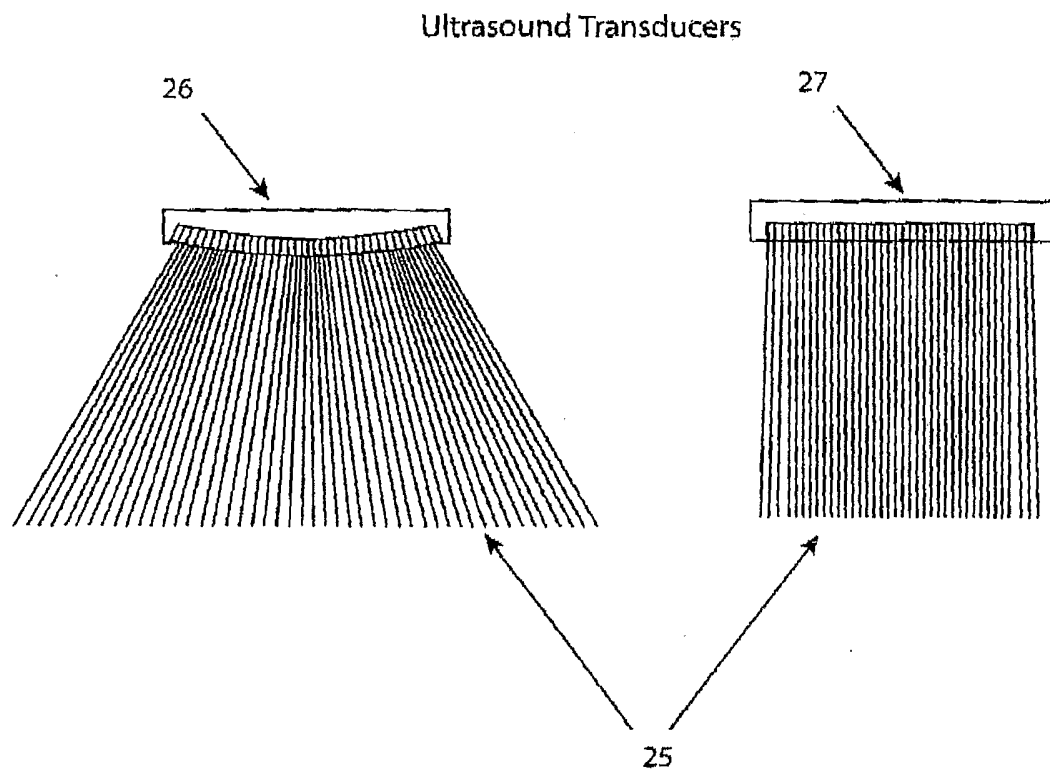
Figure 3b

A concave lens is used to focus a linear array



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Figure 4



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Figure 5

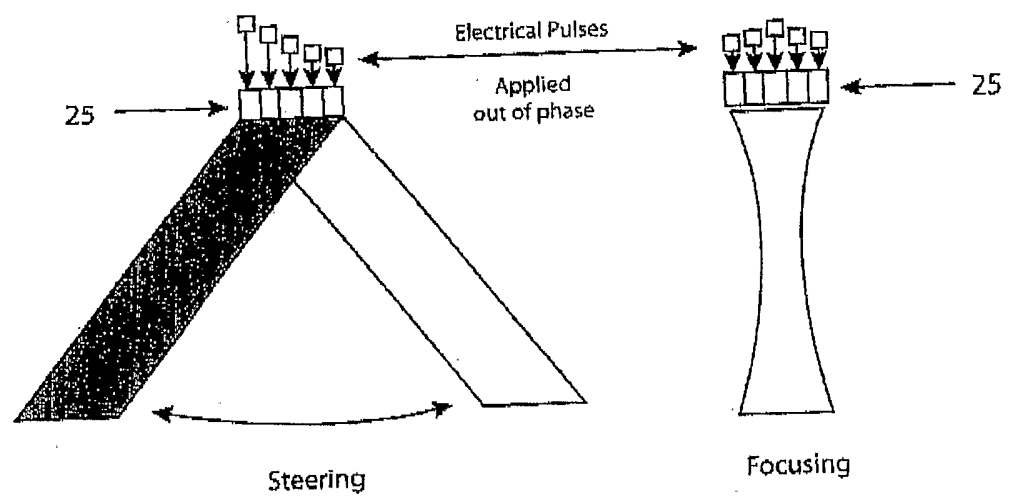
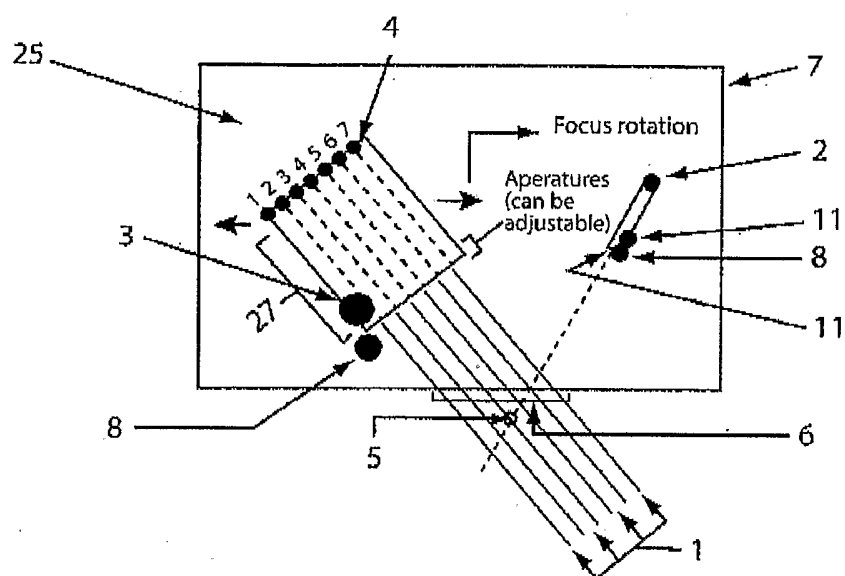
Ultrasound Transducers  
Phased Array

