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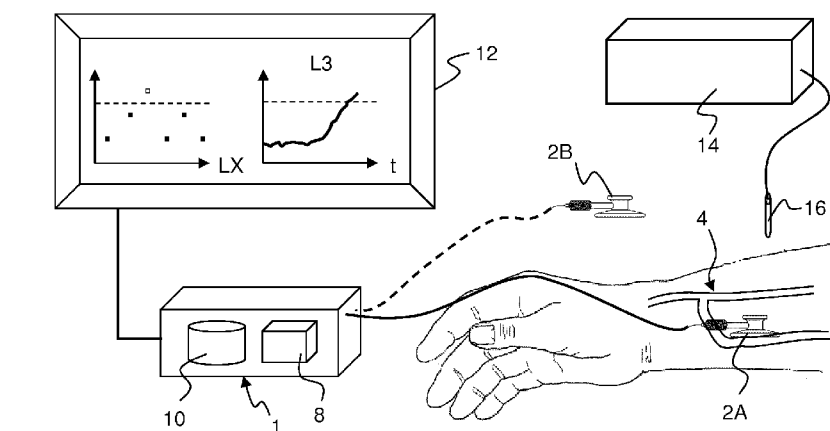


FIG. 1

(57) **Abstract:** A device (1) is arranged to monitor, in a sequence of time-separated sessions on a human subject, an arteriovenous (AV) access (4) which is configured to be connected in fluid communication with an extracorporeal fluid circuit (14). In each session, the device obtains a current signal from an acoustic sensor (2A, 2B) arranged on the human subject to detect acoustic emission created by a flow of blood through the AV access (4), and determines an acoustic envelope of the current signal. The device (1) also obtains shape-indicating data of a reference envelope which is representative of the acoustic emission at the anastomosis of the AV access (4), and processes the acoustic envelope as a function of the shape-indicating data to calculate a parameter value indicative of the status of the AV access (4), e.g. for detection of stenosis formation in the AV access (4).

MONITORING STENOSIS FORMATION IN AN ARTERIOVENOUS ACCESS

Technical Field

5 The present invention relates to signal processing techniques for monitoring stenosis formation in an arteriovenous access, such as a fistula or graft, based on acoustic signals generated in and around the access.

Background Art

10 Kidney failure is a condition that develops when the kidneys lose their ability to remove waste products and excess fluid from the blood. Dialysis treatment may be initiated when the capacity of the kidneys falls to 3-5%. The most common form of dialysis is hemodialysis. During this treatment the blood is purified from waste products and excess fluid is removed by using an external artificial kidney, a dialyzer. The
15 dialysis machine is connected to the vascular system of patient at a vascular access. The access is usually placed in one of the patient's forearms and configured as an arteriovenous (AV) fistula or graft which is designed to provide an adequate (increased) blood flow.

 The state of the vascular access may deteriorate in course of time. The most
20 common form of access failure is stenosis, which is an abnormal narrowing of the blood vessel. When the dialysis becomes inadequate as a result of too low blood flow the vascular access should be revised and remedied. This is sometimes not detected until the patient's treatment is due to begin, or acutely during treatment, and the patient has to be referred to an x-ray examination (called angiography) and/or angioplasty
25 immediately. Naturally, this is of great discomfort for the patient, and may imply reduced dialysis dose to the patient and impose additional costs on the dialysis clinic.

 To avoid this situation, clinics may perform a weekly physical examination, including inspection and palpation for pulse and thrill at different sites of the access. The clinician may also use a stethoscope to listen for sounds originating from the
30 fistula, called bruits. The characteristics of the pulse, thrill and bruit indicates e.g. the presence of stenosis. Clinics may also perform a periodic evaluation (e.g. monthly) of the vascular access, where the access flow is measured by ultrasound dilution, conductance dilution, thermal dilution, Doppler or other technique. When physical examination or periodic evaluation indicates anatomical abnormalities in the access, the
35 patient is referred to diagnostic testing in order to diagnose the presence of pathology.

 Early detection of stenosis permits correction prior to total occlusion and thereby prolongs the life of the access. Physical examination plays a major role in evaluation of

stenosis, but the disadvantage is that it should be performed by an experienced person since it is difficult for a novice to judge the status or detect a slow decay of the vascular access. It is also necessarily subjective. Many techniques for periodic evaluation require the patient to be connected to the dialysis machine. For example, pressure and
5 recirculation measurements may be conducted. However, these are late predictors of dysfunction in the vascular access and they are not very sensitive for detection of stenosis. A overview of different techniques is given in "Hemodialysis vascular access monitoring: Current concepts", by Allon, M. and Robbin, M.L., published in *Hemodialysis International* 2009; 13:153-162.

10 There is thus a need for an improved technique for monitoring a vascular access for stenosis formation, and in particular such a technique that is non-invasive, simple, inexpensive, objective and accurate.

Investigations have been made for correlating sound recordings from different vascular accesses to the stenotic state of these accesses. These investigations are
15 described in the articles "Characterisation of arteriovenous fistula's sound recordings using Principal Component Analysis", by Munguia, M. et al, 31st Annual International Conference of the IEEE EMBS, September 2-6, 2009; and "Acoustical detection of venous stenosis in hemodialysis patients using Principal Component Analysis", by Munguia, M. et al, 32nd Annual International Conference of the IEEE EMBS, August
20 31 - September 4, 2010. However, to date, the investigations have not resulted in a technique that may be put into practical use for monitoring stenosis formation.

The prior art also comprises US2002/099286, which discloses a technique for detection of vascular conditions in a human subject, e.g. with respect to occlusion or stenosis formation in an AV shunt. Sensors are placed near or on the skin surface of the
25 subject to generate an electrical signal representative of flow-induced vascular vibrations or sounds. The condition of the AV shunt is determined by comparing temporal and/or spectral information from the electrical signal to a predetermined normal or acceptable vascular condition, e.g. represented by a predetermined set of parameter values. As noted in US2002/099286, the patient to patient variability may be
30 substantial, which may make it difficult to determine the predetermined set of parameter values.

Summary

It is an object of the invention to at least partly overcome one or more limitations
35 of the prior art.

Another objective is to provide a non-invasive technique for detecting stenosis formation in a vascular access.

A further objective is to provide a technique that does not require significant training and/or experience of the operator, with respect to performing test of the vascular access or interpreting the result of the test.

One or more of these and other objects, which may appear from the description below, are at least partly achieved through devices, a method and a computer-readable medium according to the independent claims, embodiments thereof being defined by the dependent claims.

A first aspect of the invention is a device for monitoring, in a sequence of time-separated sessions on a human subject, an arteriovenous access which is configured to be connected in fluid communication with an extracorporeal fluid circuit. The device is configured to, in each session: obtain a current signal from an acoustic sensor arranged on the human subject to detect acoustic emission created by a flow of blood through the arteriovenous access; determine an acoustic envelope of the current signal; obtain shape-indicating data of a reference envelope which is representative of the acoustic emission at an anastomosis of the arteriovenous access; and process the acoustic envelope as a function of the shape-indicating data to calculate a parameter value indicative of the status of the arteriovenous access.

As is well-known to the skilled person, the anastomosis is a surgically defined structure in the arteriovenous (AV) access and is used for connecting the vein to the artery so as to provide an adequate blood flow through the AV access. Depending on implementation, the AV access may comprise a single anastomosis which directly connects the vein to the artery (e.g. in an AV fistula) or two anastomoses which connect the vein and the artery, respectively, to an intermediate artificial vessel (e.g. in an AV graft). The anastomosis is thus a well-defined structure within the AV access and is often easy to locate on the skin of a patient, e.g. by palpation or by using a stethoscope.

The present Applicant has found that the acoustic emission obtained at the anastomosis may be seen as a mixture of the acoustic emission obtained at a stenotic site and the acoustic emission obtained at a non-constricted, healthy site. It is thereby possible, in a broad sense, to use the acoustic emission obtained from the anastomosis as a reference for assessing if an AV access includes stenosis formation or not. By obtaining and using shape-indicating data of a reference envelope, which is representative of the acoustic emission at the anastomosis, the inventive device is allowed to make an objective assessment if there is stenosis formation in the AV access or not, based on an acoustic envelope obtained from an acoustic sensor which is arranged on the AV access.

Since the anastomosis is a well-defined structure which is often easy to locate on the skin of the subject, it is non-complicated to record the reference profile in a

consistent manner, e.g. on the human subject under examination, in a current session or in one or more preceding sessions. It is likewise non-complicated to obtain the reference profile in a consistent manner by recording the acoustic emission from the anastomosis of a group of human subjects, which may or may not include the human subject under examination.

In one embodiment, the reference envelope is obtained to represent the acoustic emission at the anastomosis of the human subject in one or more preceding sessions, and the current signal (i.e. the signal obtained in the current session) is obtained with the acoustic sensor arranged on the anastomosis of the human subject. Such an embodiment enables the status of the AV access to be tracked over time based on the acoustic emission from the anastomosis. This provides a simple and consistent technique for detecting the formation of stenosis in an AV access.

In an alternative embodiment, the acoustic sensor is arranged at a location on the arteriovenous access that is spatially separated from the anastomosis. Such an embodiment makes it possible to detect the precise location of stenosis formation within the AV access, by placing the acoustic sensor at different locations on the AV access and processing the resulting acoustic envelopes as a function of the shape-indicating data of the reference profile. This provides a simple and consistent technique for detecting the location of stenosis formation within an AV access.

In the alternative embodiment, the device may be configured to obtain the shape-indicating data by obtaining, in a current session, a reference signal representing a current acoustic emission at the anastomosis, and generate the shape-indicating data based at least partly on the reference signal. For example, the device may be configured to update previously stored shape-indicating data as a function of the reference signal.

In one embodiment, the shape-indicating data comprises at least two basis functions that represent the reference envelope. The basis functions may be essentially orthogonal.

In one embodiment, the basis functions are obtained by Principal Component Analysis of a plurality of characteristic envelopes obtained to represent the acoustic emission at the anastomosis of one or more human subjects. Each characteristic envelope may represent a time-average of signal segments associated with heartbeats in an envelope curve obtained from an acoustic measurement signal.

In one embodiment, the device is configured to process the acoustic envelope by: representing the acoustic envelope as a functional combination of the basis functions, and calculating a coefficient for each basis function in said functional combination.

In one embodiment, the parameter value is given by the coefficients.

In one embodiment, the coefficients define a current position in a coordinate space defined by said at least two basis functions, said device being further configured to compare the current position to a reference position in the coordinate space.

5 In one embodiment, the reference position is representative of the reference envelope.

In one embodiment, the device is configured to calculate the reference position by processing a reference signal obtained, in a current session, from an acoustic sensor arranged on the anastomosis of the human subject. The device may be further configured to obtain the current signal from a first acoustic sensor and to obtain the
10 reference signal from a second acoustic sensor.

In another embodiment, the device is configured to obtain measurement data indicative of a current flow rate of blood through the arteriovenous access, wherein at least one of the acoustic envelope and the reference envelope is determined as a function of the measurement data such that said at least one of the acoustic envelope
15 and the reference envelope is essentially independent of flow rate.

In one embodiment, the parameter value is indicative of stenosis formation in the arteriovenous access, wherein the device may be further configured to quantify the degree of stenosis formation as a function of the parameter value.

20 In one embodiment, the device is further configured to display the parameter value in real time.

In one embodiment, the acoustic envelope is determined for a time-dependent signal comprising frequencies in the range of approximately 20-2000 Hz.

