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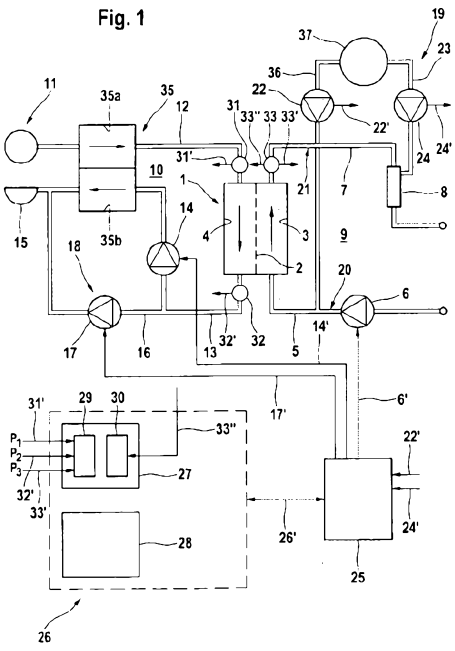
Erklärungen gemäß Regel 4.17:

[Fortsetzung auf der nächsten Seite]

(54) **Title**: METHOD FOR REGULATING THE SUPPLY OF SUBSTITUATE DURING EXTRACORPOREAL BLOOD TREATMENT AND EXTRACORPOREAL BLOOD TREATMENT DEVICE COMPRISING A UNIT FOR REGULATING THE SUPPLY OF SUBSTITUATE

(54) **Bezeichnung** : VERFAHREN ZUM REGELN DER ZUFUHR VON SUBSTITUAT BEI EINER EXTRAKORPORALEN BLUTBEHANDLUNG UND EXTRAKORPORALE BLUTBEHANDLUNGSVORRICHTUNG MIT EINER EINRICHTUNG ZUM REGELN DER ZUFUHR VON SUBSTITUAT

Fig. 1



(57) **Abstract**: The invention relates to a method for regulating the supply of substituate during an extracorporeal blood treatment using an extracorporeal blood treatment device, which comprises a dialyser (1) that is divided by a semi-permeable membrane (2) into a blood chamber (3) and a dialysis liquid chamber (4), and a unit (19) for supplying substituate. Furthermore, the invention relates to a device for extracorporeal blood treatment comprising a unit (26) for regulating the supply of substituate. The method according to the invention and the device according to the invention are based on the fact that the regulation of the supply of substituate during the extracorporeal blood treatment is effected according to the rheological load of the dialyser. In order to regulate the supply of substituate during the extracorporeal blood treatment, the rheological load on the dialyser is determined from the trans-membrane pressure at the dialyser and the flow resistance of the dialyser, and the substituate rate is increased or reduced in accordance therewith. It is therefore no longer necessary to specify dialyser parameters or blood parameters, and distinguishing between pre-dilution and post-dilution is also obsolete.

(57) **Zusammenfassung**:

[Fortsetzung auf der nächsten Seite]

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— *Erfindererklärung (Regel 4.17 Ziffer iv)*

Veröffentlicht:

— *mit internationalem Recherchenbericht (Artikel 21 Absatz 3)*

— *vor Ablauf der für Änderungen der Ansprüche geltenden Frist: Veröffentlichung wird wiederholt, falls Änderungen eingehen (Regel 48 Absatz 2 Buchstabe h)*

Die Erfindung betrifft ein Verfahren zum Regeln der Zufuhr von Substituat bei einer extrakorporalen Blutbehandlung mit einer extrakorporalen Blutbehandlungsvorrichtung, die einen durch eine semipermeable Membran (2) in eine Blutkammer (3) und eine Dialysierflüssigkeitskammer (4) unterteilten Dialysator (1) und eine Einrichtung (19) zum Zuführen von Substituat aufweist. Darüber hinaus betrifft die Erfindung eine Vorrichtung zur extrakorporalen Blutbehandlung mit einer Einrichtung (26) zum Regeln der Zufuhr von Substituat. Das erfindungsgemäße Verfahren und die erfindungsgemäße Vorrichtung beruhen darauf, dass die Regelung der Zufuhr von Substituat bei der extrakorporalen Blutbehandlung in Abhängigkeit von der rheologischen Belastung des Dialysators erfolgt. Die rheologische Belastung des Dialysators wird zur Regelung der Zufuhr von Substituat während der extrakorporalen Blutbehandlung aus dem Transmembrandruck am Dialysator und dem Strömungswiderstand des Dialysators bestimmt und die Substituatrate entsprechend der Belastung angehoben oder reduziert. Damit ist die Vorgabe von Dialysatorparametern oder Blutparametern nicht mehr notwendig und auch die Unterscheidung zwischen Prädilution oder Postdilution ist obsolet.

Method for regulating the supply of substituate in an extracorporeal blood treatment and extracorporeal blood treatment apparatus with a device for regulating the supply of substituate

The invention relates to a method for regulating the supply of substituate in an extracorporeal blood treatment with an extracorporeal blood treatment apparatus, which comprises a dialyser divided by a semipermeable membrane into a blood chamber and a dialysing fluid chamber and a device for supplying substituate. Moreover, the invention relates to an apparatus for extracorporeal blood treatment with a device for regulating the supply of substituate.

