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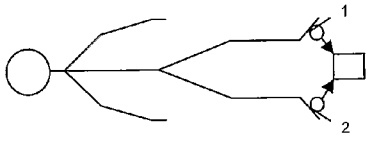
(54) Title: DVT DETECTION



(57) Abstract: A device comprising a light transmission and detection system having transducers (1, 2, 7, 8), control means (5) and output means (7). The transducers are placed at various sites on the body of a patient and the light absorbed and/or reflected at these sites is measured and signals related to vasomotor activity are collected. The output can take the form of a detailed display of the vasomotor signals collected from the transducers (1, 2, 7, 8) to a simple indication of a condition present or absent. For, example, the presence of a unilateral DVT can be detected by measuring the dissimilarity between two transducer signals from the soles of a patient's feet. The invention can also be used to provide an indication or not of for example, DVT and diabetic peripheral neuropathy.

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DVT Detection

The present invention relates to the detection of a range of clinical conditions including Deep Vein Thrombosis (DVT) and diabetic peripheral neuropathy, critical limb ischaemia, autonomic neural function and arterial and venous disease by the assessment of the vasomotor activity in the micro-circulation at individual sites on a body, and in particular, the detection of Deep Vein Thrombosis (DVT) and diabetic peripheral neuropathy.

Deep vein thrombosis (DVT) in the legs is a condition whereby a blood clot, develops in a vein causing partial or complete blockage of the vessel. The cause of the clot can be due to vessel damage, either from surgical procedures or trauma, or from a period of haemostasis due to prolonged periods of inactivity (e.g. long haul flight, disability). The perceivable consequences of a DVT can range from mild pain and swelling to a fatal pulmonary embolism.

Known tests used in clinical practices for the detection of DVT include imaging tests such as venography and duplex ultrasonography. Venography requires the injection of a radio opaque imaging medium and X-ray imaging requiring expert interpretation and is hazardous and uncomfortable to the patient, time consuming, expensive and not suitable for primary care or a General Practitioner (GP). Similarly, Duplex ultrasonography is a time consuming and expensive process not suitable for primary care or for GPs requiring highly skilled practitioners.

Plethysmography is a known test which is low cost, relatively quick, and is used in trained primary care or by a trained GP. However plethysmography requires the patient to exercise during the test which is not suitable for all patients and the test requires an expert operator and is not always reliable. There is also D-dimer assay test that

measures the clotting agents in blood and is recommended to be used in conjunction with other tests. The plethysmography and D-dimer tests are used as a front line screening means to remove as many patients as possible without a DVT from progressing to the more onerous imaging tests of duplex ultrasonography or venography.

The invention seeks to make improvements.

Accordingly, the present invention provides a device comprising a light transmission and detection system to assess vasomotor activity in the micro-circulation at individual sites on a body for the monitoring and assessment of a range of clinical conditions including suspected DVT, diabetic peripheral neuropathy, critical limb ischaemia, autonomic neural function and arterial and venous disease.

Vasomotor activity in the micro-circulation is the continuous process of contraction and dilatation of the micro-vessels and serves several important functions including blood pressure regulation, temperature regulation, tissue oxygenation and nutrition. The control of this process is both local and systemic. Local control is activated by chemical signalling from the adjacent tissues while the systemic control originates from the autonomic sympathetic nervous system, principally for the regulation of core temperature and systemic blood pressure. The resulting local blood volume variation provides information on many of the biological processes both locally and systemically.

In a preferred embodiment, the invention comprises a light transmission and detection system including wave transducers, the wave transducers placed at one or more sites on a body, control means to measure the light absorbed and/or reflected at the or more sites and provide signals relating to the absolute value at the or more sites

and/or the differential value between the sites. Preferably, the transducers are infra red wave transducers.

The present invention uses the transducers to monitor the micro-circulation blood volume variation beneath the transducer continuously. The light absorption is proportional to the volume of blood or, conversely, light reflection is inversely proportional to blood volume. For a resting patient in a stable environment, either seated or supine, the major changes of blood volume are manifestations of systemic control. Further, in the limbs, the systemic vasomotor control is symmetrical. Therefore, by placing a transducer on the sole of each foot of a healthy subject, the signal from each transducer will be similar if not identical. The presence of a unilateral DVT can be detected by measuring the dissimilarity between the two transducer signals as the distal volume of the affected leg is increased due to increased outflow resistance. This imposes altered frequency and phase characteristics in the vasomotor variation of the affected leg and therefore affects the bilateral symmetry.

In another aspect of the invention the signals received from the transducers are used in the assessment of autonomic systemic and peripheral neuropathy. Conventional systemic, autonomic function testing, analyses heart rate variability, usually derived from the ECG waveform. However, cardiac pulsation can be seen in the signal collected at most points on the skin around the body using the transducer. Therefore, heart rate variability can be derived from this signal. Analysis of the variation in the heart rate component can then be compared to the low frequency variation of the signal from the transducer, allowing a direct comparison of peripheral and systemic autonomic function. In the healthy subject both sources of variation should be similar, whereas in the patient

suffering with peripheral neuropathy alone there will be a dissimilarity.