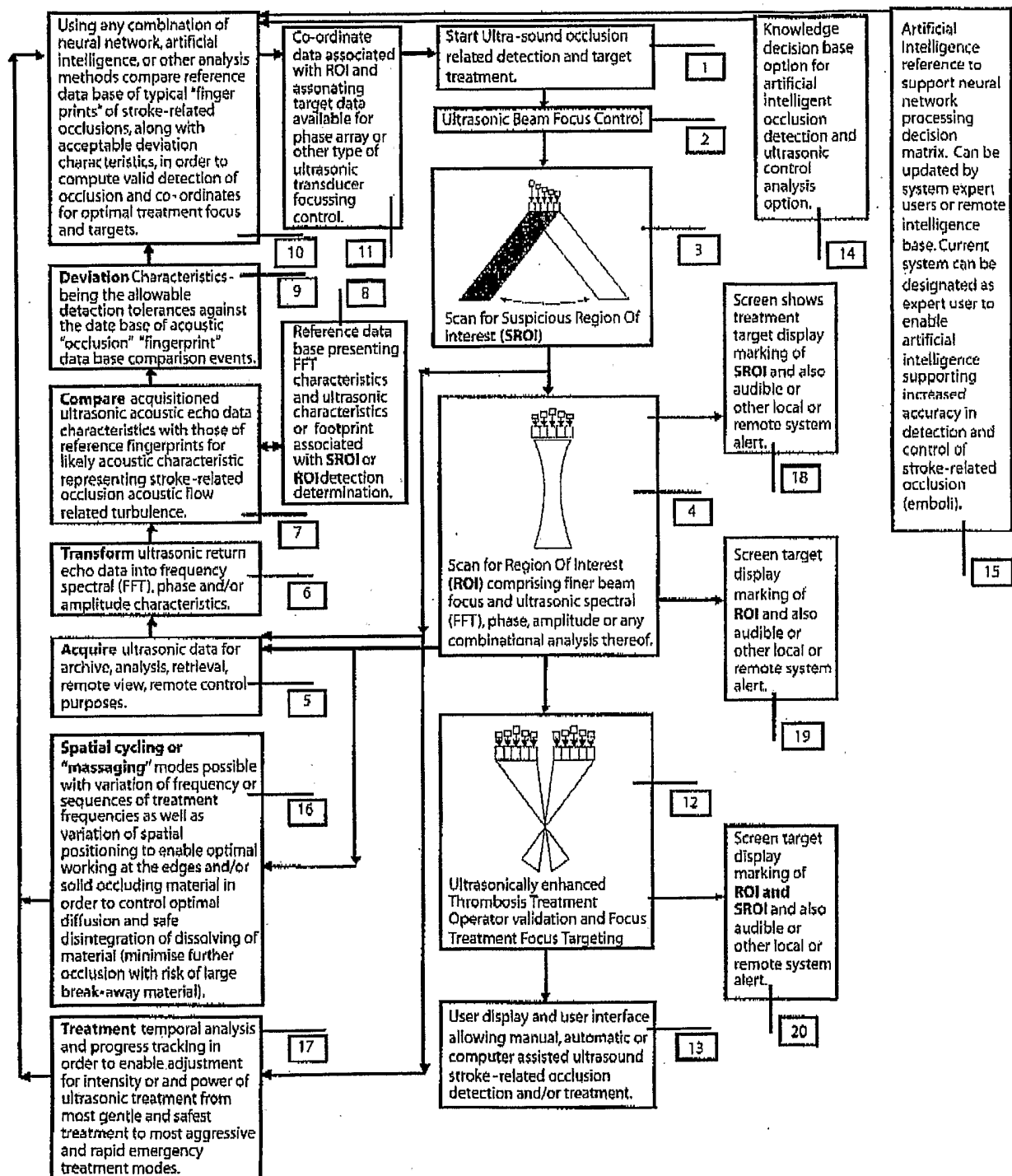
Figure 6



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Figure 7

## TYPICAL SEQUENCE OF OPERATION USING ELECTRONICALLY CONTROLLED