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(54) Title: DIFFERENTIAL FLOW-METER FOR MEASURING THE PONDERAL DECREASE IN HEMODIALYSIS TREATMENTS

(57) Abstract: A differential flow-meter (10*, 1000) for measuring the weight loss in dialysis treatments. The differential flow-meter (10*, 1000) is of the "thermal anemometer" type.

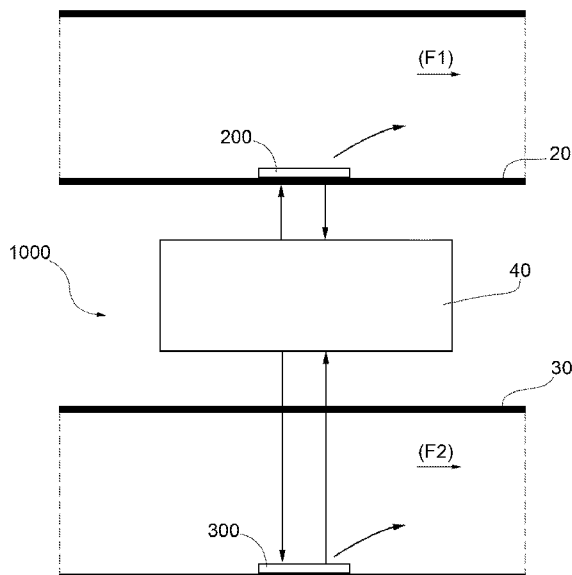


FIG. 2

WO 2014/111908 A1



TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, **Published:**
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"DIFFERENTIAL FLOW-METER FOR MEASURING THE WEIGHT LOSS IN
HAEMODIALYSIS TREATMENTS"

TECHNICAL FIELD

5 The present invention concerns a differential flow-meter for measuring the difference of flow rate, or speed, between two fluids.

 In particular, the present invention finds an advantageous application in the calculation of weight loss
10 in haemodialysis treatments.

BACKGROUND ART

 As already known, more than two million people in the whole world are presently affected by a chronic renal failure, with an annual growth rate close to 6%.

15 Currently, patients who do not undergo a kidney transplantation are treated by haemodialysis (or extracorporeal dialysis) or by peritoneal dialysis, which replaces the cleaning function of kidneys.

 In both these treatments, blood is in contact with a
20 special solution (called "dialysis fluid" or "dialysate") through a semipermeable membrane.

 In haemodialysis, the blood purification takes place out of the body, inside a special filter, the dialyzer, whereas peritoneal haemodialysis uses the peritoneum
25 natural membrane.

 Through the semipermeable membrane, blood releases

waste substances to the dialysate and yields/acquires ions by diffusion and convection, while the excess fluid (about two litres) is removed by ultrafiltration.

These processes take place using a computerized machine monitoring the total mass of liquid to be subtracted to the patient during the dialysis session, also called "weight loss".

The control system is programmed to achieve the goal of total removal of excess fluid at the end of the treatment (which usually lasts 4 hours).

This function is one of the most sensitive aspects of dialysis, since violent removal of liquids can cause significant side effects, such as, for instance, collapses and cramps.

Therefore, the control system of ultrafiltration must be made with the utmost accuracy.

Current systems of measurement of weight loss are all large and with high production costs, since they have to include several active elements.

US-A-5 861 555 describes a differential flow-meter for measuring liquid flows for biomedical applications in dialysis machines. In this system, a certain number of temperature sensors is suitably connected in order to indirectly obtain the difference between the dialysate inlet flow and the dialysate outlet flow, with the help of a further non differential flow measurement relating to the

flow rate of one or more of the channels. According to the adopted principle, the dialysis liquid is globally overheated at a temperature close to body temperature for reasons intrinsic to the dialysis treatment, and this
5 overheating is then used to carry out the differential flow measurement as well.

Moreover, US-A-2 946 220 describes a differential flow-meter for measuring gaseous fluids for chemical applications. In the claimed system, at least a pair of
10 flow-meters working according to the calorimetric principle is suitably connected (Wheatstone bridge) in order to directly obtain a differential measurement of the respective flows. According to the calorimetric principle, a total number of six resistors, four of which are
15 temperature sensors and two of which are heaters, are used and connected in a suitable way to obtain the aforesaid differential flow measurement.

For a better understanding of the present invention, figure 1 shows a schematic view of a differential flow-
20 meter substantially working according to the "calorimetric principle" (calorimetric flow-meter). In other words, according to said known principle, it is measured the temperature variation of the previously overheated fluid at the place where the temperature sensor is arranged, said
25 variation being induced by the flow rate or speed of the fluid itself.