In one embodiment, the device is configured to determine the acoustic envelope by: obtaining an envelope curve that joins one of maxima and minima in the current
25 signal, and identifying envelope segments associated with heartbeats in the envelope curve. The device may be further configured to generate an average envelope segment based on the envelope segments, and process the average signal segment to calculate the parameter value. Alternatively, the device may be further configured to generate individual parameter values for each of the envelope segments, and to calculate the
30 parameter value as an average of the individual parameter values.

A second aspect of the invention is a device for monitoring, in a sequence of time-separated sessions on a human subject, an arteriovenous access which is configured to be connected in fluid communication with an extracorporeal fluid circuit. The device comprises and is configured to operate, in each session: means for obtaining a current
35 signal from an acoustic sensor arranged on the human subject to detect acoustic emission created by a flow of blood through the arteriovenous access; means for determining an acoustic envelope of the current signal; means for obtaining shape-

indicating data of a reference envelope which is representative of the acoustic emission at an anastomosis of the arteriovenous access; and means for processing the acoustic envelope as a function of the shape-indicating data to calculate a parameter value indicative of the status of the arteriovenous access.

5 A third aspect of the invention is a method of monitoring, in a sequence of time-separated sessions on a human subject, an arteriovenous access which is configured to be connected in fluid communication with an extracorporeal fluid circuit. Each session of said method comprises: obtaining a current signal from an acoustic sensor arranged to detect acoustic emission created by a flow of blood through the arteriovenous access;
10 determining an acoustic envelope of the current signal; obtaining shape-indicating data of a reference envelope which is representative of the acoustic emission at an anastomosis of the arteriovenous access; and processing the acoustic envelope as a function of the shape-indicating data to generate a parameter value indicative of the status of the arteriovenous access.

15 In one embodiment, the reference envelope is obtained to represent the acoustic emission at the anastomosis of the human subject in one or more preceding sessions, and the current signal is obtained with the acoustic sensor arranged on the anastomosis of the human subject.

 In an alternative embodiment, the acoustic sensor is arranged at a location on the
20 arteriovenous access that is spatially separated from the anastomosis.

 In such an alternative embodiment, the step of obtaining the shape-indicating data may comprise obtaining, in a current session, a reference signal representing a current acoustic emission at the anastomosis, and generating the shape-indicating data based at least partly on the reference signal. In one embodiment, the method further comprises a
25 step of updating previously stored shape-indicating data as a function of the reference signal.

 In one embodiment, the shape-indicating data comprises at least two basis functions that represent the reference envelope, where the basis functions may be essentially orthogonal.

30 In one embodiment, the basis functions are obtained by Principal Component Analysis (PCA) of a plurality of characteristic envelopes obtained to represent the acoustic emission at the anastomosis of one or more human subjects. Each characteristic envelope may represent a time-average of signal segments associated with heartbeats in an envelope curve obtained from an acoustic measurement signal.

35 In one embodiment, the step of processing the acoustic envelope comprises a step of representing the acoustic envelope as a functional combination of the basis functions,

and a step of calculating a coefficient for each basis function in said functional combination.

In one embodiment, the parameter value may be given by the coefficients.

5 In one embodiment, the coefficients define a current position in a coordinate space defined by said at least two basis functions, and the method further comprises a step of comparing the current position to a reference position in the coordinate space, where the reference position may be representative of the reference envelope.

10 In one embodiment, the method further comprises a step of calculating the reference position by processing a reference signal obtained, in a current session, from an acoustic sensor arranged on the anastomosis of the human subject. For example, the current signal may be obtained from a first acoustic sensor and the reference signal may be obtained from a second acoustic sensor.

15 In one embodiment, the method further comprises a step of obtaining measurement data indicative of a current flow rate of blood through the arteriovenous access, and a step of determining at least one of the acoustic envelope and the reference envelope as a function of the measurement data such that said at least one of the acoustic envelope and the reference envelope is essentially independent of flow rate.

20 In one embodiment, the parameter value is indicative of stenosis formation in the arteriovenous access, and method may further comprise a step of quantifying the degree of stenosis formation as a function of the parameter value.

In one embodiment, the method further comprises a step of displaying the parameter value in real time.

In one embodiment, the acoustic envelope is determined for a time-dependent signal comprising frequencies in the range of approximately 20-2000 Hz.

25 In one embodiment, the step of determining the acoustic envelope comprises a step of obtaining an envelope curve that joins one of maxima and minima in the current signal, and a step of identifying envelope segments associated with heartbeats in the envelope curve. In such an embodiment, the method may further comprise a step of generating an average envelope segment based on the envelope segments, and a step of processing the average envelope segment to calculate the parameter value.
30 Alternatively, the method may further comprise a step of generating individual parameter values for each of the envelope segments, and a step of calculating the parameter value as an average of the individual parameter values.

35 A fourth aspect of the invention is a computer-readable medium comprising computer instructions which, when executed by a processor, cause the processor to perform the method of the third aspect.

Embodiments of the second to fourth aspects may correspond to the above-identified embodiments of the first aspect.

Still other objectives, features, aspects and advantages of the present invention will appear from the following detailed description, from the attached claims as well as
5 from the drawings.

Brief Description of Drawings

Embodiments of the invention will now be described in more detail with reference to the accompanying schematic drawings.

10 Fig. 1 is a perspective view of a device for testing an AV access for stenosis formation.

Figs 2(a)-2(b) illustrate an AV fistula without and with stenosis, respectively, and indicate different test sites on the fistula.

15 Figs 3(a)-3(b) are plots of acoustic envelopes generated from acoustic recordings at a site without and with stenosis, respectively.

Figs 4(a)-4(d) are block diagrams of different embodiments of the signal processing in the device of Fig. 1.

Fig. 5 is a flow chart of a method for monitoring stenosis formation.

20 Figs 6(a)-6(c) are plots of an acoustic signal, a raw acoustic envelope, and a acoustic envelope after noise removal, respectively.

Figs 7(a)-7(b) are plots of first and second basis functions that represent a reference envelope obtained at the anastomosis of an AV access.

25 Fig. 8 is a plot of parameter values obtained by processing recordings at an anastomosis and at healthy and stenotic sites on the AV accesses of several patients, as mapped to a parameter space.

Figs 9(a)-9(b) are plots to indicate the location of a stenotic region and a healthy region, respectively, with respect to an anastomosis region in the parameter space of Fig. 8.

30 Detailed Description of Example Embodiments

The following description is directed to a technique for monitoring an arteriovenous access for detection of stenosis formation based on acoustic signals recorded at one or more sites on the skin of a patient. The technique, in its various embodiments, may be implemented as a monitoring device, a method and a computer
35 program product. Throughout the description, the same reference numerals are used to identify corresponding elements.

Fig. 1 illustrates a monitoring device 1 according to one embodiment of the present invention. The device 1 includes an acoustic sensor 2A which is configured for application to the skin of a patient so as to pick up sound waves that originate from a confined region under the skin of the patient. The device 1 may also include a second
5 acoustic sensor 2B (and further acoustic sensors) allowing sound waves to be detected simultaneously at multiple sites on the patient. Specifically, the sensors 2A, 2B are used for sensing sound waves generated by the blood flow through an arteriovenous access (AV access) 4 located under the skin of the patient.

The device 1 further includes a signal processor 8 for acquiring and processing
10 electrical signals from the sensors 2A, 2B. The electrical signals represent sound waves and are therefore denoted "acoustic signals" in the following. The device 1 also has access to an electronic memory 10 which may be internal, as shown, or external. A display screen 12 is connected to the device 1 for displaying data ("test values") generated by the device 1.

The device 1 is configured to detect stenosis formation in the AV access 4. The
15 AV access 4 is an artificial access site which may be used for gaining access to the patient's blood stream for the purpose of treatment, analysis, diagnosis or any other medical procedure. One example is dialysis treatment, in which blood is extracted from the patient, treated in an extracorporeal blood circuit 14 and returned to the patient. As
20 shown in Fig. 1, the circuit 14 may have one or more access devices 16 (one shown), such as a needles or catheters, which are to be inserted into the AV access 4 for extraction and return of blood.

The AV access 4 may be a fistula, which is formed by surgically connecting a vein and an artery, typically in the arm of the patient. The connection point between the
25 vein and the artery is commonly known as "anastomosis". There are many variants of AV fistulas, including the radial-cephalic fistula, the brachial-cephalic fistula and the brachial-basilic fistula. Fig. 2(a) illustrates an AV fistula 4 without stenosis, in which the site of the anastomosis is indicated by reference numeral A. The site A typically has an extent of about 5-10 millimeters from the position directly over the anastomosis.

The AV access 4 may also be an AV graft, which is similar to an AV fistula in most respects, but the artery and the vein are connected using an intermediate graft tube made from synthetic or biologic material. The AV graft therefore has two anastomoses or connection points, one at the surgical connection between the artery and the graft tube and one at the surgical connection between the vein and the graft tube. AV grafts
35 are typically categorized into straight grafts and loop grafts.

As used herein, a "stenosis" refers to an abnormal narrowing of a vessel which may be caused by calcification or by the vessel being exposed to abnormal physical

stress such as turbulence or high blood pressure, causing the vessel wall to thicken. Since the blood in an AV access is typically both turbulent at some locations and at high pressure, stenosis is common in these vessels. Fig. 2(b) indicates an AV fistula with stenosis, where reference numeral L3 indicates a site with stenosis formation. Stenosis in an AV access may be treated, e.g. by percutaneous transluminal angioplasty (PTA) and surgical revision.

Returning to Fig. 1, the acoustic sensors 2A, 2B may be any type of sensor capable of detecting audible vibrations. Such sensors include microphones and accelerometers, e.g. condenser microphones and piezoelectric accelerometers. The sensor may include components for improving the acoustic coupling to the skin surface and/or reducing the impact of surrounding noise and/or enhancing certain frequencies. In the example of Fig. 1, the sensors 2A, 2B are provided with small-sized stethoscope heads.

The sounds and vibrations of an AV access may be divided into three categories:

- Thrill, which is caused by turbulence in the blood and is formed by non-audible but palpable frequency components.
- Pulse, which is the palpable pulsation representing pressure waves that are caused by the heartbeats and transmitted through the vascular system.
- Bruit, which is caused by the turbulent blood flow and is formed by audible frequency components.

The acoustic signals received by the device 1 are processed to reflect at least part of the bruit, typically in the range of 20-2000 Hz. As will be exemplified in more detail below, the device 1 is operated to acquire and analyze the acoustic signals detected on the skin of the patient in a test session. As used herein, a test session ("session") refers to an isolated event when the patient's AV access is tested for presence of stenosis. A session may last for a few minutes up to an hour, and the time period between sessions may be counted in days, weeks or even months.

In a test session, the AV access may be tested for stenosis formation at a plurality of test sites, e.g. as indicated by L1-L6 in Fig. 2. Although not indicated in Fig. 2, it is understood that the test sites may also include the anastomosis site A. The test values obtained from the recordings at the different sites may be displayed to the operator, e.g. as shown to the left on the screen 12 in Fig. 1, where the abscissa (LX) represents the different sites L1-L6 and the ordinate represents the test values. It is also conceivable that the sessions are devoted to tracking the development of stenosis at a specific site on the AV access, e.g. as shown to the right on the screen 12 in Fig. 1, where the abscissa (t) represents sessions, and the ordinate represents the test values obtained at the site L3. In another variant, exemplified in more detail further below, the acoustic signal is only

recorded from the anastomosis, i.e. within the anastomosis site A, and the test values are tracked over a sequence of test sessions. Generally, this variant does not indicate the location of the stenosis, but rather indicates the overall stenotic status of the AV access. It is realized that the different tests may be used in combination.