Various methods for machine-aided blood cleaning or blood treatment are used in chronic kidney failure in order to remove substances usually eliminated with urine and for fluid withdrawal. In haemodialysis (HD), the patient's blood is conveyed in an extracorporeal blood circuit through the blood chamber of a dialyser divided by a semipermeable membrane into the blood chamber and a dialysing fluid chamber, whilst a dialysing fluid flows through the dialysing fluid chamber. A diffuse substance exchange essentially takes place via the membrane of the dialyser. In the case of haemofiltration (HF), dialysing fluid does not flow through the dialysing fluid chamber. Only a convective substance exchange takes place. Haemodiafiltration (HDF) is a combination of the two processes.

The quantity of fluid removed from the patient via the semipermeable membrane of the dialyser in the case of haemofiltration (HF) or haemodiafiltration (HDF) is fed back to the patient during the blood treatment as substituate, which is either made available ready for use or is obtained from the dialysing fluid during the blood treatment. The substituate is fed to the extracorporeal blood circuit upstream and/or downstream of the dialyser. The supply of substituate upstream of the dialyser is referred to as pre-dilution and downstream of the dialyser as post-dilution. The substituate rate refers to the quantity of substituate that is supplied in a specific period of time to the blood flowing in the extracorporeal blood circuit.

In order to balance fresh and used dialysing fluid, which flows into and respectively out of the dialysing fluid chamber of the dialyser, use is made of balancing systems in the known blood treatment apparatuses. The balancing of fresh and used dialysing fluid ensures that no fluid or only a specific quantity of fluid is fed to or removed from the patient.

The ultrafiltration rate at which fluid is removed from the patient is dependent on the transmembrane pressure TMP, which is defined as the pressure difference between the mean blood-side pressure and the mean dialysate-side pressure in the dialyser. Methods and devices for determining the transmembrane pressure are generally known. EP 0 212 127 A1 and
WO 2009/080258 A1, for example, describe a device for determining the transmembrane pressure.

Apart from the transmembrane pressure, the longitudinal flow resistance along the hollow fibres of the semipermeable membrane of the dialyser on the blood side is of importance for an extracorporeal blood treatment, said longitudinal flow resistance being referred to below as the flow resistance of the dialyser. It is known that the attenuation of pressure pulses along the hollow fibres of the membrane of the dialyser is connected with the ratio of the amplitudes of the spectral components of the first and second harmonics to the fundamental component (WO 2008/135193 A1).

The present invention seeks to provide a method with which the regulation of the substituate rate is enabled during the extracorporeal blood treatment. Moreover, the present invention seeks to create an apparatus for extracorporeal blood treatment with an improved regulation of the substituate rate.

The method according to the invention and the device according to the invention are based on the fact that the regulation of the supply of substituate in the extracorporeal blood treatment takes place as a function of the rheological loading of the dialyser. Account has to be taken of the fact that the substituate rate is not an independent variable which can be

regulated solely as a function of the rheological loading of the dialyser, since the substituate rate is connected with the ultrafiltration rate. The method according to the invention and the device according to the invention therefore focus on proceeding from a preset substituate rate at which substituate is fed to the patient taking account of a specific ultrafiltration rate, the preset substituate rate being increased or reduced as a function of the rheological loading of the dialyser.

The rheological loading of the dialyser is determined in order to regulate the supply of substituate during the extracorporeal blood treatment and to increase or reduce the substituate rate corresponding to the loading. The selection of dialyser parameters or blood parameters is no longer necessary. Even the distinction between pre-dilution or post-dilution is obsolete.

The rheological loading of the dialyser is preferably determined on the basis of the transmembrane pressure or a variable correlating with the transmembrane pressure and the flow resistance or a variable correlating with the flow resistance, wherein the transmembrane pressure or the variable correlating with the transmembrane pressure and the flow resistance or the variable correlating with the flow resistance are ascertained during the extracorporeal blood treatment. It is unimportant here how the transmembrane pressure and the flow resistance are measured. The only decisive factor is that the transmembrane pressure and the flow resistance or variables derived from the transmembrane pressure and the flow resistance are available for the further evaluation, in order to be able to regulate the supply of substituate as a function of transmembrane pressure and flow resistance.

A preferred embodiment of the invention makes provision to ascertain a first evaluation quantity for the purpose of evaluating the transmembrane pressure or the variable correlating with the transmembrane pressure and a second evaluation quantity for the purpose of evaluating the flow resistance or the variable correlating with the flow resistance. Both ascertained evaluation quantities then form an evaluation pair, which is characteristic of the rheological loading of the dialyser. The transmembrane pressure and the flow resistance are preferably evaluated within an evaluation scale of 0-100%. The rheology in the dialyser is completely described by the evaluation pair.

In a preferred embodiment, the evaluation of the dialyser within the evaluation scale is an input parameter of a 2-dimensional matrix, which assigns to each evaluation pair (priority pair) a value which corresponds to the required change in the substituate rate.

Assigned to each evaluation pair of a large number of evaluation pairs characterising the rheological loading of the dialyser is a specific value for the amount by which the substituate rate is to be increased or reduced from a preset volume. This assignment of the evaluation pair and the amount of the change in the substituate rate can be stored in a memory. The value by which the preset substituate rate is changed is therefore available in each case for the various evaluation pairs.