The advantages of using vasomotor activity in the feet to assess DVT, vascular disease and neurological function include the ability to use a passive test requiring no movement on the part of the patient. Preferably, the neurological function test is augmented by stress testing such as valsalva manoeuvre or mild graduation of exhalation impedance. The sites to be used on the patient's body are easily accessible, requiring low cost instruments, lower level of skill than existing tests and providing reliable results.

To date, there is little work published on the use of vasomotor activity for the assessment of clinical conditions such as those of the present invention due to the poor understanding of vasomotor activity and related biological processes. We have found that the vasomotor signal provides valuable information concerning the many biological processes occurring simultaneously within healthy and unhealthy bodies.

The invention will now be described by way of example only, with reference to the following drawings, of which:

Figure 1 shows the light transmission and detection system according to the invention;

Figure 2 shows a block diagram of the transducers in Figure 1;

Figures 3a, b, c are schematic views of a preferred embodiment of the invention in Figure 1 applied to different sites on a patient;

Figure 4 is a signal output from the embodiment as applied in Figure 3a;

Figure 5 shows another preferred embodiment of the invention;

Figure 6 shows the output from the embodiment as shown in Figure 5 from the various sites of the legs of a patient; and

Figure 7 shows the signal response to increased breathing impedance and hand grip.

Figure 8 shows the vasomotor signal and extraction of the heart rate variation.

Referring to Figures 1 and 2, the invention comprises a light transmission and detection system including transducers 1, 2 comprising an LED and photo-detector with suitable amplifiers 3, 4 as shown in Figure 2. Once the transducers 1, 2 are attached to the skin the central control unit 5 calibrates them by driving the LED 1 with a voltage appropriate to detect a mid-scale voltage from the photo-detector 2. The photo-detector 2 signals are digitised by A/D1 and A/D2. The drive voltages for the LEDS are produced from the output of D/A1 and D/A2. Once the calibration process is complete the central control unit 5 collects data from the photo-detector 4 (Figure 2) at a sampling rate appropriate for the application. For DVT detection a sample rate of 6 Hz is used. A user input device 6 such as a keypad and a display for output, for example an LCD screen or LED indicators or similar is used. There is also provided an input/output port for PC connection, printer or other form of data logging device.

Figures 3a to c show a preferred embodiment of the invention using a two channel system using two transducers 1, 2 for differential signal analysis. For the purpose of DVT detection, the transducers 1, 2 are positioned on the soles of the feet of a patient as shown in Figure 3a. The configuration of 3b can give an indication of the approximate location of DVT. If the vasomotor signals are similar the DVT will be located in the thigh whereas if the vasomotor signals are dissimilar the DVT will be located in

the calf. The arrangement in Figure 3c indicates the pulse transit time between the upper and lower extremities and thus an indication of arterial stiffness. Figure 4 shows the signal derived from the soles of the feet of a healthy subject using a two channel system. The signal from each transducer is similar if not identical. The presence of a unilateral DVT is detected by measuring any dissimilarity between the two signals.

The output presented to the user can take the form of a detailed display of vasomotor signals collected from the transducers 1, 2 as shown in Figure 4 to a simple indication of a condition being present or absent. The display can be configured to the application.

The sampling rate of the transducer 1, 2 signals is such that the heart rate component can be resolved to within +/- 1 ms or better if the heart rate is of interest in the assessment being performed, for example in autonomic function testing. Otherwise sampling frequencies that meet the Nyquist requirements are adequate.

The signals acquired from each transducer 1, 2 are subject to appropriate analytical algorithms. The signals are subject to amongst others complex demodulation a mathematical technique used for investigating the vasomotor activity centred at specific frequencies with a bandwidth chosen in accordance with the application, for example DVT detection. The output of the complex demodulation algorithm consists of an amplitude signal and a phase signal which when combined, produce a time varying signal modulated by both amplitude and phase with limited bandwidth, all centred on the demodulating frequency.

As well as the arrangements shown in Figures 3a to c, another preferred embodiment has two further transducers 7, 8 applied behind the knees for a four channel system as shown in Figure 5. The signals are passed through the

stages of signal pre-processing including filtering and DC removal followed by complex demodulation at a set of chosen frequencies, for example 8 to 30 cycles per minute. The mean absolute phase differences (MAPD) from the right foot (RF) and the left foot (LF) are calculated for each frequency to produce a spectrum RFLF(MAPD) and the RFLF(MAPD) is then used by a pattern classifier such as a pre-trained artificial neural network to provide an output on a screen that there is either "DVT PRESENT" or "DVT NOT PRESENT".

