(12) STANDARD PATENT (11) Application No. **AU 2005216588 B2**
(19) AUSTRALIAN PATENT OFFICE

(54) Title
Method for the determination of hemodynamic parameters

(51) International Patent Classification(s)
A61B 5/0215 (2006.01)

(21) Application No: **2005216588** (22) Date of Filing: **2005.02.16**

(87) WIPO No: **WO05/082243**

(30) Priority Data

(31) Number	(32) Date	(33) Country
10 2004 009 871.9	**2004.02.26**	**DE**

(43) Publication Date: **2005.09.09**
(44) Accepted Journal Date: **2010.06.17**

(71) Applicant(s)
Deutsches Herzzentrum Berlin

(72) Inventor(s)
Wellnhofer, Ernst

(74) Agent / Attorney
Spruson & Ferguson, Level 35 St Martins Tower 31 Market Street, Sydney, NSW, 2000

(56) Related Art
FR 2868936
US 6290652
US 5865758
US 2004/0024294

(12) NACH DEM VERTRAG ÜBER DIE INTERNATIONALE ZUSAMMENARBEIT AUF DEM GEBIET DES PATENTWESENS (PCT) VERÖFFENTLICHTE INTERNATIONALE ANMELDUNG

(19) Weltorganisation für geistiges Eigentum
Internationales Büro

(43) Internationales Veröffentlichungsdatum
9. September 2005 (09.09.2005)

PCT

(10) Internationale Veröffentlichungsnummer
WO 2005/082243 A2

(51) Internationale Patentklassifikation[7]: A61B 5/0215

(21) Internationales Aktenzeichen: PCT/DE2005/000304

(22) Internationales Anmeldedatum:
16. Februar 2005 (16.02.2005)

(25) Einreichungssprache: Deutsch

(26) Veröffentlichungssprache: Deutsch

(30) Angaben zur Priorität:
10 2004 009 871.9
26. Februar 2004 (26.02.2004) DE

(71) Anmelder *(für alle Bestimmungsstaaten mit Ausnahme von US)*: **DEUTSCHES HERZZENTRUM BERLIN** [DE/DE]; Augustenburger Platz 1, 13353 Berlin (DE).

(72) Erfinder; und
(75) Erfinder/Anmelder *(nur für US)*: **WELLNHOFER, Ernst** [DE/DE]; Tauroggener Strasse 6, 10589 Berlin (DE).

(74) Anwalt: **NINNEMANN, Detlef**; Patentanwälte, Maikowski & Ninnemann, Postfach 15 09 20, 10671 Berlin (DE).

(81) Bestimmungsstaaten *(soweit nicht anders angegeben, für jede verfügbare nationale Schutzrechtsart)*: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Bestimmungsstaaten *(soweit nicht anders angegeben, für jede verfügbare regionale Schutzrechtsart)*: ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), eurasisches (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), europäisches (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Veröffentlicht:
— *mit einer Erklärung gemäss Artikel 17 Absatz 2 Buchstabe a; ohne Zusammenfassung; Bezeichnung von der Internationalen Recherchenbehörde nicht überprüft*

Zur Erklärung der Zweibuchstaben-Codes und der anderen Abkürzungen wird auf die Erklärungen ("Guidance Notes on Codes and Abbreviations") am Anfang jeder regulären Ausgabe der PCT-Gazette verwiesen.

(54) **Title:** METHOD FOR THE DETERMINATION OF HEMODYNAMIC PARAMETERS

(54) **Bezeichnung:** VERFAHREN ZUR BESTIMMUNG HÄMODYNAMISCHER PARAMETER

(57) **Abstract:**

(57) **Zusammenfassung:**

WO 2005/082243 A2

METHOD FOR DETERMINING HAEMODYNAMIC PARAMETERS

Description

The invention relates to a method for determining haemodynamic parameters from patient pressure signals.

For the invasive, intra-arterial and intravenous pressure measurement in cardiology, intensive medicine and anaesthesia transfer systems are used in which the pressure measurement is carried out in the body of a patient and transferred through the transfer system, which is designed for example as a catheter, to a storage medium set away from the patient body.

There is therefore the need to both store and analyse the transferred data. It is particularly of interest to determine from the incoming data haemodynamic parameters from which a doctor can deduce his diagnosis.

There is frequently the problem that the incoming signals originating in the body of the patient are subject to errors (artefacts). Such errors arise in particular in dependence on the length, cross-section, structure and properties of the catheter material. This can lead to resonances, attenuations and energy losses in the detected measured pressure value which ultimately leads to a falsification of the patient signal.