A particularly preferred embodiment of the invention makes provision such that, in order to determine the flow resistance or the variable correlating with the flow resistance, pressure pulses are generated in the extracorporeal blood circuit upstream of the dialyser and measured downstream of the dialyser, and that the pressure signal measured downstream of the dialyser is split up spectrally into a fundamental component and at least one harmonic. The flow resistance or the variable correlating with the flow resistance is then determined on the basis of the ratio of the fundamental component and the at least one harmonic. The measured pressure signal is preferably split up into one fundamental component and two harmonics.

This method has the advantage that the pressure in the extracorporeal blood circuit only needs to be measured downstream of the dialyser. As pressure pulses, it is possible to measure the pressure pulses which are generated by the blood pump disposed in the extracorporeal blood circuit upstream of the dialyser, said blood pump generally being an occluding hose pump.

The method according to the invention and the device according to the invention can make use of the sensor system which is generally present in any case in the extracorporeal blood treatment apparatus. The evaluation of the data can take place in the central control and computing unit, which is in any case present in the extracorporeal blood treatment apparatus. The device according to the invention and the method according to the invention can thus be implemented without major design expenditure.

An example of embodiment of the invention will be described in greater detail below by reference to the drawings.

In the figures:

Fig. 1 shows the main components of an extracorporeal blood treatment apparatus according to the invention in a simplified schematic representation and

Fig. 2 shows a matrix, which assigns a value corresponding to the required change in the substituate rate to each evaluation pair characteristic of the rheological loading of the dialyser.

Fig. 1 shows the main components of the blood treatment apparatus according to the invention, which is a haemo(dia)filtration apparatus, which comprises a dialyser (filter) 1 which is divided by a semipermeable membrane 2 into a blood chamber 3 and a dialysing fluid chamber 4. The inlet of blood chamber 3 is connected to one end of a blood supply line 5, into which a blood pump 6, in particular a roller pump generating pressure pulses, is incorporated, whilst the outlet of the blood chamber is connected to one end of a blood discharge line 7, into which a drip chamber 8 is incorporated. Blood supply line and blood discharge line 5, 7 form, with blood chamber 3 of the dialyser, extracorporeal blood circuit 9 of the haemodiafiltration apparatus. Blood supply line and blood discharge line 5, 7 are hose lines of a hose set (disposable) inserted into the haemodiafiltration apparatus.

Dialysing fluid system 10 of the haemodiafiltration apparatus comprises a device 11 for making available dialysing fluid, which is connected via the first section of dialysing fluid supply line 12 to the inlet of first balancing chamber half 35a of a balancing device 35. The second section of dialysing fluid supply line 12 connects the outlet of first balancing chamber half 35a to the inlet of dialysing fluid chamber 4. The outlet of dialysing fluid chamber 4 is connected via the first section of a dialysing fluid discharge line 13 to the inlet of second balancing chamber half 35b. A dialysing fluid pump 14 is incorporated into the first section of dialysing fluid discharge line 13. The outlet of second balancing chamber half 35b is connected via the second section of dialysing fluid discharge line 13 to a drain 15. An ultrafiltrate line 16, which also leads to drain 15, branches off from dialysing fluid discharge line 13 upstream of dialysing fluid pump 14. An ultrafiltration

pump 17 is incorporated into ultrafiltrate line 16. In commercially available apparatuses, balancing device 35 comprises two parallel balancing chambers which are operated anti-cyclically. For reasons of simplification, only one balancing chamber is represented here.

During the dialysis treatment, the patient's blood flows through blood chamber 3 and the dialysing fluid flows through dialysing fluid chamber 4 of the dialyser. Balancing device 35 ensures that only as much dialysing fluid can be supplied via the dialysing fluid supply line as dialysing fluid can be discharged via the dialysing fluid discharge line. A preset quantity of fluid (ultrafiltrate) can be withdrawn from the patient at a preset ultrafiltration rate with ultrafiltration pump 17. Ultrafiltration pump 17 is thus part of a device for removing fluid from the blood flowing in extracorporeal circuit 9 through membrane 2 of dialyser 1, which is referred to as ultrafiltration device 18.

In order to feed the fluid back to the patient, the haemodiafiltration apparatus comprises a substitution device 19, with which a substitution fluid (substituate) can be fed to the blood that is flowing through arterial branch 20 (pre-dilution) and/or venous branch 21 (post-dilution) of extracorporeal blood circuit 9. Substitution device 19 comprises a device 37 for making available substituate, from which a first substituate line 36, into which a first substituate pump 22 is incorporated, leads to the section of blood supply line 5 between blood pump 6 and blood chamber 3. A second substituate line 23, into which a second substituate pump 24 is incorporated, leads from device 37 for making available substituate to drip chamber 8. If the haemodiafiltration apparatus is to be operated solely with post-dilution or pre-dilution, the one or other substituate pump together with the respective substituate line can be dispensed with.

Moreover, the haemodiafiltration apparatus comprises a central control and computing unit 25, which is connected via control lines 6', 14', 17', 22', 24' to blood pump 6, dialysing fluid pump 14, ultrafiltration pump 17 and first and second substituate pump 22, 24.

The extracorporeal blood treatment apparatus comprises a device 26 for regulating the supply of the substituate, which is represented in dashed lines in fig. 1. Device 26 for regulating the supply of substituate is represented in fig. 1 as a separate device. It can however also be a component of central control and computing unit 25. Device 26 for regulating the supply of substituate is connected to central control and computing unit 25

via a data line 26', so that the regulating device can exchange data with the control unit, and in particular can correspondingly control substituate pumps 22, 24 in order to adjust substituate rate Q.

