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(54) **Blood sampling catheter**

Katheter zur Abnahme von Blut

Cathéter de prise de sang

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Description

[0001] The present invention relates to a catheter and also an apparatus for use with that catheter and a system including the catheter and apparatus. In particular, it relates to a catheter for insertion into a blood vessel allowing blood samples to be taken.

[0002] It is known, for instance, from US 2004/0102686 to carry out methods of diagnosis for identifying vulnerable plaque by identifying pathological markers such as C-reactive protein or pH change generated by the pathological site. US 2004/0102686 describes an arrangement where first and second detectors are advanced through a blood vessel with each of the detectors selected to detect the pathological marker. The detectors are spaced axially apart such that differential concentration of the pathological marker as measured by the detectors indicates the presence of the pathological site in proximity to at least one of the detectors. The use of detectors in this way is somewhat limiting and relatively expensive. Specific detectors have to be provided for respective tests, fitting these detectors in the catheter is relatively difficult and, where a variety of different catheters are provided, each requires separate regulatory approval. Furthermore, the spacing of the detectors is such that any markers for detection have been diluted throughout the blood volume such that their concentration is significantly affected by the general background level and it becomes more difficult accurately to identify the source of the markers.

[0003] US 5,533,516 describes taking a bodily sample, e.g., a cell sample, from deep within the body of a patient and collecting the sample outside the body to facilitate treatment of the patient. A sampling probe is provided in the form of an elongate catheter having a proximal portion that remains outside the body and a distal portion that can be located within the body. The distal portion includes a membrane with openings that communicate with space that communicates with a source of suction force. The catheter is positioned within the body. The sample is taken by exposing the membrane by placing it in proximity with a desired location so that the bodily sample is received by the membrane. The catheter is removed from the patient, the sample is collected outside the body, treated, disposed onto a device, such as a graft, stent, or catheter, and reintroduced into the body at a desired site.

[0004] GB 1 405 556 describes an endometrial sampler, comprising a hollow tube having a sampling end containing a plurality of sampling ports communicating with the interior of the tube, and a sleeve surrounding the tube and slidable with respect to it, the sleeve and the tube being reciprocable with respect to one another between a sampling position in which the sleeve exposes at least one of the sampling ports and a second position in which the sleeve engages a forward stop on the tube and covers all the sampling ports.

[0005] WO 2004/010874 discloses a device for sampling multiple tissue samples and fluid samples using independently controlled micro-miniature sampling devices. Samples can be collected simultaneously or in a sequence over time.

[0006] It is an object of the present invention to provide an improved means of diagnosis whilst at least reducing the problems mentioned above.

[0007] The present invention provides a method of providing a data profile, optionally as part of a method of diagnosis, whereby a blood sample is taken at a plurality of locations along a length of a blood vessel so as to provide a profile of concentration levels along that length of the blood vessel.

[0008] It is possible to collect multiple, spatially separated samples at a single instance in time (eg via multiple sheath holes), these remaining separated with no mixing. Individual collection ports can be ejected into multiple sample chambers for analysis.

[0009] Having taken blood samples in this way, it is possible to apply a variety of tests to the blood so as to provide profiles relating to any desired tests. For instance, the profiles could relate to C-reactive protein, heat-shock proteins, hydrogen ion concentration (pH), cholesterol, cells, cell surface markers, etc. By means of the profile, any background levels in the sample of blood may be calculated and the location of any problem areas may be accurately determined.

[0010] Preferably, the method involves obtaining the blood samples using a catheter which is inserted into the blood vessel at a known position, such that treatment of an identified problem area may be applied accurately with reference to the known position of the diagnostic catheter. In this way, it becomes very easy for a clinician to perform diagnosis of the blood vessel and then apply treatment specifically to the identified problem area.

[0011] According to the present invention there is provided a catheter for insertion into a blood vessel, the catheter having a sampling part arranged to capture a blood sample at a plurality of locations along a length of the blood vessel and as defined in the accompanying claim 1.

[0012] The catheter can preserve the spatial separation of samples collected at a single instance in time.

[0013] In this way, a catheter of this type can be used to conduct a number of different tests. Indeed, such tests may even be carried out simultaneously. As a result of the tests on the sample of blood, a profile of concentrations in the blood may be provided so as to enable problem areas in the blood vessel to be identified.

[0014] In general, the catheter will be arranged to capture a blood sample at at least three locations along the length of the blood vessel, but, preferably at at least five locations if not 20, 100 or more. It is considered that samples might be taken over a length of perhaps 100 cm. It is envisaged that the catheter captures blood samples at locations every 1 cm along the length or even closer, for instance 0.5 cm. The catheter has the potential to sample nano to micro litre volumes.

[0015] By collecting samples at multiple locations from

inside the blood vessel, true background levels in the serum can be found (upstream of the source) . Furthermore, the marker can be detected at a higher local concentration, because it will be collected nearer the source before it is diluted. Also, as mentioned above, the source of the marker can be located more accurately by virtue of the number of samples collected along the length of the blood vessel.