For purely introductive purposes with regard to the present invention, reference will be made to the accompanying figure 1.

In said figure 1, 10 indicates, as a whole, a differential flow-meter working according to the "calorimetric principle".

The differential flow-meter 10, of known type, comprises a first separate channel 20 and a second separate channel 30 in which two fluids flow, said fluids being same or different.

The following devices are attached on the inner wall of channel 20:

- heating means 21 of the fluid flowing according to an arrow (F1); the amount of heat supplied by the heating means 21 is controlled by a differential measuring device 40; the heating means 21 use the Joule effect to locally heat the fluid close to them; and
- temperature detecting means 22, placed close to the heating means 21; the temperature of said temperature sensor 22 being also detected by means of the differential measuring device 40.

Analogously, the following devices are attached on the inner wall of channel 30:

- heating means 31 of the fluid flowing according to an arrow (F2); the amount of heat supplied by the

heating means 21 is controlled by a differential measuring device 40; the heating means 21 use the Joule effect to locally heat the fluid close to them; and

- 5 - temperature detecting means 32 placed close to the heating means 31; the temperature of said temperature sensor 22 being also detected by means of the differential measuring device 40, which can also comprise a microprocessor processing system.

10 Furthermore, the differential measuring device can transform the instantaneous temperatures detected by the temperature sensors 22, 32 into differential flow rate or speed measurements of the two fluids passing in the two channels 20, 30.

15 For each channel, the temperature detecting means arranged close to the heating means can be formed by a single element, arranged downstream (as shown in figure 1) or upstream of the heating means (not shown), or can be formed by more elements, arranged both downstream and
20 upstream (not shown). In all the aforesaid cases, the physical principle remains the same, and all the aforesaid means would still be monitored and measured by the differential measuring device 40.

DISCLOSURE OF INVENTION

25 The present invention develops a differential system directly measuring the difference between the two flows

(weight loss) by using the principle of the "thermal anemometer" in order to obtain high sensitivity and precision and to guarantee the measurement accuracy.

This will lead to an accuracy of, at least, 5%, the
5 tolerated limit being 10%. Inside the flow-meter, the inlet and the outlet flows will flow in two adjacent channels, having the same shape and size. A sensitive element can be found on the separating element arranged between the two
10 channels, said sensitive element containing one or more resistors, self-heated thanks to the Joule effect, and directly measuring the difference of thermal dispersion between the two channels, related to the flow difference.

Main object of the present invention is therefore a differential flow-meter for biomedical applications in
15 dialysis machines, having as an objective a highly accurate and precise differential measurement of the flow rate of dialysis fluids and the possible use of the machine where a dialysis treatment is needed, including typically hot places (e.g., operating room temperatures $> 30^{\circ}\text{C}$).

20 The first objective can be reached by using a direct differential measurement (e.g., avoiding traditional flow measurements, namely of single channels, and subsequently using them for calculating their difference; or using them differently in calculations, thus avoiding a propagation of
25 errors), and trying to reduce the sensor constructive complexity, thus minimizing the source of systematic and

random manufacture errors. In the device object of the present invention, the optimal solution to these purposes is represented by a flow-meter based on the principle of the thermal anemometer, according to which a wire (resistor), specially overheated by the Joule effect, is cooled in proportion to the flow rate of the fluid touching it. The two (or four) resistors of the anemometer flow-meter are then configured as a Wheatstone bridge in order to obtain a direct differential measurement. Indicatively, the overheating is in the order of a few centigrade degrees. This method is an alternative to the more conventional calorimetric method seen in relation to figure 1, and therefore avoids having a separate heater and a separate temperature sensor. This implies a major constructive simplification, resulting in a limitation of the geometric nonidealities, thus obtaining greater measurement accuracy and precision. Moreover, the fact of having just one functional element implies a simplification in the control of the sensor, thus obtaining still the same advantage (simpler system, less error propagation).

The second objective can be reached by overheating only a negligible portion of the fluid. In fact, if the overheating functional to the flow measurement occurs only locally, close to the sensor, if necessary, it will be possible to implement a overheating, even relatively high, which, however, does not disrupt the overall temperature of

the fluid. The use of a bypass, taking a small amount of fluid, could obviate the aforesaid problem, but has the disadvantage of introducing other sources of errors, thus limiting once again the accuracy and precision of measurement.