Device 26 for regulating the supply of substituate comprises means 27 for determining the rheological loading of the dialyser and means 28 for regulating the substituate rate.

Means 27 for determining the rheological loading of the dialyser in turn comprises means 29 for determining the transmembrane pressure on the dialyser or a variable correlating with the transmembrane pressure and means 30 for determining the flow resistance of the dialyser or a variable correlating with the flow resistance. The flow resistance of the dialyser is to be understood as the longitudinal flow resistance along the hollow fibres of semipermeable membrane 2 of dialyser 1 on the blood side.

Means 29 for determining the transmembrane pressure (TMP) can be designed in different ways. The measuring device described in EP 0 212 127 A1, for example, can be used to determine the transmembrane pressure. In the present example of embodiment, means 27 for determining the transmembrane pressure comprise a first pressure sensor 31 disposed in dialysing fluid supply line 12 upstream of dialysing fluid chamber 4 of dialyser 1, a second pressure sensor 32 disposed in dialysing fluid discharge line 16 downstream of the dialysing fluid chamber of the dialyser and a third pressure sensor 33 disposed in blood return line 21 downstream of chamber 3 of dialyser 1. Pressure sensors 31, 32, 33 are connected via data lines 31', 32', 33' to means 29 for determining the transmembrane pressure. Pressure P_1 upstream and pressure P_2 downstream of the dialysing fluid chamber are measured in dialysing fluid system 10 by pressure sensors 31 and 32 and pressure P_3 downstream of the blood chamber is measured in extracorporeal blood circuit 9 by pressure sensor 33.

Means 29 for determining transmembrane pressure TMP comprise a suitable computing unit, which calculates the transmembrane pressure according to the following equation:

$$TMP = P_3 - \frac{P_1 + P_2}{2}$$

The ascertained value for transmembrane pressure TMP is evaluated as follows. In order to evaluate transmembrane pressure TMP, a first evaluation quantity HEMO Priority is calculated according to the following equation from the measured value for transmembrane pressure TMP and a preset lower limiting value for the transmembrane pressure TMP_{LIMIT_LOWER} and a preset upper limiting value for the transmembrane pressure TMP_{LIMIT_UPPER} as well as a preset value range for the transmembrane pressure TMP_{LIMIT_RANGE}. Parameters TMP_{LIMIT_LOWER}, TMP_{LIMIT_UPPER} and TMP_{LIMIT_RANGE} are ascertained empirically.

$$HEMO\_Priority = ((TMP - TMP_{LIMIT\_LOWER}) / TMP_{LIMIT\_RANGE})*100\%$$

wherein $TMP_{LIMIT\_RANGE} = TMP_{LIMIT\_UPPER} - TMP_{LIMIT\_LOWER}$

Apart from transmembrane pressure TMP, the flow resistance of the dialyser is ascertained in order to determine the rheological loading of dialyser 1.

Means 30 for determining the flow resistance comprise means for measuring pressure pulses, which are propagated in the longitudinal direction over the hollow fibres of the semipermeable membrane of the dialyser on the blood side. The pressure pulses are generated by blood pump 6, which is an occluding hose pump, in particular a roller pump. In the present example of embodiment, pressure sensor 33 disposed downstream of blood chamber 3 in blood return line 21 is used to measure the pressure pulses generated by blood pump 6. A second data line 33" therefore leads from pressure sensor 33 to means 30 for determining the flow resistance. In order to determine the flow resistance, the pressure signal measured by pressure sensor 33 is split up spectrally into a fundamental component G_0 and first and second harmonics H_1 and H_2, since the attenuation of the pressure pulses along the hollow fibres is connected with the ratio of the amplitudes of the spectral components of first and second harmonics H_1 and H_2 to fundamental component G_0. The theoretical relationship is described in WO 2008/135193 A1.

In order to regulate the substituate flow, the flow resistance is also evaluated as follows. A second evaluation quantity BLKD_priority is calculated from fundamental component G_0 and first and second harmonics H_1 and H_2 as well as empirically established parameters $K_{1,2}$, $M_{1,2}$ and α according to the following equation

$$BLKD\_Priority = \alpha \cdot \left(\frac{G_0 / H_1 - K_1}{2M_1} + \frac{G_0 / H_2 - K_2}{2M_2}\right)$$

The first and second evaluation quantities form an evaluation pair (Hemo_Priority/BLKD_Priority), which is characteristic of the rheological loading of the dialyser.

The frequency of the fundamental component of the pressure pulses results from the control of blood pump 6. The frequencies of the first and second harmonics of the fundamental component are therefore also known. The splitting-up of the continuous pressure signal into its spectral components preferably takes place with a Fourier transform, particularly preferably by digitalising the measured values of pressure sensor 33 with a discrete Fourier transform, which is carried out in a suitable computing unit.

The advantage of the analysis of the pressure pulses for the determination of the flow resistance lies in the fact that only one sensor downstream of the dialyser is required. A sensor upstream of the dialyser, on the other hand, is not required. It is however also possible to determine the flow resistance or a variable correlating with the flow resistance using measurements with four pressure sensors upstream and downstream of the dialyser on the blood side and dialysing fluid side. It is also possible to determine approximately the flow resistance or a variable correlating with the flow resistance using a measurement with two pressure sensors downstream of the dialyser on the blood side and dialysing fluid side, in that the pressures upstream of the dialyser on the blood side and dialysing fluid side are estimated on the basis of operational parameters.