5 The test values may be used by the operator to identify a need for a more detailed investigation of the AV access, through use of a conventional and typically more complex and expensive technique such as contrast angiography, duplex ultrasound or color Doppler flow. It is also conceivable that the test values are directly used by a physician or nurse to deduce, possibly in combination with conventional physical
10 examination and auscultation, if there is a need for stenosis treatment. The device may assist the operator/physician/nurse by indicating when the test values exceed a given threshold for stenosis evaluation. Such a threshold is indicated by the dashed lines on the screen 12 in Fig. 1.

 The device 1 generates the test values by analyzing the waveform of the acoustic
15 signal obtained from the sensor 2A, and specifically the envelope for acoustic pulses that are generated in synchronization with the heartbeats and which originate from the flow of blood through the AV access. Fig. 3(a) is a plot of an envelope generated from acoustic signals recorded at site L1 in Fig. 2(b), i.e. a site without stenosis, and Fig. 3(b) is a plot of a corresponding envelope generated from acoustic signals recorded at site L3
20 in Fig. 2(b), i.e. a site with significant stenosis formation.

 Generally, the test values may be generated by use of one or more reference envelopes or reference profiles that represent the waveform of a healthy (non-stenotic) site or a stenotic site. For example, either of the curves in Figs 3(a)-3(b) might be used as such a reference envelope.

25 However, it has been found that this type of reference envelope may differ between different patients, and also between different sites on one and the same patients, and even between different test sessions for the same site on the same patient. In an attempt to improve the general method outlined above, the present Applicant has found that it may be particularly advantageous to use the envelope obtained from
30 acoustic signals measured at the anastomosis site A as a reference for assessing the stenotic status of the AV access. Specifically, it has been found that it is possible to identify systematic differences between a reference envelope obtained at the anastomosis site A and the envelopes obtained at a stenotic site and at a healthy site, respectively. By designing the signal processing to emphasize and detect these
35 systematic differences, it is possible to classify an AV access as healthy or stenotic, and even to identify the location of a stenotic lesion in the AV access.

The reference envelope(s) may be obtained by processing acoustic signals recorded on the anastomosis site A in one or more previous test sessions on a dedicated patient, or from acoustic signals recorded on the anastomosis site A for a group of patients, or the reference envelope(s) may be obtained by computer or laboratory
 5 simulations. The test value for a site may be generated by comparing shape features of the envelope obtained from the acoustic signal at this site with the corresponding shape features of the reference envelope(s) obtained at the anastomosis site A. The shape features (generally denoted “shape-indicating data” herein) may include any or a combination of: the actual envelope or a section thereof (e.g. up-slope or down-slope), a
 10 curve or piece-wise linear regression slopes fitted to the envelope or a section thereof, coefficients that represent such a fitted curve/slope, and a duration/width of the envelope or a section thereof (e.g. a peak). The comparison may e.g. involve calculation of a correlation value (e.g. maximum correlation after appropriate phase shift), a sum of absolute differences, a difference in area, or a standard deviation of the differences
 15 between a measured envelope and reference envelope(s) as represented by the shape features, as well as normalized and/or weighted variants of such comparison measures.

Another approach is to represent the reference envelope at the anastomosis site A by shape-indicating basis functions, and to generate the test value for a test site by relating the acoustic envelope recorded at the test site to the basis functions. This
 20 detection principle will now be described in further detail in relation to different embodiments that are illustrated as block diagrams in Figs 4(a)-4(d). The illustrated embodiments operate on acoustic signals measured at one or more sites on an AV access of a patient, for the purpose of evaluating if there are signs of stenosis formation in the AV access, and possibly for determining the location of any stenosis lesion(s).

25 Before discussing the merits and features of the individual embodiments, a brief overview will be given of signal processing blocks that are common to all embodiments in Figs. 4(a)-4(d). It is to be understood that all signal processing blocks may be implemented by analog or digital components, or a combination thereof.

Looking at Fig. 4(a), the incoming acoustic signal S_{LX} is fed to a preprocessing
 30 (PP) or signal cleaning block 400 which removes distorting components in the raw signal, such as baseline wander and sounds not originating from the blood flow through the AV access. In the illustrated example, the preprocessing block 400 includes a high-pass filter with a cut-off frequency of 50 Hz, and a low-pass filter with a cut-off frequency of 1000 Hz.

35 The filtered signal is then received by an envelope extraction block 402, which applies a linear, time-invariant filter known as a Hilbert transformer to the filtered signal S_{LX} . This operation results in a transformed signal $\hat{S}_{LX}$, which is a 90° phase-

shifted version of the incoming signal S_{LX} . The raw envelope b_{LX} may then be derived from:

$$b_{LX}(n) = \sqrt{S_{LX}^2(n) + \hat{S}_{LX}^2(n)},$$

with n denoting time steps (samples) in the signals. In the present example, to improve processing efficiency, an approximate raw envelope is calculated from the signal S_{LX} based on the relation:

$$\hat{b}_{LX}(n) = |S_{LX}(n)| + \frac{2}{\pi} |S_{LX}(n+1) - S_{LX}(n)|.$$

The resulting raw envelope $\hat{b}_{LX}$ is then filtered with a 10 Hz low-pass filter to emphasize slowly varying signal components and yield a filtered envelope B_{LX} suited for use in stenosis detection.

The operation of the preprocessing and envelope extraction blocks 400, 402 is further exemplified in Fig. 6, which illustrates the signal S_{LX} after preprocessing, the corresponding envelope signal $\hat{b}_{LX}$, and the filtered envelope signal B_{LX} . As shown, the filtered envelope signal B_{LX} contains a time sequence of acoustic pulses, where each acoustic pulse corresponds to an individual heartbeat. It is to be understood that the acoustic pulses do not represent sounds emanating directly from the heartbeats, but sounds that are caused by the surge of blood through the AV access with every heartbeat. Each acoustic pulse has a maximum (peak value) which is flanked by a positive (rising) slope and a negative (decaying) slope.

Reverting to Fig. 4(a), the filtered envelope signal B_{LX} is received by a segmentation block 404, which separates the signal B_{LX} into one envelope segment for each pulse. Fig. 6(c) illustrates four consecutive envelope segments $\mathbf{X}_1 - \mathbf{X}_{i+3}$ extracted from the signal B_{LX} . In the following, each envelope segment is represented as a vector with N signal values, denoted $x_i(n)$. In the illustrated example, each envelope segment is extracted to represent the negative slope, since it is currently believed that the negative slopes of the acoustic pulses are more affected than the positive slopes by the presence of stenosis. However, in a variant, the entire acoustic pulse or any portion of the acoustic pulse is extracted by the segmentation block 404. It is also conceivable that each envelope segment is extracted to contain more than one acoustic pulse.

In the illustrated example, the maximum is used as a reference point within the pulses for extracting the envelope segments. Thus, an envelope segment is formed by identifying the maximum of each acoustic pulse and extracting the signal values in a

time window of given length subsequent to the maximum. The envelope segments thereby have equal length, which may be required by the analysis block 406, depending on implementation. There are of course alternative ways of generating envelope segments of equal length, e.g. by padding the extracted segments by predefined signal values, or by auto-scaling the extracted segments to a given width. It may be important, however, that the envelope segments are aligned with respect to a common feature, e.g. the maximum, such that all envelope segments have the same location with respect to the common feature.

The segmentation block 404 may be designed to generate normalized envelope segments. Normalization has been found to improve performance, if the envelope segments are to be used for extraction of basis functions, and especially if the basis functions are to be extracted from envelope segments originating from recordings on different patients. However, normalization may be omitted. If used, a normalization factor may e.g. be given by the maximum signal value of the respective envelope segment, by the dynamic of the envelope (e.g. given by the difference between the maximum value and the minimum value of the envelope), by the difference between the start and end values of the envelope, or by an energy measure for the envelope segment, e.g. given by the RMS (root mean square) or the L^2 norm of the signal values.

The analysis block 406 is based on the assumption that the envelope segments $\mathbf{X}_i$, normalized or not, may be represented by a functional combination of K basis functions ϕ_k , e.g. a linear combination such as:

$$\mathbf{X}_i = \sum_{k=1}^K W_{i,k} \cdot \phi_k ,$$

where $W_{i,k}$ is the weighting coefficient (e.g. a PCA coefficient, see below) of basis function ϕ_k for segment $\mathbf{X}_i$. Thereby, a coefficient vector $\mathbf{W}_{K,i}$ may be obtained for each segment $\mathbf{X}_i$ as:

$$\mathbf{W}_{K,i} = \Phi^T \cdot \mathbf{X}_i , \text{ with } \Phi = [\phi_1 \quad \phi_2 \quad \dots \quad \phi_K] ,$$

where Φ^T is the transpose of the basis function matrix Φ , and the coefficient vector contains K weighting coefficients, $\mathbf{W}_{K,i} = [W_{i,1} \quad W_{i,2} \quad \dots \quad W_{i,K}]^T$.

The analysis block 406 is thus designed to retrieve a set of basis functions that represent the shape of the envelope segments that are likely to be detected (or that are actually detected) at the anastomosis, and to use the basis functions to determine the coefficient vector $\mathbf{W}_{K,i}$ for an incoming envelope segment $\mathbf{X}_i$ recorded at a site LX on

the AV access. The coefficient vector $\mathbf{W}_{k,i}$ may be seen to define a position in a coordinate space defined by the basis functions and is therefore generally designated by P_{LX} and denoted a "position parameter" in the following description. To improve the quality of the position parameter, the analysis block 406 may be designed to generate an average envelope segment as an average of several envelope segments and to determine the position parameter P_{LX} (the coefficient vector) for the average envelope segment.

Another way to improve the quality of the position parameter is to generate individual coefficient vectors for individual envelope segments, and to calculate the position parameter P_{LX} as an average of the individual coefficient vectors. For example, the position parameter may be given by a mean coefficient vector $\overline{\mathbf{W}}_K$ according to

$$\overline{\mathbf{W}}_K = 1/M \sum_{i=1}^M \mathbf{W}_{K,i} ,$$

where M is the number of envelope segments.

The evaluation block 408 is designed to map the position parameter P_{LX} generated by the analysis block 406 to the coordinate space, and assess if there is any significant stenosis formation in the AV access.

Fig. 8 is a representation of a two-dimensional coordinate space, which is spanned by two weighting coefficients W_1 , W_2 associated with the basis functions ϕ_1 and ϕ_2 , respectively. Specifically, Fig. 8 illustrates the parameter values (pairs of weighting coefficients) that are generated for a set of recordings from 10 different patients, where squares ($\square$) indicate parameter values calculated for recordings on the anastomosis, circles ($\circ$) indicate parameter values calculated for sites with stenotic formation, and asterisks (*) indicate parameter values calculated for sites free from stenosis. It is seen that the parameter values essentially cluster along an arc-shaped curve in the coordinate space. Further, the stenotic parameter values and the non-stenotic ("healthy") parameter values are well-separated, and the anastomosis parameter values fall in between the stenotic and healthy positions. It may be noted that a stenotic site will result in second coefficients W_2 that, at least on average, are greater than the second coefficient W_2 for the anastomosis recordings. In contrast, a healthy site will result in second coefficients W_2 which, at least on average, are smaller than the second coefficient W_2 for the anastomosis site.