Therefore, according to the present invention, it is provided a differential flow-meter based on the principle of the "thermal anemometer" according to what defined in the attached independent claim, and preferably in any one of the claims directly or indirectly dependent on the aforesaid independent claim.

BRIEF DESCRIPTION OF THE DRAWINGS

For a better understanding of the present invention it will be now described a preferred embodiment, purely for non limitative purposes and with a reference to the attached drawings, in which:

- figure 2 shows a schematic view of a differential flow-meter made according to the present invention using the principle of the "thermal anemometer";
- figure 3 shows a blood circuit of a haemodialysis machine to which it is applied a differential flow-meter according to the present invention;
- figure 4 shows a 3D view of the differential flow-meter whose components have been assembled; and
- figure 5 shows an exploded view of the differential flow-meter of figure 4.

BEST MODE FOR CARRYING OUT THE INVENTION

In figure 2 1000 indicates, as a whole, a differential flow-meter using the principle of the thermal anemometer flow-meter, which is one of the objects of the present invention.

The differential flow-meter 1000 comprises a first separate channel 20 and a second separate channel 30 in which two fluids flow, said fluids being same or different.

A thermal device 200 is attached on the inner wall of channel 20. In said device 200, the temperature sensor 22 seen in figure 1 corresponds in principle to the heating plate 21. In particular, it is a resistor overheated thanks to the Joule effect, namely by imposing a suitably high current, with the resulting resistance increase, said resistor being cooled by the moving fluid, with the resulting temperature decrease. Therefore this resistance variation is inversely proportional to the fluid flow rate.

Analogously, a thermal device 300 is attached on the inner wall of channel 30. In said device 300, the temperature sensor 32 seen in figure 1 corresponds in principle to the heating plate 31.

In this way the variation of heat flow from the plate to the fluid can be measured by means of the differential measuring device 40.

In figure 3, 100 indicates, as a whole, a blood circuit of a haemodialysis machine (not shown in its

entirety).

The blood circuit 100 comprises a dialyzer 50 fed, on the one side, by the dialysate through a duct 51 and, on the other side, by the arterial blood flowing through a duct 52 thanks to a peristaltic pump 53. The exchange of impurities between the blood and the dialysate takes place according to the previously described system.

The "dirty" dialysate exits the dialyzer 50 flowing in a duct 54, whereas the treated blood is re-introduced in the human body (BD) through a channel 55 connected to a patient's vein.

In a known way, in the duct 52 a certain amount of heparin is pumped into the arterial blood by means of a pumping device 56 in order to avoid blood coagulation.

The duct 52 is provided with a device 57 for measuring the arterial pressure. Analogously, the duct 55 is associated to a device 58 for measuring the venous pressure and for detecting the presence of unwanted air.

Figures 4,5 show a further embodiment of a differential flow-meter 10* object of the present invention.

The differential flow-meter 10*, 1000 can be connected to the ducts 51, 54 of the blood circuit 100 (figure 3) to calculate the so-called "weight loss", namely the liquid mass subtracted to the patient.

In an alternative embodiment, the person skilled in

the art also finds obvious to connect the differential flow-meter 10*, 1000 to the two blood ducts 52, 55 (figure 3).

As shown in figures 4, 5 the differential flow-meter 10* comprises two channels 20*, 30*.

In the embodiment shown in figures 4, 5, channels 20*, 30* are identical, but they could also have different shapes.

Each channel 20*, 30* is aligned along a respective longitudinal symmetry axis (Y1), (Y2), which, in use, are parallel to each other.

In particular, channel 20* (but this obviously applies also for channel 30*) comprises two cylindrical end portions (PC) connected to a central prismatic portion (PP).

The two cylindrical end portions (PC) are used for the insertion of the remaining portions of the duct in which they are inserted (pair of ducts 51, 54; or, alternatively, pair of ducts 52, 55).

The central prismatic portion (PP), in turn, is provided with a flat back face (FP), on which a back groove (SC) is made, and a flat front face (FA) with an inspection window (WN), covered in use by a transparent panel (PN) (figure 5) to allow the visual inspection of the fluid flowing in said central prismatic portion (PP).

The back groove (SC) supports in use (figure 4) a

micro-machined chip 90, advantageously made of silicon, integrating the thermal devices 200, 300 and the differential measuring device 40 seen in relation to the embodiment shown in figure 2.

5 More precisely, the chip 90 is glued and connected (for instance by means of the "wire-bonding" technique) to a substrate 91 (for instance a PCB, which stands for "Printed Circuit Board") containing all the electrical connections for data control and acquisition; the two
10 channels on the substrate 91 bearing the two flows must have a suitable opening for housing the chip 90.