Since the rheological loading of the dialyser is determined both on the basis of the transmembrane pressure and the flow resistance, the measurement of the transmembrane pressure is sufficient with only two or three pressure sensors instead of the known measurement with four pressure sensors, although the two-point and the three-point measurement of the transmembrane pressure have not always proved to be reliable in practice, since an unsteady behaviour in the region of particularly high transmembrane pressures can occur with the two-point and the three-point measurement.

In the present example of embodiment, the transmembrane pressure and the flow resistance are evaluated in such a way that the evaluation quantities are scaled within an evaluation scale of 0 to 100%. The rheological loading of the dialyser can be completely described as a point in a two-dimensional coordinate system. The regulation of the substituate rate is based on keeping the rheological loading inside a target area of the matrix. The regulation takes place irrespective of whether a post-dilution or pre-dilution is present.

Fig. 2 shows the two-dimensional matrix, which assigns to each evaluation pair (priority pair) a value which corresponds to the required change in the substituate rate. Consequently, a specific value for the amount of the change in the preset substituate rate is assigned to each value pair stored in the matrix. Inside the matrix there is a nominal line (value range) which connects the evaluation pairs to one another which correspond to the desired dialyser loading. The nominal line is a line which consists mathematically of the connection in a line running linearly to the priorities and a circular line running around the priority pair (0,0). If the priority pair lies on the nominal line, the substituate rate remains unchanged. The nominal line (value range) is marked in fig. 1 as an unshaded area. The amount of the change in the substituate rate is represented in fig. 1 by the density of the shading. The scale on the right in fig. 1 assigns corresponding changes in the substituate rate to the shaded areas in the coordinate system on the left. The control target here is the unshaded area (0 %), which is equivalent to an unchanged substituate dose.

Required substituate rate change α is determined from the matrix in device 26 for regulating the supply of substituate. The substituate rate to be newly adjusted $Q_{sub,\,new}$ is calculated as follows:

$$Q_{sub,new} = Q_{sub,old}\,(1 + \alpha)$$

A specific ultrafiltration rate, which is set using ultrafiltration device 18, is preset for the extracorporeal blood treatment. Furthermore, a selection is made as to whether fluid is to be supplied to or removed from the patient or whether fluid is neither to be supplied to nor removed from the patient. If, for example, fluid is to be removed from the patient, central control and computing unit 25 presets a specific substituate rate. This substituate rate is

then rated in such a way that less substituate is supplied to the extracorporeal blood circuit than fluid is removed via membrane 2 of dialyser 1 by ultrafiltration device 18. This preset substituate rate is increased or reduced by device 26 in order to regulate the supply of substituate according to the method described above. The extracorporeal blood treatment is thus carried out under optimum conditions for the dialyser.

The regulation of the substituate addition provides not only for a change in the substituate rate, but also a distribution of the supply of substituate upstream and downstream of the dialyser (pre-dilution and post-dilution). In the case of the supply of substituate both upstream and downstream of the dialyser, the total dilution quantity for post- and pre-dilution is changed according to the matrix. As a determining parameter for a change instruction for the total dilution quantity, use is made here of the distance of the value pair in the coordinate system characteristic of the rheological loading of the dialyser from the coordinate origin (0,0) and the angle between the imaginary line, which runs through the coordinate origin (0,0) and the characteristic evaluation pair, and the X-axis or alternatively the Y-axis. Device 26 for regulating the supply of substituate, together with central control and computing unit 25, then sets the flow rates of substituate pumps 22 and 30 in accordance with the ascertained distance and angle.

Throughout this specification and the claims which follow, unless the context requires otherwise, the word "comprise", and variations such as "comprises" or "comprising", will be understood to imply the inclusion of a stated integer or step or group of integers or steps but not the exclusion of any other integer or step or group of integers or steps.

The reference in this specification to any prior publication (or information derived from it), or to any matter which is known, is not, and should not be taken as, an acknowledgement or admission or any form of suggestion that that prior publication (or information derived from it) or known matter forms part of the common general knowledge in the field of endeavour to which this specification relates.

The Claims defining the invention are as follows:

1. A method for regulating the supply of substituate in an extracorporeal blood treatment with an extracorporeal blood treatment apparatus, which includes:

a dialyser divided by a semipermeable membrane into a blood chamber and a dialysing fluid chamber, the blood chamber being part of an extracorporeal blood circuit and the dialysing fluid chamber part of a dialysing fluid system;

a device for supplying substituate at a preset substituate rate to the extracorporeal blood circuit,

characterised in that

the transmembrane pressure or a variable correlating with and depending of the transmembrane pressure and the flow resistance of the dialyser or a variable correlating with and depending of the flow resistance are ascertained,

wherein the rheological loading of the dialyser is determined on the basis of the transmembrane pressure or a variable correlating with and depending of the transmembrane pressure and the flow resistance of the dialyser or a variable correlating with and depending of the flow resistance, and

wherein the substituate rate is regulated as a function of the rheological loading of the dialyser.