It is realized that, given the data in Fig. 8, there are a multitude of different ways of assessing if a single or a plurality of parameter values P_{LX} determined by the analysis block 406 indicate stenosis formation or not. For example, a statistical test may be applied to assign the parameter value(s) P_{LX} to either a stenotic region (Fig. 9(a)) or a healthy region (Fig. 9(b)), or neither. The degree of stenosis may be quantified by

evaluating a distance from the parameter value(s) P_{LX} in the coordinate space, e.g. to a given reference point of the healthy/stenotic/anastomosis region, e.g. its center of gravity. The distance may e.g. be given as an Euclidian distance, a distance in one or more parameter dimensions (e.g. W_2), or a distance along the arc-shaped curve.

5 Depending on implementation, the evaluation block 408 may e.g. output a test value, which may be formed by the parameter value as such, a value that quantifies the degree of stenosis, a value that indicates a probability for stenosis, or an indication if the site is deemed either stenotic or healthy. The test value, and any other output data, may be displayed to the operator, e.g. as discussed above in relation to Fig. 1, or otherwise
10 output or stored in electronic memory.

In the illustrated examples, the basis functions are determined by a basis function generation block 406' which generally operates on a plurality of characteristic envelopes obtained to represent the acoustic emission at the anastomosis of one or more patients. The characteristic envelopes may be formed from envelope segments obtained from
15 recordings at the anastomosis of one or more AV accesses. To improve the quality of the basis functions, the block 406' may be configured to form each characteristic envelope as a time-average of some envelope segments that are generated by the segmentation block 404, i.e. an average formed by aligning and averaging the envelope segments. The recordings may originate from the current patient or from a group of
20 different patients, which may or may not include the current patient. The block 406' may operate a Principal Component Analysis (PCA) on a large ensemble of characteristic envelopes so as to determine an appropriate set of basis functions that describe the characteristic envelopes. PCA, which is well-known to the skilled person, is a mathematical procedure that uses an orthogonal or essentially orthogonal
25 transformation to convert a set of observations of possibly correlated variables into a set of values of essentially uncorrelated variables called principal components, which correspond to the above-mentioned basis functions. The number of principal components is less than or equal to the number of original variables. This transformation is defined in such a way that the variance of the first principal
30 component is maximized, and each succeeding component in turn has the highest variance possible under the constraint that it be essentially orthogonal to (uncorrelated with) the preceding components. PCA is also known as the discrete Karhunen-Loève transform (KLT), the Hotelling transform or Proper Orthogonal Decomposition (POD).

In one example, the basis functions are generated by applying PCA to the
35 envelope segments $\mathbf{X}_i$ as follows:

1. Subtract the mean from each envelope segment $\mathbf{X}_i$.

2. Calculate a correlation/covariance matrix $\mathbf{R}_i$ for each envelope segment $\mathbf{X}_i$.
3. Calculate a mean correlation matrix, $\bar{\mathbf{R}}$, by averaging the different correlation matrices $\mathbf{R}_i$.
- 5 4. Calculate the eigenvectors and eigenvalues of the mean correlation matrix $\bar{\mathbf{R}}$, select the eigenvector corresponding to the largest eigenvalue as the most significant (first) basis function, etc, and include the K most significant basis functions in the basis function matrix Φ .

10 The number K may e.g. be selected such the total energy of the basis functions at least represents a minimum fraction of the total energy of the envelope segments, where the minimum fraction may be given by a value in the range of 75-99%. An example of a technique for determining the energy content of a basis function is found in "Bioelectrical Signal Processing in Cardiac and Neurological Applications", by Sörnmo and Laguna, Elsevier/Academic Press, Amsterdam, 2005.

15 Experiments indicate that $K = 2$ may be sufficient, although a larger or smaller number of basis functions may be used. Figs 7(a)-7(b) illustrate a first basis function ϕ_1 and a second basis function ϕ_2 , which have been determined for a set of envelope segments obtained from recordings at an anastomosis. The most significant basis
 20 function ϕ_1 may be seen as reflecting the average shape of the envelope segments, while the second basis function ϕ_2 may be seen as representing delayed contributions to the envelope segments. The illustrated basis functions have been obtained for envelope segments that contain both the positive and negative slopes of the acoustic pulses. If the segments contain only the negative slope of the acoustic pulses, as indicated in Fig.
 25 6(c), the basis functions may be given by the curve portion to the right of the dashed line in Fig. 7(a) and Fig. 7(b), respectively.

Reverting now to Figs 4(a)-4(d), these embodiments are intended to present different ways of using basis functions that represent the envelope (waveform) at the anastomosis, for assessing stenosis formation in an AV access. Unless stated otherwise,
 30 the different blocks 400-408 perform the operations described in the foregoing.

In the embodiment of Fig. 4(a), the basis functions Φ are pre-calculated and stored in memory 10. As indicated by the dashed box, the basis functions Φ may be generated by processing an acoustic signal S_A recorded on an anastomosis. In Fig. 4(a), the signal S_A may represent one signal recorded at one session, or several signals
 35 recorded at different sessions. The signal S_A may thus be recorded in one or more preceding sessions on the patient currently under examination, or it may be recorded on a group of different patients, possibly including the current patient. The generation

block 406' operates on envelope segments obtained from the signal S_A to calculate the basis functions Φ , which are later retrieved by the analysis block 406 for generating the position parameter P_{LX} from an acoustic signal S_{LX} recorded in a current session at a specific site LX on the AV access, where the site LX may but need not be spaced from the anastomosis A. The P_{LX} value(s) is then evaluated by block 408. This embodiment assumes that the pre-stored "global" or "general" basis functions Φ provide a sufficiently accurate representation of the envelope profile at the anastomosis of the current patient. In a variant, the global basis functions may be generated by computer or laboratory simulations of flow paths through an anastomosis.

In the embodiment of Fig. 4(b), pre-stored basis functions are intermittently updated, based on an acoustic signal S_A recorded on the anastomosis of the current patient. The signal S_A may be recorded in the same session as the signal S_{LX} , or in a preceding session. There are many different ways of updating the pre-stored basis functions. In the illustrated embodiment, the block 406' generates basis functions by processing envelope segments extracted from the signal S_A , and an updating block 410 modifies the stored basis functions as a function of the generated basis functions. For example, the generated basis functions may modify the stored basis function in proportion to the number of sessions used for generating the stored basis function. For example, if the stored basis functions originate from 1000 sessions, the generated basis functions are given a weight of 1/1000. Of course, other updating functions and weights may be used. It is to be noted that the stored basis functions may be truly global for use by all patients, group-wise global for use by a dedicated group of patients (e.g. patients with a given type of AV access, or a given vascular status), or individual for use by the current patient. It is realized that the updating in Fig. 4(b) may improve the quality of the stored basis function, and thereby potentially improve the performance of the evaluation block 408. For example, the updating enables the truly global basis functions to be based on a larger set of data, and the group-wise global and individual basis functions to be (gradually) adapted to the dedicated group of patients and the current patient, respectively.

In a variant, the updating block 410 replaces the pre-stored set of basis functions by the generated basis functions.

In another variant, the basis functions are updated by a complete recalculation based on the envelope segments extracted from the signal S_A , and the envelope segments obtained in previous sessions, for this and/or other patients. In such an embodiment, blocks 406' and 410 may be combined, and memory 10 may be arranged to store all previously extracted envelope segments. The combined block 406, 410 thus regenerates a set of basis functions based on newly and previously extracted envelope

segments and stores the set of basis functions and the newly extracted envelope segments in memory 10.

It is to be noted that the embodiment in Fig. 4(b), like the embodiment in Fig. 4(a), may be implemented with the signal S_{LX} being obtained at the anastomosis A.

5 In the embodiment of Fig. 4(c), the signal S_A and the signal S_{LX} are recorded in the same session, and the P_A value obtained for the signal S_A is used as a reference position by the evaluation block 408. In this embodiment, the signal S_{LX} is recorded at a test site spaced from the anastomosis A. In one implementation, the signal S_A may first be input for processing by blocks 400-408, resulting in a P_A value, and then the signal
10 S_{LX} may be input for processing by blocks 400-406, resulting in a P_{LX} value. The evaluation block 408 may then assess the likelihood of stenosis formation at the site LX based on the relative placement of the P_A and P_{LX} values in the coordinate space (cf. Figs 8-9). By obtaining the P_A and P_{LX} values in one and the same session, possibly simultaneously using two acoustic sensors (cf. 2A, 2B in Fig. 1), the influence of
15 varying conditions within the AV access may be taken into account. For example, it is currently believed that the flow rate of blood through the AV access may vary between sessions, or even within a session, and that these variations may modify the shape and/or location of the stenotic, anastomosis and healthy regions in the coordinate space (cf. Fig. 9).

20 As an alternative to the use of two acoustic sensors as exemplified in Fig. 4(c), a single acoustic sensor (cf. 2A in Fig. 1) for recording the signal S_{LX} may be used in combination with standard equipment for measurement of the current access flow, e.g. in the cross-sectional area of the test site LX. The current acoustic envelope obtained from the signal S_{LX} may then be normalized or otherwise transformed as a function of
25 the measured blood flow through the AV access, thereby making the current acoustic envelope essentially independent of current access flow. This will reduce the influence of temporal variations in access flow on the calculated parameter values. For example, the current acoustic envelope may be given with respect to a standard access flow. For example, the current acoustic envelope may be normalized/transformed through an
30 empirical or theoretical model that relates the acoustic signal obtained from an acoustic sensor at a test site to the blood flow through the AV access. A similar normalization/transformation may be operated on the reference envelope that is obtained from the signal S_A . This type of normalization/transformation may be used in any of the embodiments disclosed herein.

35 The embodiment of Fig. 4(c) also includes a stability detection block 412 which determines if the P_A values obtained in successive sessions are sufficiently stable, e.g. if the P_A values remain within a given zone in the coordinate space. Any lack of stability

may, e.g., be caused by formation of stenosis in the access and/or variations in access flow, blood pressure, water status, or body position of the patient between sessions. If the P_A values are deemed sufficiently stable, the generation block 406' is caused to generate a set of basis functions based on the envelope segments obtained from the signal S_A , whereupon the update block 410 stores an updated set of basis functions in memory 10. The updating may be executed as described in relation to Fig. 4(b). The updating may be made either before or after the blocks 400-406 operate on the signal S_{LX} .

In a variant, not shown, the stability detection may be included in the evaluation block 408 for the purpose of to assessing the stability of individual P_A values or P_{LX} values generated during the current test session. A sufficiently large dispersion in the P_A or P_{LX} values may cause the monitoring device 1 to abort the test session and/or output an indication, e.g. on the screen 12, for the operator to check the positioning of the acoustic sensor(s) 2A, 2B. This type of stability detection may be used in any of the embodiments disclosed herein.

In the embodiment of Fig. 4(d), acoustic signals are only recorded on the anastomosis A and processed for calculation of P_A values. As illustrated, the evaluation block 408 detects stenosis formation within the AV access by comparing the P_A value obtained for a signal S_A recorded in a current session t with the P_A value(s) obtained in one or more preceding sessions, here represented by session $t-m$. Thus, in this embodiment, stenosis formation is detected by tracking the P_A value over a number of sessions. As stenosis is formed within the AV access, the flow of blood through the access will change and cause a slight change in the shape of the envelope segments extracted from the signal S_A . This change may be represented as a change in the P_A values over a sequence of sessions. The analysis block 406 may e.g. operate on basis functions that are pre-stored as in Fig. 4(a), or updated as in Fig. 4(c). One advantage of the embodiment in Fig. 4(d) is that the recordings are made on a single site on the patient, the anastomosis, which is well-defined and often easy to find for the operator.