[0016] Since the marker can be detected at a higher local concentration, the levels of the marker can be determined more sensitively. In particular, the level of the marker will be higher in relation to the background level. Hence, the marker can be detected even if the patient has an elevated background level of inflammatory marker.

[0017] The arrangement allows future coronary events to be predicted more accurately so that patients at severe risk of MI (myocardial infarction) and/or stroke can monitored or given prophylactic treatment. Also, low risk patients can be identified more accurately and managed more economically than previously.

[0018] Unstable plaques in the blood vessel can be located accurately which allows targeted local therapy, such as stenting.

[0019] With the arrangement of the present invention, the progress/effectiveness of chemical therapy can be monitored in more detailed than before. Furthermore, the process is compatible with clinical procedures as the catheter could collect samples within blood vessels during routine exploratory procedures. The process is compatible with clinical budgets, since the catheter of the present invention is relatively straightforward to construct and, hence, relatively inexpensive.

[0020] It is not necessary for the catheter to contact the vessel wall or to use suction to pull the vessel wall to the device. Indeed, it is preferred not to. It is preferred not to damage the endothelium (inner wall of artery) and to collect blood and biological samples in close proximity to the wall.

[0021] By virtue of the sleeve, the openings may be kept closed until the catheter is located at a desired position. Although-this is highly advantageous in some embodiments, where blood samples are actively drawn into individual openings. It is recognised that in some arrangements that are outside the scope of the claims, the sleeve may not be necessary.

[0022] The through-holes of the sleeve are arranged in an array corresponding to the array of openings of the sample member. At first, the through-holes are out of alignment with the openings, but movement of the sleeve relative to the sample member brings the through-holes into alignment with the openings.

[0023] Preferably, the sampling part includes a respective plurality of pockets for receiving blood from the openings.

[0024] In this way, the pockets provide respective storage chambers for each opening.

[0025] Preferably, each of said pockets is at least partially evacuated such that, upon exposure by the sleeve, the pockets suck in blood from outside the catheter.

[0026] The sleeve thus seals the opening and pockets so as to maintain a low pressure (relative to atmosphere) in the pockets whilst the catheter is positioned in the blood vessel. When the sleeve is moved to expose the pockets, the low pressure draws in blood from outside the catheter.

[0027] Alternatively, the sampling member may include a vacuum passageway connecting each of the pockets, the vacuum passageway allowing suction to be applied to each of the pockets.

[0028] In this way, by connecting the vacuum passageway to an external low pressure source, blood samples may be drawn through the openings as required.

[0029] The pockets and the vacuum passageway may be pre-filled with a fluid, such as saline, which can be drawn out of the catheter so as to draw blood into the pockets from outside the catheter.

[0030] Pre-filling the pocket and vacuum passageway in this way, as with evacuating the pockets, reduces the release of bubbles into the blood flow.

[0031] As an alternative, the sampling part may include a respective plurality of vacuum passageways connected to respective openings so as to allow suction to be applied individually to each opening.

[0032] In this way, sampling from each opening can be individually controlled.

[0033] The catheter may further include a respective plunger within the or each vacuum passageway moveable away from the openings so as to draw blood through the openings from outside the catheter.

[0034] It will be appreciated that movement of the plunger in a vacuum passageway will cause blood to flow into the respective opening. Where the openings are provided with individual respective vacuum passageways and plungers, the samples taken by those openings can be individually controlled.

[0035] The sampling part may further include a respective plurality of pistons in the pockets whereby movement of the pistons away from the respective openings sucks blood into the respective pockets.

[0036] The pistons act like the plungers mentioned above, but are provided within pockets, rather than the vacuum passageways.

[0037] Preferably, the pistons are moveable in the axial direction to suck blood into the respective pockets and the sampling part further includes an axially extending actuator to which all of the pistons are attached and by which the pistons may be moved.

[0038] This provides a convenient arrangement for simultaneously actuating the pistons of all of the pockets.

[0039] A membrane layer may be provided covering the openings, the membrane layer allowing plasma through the openings.

[0040] In this way, plasma may be sampled whilst leaving platelets etc outside the catheter. This increases the concentration of the test sample and allows reduction in the collection volume.

[0041] As described above, preferably, the sampling part is arranged to capture a plurality of discrete samples along said length of the blood vessel. Many diagnostic chemistry processes require samples of approximately 50μl and, hence, for many embodiments each discrete sample is substantially of this value. However, the discrete samples may be between 0.1 μl and 100 μl, more preferably between 20 μl and 50 μl.

[0042] The sampling part may include an axially elongate sample member comprising a continuous absorbent material. This can be used in conjunction with the axial array of openings, such that each opening feeds a respective sample into a respective part of the same continuous absorbent material. A sleeve is used in conjunction with this. Alternatively, however, the continuous absorbent material may be provided so as to continuously sample blood along its length, although such an arrangement is outside the scope of this invention. Again, a sleeve may be provided to control exposure of the material to the blood outside the catheter. The sample member can be directly analysed to measure differences in samples along the length of the device.

[0043] The present invention also provides an apparatus for analysing blood samples captured by a catheter as described above, the apparatus being arranged to analyse blood taken from a plurality of locations along said length of the blood vessel and to provide a profile of concentration levels for one or more pathological markers along said length of the blood vessel.