For a four channel system as shown in Figure 5, there will be six MAPDs as shown in Figure 6:-

Right Foot Left Foot : RFLF = mean(abs(RF(Φ) - LF(Φ))),
Right Knee Left Knee : RKLK = mean(abs(RK(Φ) - LK(Φ))),
Right Foot Right Knee : RFRK = mean(abs(RF(Φ) - RK(Φ))),
Left Foot Left Knee : LFLK = mean(abs(LF(Φ) - LK(Φ))),
Right Foot Left Knee : RFLK = mean(abs(RF(Φ) - LK(Φ))),
Right Knee Left Foot : RKLF = mean(abs(RK(Φ) - LF(Φ))),

giving six times the diagnostic information of the two channel system, described above.

In addition to detecting DVT, the present invention can monitor and assess a range of clinical conditions including diabetic peripheral neuropathy, critical limb ischaemia, autonomic neural function and arterial and venous disease.

In each of these conditions the vasomotor activity of the micro circulation possesses a unique signature which is extracted and assessed using the appropriate signal processing algorithms. These algorithms are tuned to the appropriate frequency bands determined by the clinical condition of interest. The algorithms exploit the property of vasomotor symmetry between the left and right feet and also use the similarity between the low frequency components of the vasomotor activity and the low frequency components of heart rate variation. As shown in Figure 8, the device according to the invention, extracts from the

vasomotor signal the heart rate variation and direct comparison of the simultaneous low frequency heart rate variation and the low frequency vasomotor variation provides information relating to diabetic sympathetic neuropathy, any dissimilarity between the two components indicating diabetic sympathetic neuropathy.

Figure 7 shows the changes in vasomotor activity related to increased breathing resistance and the hand grip test of a healthy person. These tests affect systemic blood pressure and cardiac output which in turn cause neurologically mediated responses in heart rate and peripheral vasomotor activity as observed with the transducers on the soles of the feet. Any changes from the signals in Figure 7 between the resting phase and the increased breathing resistance and the hand grip test will indicate diabetic sympathetic neuropathy since the pathology of the sympathetic nerve fibres which innovate the micro-blood vessels within the feet will cause significant change in vasomotor behaviour.

CLAIMS

1. A device comprising a light transmission and detection system to assess vasomotor activity at individual sites on a body for the monitoring and assessment of a range of clinical conditions including suspected DVT and diabetic peripheral neuropathy.

2. A device as claimed in claim 1, wherein the device comprises a multi channel light transmission and detection system, including one or more wave transducers, the wave transducers placed at one or more sites on a body, control means to continuously measure the light absorbed at the or more sites and provide signals relating to the absolute value at the or more sites.

3. A device as claimed in claim 1, wherein the device comprises a multi channel light transmission and detection system, including one or more wave transducers, the wave transducers placed at one or more sites on a body, control means to continuously measure the light reflected at the or more sites and provide signals relating to the absolute value at the or more sites.

4. A device as claimed in claim 2, wherein the control means measure the light absorbed at the or more sites and provide signals relating to the differential value between the sites.

5. A device as claimed in claim 3, wherein the control means measure the light reflected at the or more sites and provide signals relating to the differential value between the sites.

6. A device as claimed in claims 1, 2 or 3 wherein the signals relating to the simultaneous low frequency heart rate variation and the low frequency vasomotor variation are extracted and compared.