It is to be understood that the monitoring device may be configured to combine two or more of the embodiments in Figs 4(a)-4(d), or selected operations thereof. For example, it is conceivable to combine the analysis in Fig. 4(d) with the updating in Fig. 4(b) or Fig. 4(c). In one example, steps 400-408 in Fig. 4(d) are first executed to verify the signal S_A by computing and evaluating the P_A values of the current session, before basis functions are computed based on the signal S_A (by step 406' in Figs 4(b)-4(c))) and/or are used for updating the set of basis functions that are stored in memory 10 (by step 410 in Figs 4(b)-4(c))). For example, if the P_A values of the current session are

found to deviate significantly from the P_A values of preceding session(s), the monitoring device may refrain from updating the basis functions.

All of the above embodiments may be summarized in the flow chart of Fig. 5. A new session is started when a patient arrives at a test station for stenosis monitoring.

5 One or more acoustic sensors are applied to the skin of the patient, at one or more sites on the AV access. In step 50, one or more acoustic signals are obtained from the one or more sites. In step 51, one or more acoustic envelopes are determined for each signal. The acoustic envelopes may correspond to the above-described envelope segments. In step 52, shape-indicating data of a reference profile is obtained. In the embodiments of
10 Fig. 4, the reference profile corresponds to the set of basis functions that represent the envelope segment at the anastomosis. As explained above, the set of basis functions may, but need not, be obtained from an acoustic signal recorded on the anastomosis of the current patient. In step 53, a parameter value is generated. The parameter value may correspond to the P_{LX} value generated in the embodiments of Figs 4(a)-4(c) or the P_A
15 value generated in the embodiments of Figs 4(c)-4(d). In step 54, the status of the AV access is evaluated, based on the parameter value. In the foregoing embodiments, the "status" refers to signs of stenosis formation in the AV access. In step 55, information on the status and/or the parameter value as such is output, e.g. for storage in computer memory or for display to the operator on a screen. Then, the session ends and the
20 patient is disconnected from the test station.

The above-described monitoring device (cf. 1 in Fig. 1) and its signal processing (e.g. blocks 400-412 in Fig. 4) may be implemented by special-purpose software (or firmware) run on one or more general-purpose or special-purpose computing devices. In this context, it is to be understood that each "element" or "means" of such a computing
25 device refers to a conceptual equivalent of a method step; there is not always a one-to-one correspondence between elements/means and particular pieces of hardware or software routines. One piece of hardware sometimes comprises different means/elements. For example, a processing unit serves as one element/means when executing one instruction, but serves as another element/means when executing another
30 instruction. In addition, one element/means may be implemented by one instruction in some cases, but by a plurality of instructions in some other cases. Such a software controlled computing device may include one or more processing units, e.g. a CPU ("Central Processing Unit"), a DSP ("Digital Signal Processor"), an ASIC ("Application-Specific Integrated Circuit"), discrete analog and/or digital components,
35 or some other programmable logical device, such as an FPGA ("Field Programmable Gate Array"). The surveillance device may further include a system memory (cf. 10 in Fig. 1) and a system bus that couples various system components including the system

memory to the processing unit. The system bus may be any of several types of bus structures including a memory bus or memory controller, a peripheral bus, and a local bus using any of a variety of bus architectures. The system memory may include computer storage media in the form of volatile and/or non-volatile memory such as read only memory (ROM), random access memory (RAM) and flash memory. The special-purpose software, and the basis functions, envelope segments, test values etc, may be stored in the system memory, or on other removable/non-removable volatile/non-volatile computer storage media which is included in or accessible to the computing device, such as magnetic media, optical media, flash memory cards, digital tape, solid state RAM, solid state ROM, etc. The surveillance device may include one or more communication interfaces, such as a serial interface, a parallel interface, a USB interface, a wireless interface, a network adapter, etc, as well as one or more data acquisition devices, such as an A/D converter. The special-purpose software may be provided to the surveillance device on any suitable computer-readable medium, including a record medium, a read-only memory, or an electrical carrier signal. It is also conceivable that certain signal processing is fully or partially implemented by dedicated hardware, such as an FPGA, an ASIC, or an assembly of discrete electronic components (resistors, capacitors, operational amplifier, transistors, filters, etc), as is well-known in the art.

20

While the invention has been described in connection with what is presently considered to be the most practical and preferred embodiments, it is to be understood that the invention is not limited to the disclosed embodiments, but on the contrary, is intended to cover various modifications and equivalent arrangements included within the spirit and the scope of the appended claims.

25

For example, the acoustic envelope may be generated by any technique for generating an envelope curve that joins one of maxima and minima in a signal. In one example, the envelope curve is obtained by calculating the sum of absolute/squared signal values within an integration time window, which is selected to contain a plurality of signal values while being smaller than the spacing of the acoustic pulses (cf. Fig. 6). By sliding the integration time window along the acoustic signal, and calculating the sum for each of a number of partially overlapping integration time windows, the resulting sequence of sums will approximate the envelope of the monitoring signal. In another example, a conventional envelope detector or envelope follower may be used for generating the envelope curve. It is also to be understood that the envelope curve may be generated to represent either the amplitude modulation or the energy modulation

35

in the signal, where the energy modulation may be given by the amplitude values squared.

It is also conceivable that segmentation is done before envelope extraction. For example, if the timing of the heartbeats is available, e.g. from a timing signal generated by a pulse meter, an ECG, etc connected to the patient, the segments may be identified in the (preprocessed) acoustic signal S_A , S_{LX} based on the timing signal. Of course, the segmentation of the envelope curve (e.g. by block 404 in Fig. 4) may also use such a timing signal.

It is also possible to omit the segmentation altogether, and extract the shape-indicating data "on the fly". To give one example, the duration of the acoustic pulses may be directly obtained from an envelope curve, by counting the number of samples that fall between first and second predefined features of the acoustic pulses. The predefined features may e.g. be a peak of the acoustic pulse and/or a predefined level above the base level between consecutive acoustic pulses.

Further, the basis functions may be generated using other techniques than PCA, e.g. Independent Component Analysis (ICA), Fourier analysis/series, and Wavelet analysis. Still further, the basis functions are not necessarily generated to be orthogonal.

Theoretically, the basis functions may have any shape, as long as they may be used to represent (or at least partly represent) the envelope segments.

As noted above, the acoustic emission of interest may consist of frequencies in the approximate range of 20-2000 Hz, and often in the approximate range of 50-800 Hz. Generally, the acoustic envelope is generated to represent frequencies in a range of 20-2000 Hz, and preferably in a range defined by a lower cut-off frequency of about 20, 30, 50, 100, 150, 200, 250 or 300 Hz, and an upper cut-off frequency of 2000, 1000, 900, 800, 700, 600, 500 or 400 Hz. It is conceivable to process the acoustic signal, before envelope generation, to isolate frequencies in an even smaller range. In another variant, envelope curves are generated for different (two or more) frequency ranges in the acoustic signal, whereupon these envelope curves are processed separately or in combination in order to assess the stenotic status of the AV access.

The design and use of the acoustic sensors may be optimized in many different ways. In one example, an arm sleeve (cuff) may be equipped with numerous acoustic sensors arranged to allow supervision of plural sites across the AV access. The resulting acoustic signals may be analyzed individually or combined to allow e.g. interpolation of sounds between the sensors. In another example, the acoustic sensor may be arranged in a housing of transparent material to facilitate accurate positioning at the selected test site, and the housing may be further provided with a sighting reference, such as a cross hair.

The monitoring device 1 in Fig. 1 may be connected to a loudspeaker or headphone(s), so that the monitoring device may be used interactively by the operator to optimize positioning by auscultation, e.g. by listening to the acoustic signal generated by the acoustic sensor(s) 2A, 2B. The operator may also use the monitoring device 1 to
5 compare the actual sound with previously recorded sounds that represent the healthy/un-healthy states generally or for the patient under test. This feature may e.g. be used for education of inexperienced medical personnel.

It is also to be understood that the monitoring device may be configured to extract frequency parameters from the acoustic signal or the acoustic envelope, and use the
10 frequency parameters to supplement or even replace the test values generated by the above-described shape (waveform) analysis of the acoustic envelope. In one such embodiment, the monitoring device is configured to, in each session: obtain a current signal from an acoustic sensor arranged on the human subject to detect acoustic emission created by a flow of blood through an AV access; calculate a value of a
15 frequency parameter of the current signal; obtain a reference value of the frequency parameter for the acoustic emission at the anastomosis of the AV access, and assess the status of the AV access as a function of a comparison of the value and the reference value. The frequency parameter may be calculated for the current signal or the acoustic envelope and may, e.g., include any one of a signal magnitude (amplitude, energy, etc)
20 in a given frequency range, a relation of signal magnitudes in different frequency ranges, a characteristic feature of the power spectral density such as shape, magnitude, peak frequency, mean frequency, etc. The current signal may correspond to the signal S_{LX} described in relation to Figs 1-4, and the reference value may be obtained based on a reference signal such as the signal S_A described in relation to Figs 1-4.

25 In a further alternative, a multivariate prediction model is used for evaluating the stenotic status as a function of one or more shape features of an acoustic envelope. The multivariate prediction model may be obtained using any known technique, such as PLS (Partial Least Squares) regression. For example, PLS regression may be operated on a set of reference envelopes, where each reference envelope represents a certain stenotic
30 status (e.g. either a healthy site or a stenotic site, or a quantitative degree of stenosis), to generate a model F between observable variables X (shape features of the reference envelopes) and predictable variables Y (the stenotic status). During a test session on a patient, the model F is then used for predicting the stenotic status based on an acoustic envelope derived from an acoustic signal recorded at a test site on the patient, by
35 inputting the shape feature(s) of the acoustic envelope into the model, $Y=F(X)$, which outputs a prediction of the stenotic status at the test site. In one such embodiment, the monitoring device is configured to, in each session: acquire a current signal from an

acoustic sensor arranged on the human subject to detect acoustic emission created by a flow of blood through an AV access, obtain a multivariate model generated for a set of reference envelopes, and operate the multivariate model on shape-indicating data of the acoustic envelope to calculate a parameter value indicative of the status of the AV
5 access.

CLAIMS

1. A device for monitoring, in a sequence of time-separated sessions on a human subject, an arteriovenous access (4) which is configured to be connected in fluid communication with an extracorporeal fluid circuit (14), said device being configured to, in each session:
- 5 obtain a current signal from an acoustic sensor (2A, 2B) arranged on the human subject to detect acoustic emission created by a flow of blood through the arteriovenous access (4),
- 10 determine an acoustic envelope of the current signal,
- obtain shape-indicating data of a reference envelope which is representative of the acoustic emission at an anastomosis of the arteriovenous access (4), and
- process the acoustic envelope as a function of the shape-indicating data to calculate a parameter value indicative of the status of the arteriovenous access (4).
- 15 2. The device of claim 1, wherein the reference envelope is obtained to represent the acoustic emission at the anastomosis of the human subject in one or more preceding sessions, and wherein the current signal is obtained with the acoustic sensor (2A, 2B) arranged on the anastomosis of the human subject.
- 20 3. The device of claim 1, wherein the acoustic sensor (2A, 2B) is arranged at a location on the arteriovenous access (4) that is spatially separated from the anastomosis.
4. The device of claim 3, which is configured to obtain the shape-indicating data by: obtaining, in a current session, a reference signal representing a current acoustic emission at the anastomosis, and generating the shape-indicating data based at least partly on the reference signal.
- 25 5. The device of claim 4, which is configured to update previously stored shape-indicating data as a function of the reference signal.
- 30 6. The device of any preceding claim, wherein the shape-indicating data comprises at least two basis functions that represent the reference envelope.
- 35 7. The device of claim 6, wherein the basis functions are essentially orthogonal.