2005216588 31 May 2010

One method for correcting such artefacts which are conditioned through the transfer system, is known from DE 198 20 844 A1; one method for determining and monitoring the transfer function of the transfer system is described in DE 100 49 734 A1.

However artefacts also often occur which are not conditioned by transfer errors, such as for example motion artefacts which happen through manipulation on the catheter or knocking of the catheter in the vessel or through a break in the pressure measurement when changing the catheter or injection, as well as such artefacts which arise on flushing through the system. The haemodynamic parameters which are calculated from such falsified patient signals can thus not provide the doctor with a suitable foundation on which to base his diagnosis.

Object of the Invention

It is the object of the present invention to substantially overcome or ameliorate one or more of the disadvantages of the prior art.

Summary of the Invention

The present invention provides a method for determining haemodynamic parameters from patient pressure signals, wherein the method comprises the steps:

a) receiving patient pressure signals from a measurement receiver to which vessel pressures measured in the body of a patient are supplied,

b) selecting and determining a patient pressure signal as reference pressure signal from the patient pressure signals sent from the measurement receiver,

c) dividing the patient pressure signals and reference pressure signal into segments,

d) examining these segments for artefacts with methods in the time range by using the first derivative with respect to time of the pressure signals wherein artefact-afflicted segments are discarded,

e) determining the start and end of a heart beat by means of the reference pressure signal, and

f) using the non-discarded segments of the patient pressure signals for calculating haemodynamic parameters.

Preferably, the examination of the segments for artefacts is carried out with methods in the time and frequency range.

Preferably, an analysis of the derivatives with respect to time is carried out for determining the signal type.

2005216588 31 May 2010

Preferably, for determining the signal type, a discriminant analysis or logistic regression is carried out based on beat-wise analysis of the pressure curve in the time and frequency range.

Preferably, to calculate the beat volume as haemodynamic parameter a beat-wise multiple regression based on parameters from standardised Fourier spectra and analysis of the pressure curve and their derivatives is undertaken in the time range.

Preferably, for calibrating the beat volume as haemodynamic parameter is used the size or weight or sex or age or a combination thereof.

Preferably, an evaluation typical of the signal-type is carried out.

Preferably, a low frequency analysis is carried out.

Preferably, the calculated haemodynamic parameters are stored electronically or displayed on an output unit.

Preferably, the output unit is a monitor.

Description of the Preferred Embodiments

After receiving patient signals through a measured value receiver according to step a) and before selecting and determining a patient pressure signal as reference pressure signal from the patient pressure signals sent by the measured value receiver according to step b) it is possible to carry out where required a preliminary processing of the signals for correcting the artefacts conditioned through the transfer system using the methods described in DE 198 20 844 A1 and DE 100 49 734 A1. The artefacts conditioned through the transfer system are thereby corrected.

By selecting and determining a patient pressure signal as reference pressure signal according to step b) it is ensured that a reliable stable recognition of the heart beats is carried out.

The division of the patient pressure signals and reference pressure signals into segments according to step c) enables a high-resolution examination and processing of the pressure signals in the following steps.

Step d) serves to identify motion artefacts, rinsing artefacts and/or other flagrant mechanical artefacts, as well as signal breaks and noise artefacts for each signal, including the reference signal. For this an investigation is made into the relevant deviation of the derivative of the signal from for example a smoothed copy of the relevant signal, or the differences of mean, minimum and maximum,

the deviation of the signal from a regression line and further analyses in the time and frequency range. By separating out flagrant artefacts it is ensured that only suitable patient pressure signal segments are included for calculating haemodynamic parameters.

There are basically two possibilities for determining artefacts, namely both segment-wise and beat-wise.

By one segment is thereby meant a specific time section which is to be defined and in which the relevant pressure signal is considered. One segment can thereby comprise for example 500 ms. For a beat-wise artefact determination, on the other hand, a time section is used which corresponds to one beat period.

Fixing the time of the beginning and end of a heart beat with the aid of the reference pressure signal according to step e) enables the local search for the start and end of the corresponding heart beat from other patient pressure signals.

The non-discarded patient pressure signal segments can now serve according to step f) for calculating haemodynamic parameters which are based on unfalsified pressure data.

As will be described below different haemodynamic parameters can be calculated with the aid of the method according to the invention. More particularly the patient pressure signals and/or reference pressure signals are used as the basis for determining the type of signal, determining the cardiac output, determining the beat at the reference signal, for an evaluation typical of the type of signal and for a low frequency analysis (of the so-called Mayer waves).