PHASED ARRAY TRANSDUCERS



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Figure 8a

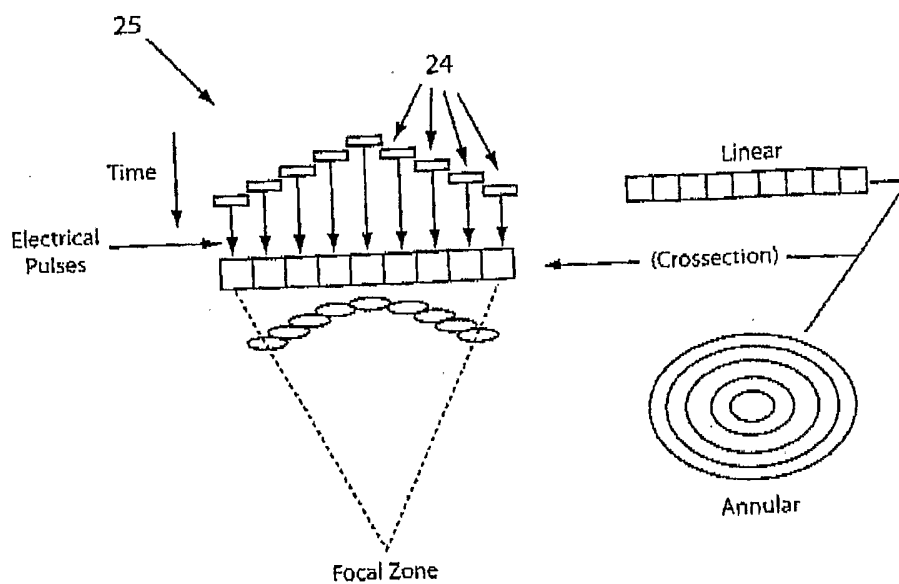
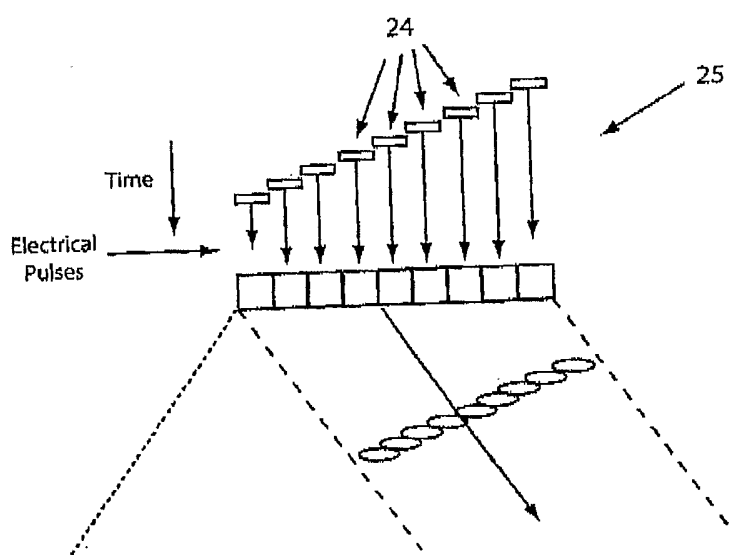