[0044] The apparatus is preferably arranged to provide a profile of cardiac inflammatory marker along the length of the blood vessel.

[0045] It is preferably further arranged to calculate from the profile the marker background level of the sample of blood.

[0046] It is preferably further arranged to predict, from elevated portions of the profile, the location of problem areas along the length of the blood vessel.

[0047] According to the present invention, there is also provided a catheter system including both the catheter and the apparatus described above.

[0048] By means of the present invention, gradients can be measured by collecting separate samples of whole blood at multiple locations in a linear path along the longitudinal axis of the blood vessel. Either at the time of collection or immediately after collection, the samples from different locations are kept as separate discrete entities. The collected samples are extracted from the body and analysed using, for instance, antibody- based methods to determine the concentration of inflammatory marker(s) in each separate sample. The concentration of the markers can be plotted against their location along the length of the sampling catheter.

[0049] The catheter may take samples not only along the length of the blood vessel, but also radially around the outer periphery of the catheter. In this case, the concentration markers can be plotted against their location in three dimensions.

[0050] The plot can be referenced to the precise position in the blood vessel where the samples were taken. This may be determined by X-ray/fluoroscopy or merely with reference to the reference guide as described above. This shows the gradient of the markers as the rate of change of concentration along the length of the blood vessel. The gradient can be used to determine the markers more sensitively than with previous techniques and can locate vulnerable plaques allowing the potential of targeted local therapy, e.g. stenting, as described above.

[0051] The catheter can be used in combination with other diagnostic and imaging devices and systems incorporating acoustic (e. g. Intravascular Ultrasound IVUS, etc.) and/or electromagnetic sensing/imaging modalities (e. g. Optical coherence tomography, Angioscopy, Thermography, Spectroscopy, Magnetic Resonance Imaging, Electron beam computed tomography, etc.). Hybrid devices can be provided with combined sensing platforms in a single device e. g. a catheter according to the present invention with an IVUS probe at the end. The advantage of combined devices is that it would enable clinicians to use a single procedure to examine the vessels with a familiar technique, such as IVUS, and, in areas of concern, collect blood using the catheter of the present invention.

[0052] It will be appreciated that, although the catheter has been described with reference to its use in a blood vessel, it can also be used inserted into other parts of the body.

[0053] The invention will be more clearly understood from the following description given by way of example only, with reference to the accompanying drawings, in which:

Figures 1(a) to (g) illustrate schematically a general method of treatment and diagnosis, these being provided by way of background information to aid in the understanding of the invention;

Figures 2(a), (b) and (c) illustrate an exemplary catheter;

Figures 2(d) and (e) illustrate a catheter embodying the present invention;

Figure 3 illustrates an exemplary catheter;

Figure 4 illustrates an exemplary catheter;

Figure 5 illustrates an exemplary catheter;

Figures 6(a) and (b) illustrate a catheter embodying the present invention;

Figures 7(a) and (b) illustrate a catheter embodying the present invention;

Figures 8(a) and (b) illustrate a catheter embodying the present invention;

Figures 9(a) and (b) illustrate a catheter embodying the present invention;

Figures 10(a) and (b) illustrate a catheter embodying the present invention;

Figures 1 I(a) and (b) illustrate an absorbent planar member; and

Figure 12 illustrates, schematically, a membrane for

covering openings of catheters embodying the present invention;

Figures 13(a), (b) and (c) illustrate an exemplary catheter;

Figures 14(a), (b) and (c) illustrate an exemplary catheter;

Figure 15 illustrates an exemplary catheter with a positioning device and a suction device; and

Figure 16 illustrates an exemplary catheter with a sample collector.

[0054] Methods of obtaining profiling data, diagnosis and treatment using an examplary catheter will be described with reference to the schematic representations given in Figure 1(a) to (g).

[0055] As shown in Figure 1, a reference guide (2) is inserted into a blood vessel (4) at a fixed position relative to the blood vessel (4). Then, as illustrated in Figure 1 (b) a sampling part (6) is inserted through an axial duct (8) of the reference guide (2). Preferably, some form of indexing is provided such that, when fully inserted, the sampling part (6) has a predetermined relative positioning with the reference guide (2).

[0056] Various different arrangements will be described below, but, as illustrated in Figure 1(b), the sampling part includes plurality of openings (10) for taking a plurality of blood samples along a length of the blood vessel (4) determined according to the position of the reference guide (2). As will be described below, the samples of blood taken by the opening (10) are used to identify a problem area in the blood vessel, such as plaque (12). The catheter need only be located in close proximity to a vessel wall (not in contact) and hence collect biological and chemical entities from very near the surface of the plaque. The sampling part (6) may be withdrawn from the reference guide (2) as illustrated in Figure 1(c) and provided to an apparatus (14) as illustrated schematically in Figure 1(d). The apparatus (14) analyses the blood samples and provides at an output a map of single/multiple biochemical marker gradients (16) along the length of the blood vessel (4). As illustrated in Figures 1(e) and (f), a treatment catheter (18) may then be deployed to the exact position of the zone of interest, e. g. vulnerable plaque, using the reliable positional reference of the reference guide (2) and using the information of the marker gradient from the apparatus (14).