1. Beat determination on the reference signal

A threshold value determination dependent on the type of signal takes place for the derivative of the pressure according to time. By means of a flooding algorithm a search is made for the peaks of this derivative, followed by an examination whether it is a local maximum. For this, the second derivative is investigated in a local surrounding. Finally a check is carried out for plausibility dependent on the type of signal.

The determination of the start and end of the beat is then carried out in the other signals using the results of this first step.

2. Determining the type of signal (facultative)

Based on the time definition of the length of the heart beat, an investigation is made from the relevant pressure signals and their first and second derivative according to time of corresponding sections in order to identify the type of signal whereby it is possible to use as signal type for example the left-ventricular, systemic arterial, pulmonal-arterial, right-ventricular, right-atrial or pulmonal-capillary closure pressure. For the purpose of identifying the type of signal a feature extraction is carried out by determining in addition to the pulsatility index, the maximum derivative of the pressure according to time, statistical parameters (medians, mean values and moments as well as parameters from the Fourier transformation of the beat curve and their derivatives. Further features are obtained from breaking down the curve into two halves relative to the time axis and/or an investigation of higher moments or cumulants of the curve in the complex graph. The time axis thereby forms the real part and the pressure the imaginary part of the complex graph.

Determining the type of signal is carried out by combining a score system, a stepwise logistic regression and/or a discriminant analysis and plausibility check.

The logistic regression or discriminant analysis uses both values from the time range and also characteristics of the Fourier transformation of the relevant beat.

3. Cardiac output determination

Determining the cardiac output also takes place based on the time definition of a heart beat length.

The determination algorithm for determining a cardiac output thereby has a facultative measuring-position-dependent multiple regression for resistance, beat volume and cardiac output, a plausibility check as well as a fine correction. The multiple regression uses both values from the time range and also characteristics of the Fourier transformation of the relevant beat. This is thereby not a pulse contour analysis.

4. Evaluation typical of a signal type

Specific haemodynamic parameters are calculated in dependence on the type of pressure signals measured.

The calculation of the following parameters is thus possible for ventricle pressure signals:

Systolic, minimal and endiastolic pressures, maximum and minimum of the derivative of the pressure according to time, time tension index (TTI), maximum shortening speed (VPM), developed pressure, pulsatility, relaxation time (tau).

For artery pressures it is possible to determine systolic, diastolic and mean pressure, as well as maximum and minimum of the derivative of the pressure according to time. Furthermore ejection time, pulse pressure and a pulsatility index can also be calculated.

V-wave, A-wave, maximum, minimum and mean pressure can be determined for auricle pressures.

5. Low Frequency Analysis (Mayer waves)

For low frequency analysis a power spectrum estimation is carried out by means of an eigenvalue process (with four to six sub chambers). The power spectrum thus obtained is logarithmed. A further power spectrum estimation by means of an eigenvalue process (with two sub chambers) supplies a severely smoothed spectrum which represents substantially the very low frequency component. The logarithmed very low frequency component is subtracted from the logarithmed total power spectrum power. The very low frequency component is thereby removed.

Then two maxima and the minimum in between are then identified. The positions of the low frequency component and the high frequency component are identical with those of the delogarithmed residual spectrum after removing the very low frequency component.

A delogarithmization of the residual spectrum and a determination of the power integral of the low and high frequency components are then carried out.

To determine the type of signal advantageously an analysis of the first derivative according to time is then carried out whereby the function f2 of the reference pressure signal is dependent on the time. To calculate the cardiac output as haemodynamic parameter the first and second derivative of a function f1 is determined according to the time whereby the function f 1 of the patient pressure signals is dependent on the time.

The determined haemodynamic parameters can advantageously be stored on a output unit more particularly an electronic data medium such as a memory disc, network or patient information system and/or displayed on a monitor. The parameters can furthermore be transferred directly into a patient information system.

In one development of the invention the method has an automatic identification based on a logistical analysis of the type of the measured patient pressure, more particularly a pressure of the left ventricle, the aorta, the right ventricle, the pulmonal artery, the pulmonal capillary closure pressure as well as the right auricle.

The method according to the invention for determining haemodynamic parameters will be explained in further detail with reference to the drawings. They show:

Figure 1 a block circuit diagram of a device which is suitable for carrying out the method for determining haemodynamic parameters;

Figure 2 a flow chart of the method for determining haemodynamic parameters;

Figure 3 a graphic representation of the first derivative of the pressure signal of the left ventricle over time and

Figure 4 a graphic representation of the first derivative of the pressure signal of the aorta over time.