8. The device of claim 6 or 7, wherein the basis functions are obtained by Principal Component Analysis of a plurality of characteristic envelopes obtained to represent the acoustic emission at the anastomosis of one or more human subjects.

5 9. The device of claim 8, wherein each characteristic envelope represents a time-average of signal segments associated with heartbeats in an envelope curve obtained from an acoustic measurement signal.

10 10. The device of any one of claims 6-9, which is configured to process the acoustic envelope by: representing the acoustic envelope as a functional combination of the basis functions, and calculating a coefficient for each basis function in said functional combination.

15 11. The device of claim 10, wherein the parameter value is given by the coefficients.

20 12. The device of claim 10 or 11, wherein the coefficients define a current position in a coordinate space defined by said at least two basis functions, said device being further configured to: compare the current position to a reference position in the coordinate space.

 13. The device of claim 12, wherein the reference position is representative of the reference envelope.

25 14. The device of claim 12 or 13, which is configured to calculate the reference position by processing a reference signal obtained, in a current session, from an acoustic sensor (2A, 2B) arranged on the anastomosis of the human subject.

30 15. The device of claim 14, which is configured to obtain the current signal from a first acoustic sensor (2A) and to obtain the reference signal from a second acoustic sensor (2B).

35 16. The device of any one of claims 1-14, which is configured to obtain measurement data indicative of a current flow rate of blood through the arteriovenous access (4), wherein at least one of the acoustic envelope and the reference envelope is determined as a function of the measurement data such that said at least one of the acoustic envelope and the reference envelope is essentially independent of flow rate.

17. The device of any preceding claim, wherein the parameter value is indicative of stenosis formation in the arteriovenous access (4).

5 18. The device of claim 17, which is further configured to quantify the degree of stenosis formation as a function of the parameter value.

19. The device of any preceding claim, which is further configured to display the parameter value in real time.

10

20. The device of any preceding claim, wherein the acoustic envelope is determined for a time-dependent signal comprising frequencies in the range of approximately 20-2000 Hz.

15 21. The device of any preceding claim, which is configured to determine the acoustic envelope by: obtaining an envelope curve that joins one of maxima and minima in the current signal, and identifying envelope segments associated with heartbeats in the envelope curve.

20 22. The device of claim 21, which is further configured to generate an average envelope segment based on the envelope segments, and process the average envelope segment to calculate the parameter value.

23. The device of claim 21, which is further configured to generate individual
25 parameter values for each of the envelope segments, and to calculate the parameter value as an average of the individual parameter values.

24. A device for monitoring, in a sequence of time-separated sessions on a human
subject, an arteriovenous access (4) which is configured to be connected in fluid
30 communication with an extracorporeal fluid circuit (14), said device comprising and being configured to operate, in each session:

means (8; 400) for obtaining a current signal from an acoustic sensor (2A, 2B) arranged on the human subject to detect acoustic emission created by a flow of blood through the arteriovenous access (4),

35 means (402, 404) for determining an acoustic envelope of the current signal,

means (406, 406') for obtaining shape-indicating data of a reference envelope which is representative of the acoustic emission at an anastomosis of the arteriovenous access (4), and

5 means (406, 408) for processing the acoustic envelope as a function of the shape-indicating data to calculate a parameter value indicative of the status of the arteriovenous access (4).

25. A method of monitoring, in a sequence of time-separated sessions on a human subject, an arteriovenous access (4) which is configured to be connected in fluid
10 communication with an extracorporeal fluid circuit (14), each session of said method comprising:

obtaining a current signal from an acoustic sensor arranged to detect acoustic emission created by a flow of blood through the arteriovenous access (4),

determining an acoustic envelope of the current signal,

15 obtaining shape-indicating data of a reference envelope which is representative of the acoustic emission at an anastomosis of the arteriovenous access (4), and

processing the acoustic envelope as a function of the shape-indicating data to generate a parameter value indicative of the status of the arteriovenous access (4).

20 26. A computer-readable medium comprising computer instructions which, when executed by a processor, cause the processor to perform the method of claim 25.

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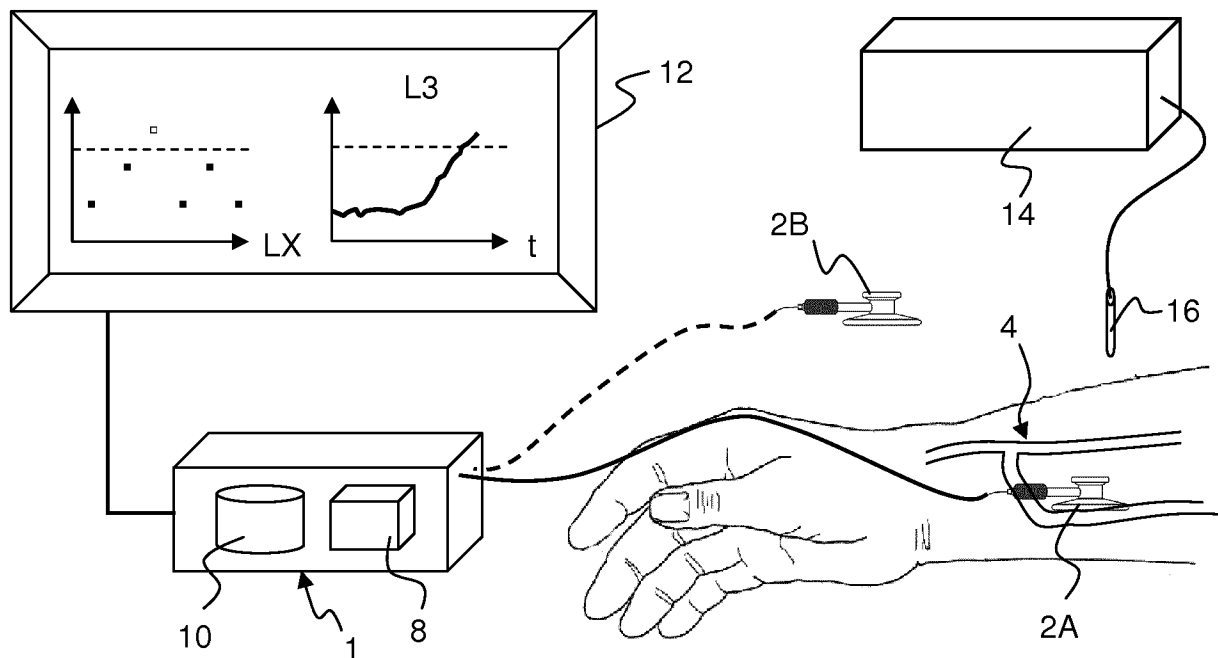


FIG. 1

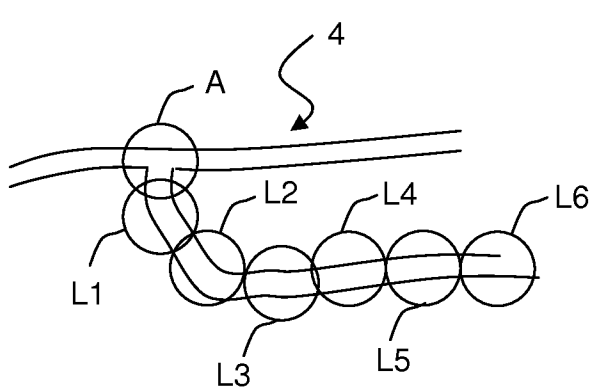


FIG. 2(a)

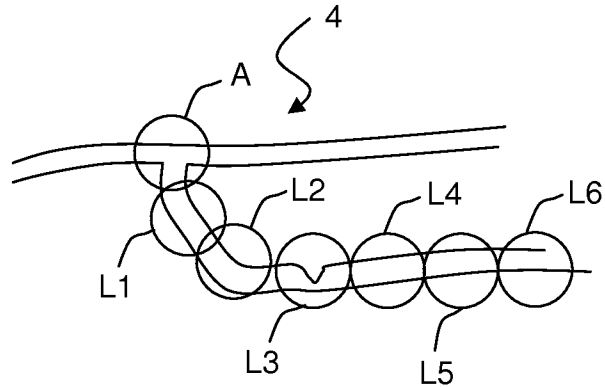


FIG. 2(b)

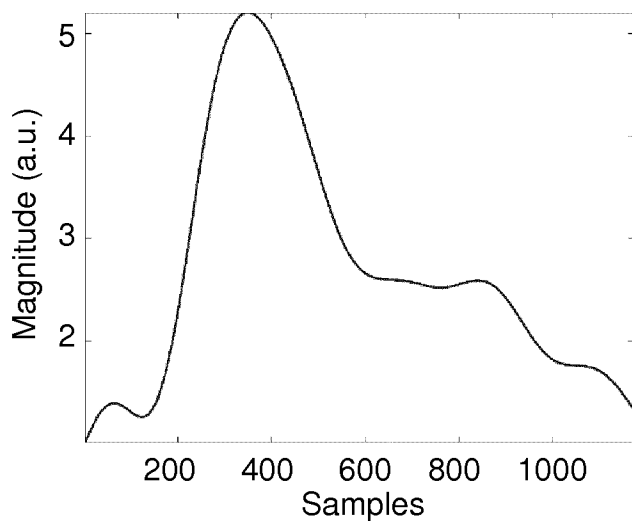


FIG. 3(a)

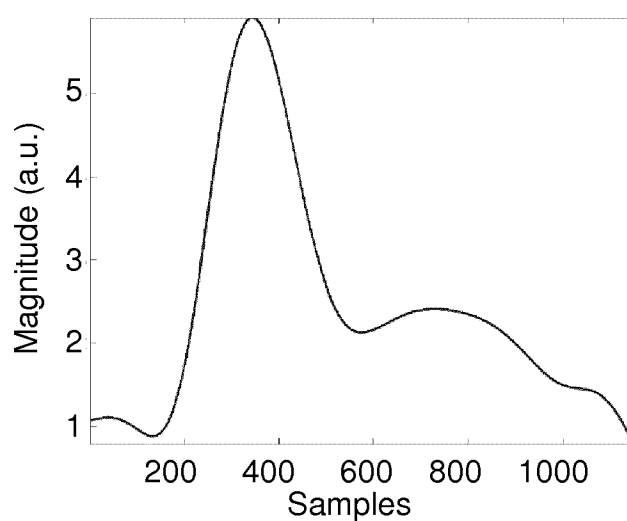


Fig. 3(b)

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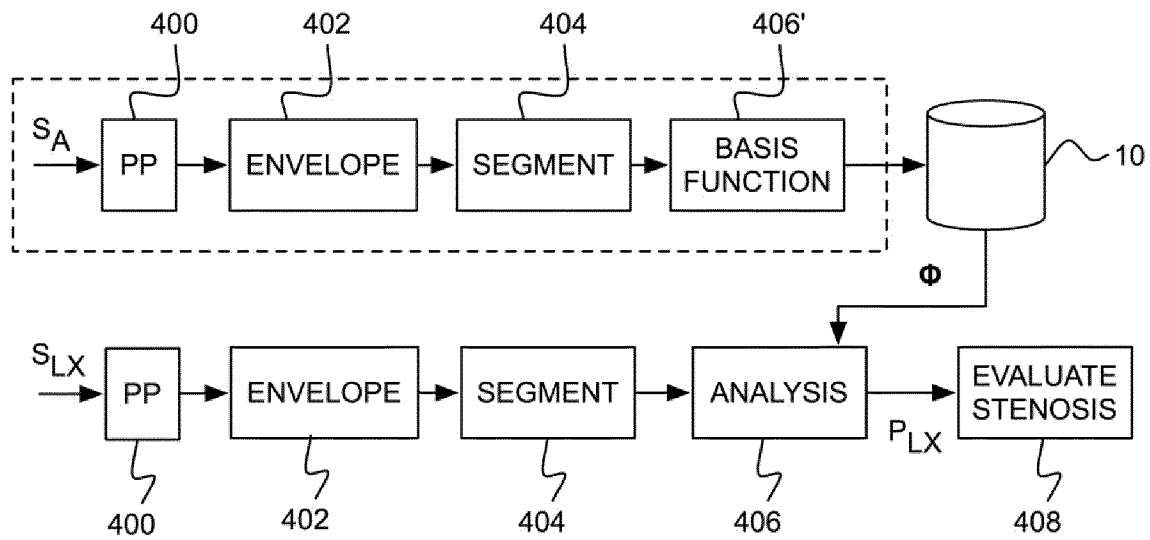