Once assembled, the differential flow-meter 10*, 1000 is as shown in figure 4.

15 In short, according to the preferred embodiment shown in figures 4, 5, the present invention refers to a differential flow-meter 10*, 1000 for measuring the difference of flow rate, or speed, between two fluids.

The differential flow-meter 10* is identical to the differential flow-meter 100 shown in figure 2 and is
20 characterized in that it comprises:

a) a first separate channel 20* and a second separate channel 30* in which two fluids flow, said fluids being same or different; and

b) a chip 90 located on either side of the two
25 channels 20*, 30* so that a first portion 90A of the chip 90 is touched only by a first fluid flowing in the first

channel 20*, and so that a second portion 90B of the chip 90 is touched only by a second fluid flowing in the second channel 30*.

Moreover, the chip 90 can measure and compare, by means of the method seen with regard to figure 2, any possible electrical resistance change in the first portion 90A and in the second portion 90B in order to calculate any possible change of flow rate or speed occurring in the fluids flowing in the two channels 20*, 30*.

The silicon micro-machining technology can be used to manufacture the sensitive portion of the differential flow-meter 10. This technology, starting from the silicon planar processing techniques, allows to create miniaturized planar and 3D structures, such as resistors resting on elastic membranes.

The silicon micro-machining techniques allow the manufacture of very small objects at low costs. Small size, combined with reduced costs and accuracy, allow the creation of dialysis machines which are cheaper, smaller, lighter and with lower operating costs. In particular, the operating costs are drastically reduced and, with no active element in motion, breakage and maintenance are rare and cheaper.

The objective of the device object of the present invention is the direct measurement of the difference of (mass or volume) flow rate, or speed, between two separate

channels bearing the two flows.

The fluids forming the two flows can have same or different chemical composition, and can have same or different physical conditions (for instance density, temperature, speed, pressure).

The sensitive elements are connected and controlled in such a way to be directly affected by the difference of the two flows in question. A Wheatstone bridge connection can be used to this purpose, so that the measurement of the unbalance of the Wheatstone bridge is proportional to the flow difference in the two channels.

It should be noted that the measurement in question cannot ignore the fluid temperature, which must therefore be known (measured by the sensor) and suitably balanced.

The sensor manufacture comprises two steps:

1. micro-machining of silicon chips, containing all necessary sensitive elements and heaters; and

2. assembling of the aforesaid chip with other functional parts (substantially PCBs and fluidic channels), in order to obtain a flow sensor which can be used under desired thermal, fluidic and electrical conditions.

In short, the micro-machining consists in the creation of a suitable network of resistors, electrically insulated with regard to the fluid and thermally insulated with regard to the substrate. Indicatively, the manufactured resistors have a micrometre-sized section and a millimetre-

sized length.

The sensor assembly can be carried out as follows. The chip bearing the sensitive elements configured in a differential manner is glued and connected (for instance by means of wire-bonding) to a substrate (for instance PCB) having all electrical connections for data control and acquisition; the two channels bearing the two flows must have a suitable opening for housing the chip.

In a second alternative embodiment (not shown), the two channels of the differential flow-meter are formed in at least one block, one face of which is closed by a layer of suitable material (e.g. silicon) on which the elements 200, 300 and the differential measuring device 40 are formed.

In a third embodiment, the sensitive elements (thermorestistances) are made by means of thermopiles or thermistors.

The main advantages of the differential flow-meter of the present invention are as follows:

- high sensitivity and resolution;
- reduced size;
- low production costs; and
- better reliability over time.

CLAIMS

1. Differential flow-meter (10*, 1000) comprising a first
separate channel (20) and a second separate channel
(30) in which two fluids flow, said fluids being same
or different;

said first channel (20) comprising the following
devices:

- first heating means (21) of the fluid flowing
according to an arrow (F1); the amount of heat
supplied by said first heating means (21) being
controlled by a differential measuring device (40);

- first temperature detecting means (22), placed
close to said first heating means (21); the
temperature of said first temperature detecting
means (22) being also detected by means of the
differential measuring device (40); and

said second channel (30) comprising the following
devices:

- second heating means (31) of the fluid flowing
according to an arrow (F2); the amount of heat
supplied by said second heating means (31) being
controlled by said differential measuring device
(40);

- second temperature detecting means (32), placed
close to said second heating means (31); the
temperature of said second temperature detecting

means (32) being also detected by means of the differential measuring device (40);

wherein said differential measuring device (40) can transform the instantaneous temperatures detected by the temperature detecting means (22, 32) into differential flow rate or speed measurements of the two fluids passing in the two channels (20, 30);

differential flow-meter (10) characterized in that said first temperature detecting means (22) are at least partially integral to said first heating means (21) in a first thermal device (200), and/or said second temperature detecting means (32) are at least partially integral to said second heating means (31) in a second thermal device (300).