7. A device as claimed in any one of the preceding claims wherein the transducers are infra red wave transducers.

Figure 1

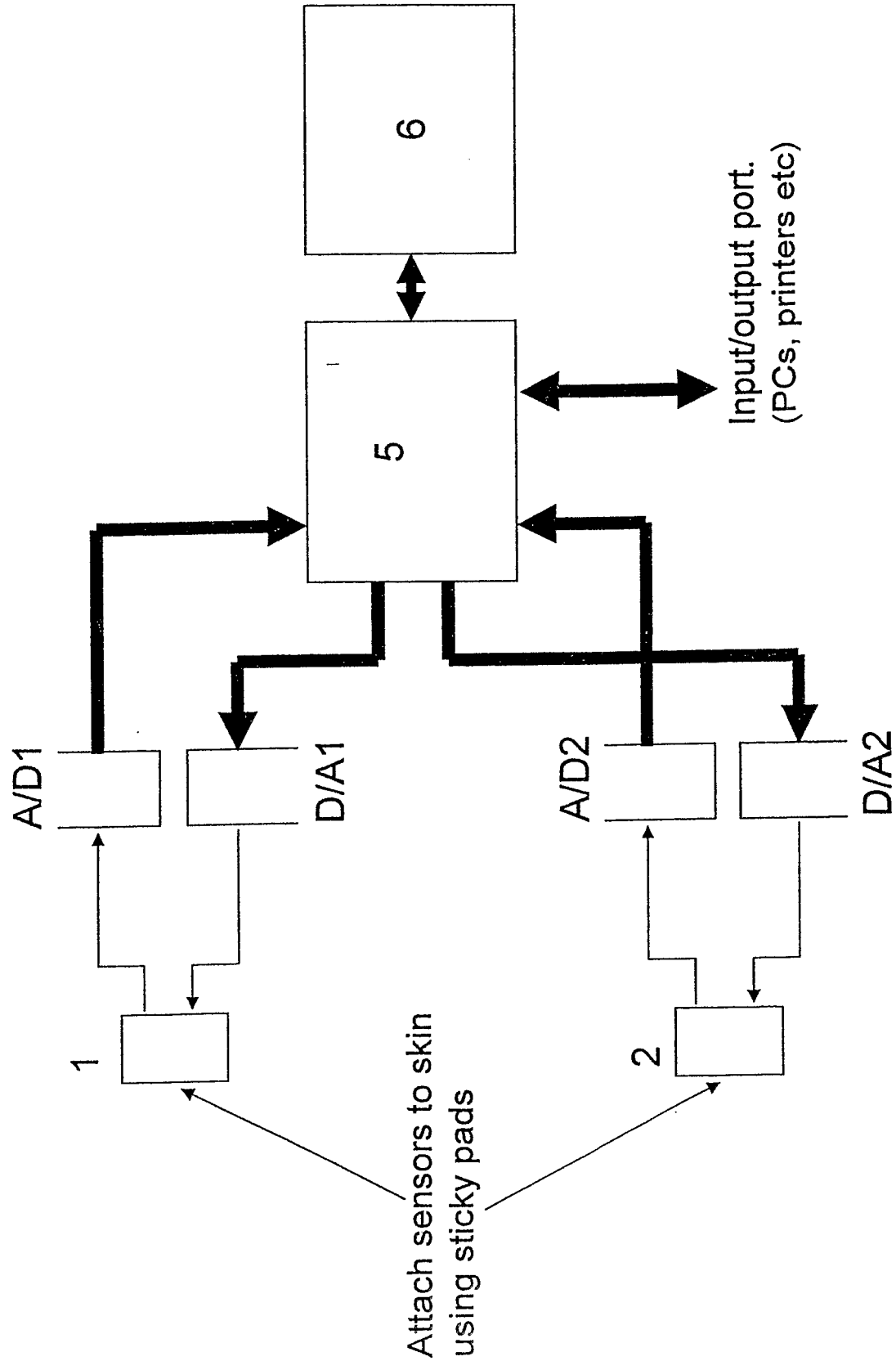
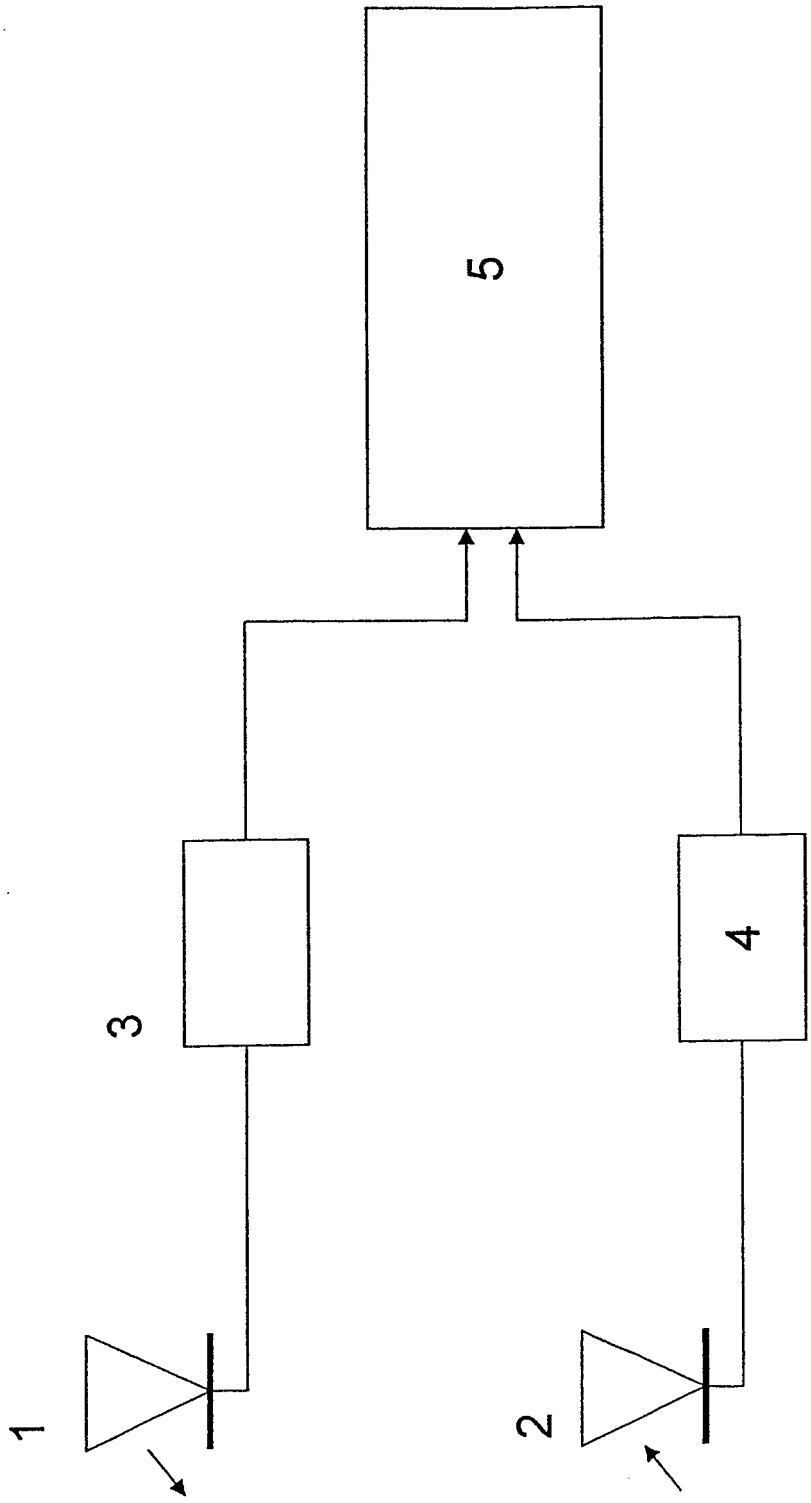