FIG. 4(a)

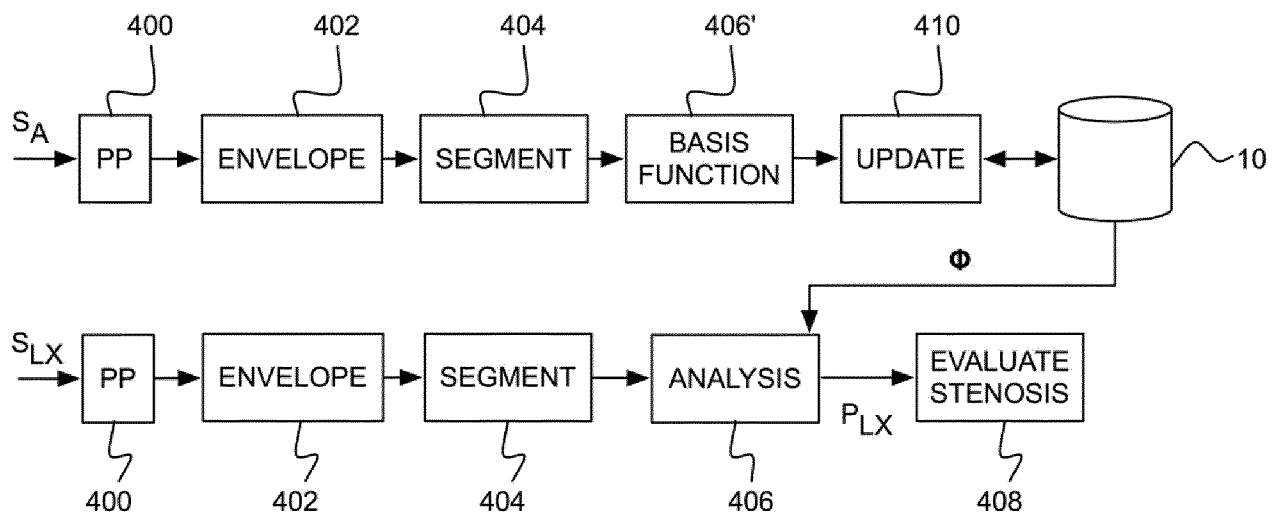


FIG. 4(b)

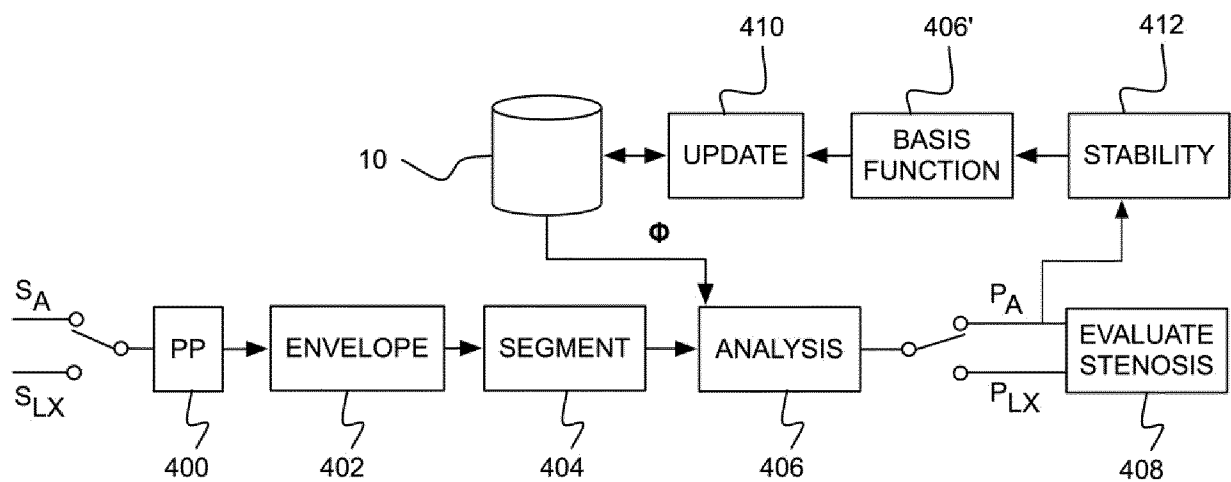


FIG. 4(c)

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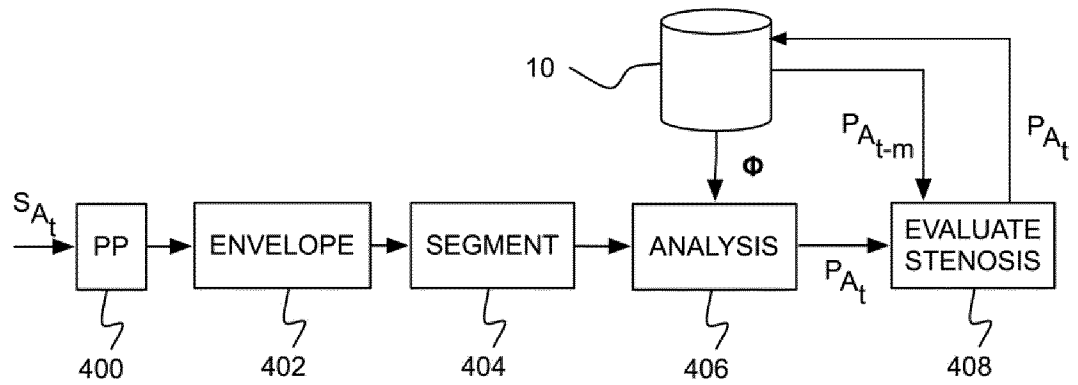


FIG. 4(d)