2. Differential flow-meter (10*, 1000) according to Claim 1, characterized in that said first and said second thermal devices (200, 300) are integrated in a micro-machined chip (90).

3. Differential flow-meter (10*, 1000) according to any one of the preceding Claims, characterized in that the sensitive elements of said differential measuring device (40; 90) comprise at least some Wheatstone bridges, and in that the differential measurement is carried out by measuring the unbalance of said Wheatstone bridges.

4. Differential flow-meter (10*, 1000) according to any

one of the preceding Claims, characterized in that each channel (20*, 30*) comprises cylindrical end portions (PC) connected to a central prismatic portion (PP).

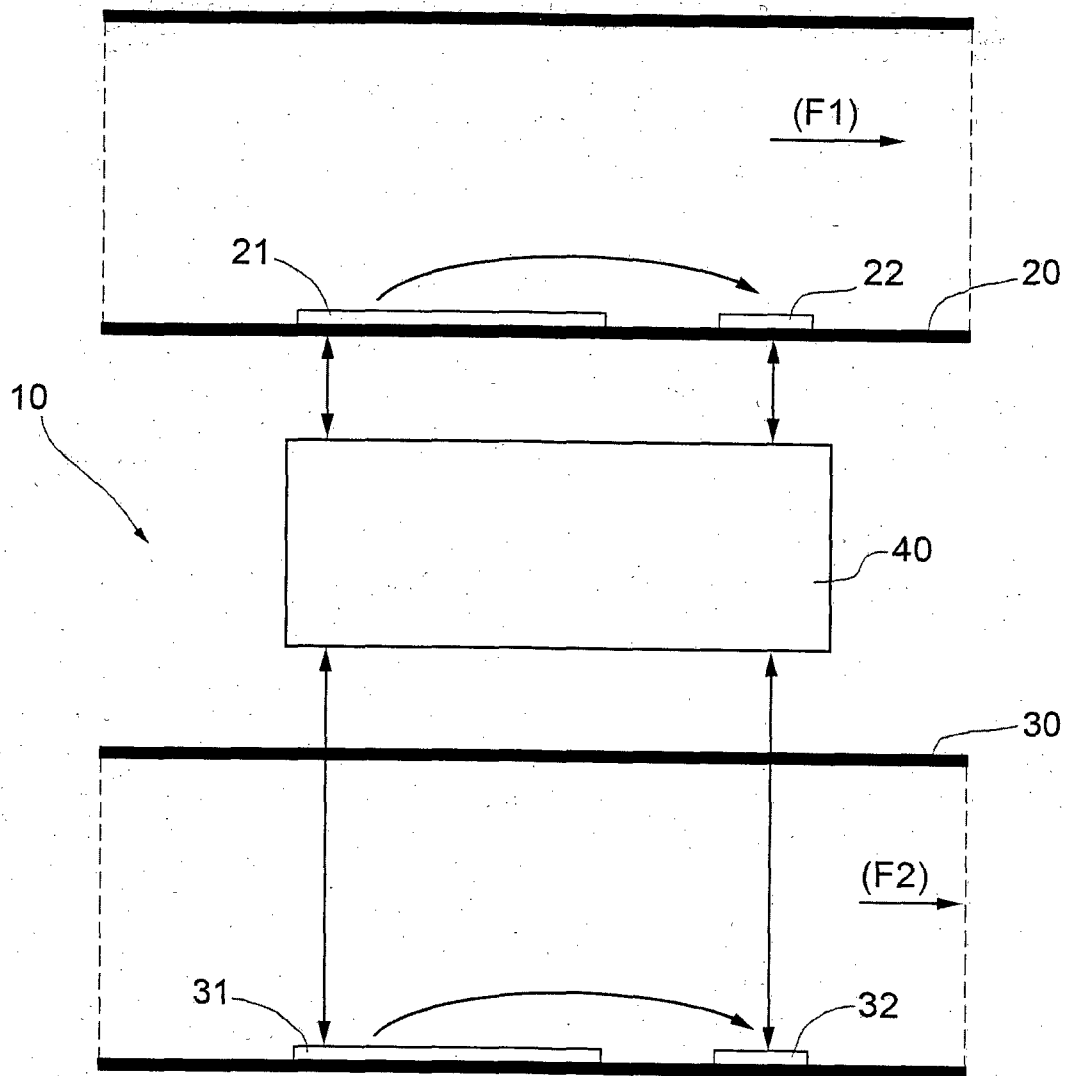
5 5. Haemodialysis machine characterized in that it comprises at least a differential flow-meter (10*, 1000) according to any one of Claims 1-4.