[0057] In the example illustrated in Figures 1(f) and (g), the treatment catheter (18) deploys a localized drug delivery vehicle such as a drug-eluting stent. Those familiar with the state of the art in drug-eluting stents will recognize that this may be either a permanent or a transient biodegradable device.

[0058] It is also possible to provide a catheter with an integrated treatment part which can be indexed to an appropriate position after diagnosis.

[0059] The present invention is applicable to observing not only biomarkers, where a biomarker can be considered a "biological entity that can give information regarding disease state", but also chemical entities e. g. Nitric Oxide that are also produced by those biological entities. Examples of biomarkers relevant to vulnerable plaque include:

CRP, PAPPA, Myeloperoxidase, MMP 9, sCD40L, PLGF, Neopterin, Soluble P-Selectin, sVCAM-1, sICAM-1, Soluble CD40L, VCAM-I, ICAM-I, P-Selectin, E- Selectin.

[0060] Figures 2(a), (b) and (c) illustrate schematically an example of a catheter arrangement useful for an understanding of the present invention.

[0061] The sampling part (6) includes a sample member (22) in which an axial array of a plurality of pockets (24) are formed. Each of the pockets (24) forms, at the outer surface of the sample member (22), a corresponding opening (26).

[0062] Sampling part (6) is also provided with an elongate sleeve (28) defining an axial passage (30) for housing the sample member (22). In this respect, Figures 2 (a), (b) and (c) are highly schematic and the upstream end of the elongate sleeve (28) (to the left as illustrated) extends beyond the Figure. The sampling part (6) can be positioned as described with reference to Figures 1 (a) to (g). With the sample member then in place, the sleeve (28) may be withdrawn from the sample member (22) as illustrated by arrow (32). The sleeve (28) includes a through hole (34). By withdrawing the sleeve (6) as illustrated in Figures 2(b) and (c), the through hole (34) moves in turn over each of the openings (26) so as to allow the respective pockets (24) to be filled with blood from outside the catheter.

[0063] A corresponding embodiment of the present invention is illustrated in Figures 2(d) and (e) where there is provided a plurality of through holes (34), in particular, a through hole (34) corresponding to each opening (26). In this case, the sleeve (28) is originally positioned such that all of its through holes are positioned adjacent parts of the sample member (22) where openings (26) are not provided. In this respect, they could be positioned radially or axially displaced from the openings (26). The sleeve (28) can then be moved so as to bring its through holes into alignment with the openings (26).

[0064] Figure 3, which is provided by way of background material that is useful for understanding the invention, illustrates an exemplary catheter like that illustrated in Figures 2(a), (b) and (c), but where the pockets (24) are evacuated prior to use. In other words, they have an internal pressure which is less than atmospheric and preferably significantly less than atmospheric.

[0065] When the sleeve (28) is moved to bring the through hole (34) adjacent the opening (26) of a pocket (24), the low pressure space thus draws in blood from outside the catheter. This helps prevent bubble release during collection and improves blood flow into the pocket.

[0066] In the arrangement of Figure 4, which is provided by way of background material that is useful for un-

derstanding the invention, instead of prior evacuation of the pockets (24), the pockets (24) are all interconnected by a vacuum passageway (36). The vacuum passageway (36) is connected to a source of suction such that when any through hole (34) connects a pocket (24) to the blood surrounding the catheter, blood is drawn into the pocket (24) as a result of the reduced pressure.

[0067] In the arrangement of Figure 5, which is provided by way of background material that is useful for understanding the invention, the pockets and, preferably, the vacuum passageway are pre-filled with a liquid, such as saline. Suction on the vacuum passageway withdraws the liquid from the pockets, such that they are replaced with blood from outside the catheter. The use of liquid (38) in this way helps prevent bubble release during collection.

[0068] As mentioned above, the sleeve (28) of the catheter according to the invention is provided with a plurality of through holes (34) corresponding to respective openings (26) and pockets (24). Figures 6(a) and (b) illustrate embodiments based on the arrangements of Figures 3 and 4 modified in this way. Figures 7(a) and (b) illustrate an embodiment based on the arrangement of Figure 5 modified in this way.

[0069] It is possible to use a plunger (40) in a vacuum passageway (38) in order to draw blood in through the openings (26). The embodiment of Figures 8(a) and (b) is based on an arrangement where individual respective vacuum passageways (38) are provided for each respective opening (26). As with the exemplary arrangements of Figures 4 and 5, an external vacuum source could be used to draw blood in through the openings (26). However, in the illustrated embodiment, respective plungers (40) are provided for each vacuum passageway (38). By withdrawing the plungers (44) away from the openings (26), samples of blood are drawn into the sample member (22) as illustrated in Figure 8(b). Although individual pockets could be provided for each opening (26), in the illustrated embodiment, the vacuum passageways (38) effectively themselves form pockets. It will also be appreciated that, in this embodiment, a sleeve is not necessary, though, for certain applications, might be desirable.