Figure 1 shows the principle structure of an invasive pressure measurement wherein a catheter 2 forming the transfer system is moved through the venous or arterial system of a patient 1 into the vicinity of the point where the pressure measurement is to be performed. A pressure converter 3 generates in dependence on the patient pressure signals electrical signals which are supplied to an analog/digital converter 4. The signals converted in the analog/digital

converter 4 are then forwarded to a measurement receiver in the form of a signal-analysis and processing unit 5 in which the method according to the invention for determining haemodynamic parameters is carried out. The calculated haemodynamic parameters are then forwarded to an output unit 6 more particularly in the form of an electronic data medium or monitor.

Figure 2 shows a flow chart of the method for determining haemodynamic parameters.

According to this method, first a selection of a patient pressure signal as a reference pressure signal is carried out from the received patient pressure signals. After dividing the patient pressure signals and the reference pressure signal into segments, a check is made on these segments for artefacts with processes in the time and where necessary frequency range. For this the first and second derivative of the pressure signals is determined according to time.

A beat determination is then carried out on the reference signal and/or on further signals. A beat-wise examination of the artefacts is then carried out on the basis of the length of a heat beat. Such artefacts are for example motion artefacts which arise through manipulation on the catheter, knocking of the catheter in the vessel, interruption in the pressure measurement when changing catheter, injection or flushing of the system. Those segments which are identified as afflicted with artefacts are discarded. As an optional measure an automatic beat type determination can now be carried out.

A signal-specific evaluation is carried out on the basis of the beat-wise artefact examination. A cardiac output determination and/or low frequency analysis are optionally carried out.

The calculated haemodynamic parameters can be displayed on an output unit e.g. a monitor. In an advantageous embodiment of the invention the results can

be integrated into the digital patient files and/or an automatic findings report or text processing to the doctor's notes.

Figure 3 shows a graphic representation of a left ventricular (LV) patient pressure signal 7 and the associated first derivative 8 over time. On the abscissa is entered the time in seconds, on the ordinate the pressure in millimetres mercury column (mmHg) and the first derivative of the pressure according to time in millimetres mercury column per second (mmHg/sec), scaled down by factor 0.01 for graphic reasons.

Different haemodynamic parameters are determined using the method according to the invention. Patient pressure signals are thereby received from a measurement receiver which measures vessel pressures in the body of the patient.

After checking for (flagrant) artefacts only patient pressure signal segments with sufficient quality are analysed. After selecting and determining a patient pressure signal as reference pressure signal from the patient pressure signals 7 sent by the measurement receiver, the time range of one heart beat is found and the start and end of the heart beat around this time is determined on the actual patient pressure signal. In the illustrated case the reference signal was a femoral pressure signal.

The ventricle beat precedes a beat of this reference signal. The maximum of the first derivative of the ventricle pressure signal beat within a time vicinity (e.g. 100 ms) of the maximum of the first derivative of the femoral pressure signal beat is sought and then starting from this point the beginning of the steep rise of the ventricle pressure signal is sought (end diastole of the previous beat , 9). The end of the beat is thus precisely determined. After determining the heart beat at the actual pressure signal a beat wise examination of artefacts still takes place once more.

The non-discarded patient pressure signals are used for calculating haemodynamic parameters. The curve shows the result of an automatic analysis. The beat starts at the rise of the pressure curve with the end diastole of the previous beat 9. The maximum of the derivative 10 is located at the point of the steepest rise. The next points to follow in time sequence are the systolic maximum 11 of the pressure, the minimum 12 of the derivative at the steepest drop in pressure, the minimum of the pressure 13 in the beat range and the end diastole 14 of the actual beat. From the beat length is calculated the heart frequency (HF) at for example 85 beats per minute, from the beat is furthermore determined the mean pressure at 67 mmHg, the developed pressure (DP) as pressure maximum minus end-diastolic pressure at 127 mmHg, the dimension-less pulsatility index (PI) as pressure amplitude through mean pressure at 2, 1999, the relaxation time (tau) according to five different methods known to the expert from literature at tau = 16 msec, the maximum shortening speed (VPM) after a calculation likewise known to the expert at VPM = 2,8478 Hz and the time tension index (TTI) as integral of the pressure in the systole at TTI = 44,7269 mmHg*sec.

The calculated parameters can then be displayed on an output unit 6 as data files, on the screen or on a monitor.

Figure 4 shows a graphic representation of a patient pressure signal 7' from the aorta (AO) and the associated first derivative 8' over time. On the abscissa is entered the time in seconds, on the ordinate the pressure in millimetre mercury column (mmHg) and the first derivative of the pressure according to time in millimetre mercury column per second (mmHg/sec) , scaled down by factor 0.01 for graphic reasons.