6. Haemodialysis machine according to Claim 5, characterized in that the two channels (20*, 30*) of
10 said differential flow-meter (10*, 1000) are hydraulically connected to two ducts (51, 54) in which the dialysate flows in order to calculate the weight loss.

7. Haemodialysis machine according to Claim 5,
15 characterized in that the two channels (20*, 30*) of said differential flow-meter (10*, 1000) are hydraulically connected to two ducts (52, 55) in which the blood flows in order to calculate the weight loss.

20

25



PRIOR ART

FIG.1

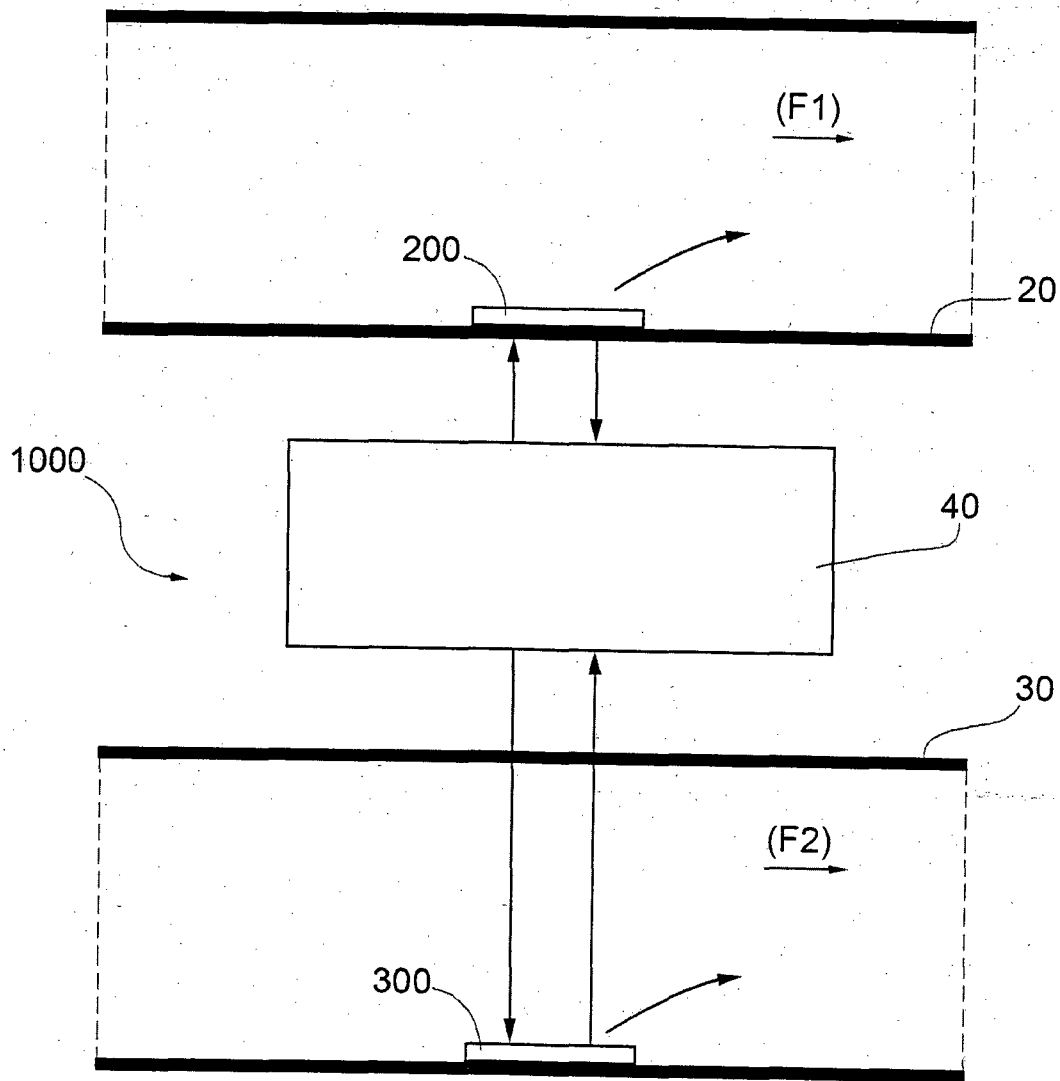


FIG.2