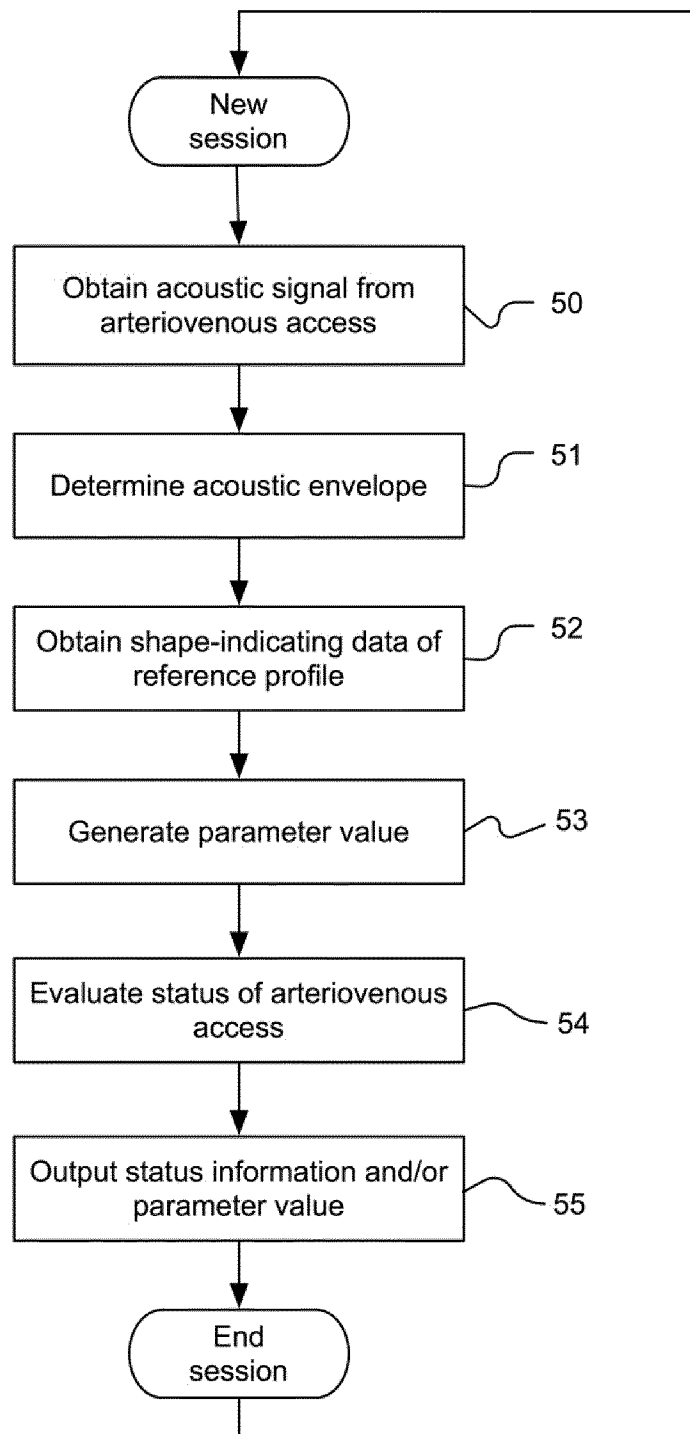


FIG. 5

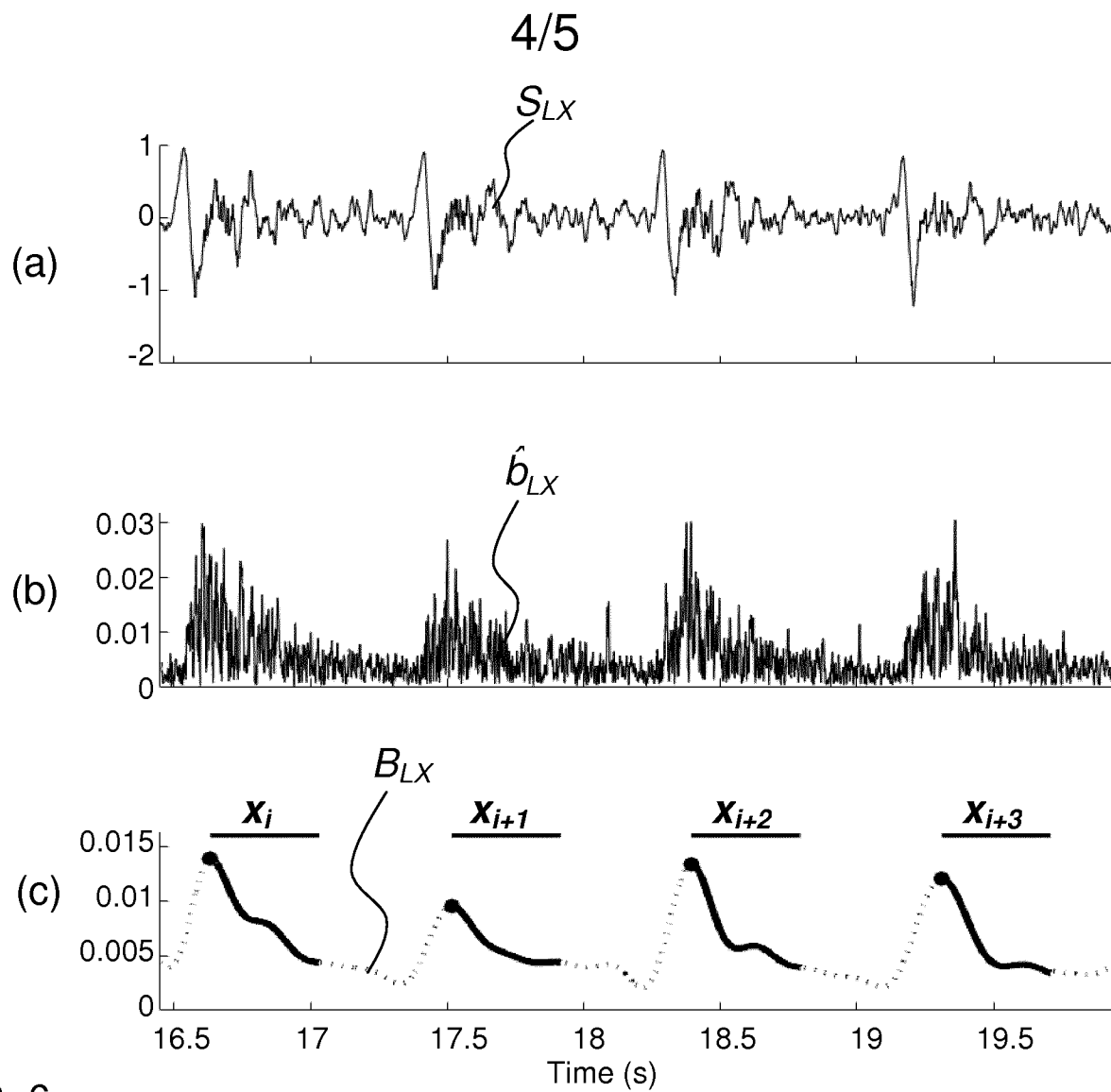


FIG. 6

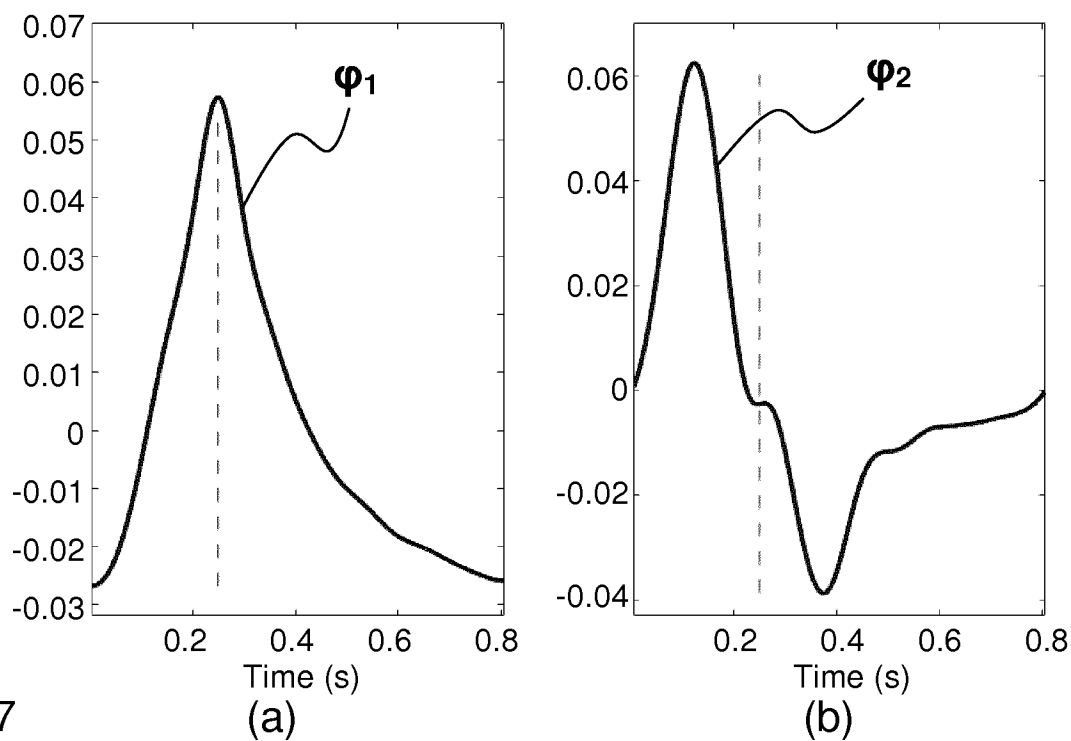


FIG. 7

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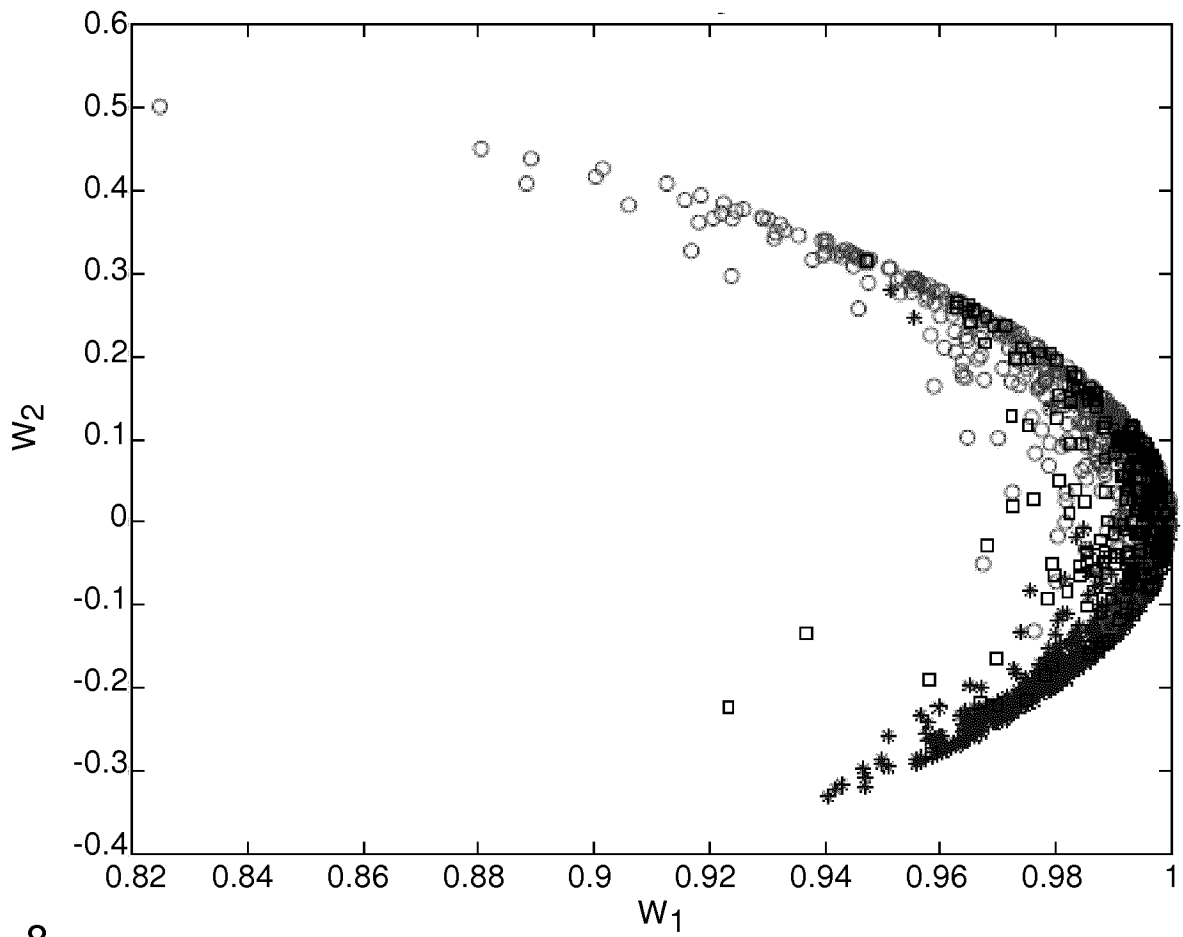


FIG. 8

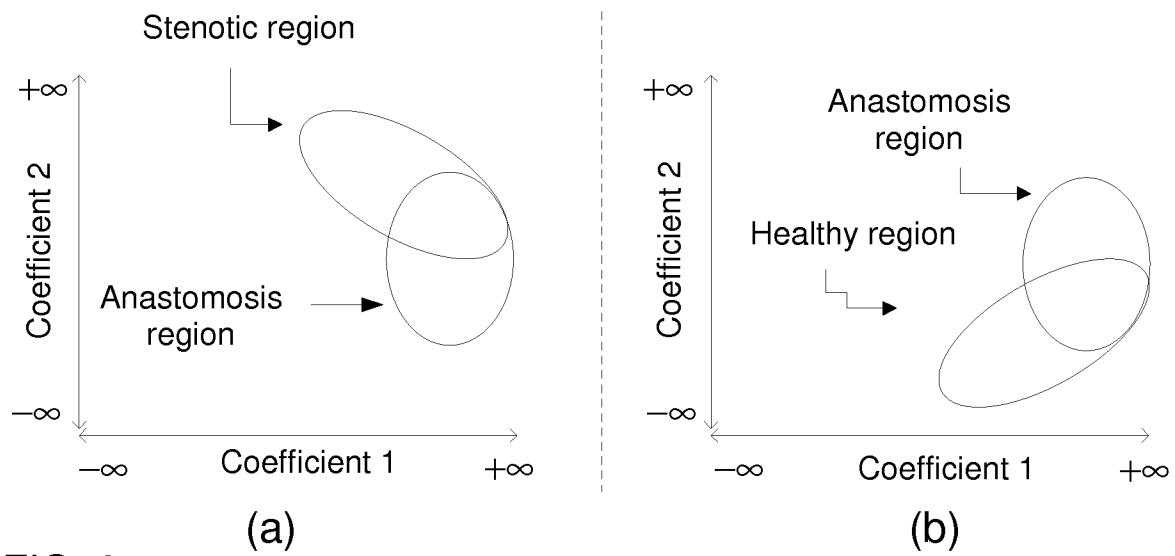


FIG. 9

INTERNATIONAL SEARCH REPORT

International application No
PCT/EP2012/059522

A. CLASSIFICATION OF SUBJECT MATTER
INV. A61M1/36
ADD.

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

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
A61M 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 practicable, search terms used)

EPO-Internal, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 2008/195021 A1 (ROGER RODOLFO G [US] ET AL) 14 August 2008 (2008-08-14) paragraphs [0001], [0021], [0098], [0101]; figures 2-3 -----	1-26
X	WO 2010/146371 A2 (QUANTA FLUID SOLUTIONS LTD [GB]; BUCKBERRY CLIVE [GB]) 23 December 2010 (2010-12-23) page 9, lines 30-32; claim 1; figures 1,2 -----	1,2, 4-15, 19-26
A	WO 93/00938 A1 (HOSPAL LTD [CH]) 21 January 1993 (1993-01-21) page 8, lines 28-35 -----	1
A	WO 2009/038834 A1 (BAXTER INT [US]; BAXTER HEALTHCARE SA [CH]; BENNISON CORRIE [US]) 26 March 2009 (2009-03-26) paragraphs [0011], [0041] - [0043], [0049]; figure 1 -----	1-26



Further documents are listed in the continuation of Box C.



See patent family annex.

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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

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"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

5 September 2012

Date of mailing of the international search report

13/09/2012

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Authorized officer

Westsson, David

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

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