The beat identification, automatic analysis and representation corresponds to the beat identification, automatic analysis and representation described in connection with Figure 2. Instead of the developed pressure, with arterial pressures the pulse pressure (PP) and the ejection time (ET) in milliseconds (msec) are determined.

A calculation of the beat volume (ml/min), the cardiac output (CO) in litres per minute (l/min) and the system resistance (Res) is provided facultatively.

In the illustrated example the following haemodynamic parameters are calculated: the pulse pressure is determined at PP= 76 mmHg, the ejection time amounts to ET = 306 msec, the cardiac output CO = 7 l/min and the system resistance result at Res = 13.4 Wood units. Furthermore a heart frequency HF is calculated as 84 beats per minute. The mean pressure is determined at 94 mmHg and the dimension-less pulsatility index (PI) is determined at 0.83076.

2005216588 21 Feb 2006

The claims defining the invention are as follows:

1. Method for determining haemodynamic parameters from patient pressure signals, wherein the method comprises the steps:

   a) receiving patient pressure signals from a measurement receiver to which vessel pressures measured in the body of a patient are supplied,

   b) selecting and determining a patient pressure signal as reference pressure signal from the patient pressure signals sent from the measurement receiver,

   c) dividing the patient pressure signals and reference pressure signal into segments,

   d) examining these segments for artefacts with methods in the time range by using the first derivative with respect to time of the pressure signals wherein artefact-afflicted segments are discarded,

   e) determining the start and end of a heart beat by means of the reference pressure signal, and

   f) using the non-discarded segments of the patient pressure signals for calculating haemodynamic parameters.

2. Method according to claim 1, wherein the examination of the segments for artefacts is carried out with methods in the time and frequency range.

3. Method according to claim 1 or 2, wherein an analysis of the derivatives with respect to time is carried out for determining the signal type.

4. Method according to claim 1 or 2, wherein, for determining the signal type, a discriminant analysis or logistic regression is carried out based on beat-wise analysis of the pressure curve in the time and frequency range.

2005216588 31 May 2010

5. Method according to any one of the preceding claims, wherein to calculate the beat volume as haemodynamic parameter a beat-wise multiple regression based on parameters from standardised Fourier spectra and analysis of the pressure curve and their derivatives is undertaken in the time range.

6. Method according to claim 5, wherein for calibrating the beat volume as haemodynamic parameter is used the size or weight or sex or age or a combination thereof.