2. The method according to claim 1, characterised in that, in order to evaluate the transmembrane pressure or the variable correlating with and depending of the transmembrane pressure, a first evaluation quantity HEMO_Priority is ascertained and that, in order to evaluate the flow resistance or the variable correlating with and depending of the flow resistance, a second evaluation quantity BLKD_priority is ascertained, wherein the two ascertained evaluation quantities form an evaluation

pair (HEMO_Priority / BLKD_Priority) characteristic of the rheological loading of the dialyser.

3. The method according to claim 2, characterised in that a specific value for the amount of the change in the substituate rate from a preset value is assigned to each evaluation pair of a large number of evaluation pairs characterising the rheological loading of the dialyser, wherein the amount of the change in the substituate rate is determined from the ascertained evaluation pair characterising the rheological loading of the dialyser on the basis of the assignment of the evaluation pair and the amount of the change in the substituate rate.

4. The method according to claim 3, characterised in that the preset substituate rate is increased or reduced by the ascertained value.

5. The method according to claim 2 or 3, characterised in that, in order to evaluate the transmembrane pressure or the variable correlating with and depending of the transmembrane pressure, the first evaluation quantity HEMO_Priority is calculated

according to the following equation:

$$HEMO\_Priority = ((TMP - TMP_{LIMIT\_LOWER}) / TMP_{LIMIT\_RANGE})*100\%$$

with $TMP_{LIMIT\_RANGE} = TMP_{LIMIT\_UPPER} - TMP_{LIMIT\_LOWER}$

wherein TMP_{LIMIT_LOWER}, TMP_{LIMIT_UPPER} and TMP_{LIMIT_RANGE} are empirically ascertained parameters.

6. The method according to any one of claims 1 to 5, characterised in that, in order to determine the flow resistance or the variable correlating with and depending of the flow resistance, pressure pulses are generated in the extracorporeal blood circuit upstream of the dialyser and measured downstream of the dialyser, and that the

pressure signal measured downstream of the dialyser is split up spectrally into a fundamental component and at least one harmonic, wherein the flow resistance or the variable correlating with and depending of the flow resistance is determined on the basis of the ratio of the fundamental component and the at least one harmonic.

7. The method according to claim 6, characterised in that, in order to evaluate the flow resistance or the variable correlating with and depending of the flow resistance, the second evaluation quantity BLKD_priority is calculated from fundamental component G_0 and first and second harmonics H_1 and H_2 as well as empirically established parameters $K_{1,2}$, $M_{1,2}$ and α

according to the following equation

$$BLKD\_Priority = \alpha \cdot \left(\frac{G_0/H_1 - K_1}{2M_1} + \frac{G_0/H_2 - K_2}{2M_2}\right)$$

8. The method according to any one of claims 1 to 7, characterised in that the pressure in the extracorporeal blood circuit and in the dialysing fluid system is measured in order to determine the transmembrane pressure.

9. The method according to any one of claims 2 to 8, characterised in that the substituate is supplied to the extracorporeal blood circuit upstream and/or downstream of the dialyser, wherein the ratio between the quantity of the substrate supplied upstream and/or downstream is regulated on the basis of the ascertained evaluation pair, which is characteristic of the rheological loading of the dialyser.

10. An apparatus for extracorporeal blood treatment with

a dialyser divided by a semipermeable membrane into a blood chamber and a dialysing fluid chamber, wherein the blood chamber is part of an extracorporeal blood circuit and the dialysing fluid chamber is part of a dialysing fluid system;

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a device for supplying substituate at a preset substituate rate to the extracorporeal blood circuit and

a device for regulating the supply of substituate,

characterised in that

the device for regulating the supply of substituate includes:

means for determining the rheological loading of the dialyser and

means for regulating the substituate rate, which are configured such that the substituate rate is regulated as a function of the rheological loading of the dialyser

wherein the means for determining the rheological loading of the dialyser include means for determining the transmembrane pressure or a variable correlating with and depending of the transmembrane pressure and the flow resistance of the dialyser or a variable correlating with and depending of the flow resistance, wherein the means for determining the rheological loading of the dialyser are configured such that the rheological loading of the dialyser is determined on the basis of the transmembrane pressure or a variable correlating with and depending of the transmembrane pressure and the flow resistance of the dialyser or a variable correlating with and depending of the flow resistance.

11. The apparatus according to claim 10, characterised in that the means for determining the rheological loading of the dialyser are configured such that a first evaluation quantity HEMO_Priority is ascertained in order to evaluate the transmembrane pressure or the variable correlating with and depending of the transmembrane pressure and that a second evaluation quantity BLKD_priority is ascertained in order to evaluate the flow resistance or the variable correlating with

and depending of the flow resistance, wherein the two ascertained evaluation quantities form an evaluation pair (HEMO_Priority / BLKD_Priority) characteristic of the rheological loading of the dialyser.

12. The apparatus according to claim 11, characterised in that the means for regulating the preset substituate rate are configured such that a specific value for the amount of the change in the substituate value from a preset value is assigned to each evaluation pair of a large number of evaluation pairs characteristic of the rheological loading of the dialyser, wherein the amount of the change in the substituate value is determined from the ascertained evaluation pair characteristic of the rheological loading of the dialyser on the basis of the assignment of the evaluation pair and the amount of the change in the substituate rate.

13. The apparatus according to claim 12, characterised in that the means for regulating the preset substituate rate are configured such that the preset substituate rate is increased or reduced by the ascertained value.