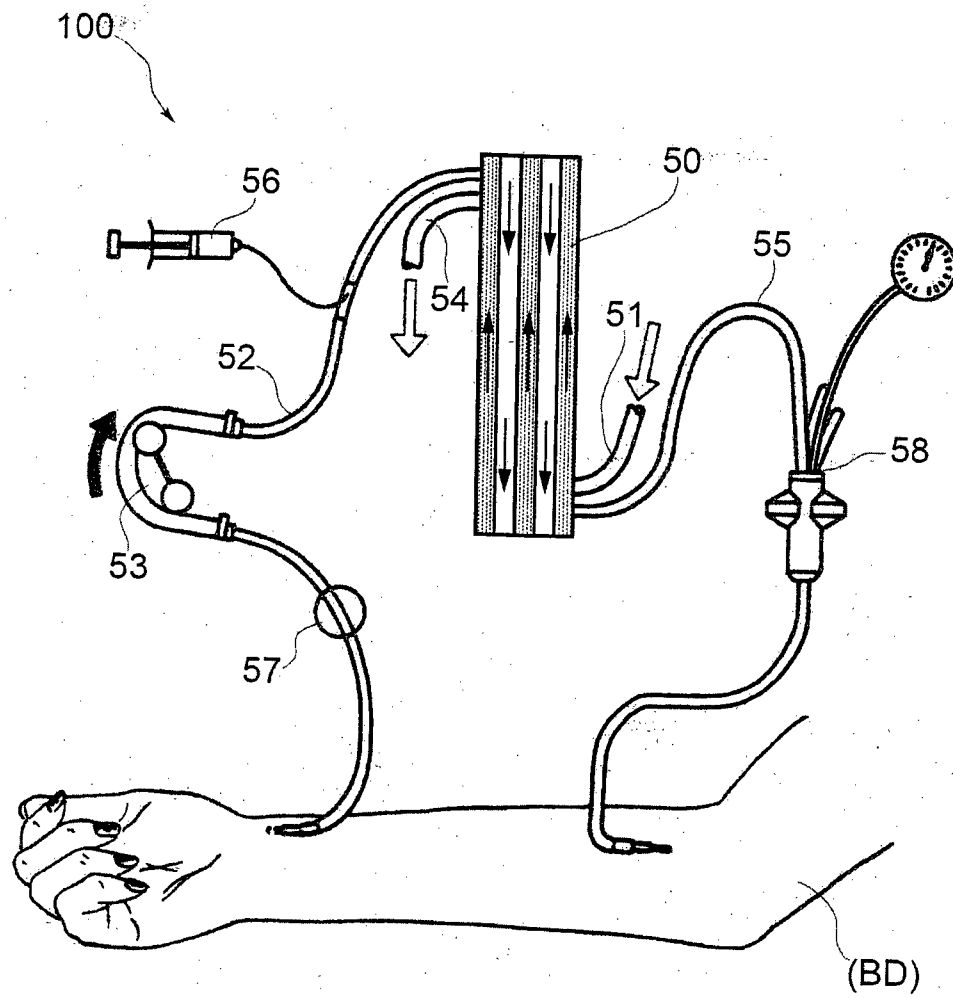


FIG.3

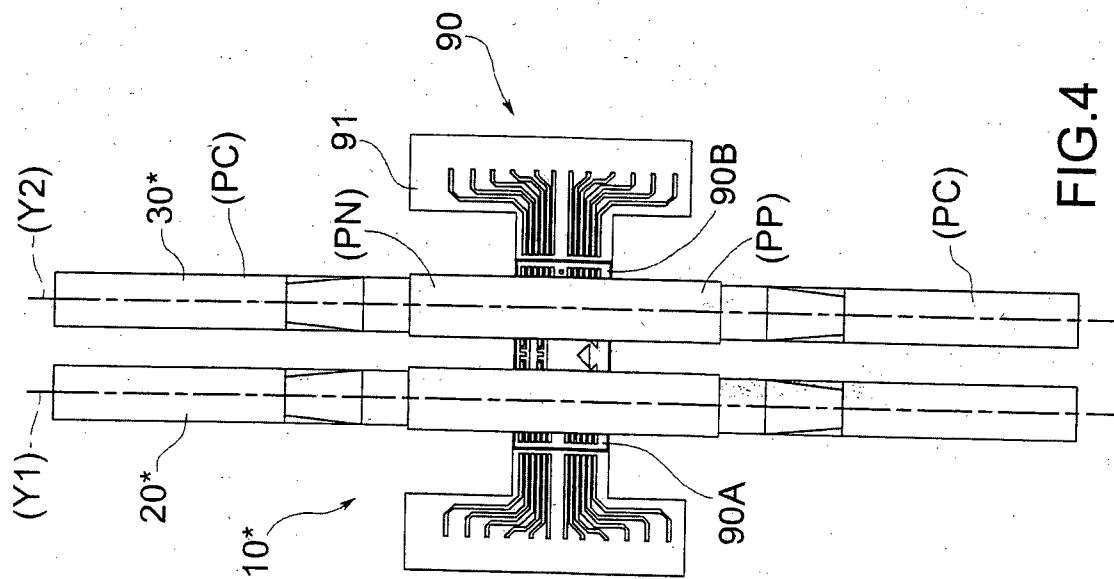


FIG. 4

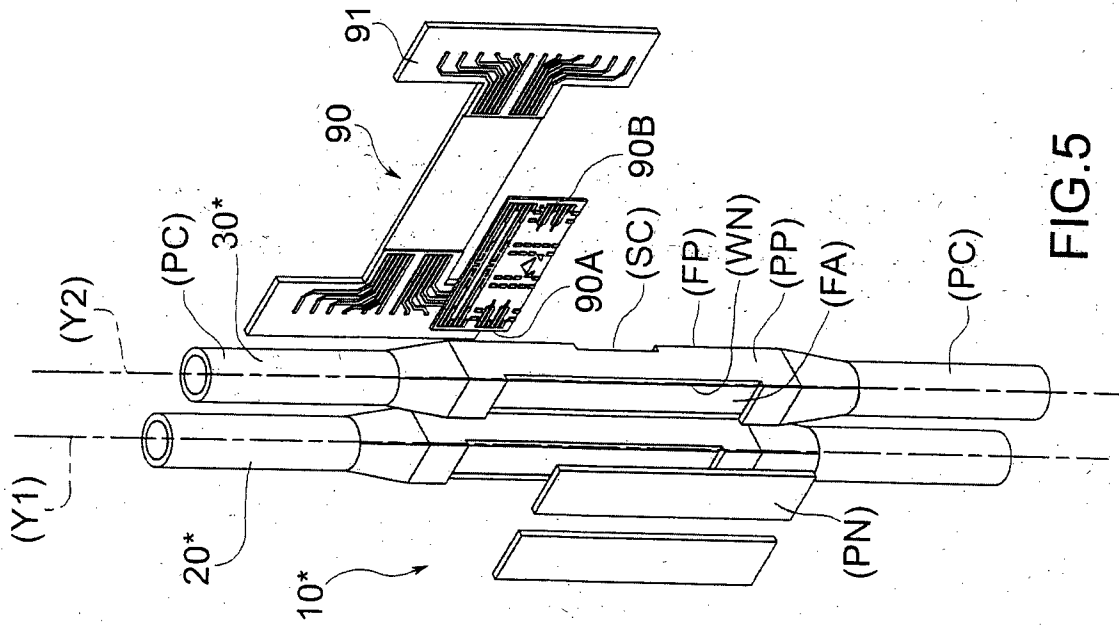


FIG. 5

INTERNATIONAL SEARCH REPORT

International application No
PCT/IB2014/058447

A. CLASSIFICATION OF SUBJECT MATTER INV. G01F23/30 G01F23/72 G01F1/68 G01F1/684 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) G01F A61M		
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 2 946 220 A (MARCEL COGNAT ET AL) 26 July 1960 (1960-07-26)	1,3,4
Y	the whole document -----	2
X	US 5 861 555 A (HOBRO STURE [SE] ET AL) 19 January 1999 (1999-01-19)	1,4-7
Y	the whole document ----- DE 10 2011 002947 B3 (SIEMENS AG [DE]) 26 January 2012 (2012-01-26)	2
	the whole document -----	
☐ Further documents are listed in the continuation of Box C. ☒ See patent family annex.		
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Date of the actual completion of the international search 8 April 2014	Date of mailing of the international search report 15/04/2014	
Name and mailing address of the ISA/ European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016	Authorized officer De Masi, Rita	

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

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