7. Method according to any one of the preceding claims, wherein an evaluation typical of the signal-type is carried out.

8. Method according to any one of the preceding claims, wherein a low frequency analysis is carried out.

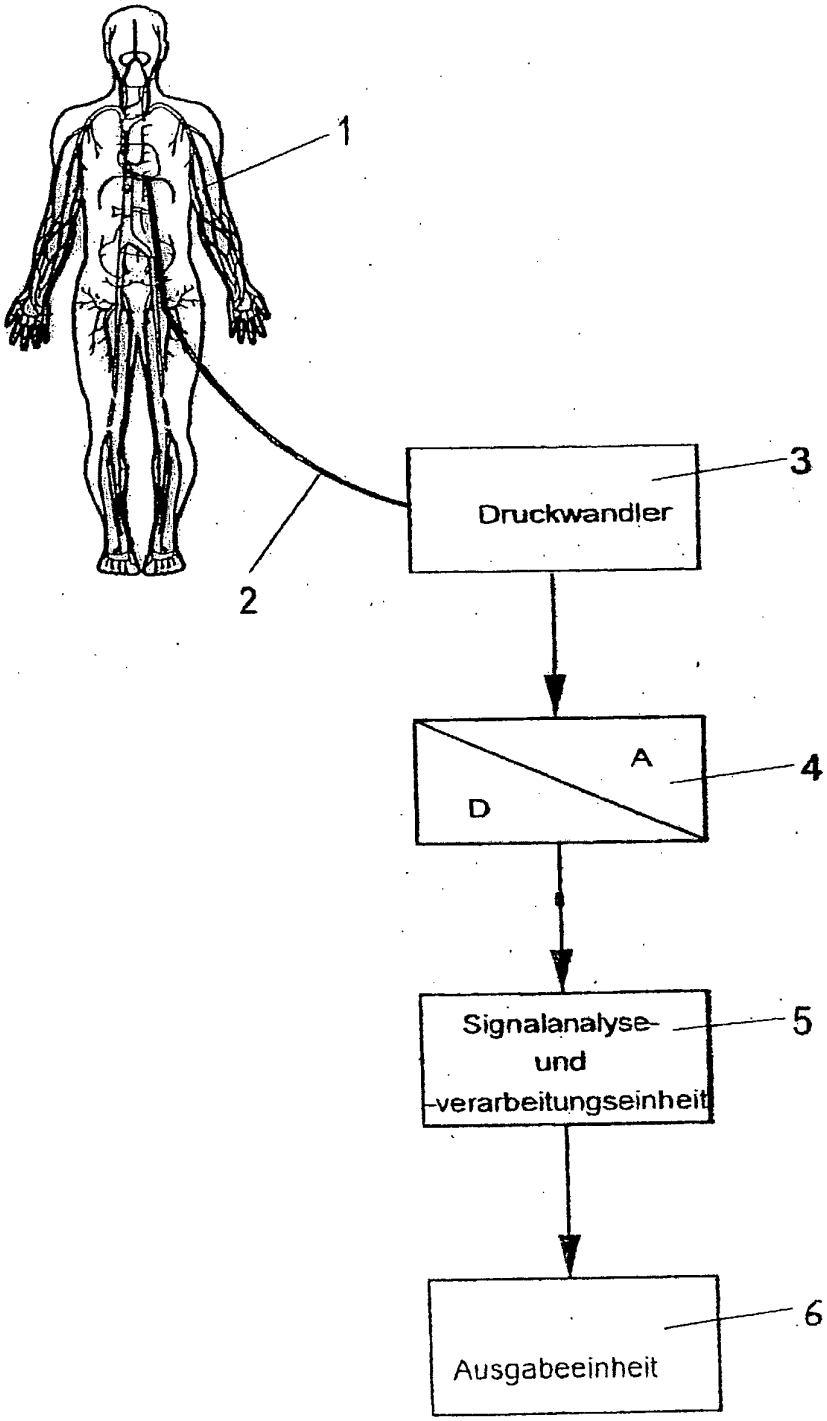
9. Method according to any one of the preceding claims, wherein the calculated haemodynamic parameters are stored electronically or displayed on an output unit.

10. Method according to claim 9, wherein the output unit is a monitor.

11. Method for determining haemodynamic parameters from patient pressure signals, said method substantially as hereinbefore described with reference to the accompanying drawings.

Dated 28 May 2010
Deutsches Herzzentrum Berlin
Patent Attorneys for the Applicant/Nominated Person
SPRUSON & FERGUSON

Fig. 1


1
2
Druckwandler
3
A
D
4
Signalanalyse- und verarbeitungseinheit
5
Ausgabeeinheit
6