6
5
Input/output port.
(PCs, printers etc)
A/D1
D/A1
A/D2
D/A2
1
2
Attach sensors to skin
using sticky pads

Figure 2



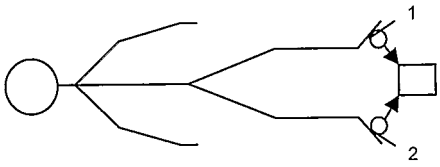


Figure 3a

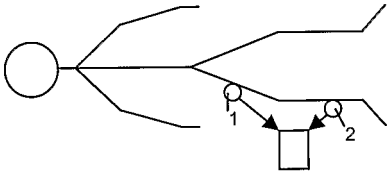


Figure 3b

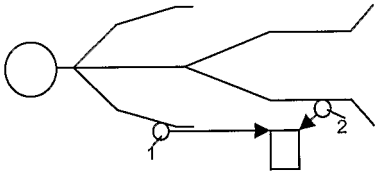
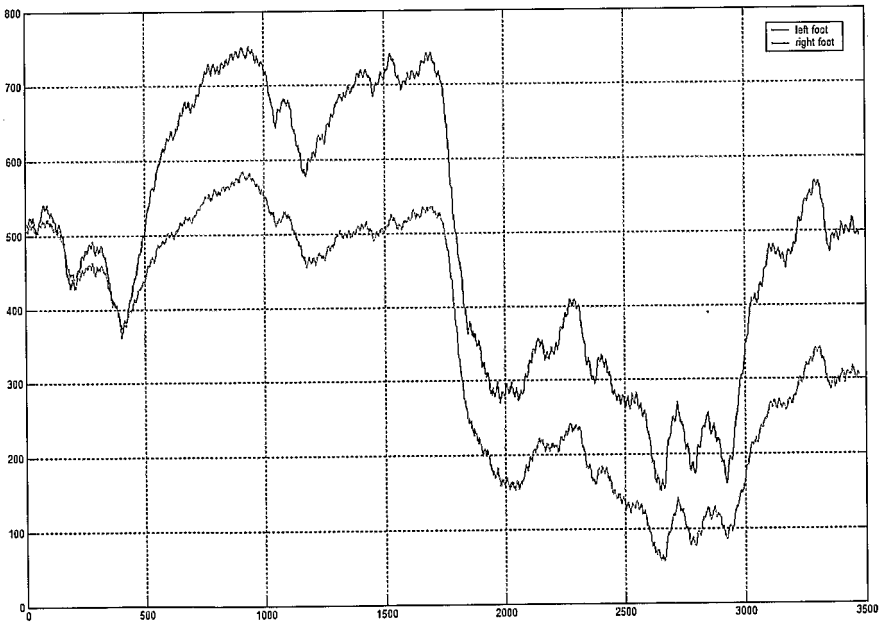