Figure 8b



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Figure 9a

## Pulse rate

- Number of separate pulses that are produced each second
- Remember – the transducer must act as a transmitter and a receiver
- Common pulse rate for abdominal imaging is 1,000 pulses/second
- Different and unrelated to frequency

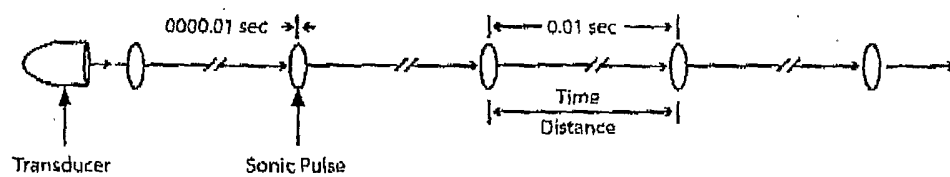
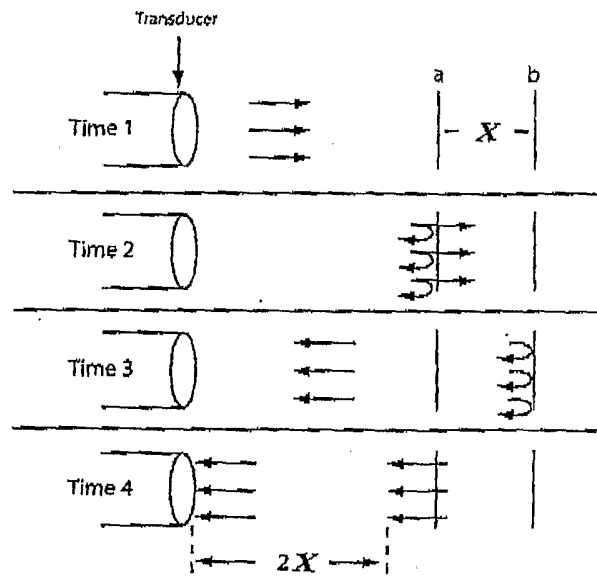


Figure 9b

## Depth (axial) Resolution

This figure shows a time sequence of an ultrasonic pulse resolving two surfaces, a and b, separated by  $X$  distance





## INTERNATIONAL SEARCH REPORT

International application No.