[0070] In the embodiment of Figures 9(a) and (b), individual respective pistons (42) are provided in each pocket (24). Although arrangements are possible where the pistons (42) are movable individually, in the illustrated embodiment, all of the pistons are attached to an axially extending actuator (44). By moving the actuator (44) axially away from the far end of the catheter and, hence, away from the openings (26), blood is drawn into the pockets (24). The volumes of the pockets (24) prior to sampling can be evacuated prior to use so as to enable the pistons (42) to move. Alternatively, the pockets could be prefilled with a fluid which is driven out by the pistons (42) to an outlet channel or even to the blood vessel.

[0071] Rather than form individual pockets in the sample member (22), the sample member (22) can include a single continuous absorbent member which extends along the length of blood vessel to be diagnosed.

[0072] Figures 10(a) and (b) illustrate an embodiment with a single continuous absorbent member (46) within the sample member (22). In a manner similar to that described for the embodiment of Figures 7(a) and (b), the sleeve 28 with its through holes (34) can be moved from a position as illustrated in Figures 10(a) where the through holes (34) and openings (26) are not in alignment to a position as illustrated in Figure 10(b) where they are in alignment. When the through holes (34) and openings (26) are in alignment, blood flows into the sample member (22) and is absorbed into the absorbent member (46) at predetermined positions along its length. Subsequently, samples can be taken from those predetermined positions. Also, the absorbent member (46) can be interrogated with micron resolution in an external device, for instance using fluorescent tags etc.

[0073] As illustrated in Figure 11(a), the absorbent member (46) can comprise a planar member which is rolled into a cylinder and can then be unrolled as illustrated in Figure 111(b). This provides additional three dimensional information because the sampling is being taken not only along the length of the blood vessel, but also at different radial angles around its periphery. As illustrated in Figures 11 (a) and (b) the part (48) of the sample adjacent the problem area (12) will contain a variation, such as concentration, indicating the problem area (12). In this respect, the absorbent material can be interrogated with micron resolution in an external device, for instance fluorescent tags etc.

[0074] It will be appreciated that, although the embodiments described above have been described only with an axial array of openings and pockets, it is also possible to provide an array which additionally extends around the periphery of the catheter in a radial fashion. In this way, a three dimensional sample can be taken.

[0075] As illustrated in Figure 12, from which the sleeve (28) has been omitted for clarity, a membrane (50) may be used to cover the opening (26). This is also applicable where a pocket (24) is not used. The membrane allows plasma to pass through it, but not other parts of the blood. In this way, it increases the useful concentration of the test sample and, therefore, can reduce the required collection volume.

[0076] In one exemplary arrangement, which is included by way of background information to aid in understanding the invention, as illustrated in Figures 13(a), (b) and (c), similar to the embodiment of Figure 11 (a) and (b), a single continuous absorbent member (46) may be exposed in its entirely by withdrawing the sleeve (28). As a result, the blood absorbed into the absorbent member (46) represents a sample at a plurality of locations along the length of the blood vessel.

[0077] It is also possible to provide a suction tube in the centre of the absorbent member separated from, the absorbent member by a membrane that allows air to pass through but not blood or biomarkers. This would help

draw blood into the absorbent material but would prevent any pooling or mixing of the collected samples in the suction tube. A single suction tube can be provided like that illustrated in Figures 4, 5, 6(b), 7(a) or 7(b). Alternatively, multiple tubes could be provided like those illustrated in Figures 8 (a) and (b) or individual suction chambers like those illustrated in Figures 9(a) and (b).

[0078] It is also possible, but outside the scope of this invention, to capture a blood sample at a plurality of locations along the length of the blood vessel by using only a single opening or inlet port. Figures 14(a), (b) and (c), which are provided by way of background material that is useful for understanding the invention, illustrate highly schematically a sampling part having an opening (26) forming an inlet port at a distal end and vacuum passageway (38) forming an axial channel running from the inlet port to a proximal end. By pulling the sampling part (6) along the length of the blood vessel (4) whilst applying suction to the axial channel at the outlet port, sequential slugs of blood may be sampled at known/positions. The resulting slugs of blood in the vacuum passageway (38) forming the axial channel represent a blood sample at plurality of locations along the length of the blood vessel. Figure 15, which is provided by way of background material that is useful for understanding the invention, illustrates schematically the positioning device (52) and suction device (54) required for this.

[0079] Blood contained in the vacuum passageway (38) forming the axial channel can then be dispensed into a sample collector having a plurality of discrete sample reservoirs.

[0080] This is illustrated in Figure 16 in relation to an exemplary arrangement, which is provided by way of background material that is useful for understanding the invention, where blood is sampled continuously and dispensed consecutively into sample reservoirs (56) of a sample collector (58). Of course, this is also preferably provided in conjunction with a positioning device.