Figure 3c

Figure 4



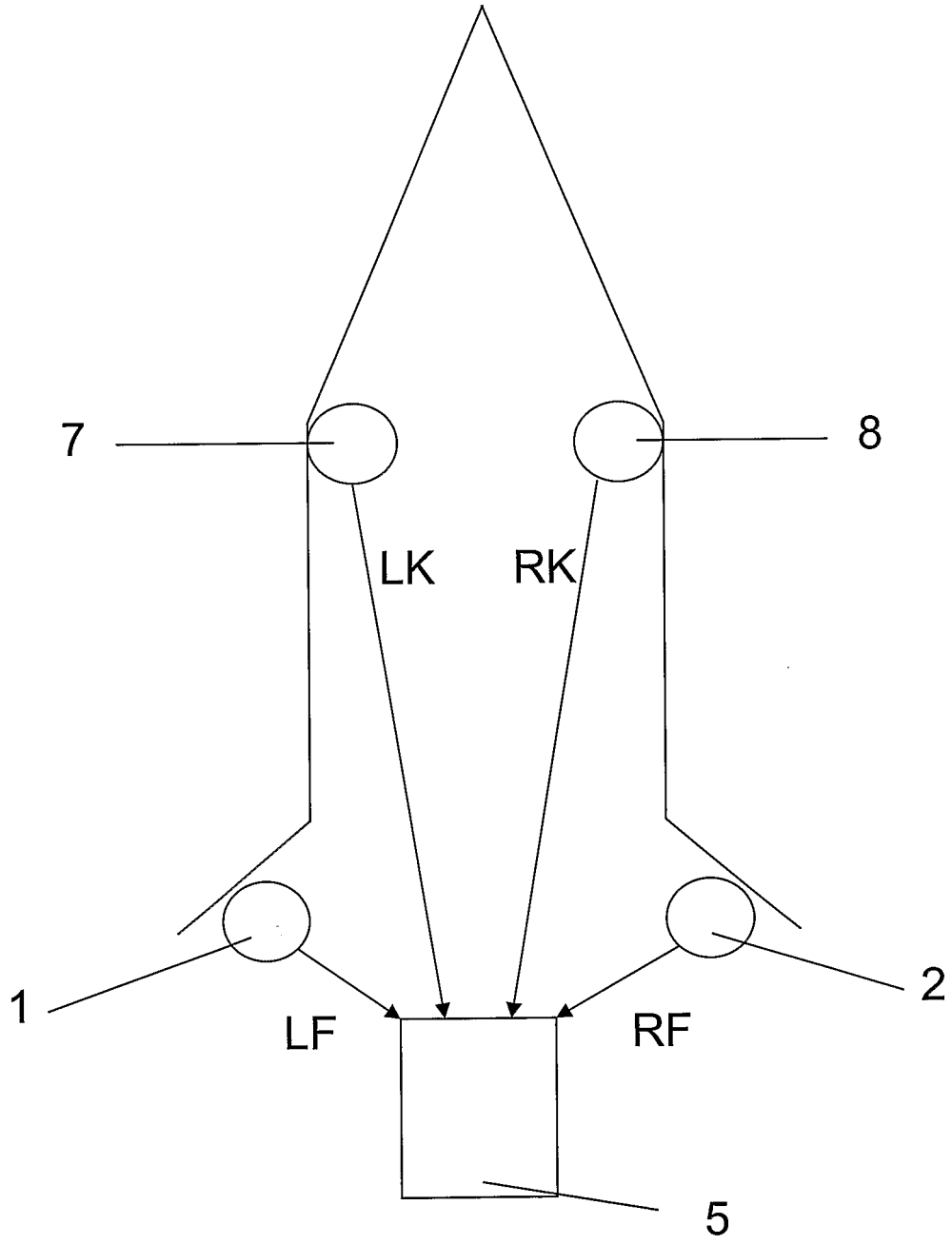


Figure 5

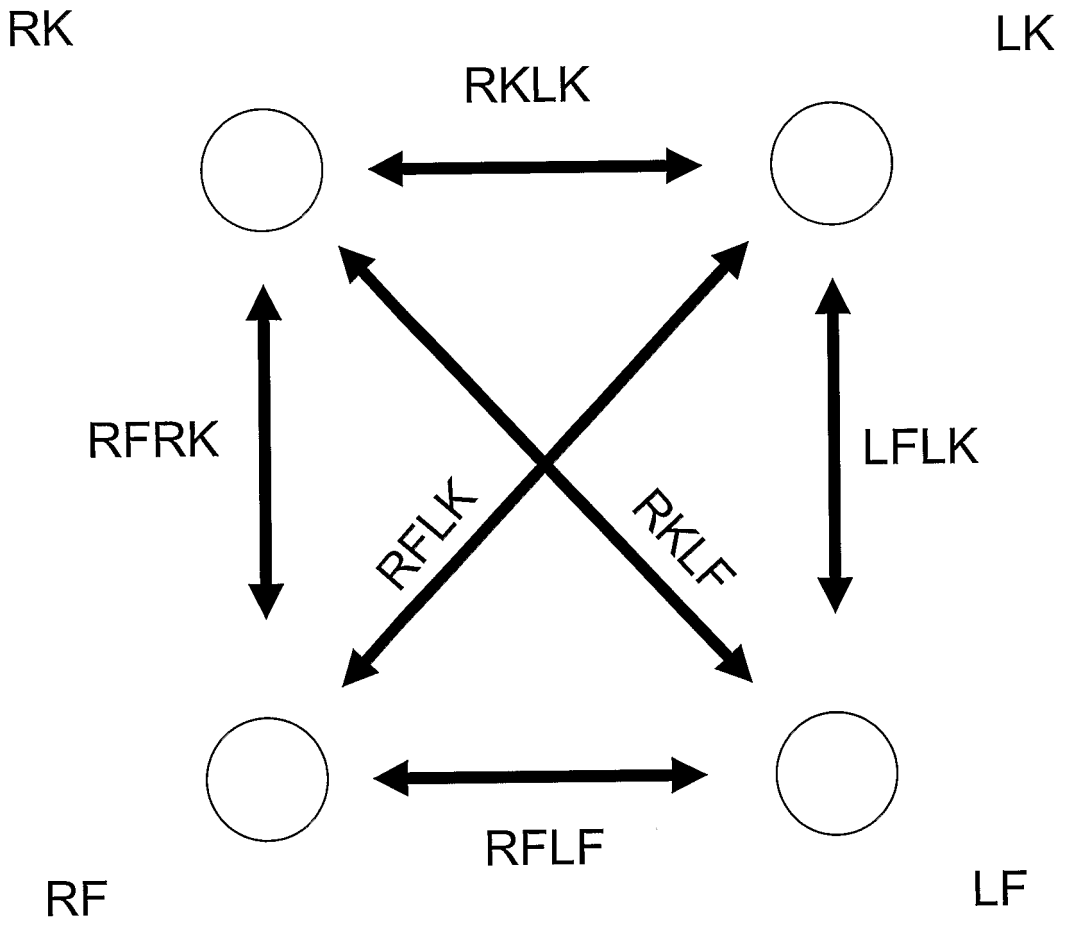