PCT/AU2006/000620

## A. CLASSIFICATION OF SUBJECT MATTER

Int. Cl. *A61B 8/08* (2006.01) *A61B 8/06* (2006.01)  
*G01N 29/26* (2006.01) *A61N 7/00* (2006.01)

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)

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 practicable, search terms used)

DWPI: IPC A61B & Keywords (Image, Scan, Vessel, Occlusion, Blockage, Ultrasound, Sonication, Transducer, Locate, Spatial, Focus, Array, Automatic) and similar terms; Espac & Keywords (Transcranial, Ultrasound, Apparatus, Diagnosis, Treatment, Occlusion, Vessel)

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 5844140 A (SEALE) 1 December 1998 See whole document.	1-53
X	WO 2001/069283 A2 (THE REGENTS OF THE UNIVERSITY OF CALIFORNIA) 20 September 2001 See whole document.	1, 4-11, 17, 18-20, 28-29
X	WO 2001/032258 A2 (UNIVERSITY OF CINCINNATI) 10 May 2001 See whole document.	1, 4, 6-11, 17, 29-31
X	US 6186949 B1 (HATFIELD et al.) 13 February 2001 See whole document.	1-12, 17, 19-24, 29-35, 42, 45, 51

☒ Further documents are listed in the continuation of Box C☒ See patent family annex

* Special categories of cited documents:	"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"A" document defining the general state of the art which is not considered to be of particular relevance	"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"E" earlier application or patent but published on or after the international filing date	"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"&" document member of the same patent family
"O" document referring to an oral disclosure, use, exhibition or other means	
"P" document published prior to the international filing date but later than the priority date claimed	

Date of the actual completion of the international search  
28 August 2006

Date of mailing of the international search report  
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Name and mailing address of the ISA/AU  
 AUSTRALIAN PATENT OFFICE  
 PO BOX 200, WODEN ACT 2606, AUSTRALIA  
 E-mail address: pct@ipaustalia.gov.au  
 Facsimile No. (02) 6285 3929

Authorized officer  
**KAREN VIOLANTE**  
 Telephone No : (02) 6283 7933

## INTERNATIONAL SEARCH REPORT

International application No.

PCT/AU2006/000620

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 5379770 A (VAN VEEN) 10 January 1995 See whole document.	1, 4-11, 19-24, 28-35, 42, 47, 51
X	WO 1989/007907 A1 (LABORATORY EQUIPMENT CORP.) 8 September 1989 See whole document.	1-4, 6, 11-12
X	US 3735755 A (EGGLETON et al.) 29 May 1973 See whole document.	1-12, 17-24, 28-29
A	WO 2004/103184 A2 (BORDERS NHS BOARD) 2 December 2004 See whole document.	
A	WO 2000/049946 A1 (ECHOCATH INC) 31 August 2000 See whole document.	
A	US 5951476 A (BEACH) 14 September 1999 See whole document.	
A	US 6547737 B2 (NJEMANZE) 15 April 2003 See abstract and figures.	
A	US 5409005 A (BISSONNETTE et al.) 25 April 1995 See abstract and figures.	

# INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No.

PCT/AU2006/000620

This Annex lists the known "A" publication level patent family members relating to the patent documents cited in the above-mentioned international search report. The Australian Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

Patent Document Cited in Search Report				Patent Family Member			
US	5844140						
WO	2001069283	AU	45831/01	EP	1330815	US	6490469
		US	2001037075				
WO	2001032258	AU	15799/01	CA	2389669	EP	1225837
US	6186949	DE	10119814	DE	19913198	EP	0947853
		EP	1046928	IL	129153	JP	11318902
		JP	2000316860	JP	2000333957	JP	2002000607
		US	6074348	US	6210332	US	6312384
		US	6406430				
US	5379770						
WO	1989007907	EP	0425495	EP	0596513	US	4951653
		US	5054470				
US	3735755						
WO	2004103184	AU	2004241786				
WO	2000049946	US	6176829				
US	5951476						
US	6547737	US	2002103436				
US	5409005						
Due to data integration issues this family listing may not include 10 digit Australian applications filed since May 2001.							
END OF ANNEX							