14. The apparatus according to any one of claims 11 to 13, characterised in that the means for determining the rheological loading of the dialyser are configured such that, in order to evaluate the transmembrane pressure or the variable correlating with and depending of the transmembrane pressure, the first evaluation quantity HEMO_Priority is calculated

according to the following equation:

$$HEMO\_Priority = ((TMP - TMP_{LIMIT\_LOWER}) / TMP_{LIMIT\_RANGE})*100\%$$

with $TMP_{LIMIT\_RANGE} = TMP_{LIMIT\_UPPER} - TMP_{LIMIT\_LOWER}$

wherein TMP_{LIMIT_LOWER}, TMP_{LIMIT_UPPER} and TMP_{LIMIT_RANGE} are empirically ascertained parameters.

15. The apparatus according to any one of claims 10 to 14, characterised in that the means for determining the rheological loading of the dialyser include means for measuring pressure pulses generated in the extracorporeal blood circuit upstream of the dialyser, and that the means for determining the rheological loading of the dialyser are configured such that, in order to determine the variable correlating with and depending of the flow resistance of the dialyser, the pressure signal measured downstream of the dialyser is split up into a fundamental component and at least one harmonic, wherein the flow resistance or the variable correlating with and depending of the flow resistance is determined on the basis of the ratio of the fundamental component and the at least one harmonic.

16. The apparatus according to claim 15, characterised in that the means for determining the rheological loading of the dialyser are configured such that, in order to evaluate the flow resistance or the variable correlating with and depending of the flow resistance, second evaluation quantity BLKD_priority is calculated from fundamental component G_0 and first and second harmonics H_1 and H_2 as well as empirically established parameters $K_{1,2}$, $M_{1,2}$ and α

according to the following equation:

$$BLKD\_Priority = \alpha \cdot \left(\frac{G_0 / H_1 - K_1}{2M_1} + \frac{G_0 / H_2 - K_2}{2M_2}\right)$$

17. The apparatus according to any one of claims 10 to 16, characterised in that the means for determining the transmembrane pressure include means for measuring the pressure in the extracorporeal blood circuit and in the dialysing fluid system.

18. The apparatus according to any one of claims 11 to 17, characterised in that the device for supplying substituate at a preset substituate rate to the extracorporeal blood circuit is configured such that the substituate is supplied to the extracorporeal

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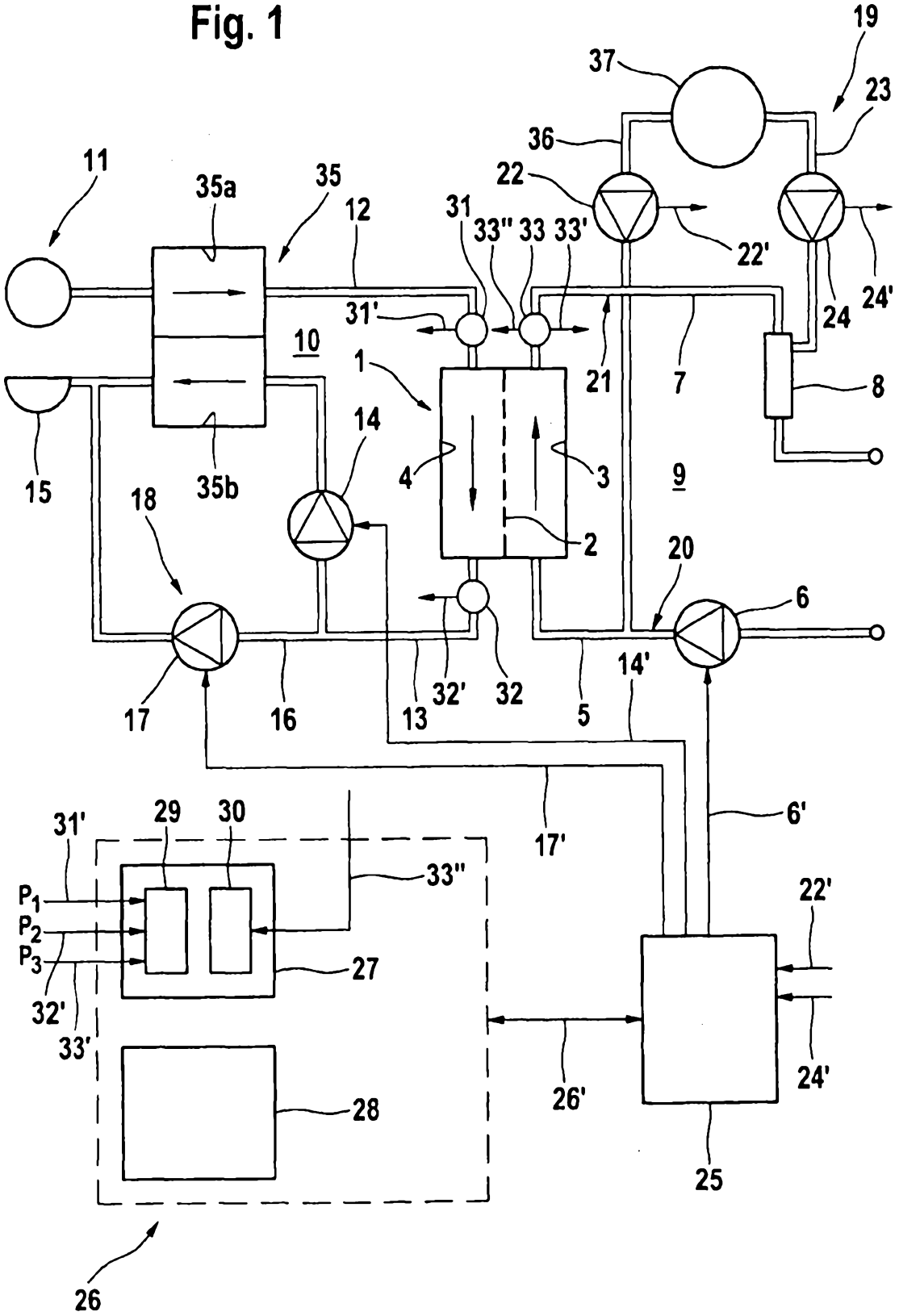
blood circuit upstream and/or downstream of the dialyser, wherein the device for regulating the supply of substituate is configured such that the ratio between the quantity of the substituate supplied upstream and downstream is regulated on the basis of the ascertained evaluation pair characteristic of the rheological loading of the dialyser.