Figure 6

Figure 7

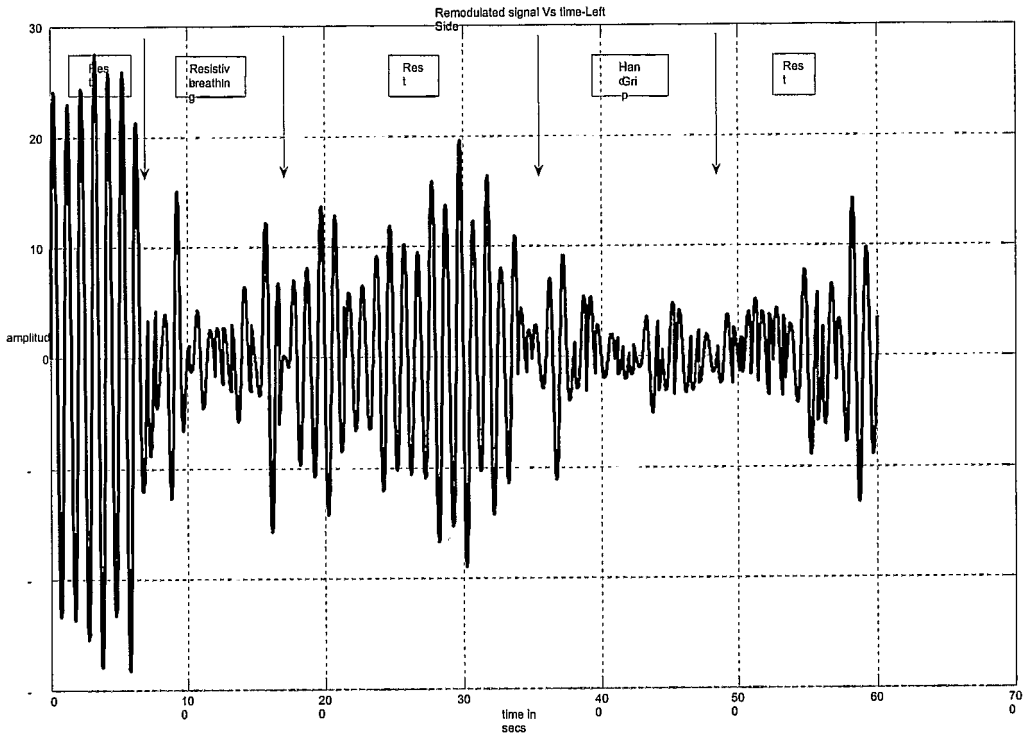
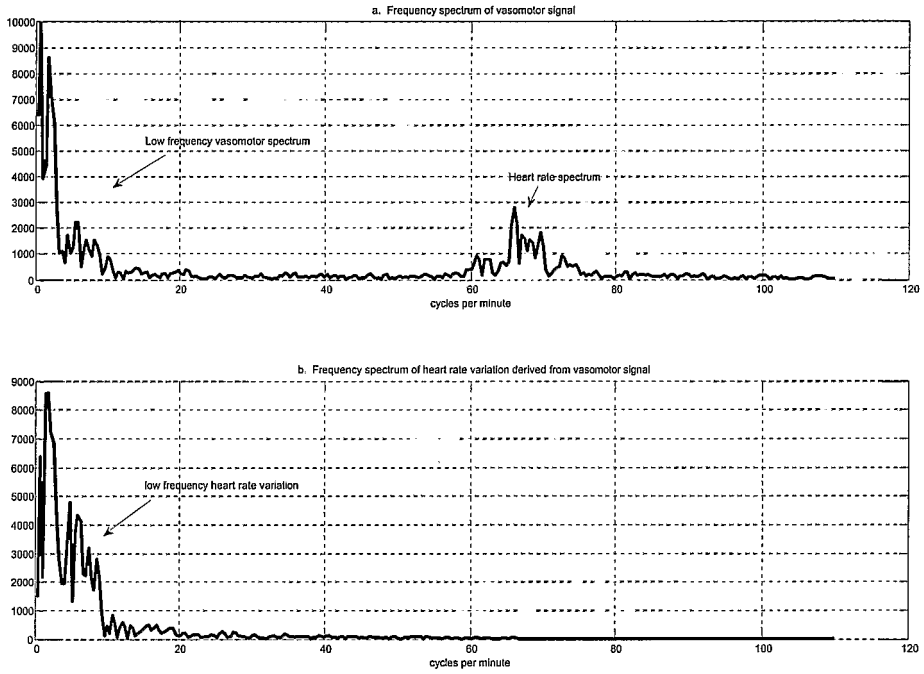