Claims

1. A catheter for insertion into a blood vessel (4), the catheter having a sampling part (6) arranged to collect a plurality of spatially separated discrete blood samples simultaneously from a plurality of locations along a length of the blood vessel and to preserve the spatial separation of those discrete blood samples, wherein the sampling part includes:

   an axially elongate sample member (22) having an axial array of a plurality of openings (26) for receiving blood from outside the catheter at intervals along a length of the blood vessel (4); and an elongate sleeve (28) coaxial with the sample member (22), the sleeve defining an axial passage (30) for housing the sample member and including a plurality of through holes (34) corresponding to respective openings (26), wherein the through holes are positioned so that, with relative movement between the sleeve (28) and the sample member (22), all of the openings (26) are exposed simultaneously to blood outside the catheter so as to collect a respective plurality of discrete blood samples along the length of the blood vessel (4).

2. A catheter according to claim 1, wherein the sampling part (6) includes:

   a respective plurality of pockets (24) for receiving blood from the openings (26).

3. A catheter according to claim 2, wherein each of said pockets (24) is at least partially evacuated such that, upon exposure by the sleeve (28), the pockets suck in blood from outside the catheter.

4. A catheter according to claim 2, wherein the sampling member (6) further includes:

   a vacuum passageway (36) connecting each of the pockets (24), the vacuum passageway allowing suction to be applied to each of the pockets.

5. A catheter according to claim 4, wherein the pockets (24) and the vacuum passageway (36) are pre-filled with a fluid which can be drawn out of the catheter so as to draw blood into the pockets from outside the catheter.

6. A catheter according to claim 1 or 2, wherein the sampling part (6) includes:

   a respective plurality of vacuum passageways (38) connected to respective openings (26) so as to allow suction to be applied individually to each opening.

7. A catheter according to claim 6, further including:

   a respective plunger (40) within each vacuum passageway (38) moveable away from the opening (26) so as to draw blood through the opening from outside the catheter.

8. A catheter according to claim 2, wherein the sampling part (6) further includes a respective plurality of pistons (42) in the pockets (24) whereby movement of the pistons away from respective openings (26) sucks blood into the respective pockets.

9. A catheter according to claim 8, wherein the pistons (42) are movable in the axial direction to suck blood into the respective pockets (24) and the sampling

part (6) further includes an axially extending actuator (44) to which all of the pistons are attached and by which the pistons may be moved.

10. A catheter according to any preceding claim, further including:

a membrane layer (50) covering the pockets (24), the membrane layer allowing blood plasma into the pockets.

11. A catheter according to any preceding claim, wherein each discrete sample is between 10μl and 50μl.

12. A catheter according to any preceding claim, wherein the sampling part (6) includes an axially elongate sample member (22) comprising a continuous absorbent material (46).

13. A catheter according to any preceding claim, comprising an array of axially and radially spaced openings (26) along a length of the sample member (22).

14. A catheter system including a catheter according to any preceding claim and an apparatus for analysing the discrete blood samples captured by the catheter, the apparatus being arranged to analyse blood taken from a plurality of locations along said length of the blood vessel (4) and to provide a profile of concentration levels for one or more pathological markers along said length of the blood vessel.

15. A catheter system according to claim 14, in which the marker is an inflammatory marker.

16. A catheter system according to claim 14 or 15, further comprising means to calculate from the concentration profile the background level of the marker in the sample blood.

17. A catheter system according to any of claims 13 to 16, in which the profile is output as a 2D or 3D mapping of concentration levels for one or more markers against location along the length of the blood vessel.

18. A method for generating a data profile for one or more biomarkers at a site of interest in a blood vessel (4), which method comprises analysing a plurality of discrete, spatially separated, blood samples that have been taken from respective locations along a length of the blood vessel, by measuring the concentration of the one or more biomarkers in each of the samples and generating a data profile of the concentration levels for the biomarkers along the length of said blood vessel.

19. A method according to claim 18, in which the number of samples is at least 3, preferably at least 5, more preferably at least 20 and most preferably at least 100.

20. A method according to claim 18 or 19, in which the biomarkers tested for include one or more of: CRP, PAPPA, Myeloperoxidase, MMP 9, sCD40L, PLGF, Neopterin, Soluble P-Selectin, SVCAM-1, sICAM-1, Soluble CD40L, VCAM-1, ICAM-1, P-Selectin and E-Selectin.

21. A method according to.any of claims 18 to 20, in which the data is output as a map of one or more biomarker gradients along the length of said blood vessel (4).

Patentansprüche

1. Ein Katheter zum Einführen in ein Blutgefäß (4), wobei der Katheter ein Probenentnahmeteil (6) aufweist, das so gestaltet ist, dass es eine Vielzahl von räumlich getrennten, einzelnen Blutproben gleichzeitig von einer Vielzahl von Stellen entlang einer Teilstrecke des Blutgefäßes entnehmen und die räumliche Trennung dieser einzelnen Blutproben erhalten kann, wobei das Probenentnahmeteil umfasst:

ein axial langgestrecktes Probenelement (22), das eine axiale Anordnung einer Vielzahl von Öffnungen (26) zur Aufnahme von Blut von außerhalb des Katheters in Abständen entlang einer Teilstrecke des Blutgefäßes (4) aufweist; und
eine langgestreckte Hülle (28), die koaxial zum Probenelement (22) angeordnet ist, wobei die Hülle einen axialen Durchgang (30) zur Unterbringung des Probenelements umgrenzt und eine Vielzahl von Durchgangslöchern (34) umfasst, die den jeweiligen Öffnungen (26) entsprechen, wobei die Durchgangslöcher so positioniert sind, dass mit einer relativen Bewegung zwischen der Hülle (28) und dem Probenelement (22) alle Öffnungen (26) gleichzeitig mit Blut von außerhalb des Katheters in Kontakt gebracht werden, so dass eine entsprechende Vielzahl von einzelnen Blutproben entlang der Teilstrekke des Blutgefäßes (4) entnommen werden kann.