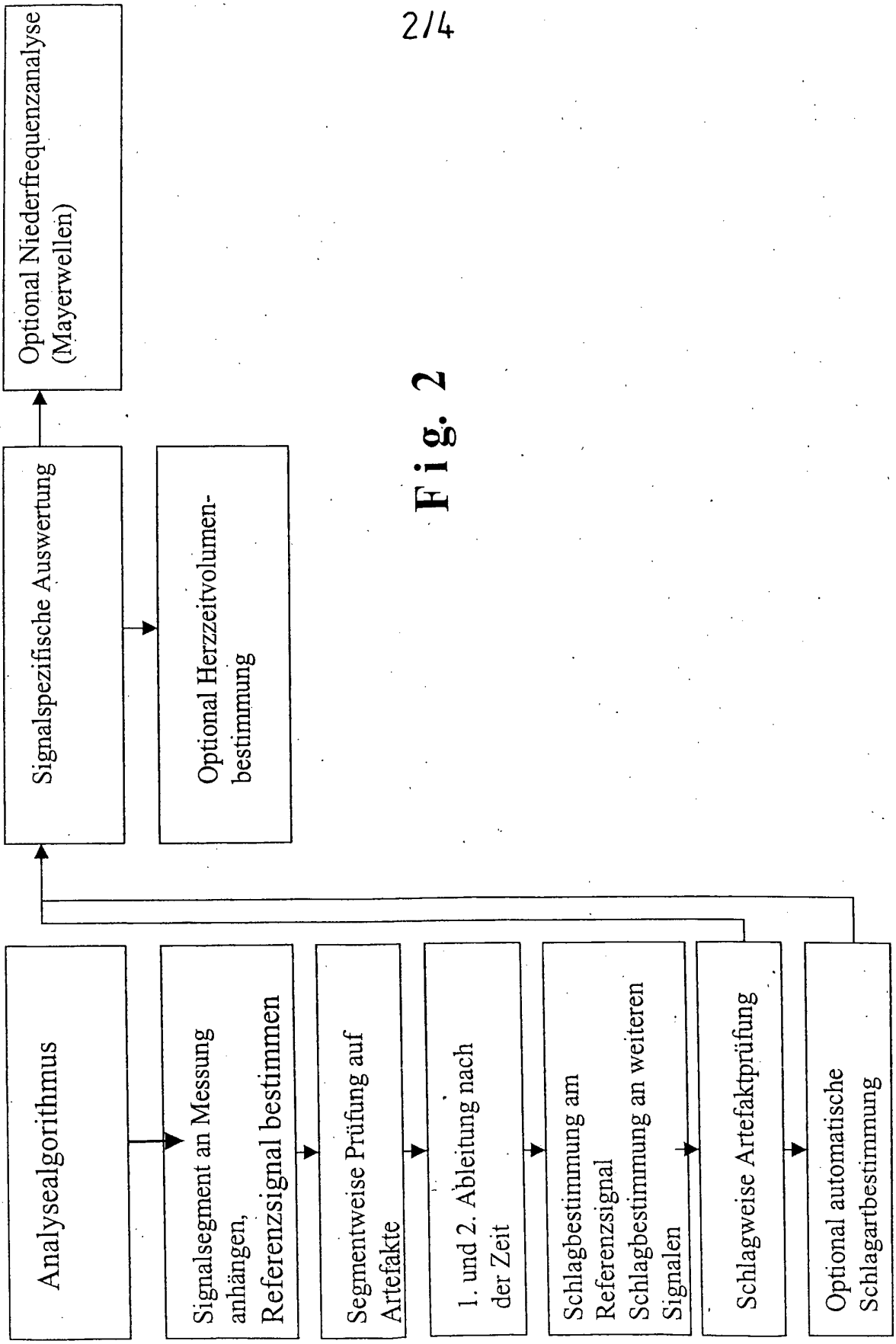

Analysealgorithmus
Signalsegment an Messung anhängen, Referenzsignal bestimmen
Segmentweise Prüfung auf Artefakte
1. und 2. Ableitung nach der Zeit
Schlagbestimmung am Referenzsignal Schlagbestimmung an weiteren Signalen
Schlagweise Artefaktprüfung
Optional automatische Schlagartbestimmung
Signalspezifische Auswertung
Optional Herzzeitvolumen-bestimmung
Optional Niederfrequenzanalyse (Mayerwellen)