Remodulated signal Vs time-Left Side
Res
Resistiv breathin g
Res t
Han dGri p
Res t
amplitud
30
20
10
0
0
10 0
20 0
30
40 0
50 0
60
70 0
time in secs

Figure 8


a. Frequency spectrum of vasomotor signal
Low frequency vasomotor spectrum
Heart rate spectrum
cycles per minute
b. Frequency spectrum of heart rate variation derived from vasomotor signal
low frequency heart rate variation
cycles per minute

INTERNATIONAL SEARCH REPORT

ıational Application No
/GB2005/004022

A. CLASSIFICATION OF SUBJECT MATTER
A61B5/026 A61B5/00

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

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)
EPO-Internal

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 2004/073514 A (HUNTLEIGH TECHNOLOGY PLC; GOUGH, NIGEL) 2 September 2004 (2004-09-02) abstract page 1, lines 3-10 page 3, line 32 - page 4, line 4 page 4, line 27 - page 5, line 5	1-3,7
X	US 5 991 654 A (TUMEY ET AL) 23 November 1999 (1999-11-23) abstract column 2, line 55 - column 3, line 37	1,7
X	US 5 282 467 A (PIANTADOSI ET AL) 1 February 1994 (1994-02-01) column 4, lines 3-53	1,7

-/--

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

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"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

"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

"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

"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.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
13 January 2006	24/01/2006

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Rivera Pons, C

INTERNATIONAL SEARCH REPORT

ational Application No
/GB2005/004022

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 5 090 417 A (MOLLAN ET AL) 25 February 1992 (1992-02-25) column 2, lines 21-25	4,5

INTERNATIONAL SEARCH REPORT

Information on patent family members

ational Application No
/GB2005/004022

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 2004073514 A	02-09-2004	AU 2004212761 A1	02-09-2004
		EP 1594399 A1	16-11-2005
US 5991654 A	23-11-1999	NONE	
US 5282467 A	01-02-1994	NONE	
US 5090417 A	25-02-1992	NONE	

专利名称(译)	DVT检测		
公开(公告)号	EP1824382A1	公开(公告)日	2007-08-29
申请号	EP2005801375	申请日	2005-10-19
[标]申请(专利权)人(译)	HUNTLEIGH TECH PLC卢顿		
申请(专利权)人(译)	HUNTLEIGH PLC技术		
当前申请(专利权)人(译)	HUNTLEIGH科技有限公司		
[标]发明人	GOUGH NIGEL		
发明人	GOUGH, NIGEL		
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CPC分类号	A61B5/0059 A61B5/02007 A61B5/4035 A61B5/6829		
优先权	2004023289 2004-10-20 GB		
其他公开文献	EP1824382B1		
外部链接	Espacenet		

摘要(译)

一种装置，包括具有换能器（1,2,7,8）的光传输和检测系统，控制装置（5）和输出装置（7）。将换能器放置在患者身体的不同部位，测量在这些部位吸收和/或反射的光，并收集与血管舒缩活动有关的信号。输出可以采取从换能器（1,2,7,8）收集的血管舒缩信号的详细显示的形式，以简单地指示存在或不存在的病症。例如，可以通过测量来自患者脚底的两个换能器信号之间的不相似性来检测单侧DVT的存在。本发明还可用于提供或不提供例如DVT和糖尿病周围神经病的指征。