19. A method for regulating the supply of a substituate in an extracorporeal blood treatment with an extracorporeal blood treatment apparatus, substantially as herein described.

20. An apparatus for extracorporeal blood treatment, substantially as herein described.

Fig. 1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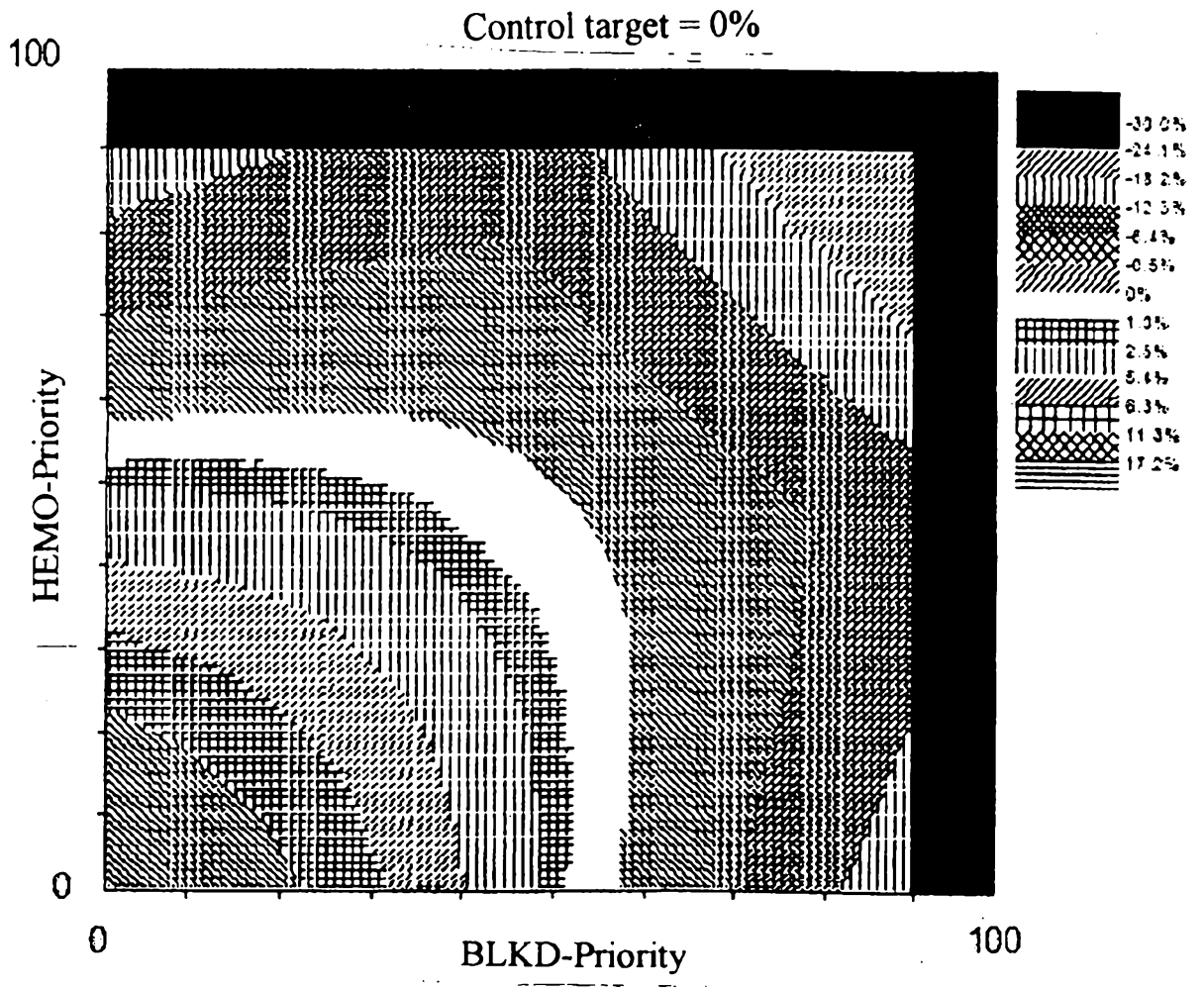
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