2. Ein Katheter gemäß Anspruch 1, wobei das Probenentnahmeteil (6) umfasst;
eine entsprechende Vielzahl von Fächern (24) zur Aufnahme von Blut aus den Öffnungen (26).

3. Ein Katheter gemäß Anspruch 2, wobei jedes der Fächer (24) mindestens teilweise luftleer ist, so dass die Fächer, wenn sie in Kontakt mit der Hülle (28)

gebracht werden, Blut von außerhalb des Katheters in sich hineinsaugen.

4. Ein Katheter gemäß Anspruch 2, wobei das Probenentnahmeteil (6) weiterhin umfasst:

einen Vakuumdurchgang (36), der die einzelnen Fächer (24) verbindet, wobei der Vakuumdurchgang es ermöglicht, eine Saugwirkung auf jedes der Fächer auszuüben.

5. Ein Katheter gemäß Anspruch 4, wobei die Fächer (24) und der Vakuumdurchgang (36) mit einer Flüssigkeit vorgefüllt sind, die aus dem Katheter herausgezogen werden kann, so dass Blut von außerhalb des Katheters in die Fächer hineingezogen wird.

6. Ein Katheter gemäß Anspruch 1 oder 2, wobei das Probenentnahmeteil (6) umfasst:

eine entsprechende Vielzahl von Vakuumdurchgängen (38), die mit den entsprechenden Öffnungen (26) verbunden sind, so dass die Saugwirkung für jede der Öffnungen einzeln ausgeübt werden kann.

7. Ein Katheter gemäß Anspruch 6, der weiterhin umfasst:

einen entsprechenden Stößel (40) innerhalb jedes Vakuumdurchgangs (38), der von der Öffnung (26) weg beweglich ist, so dass Blut von außerhalb des Katheters durch die Öffnung hineingezogen werden kann.

8. Ein Katheter gemäß Anspruch 2, wobei das Probenentnahmeteil (6) weiterhin eine entsprechende Vielzahl von Kolben (42) in den Fächern (24) umfasst, wobei durch die Bewegung der Kolben weg von den jeweiligen Öffnungen (26) Blut in die entsprechenden Fächer gesaugt wird.

9. Ein Katheter gemäß Anspruch 8, wobei die Kolben (42) in axialer Richtung bewegt werden können, um Blut in die jeweiligen Fächer (24) hineinzusaugen, und wobei das Probenentnahmeteil (6) weiterhin einen sich axial erstreckenden Betätiger (44) umfasst, an dem alle Kolben befestigt sind und durch den die Kolben bewegt werden können.

10. Ein Katheter gemäß einem beliebigen der vorhergehenden Ansprüche, der weiterhin umfasst:

eine Membranschicht (50), die die Fächer (24) bedeckt, wobei die Membranschicht Blutplasma in die Fächer hineinlässt.

11. Ein Katheter gemäß einem beliebigen der vorhergehenden Ansprüche, wobei jede einzelne Probe zwischen 10 μl und 50 μl beträgt.

12. Ein Katheter gemäß einem beliebigen der vorhergehenden Ansprüche, wobei das Probenentnahmeteil (6) ein axial langgestrecktes Probenelement (22) umfasst, das ein durchgängiges saugfähiges Material (46) umfasst.

13. Ein Katheter gemäß einem beliebigen der vorhergehenden Ansprüche, der eine Reihe von axial und radial im Abstand voneinander angeordneten Öffnungen (26) entlang einer Teilstrecke des Probenelements (22) umfasst.

14. Ein Kathetersystem, das einen Katheter gemäß einem beliebigen der vorhergehenden Ansprüche und einen Apparat zur Analyse der einzelnen Blutproben, die von dem Katheter entnommen wurden, umfasst, wobei der Apparat so angeordnet ist, dass er Blut analysiert, das von einer Vielzahl von Stellen entlang der Teilstrecke des Blutgefäßes (4) entnommen wurde, und dass er ein Profil von Konzentrationsspiegeln für einen oder mehrere pathologische Marker entlang der Teilstrecke des Blutgefäßes liefert.

15. Ein Kathetersystem gemäß Anspruch 14, wobei der Marker ein Entzündungsmarker ist.

16. Ein Kathetersystem gemäß Anspruch 14 oder 15, das weiterhin ein Mittel zur Berechnung des Hintergrundspiegels des Markers im Probenblut aus dem Konzentrationsprofil umfasst.