Fig. 2

Fig. 3

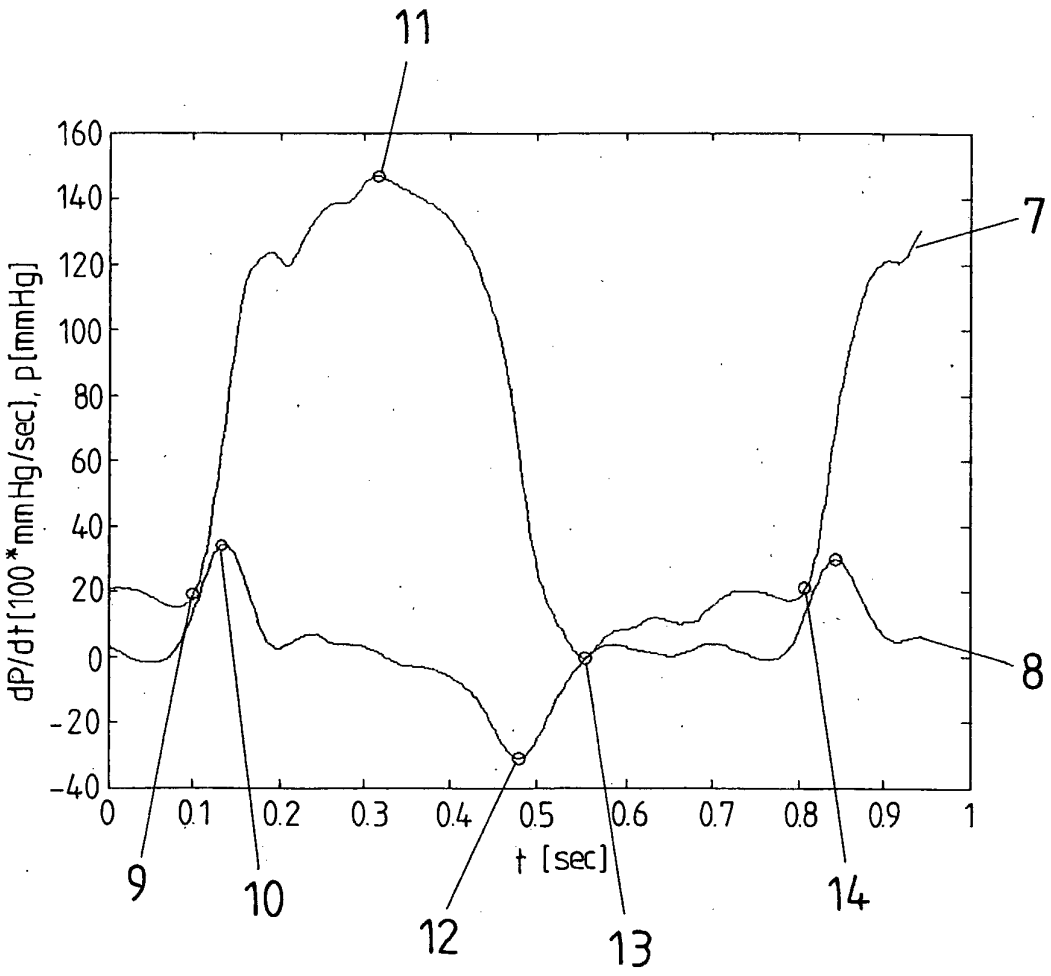
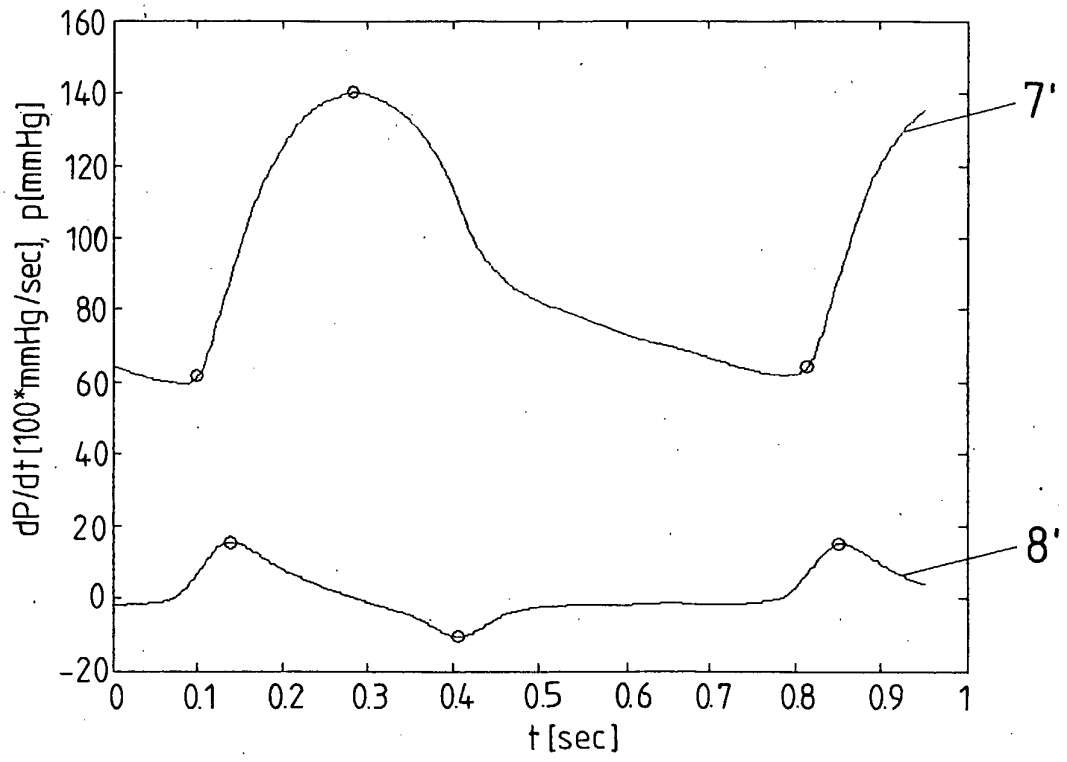

11
160
140
120
100
80
60
40
20
0
-20
-40
dP/dt [100 * mmHg/sec], p [mmHg]
0
0.1
0.2
0.3
0.4
0.5
0.6
0.7
0.8
0.9
1
t [sec]
7
8
9
10
12
13
14

Fig. 4


160
140
120
100
80
60
40
20
0
-20
dP/dt [100*mmHg/sec], p[mmHg]
0
0.1
0.2
0.3
0.4
0.5
0.6
0.7
0.8
0.9
1
t [sec]
7'
8'