17. Ein Kathetersystem gemäß einem beliebigen der Ansprüche 13 bis 16, bei dem die Ausgabe des Profils als zwei- oder dreidimensionale Abbildung erfolgt, auf der die Konzentrationsspiegel für einen oder mehrere Marker jeweils der entsprechenden Stelle entlang der Teilstrecke des Blutgefäßes zugeordnet sind.

18. Eine Methode zur Erzeugung eines Datenprofils für einen oder mehrere Biomarker an einer Stelle in einem Blutgefäß (4), die von Interesse ist, wobei die Methode die Analyse einer Vielzahl von einzelnen, räumlich getrennten Blutproben umfasst, die aus den jeweiligen Stellen entlang einer Teilstrecke des Blutgefäßes entnommen wurden, indem die Konzentration von einem oder mehreren Biomarkern in jeder der Proben gemessen wird und ein Datenprofil der Konzentrationsspiegel für die Biomarker entlang der Teilstrecke des Blutgefäßes erzeugt wird.

19. Eine Methode gemäß Anspruch 18, in der die Anzahl der Proben mindestens 3 beträgt, wobei eine Mindestanzahl von 5 vorzuziehen ist, eine Mindestan-

zahl von 20 noch mehr vorzuziehen ist und eine Mindestanzahl von 100 am meisten vorzuziehen ist.

20. Eine Methode gemäß Anspruch 18 oder 19, in der die Biomarker, auf die getestet wird, einen oder mehr der Folgenden umfassen: CRP, PAPPA, Myeloperoxidase, MMP 9, sCD40L, PLGF, Neopterin, lösliches P-Selectin, SVCAM-1, sICAM-1, lösliches CD40L, VCAM-1, ICAM-1, P-Selectin und E-Selectin.

21. Eine Methode gemäß einem beliebigen der Ansprüche 18 bis 20, in der die Datenausgabe als Abbildung eines oder mehrerer Biomarkergradienten entlang der Teilstrecke des Blutgefäßes (4) erfolgt.

Revendications

1. Cathéter à introduire dans un vaisseau sanguin (4), ledit cathéter possédant un segment d'échantillonnage (6) disposé de manière à prélever simultanément une pluralité d'échantillons sanguins discrets espacés spatialement en une pluralité de positions le long d'une longueur du vaisseau sanguin et à préserver l'intervalle spatial de ces échantillons sanguins discrets, en discontinu, dans lequel le segment d'échantillonnage comprend :

un membre échantillonneur allongé axialement (22) portant une série axiale d'une pluralité d'orifices (26) pour recevoir le sang à l'extérieur du cathéter à intervalles le long d'une longueur du vaisseau sanguin (4) ; et
un manchon allongé (28) coaxial avec le membre échantillonneur (22), ledit manchon définissant un passage axial (30) pour loger le membre échantillonneur et incluant une pluralité de canaux (34) correspondant aux orifices respectifs (26), dans lequel les canaux sont positionnés de manière à ce que, grâce à un mouvement relatif entre le manchon (28) et le membre échantillonneur (22), tous les orifices (26) sont simultanément exposés au sang à l'extérieur du cathéter afin de prélever une pluralité respective d'échantillons sanguins discrets le long de la longueur du vaisseau sanguin (4).

2. Cathéter selon la revendication 1, dans lequel le segment d'échantillonnage (6) inclut :

une pluralité respective de poches (24) destinées à recevoir le sang sortant des orifices (26).

3. Cathéter selon la revendication 2, dans lequel chacune desdites poches (24) est au moins partiellement évacuée de telle sorte que, dès l'exposition par le manchon (28), les poches aspirent le sang à l'extérieur du cathéter.

4. Cathéter selon la revendication 2, dans lequel le membre échantillonneur (6) inclut, en outre :

un passage sous vide (36) reliant chacune des poches (24), le passage sous vide permettant l'application d'une aspiration dans chacune des poches.

5. Cathéter selon la revendication 4, dans lequel les poches (24) et le passage sous vide (36) sont préremplis d'un liquide qui peut être aspiré hors du cathéter afin d'aspirer le sang à l'extérieur du cathéter et le transférer dans les poches.

6. Cathéter selon la revendication 1 ou 2, dans lequel le segment d'échantillonnage (6) comprend :

une pluralité respective de passages sous vide (38) reliés aux orifices respectifs (26) de manière à permettre l'application de l'aspiration individuellement à chaque orifice.

7. Cathéter selon la revendication 6, comprenant, en outre :

un plongeur respectif (40) à l'intérieur de chaque passage sous vide (38) pouvant être éloigné de l'orifice (26) afin d'aspirer le sang à l'extérieur du cathéter et le transférer dans l'orifice.

8. Cathéter selon la revendication 2, dans lequel le segment d'échantillonnage (6) comprend, en outre, une pluralité respective de pistons (42) dans les poches (24), par lesquels le mouvement des pistons pour les éloigner des orifices respectifs (26) aspire le sang dans les poches respectives.

9. Cathéter selon la revendication 8, dans lequel les pistons (42) peuvent se déplacer dans le sens axial pour aspirer le sang dans les poches respectives (24) et le segment d'échantillonnage (6) inclut, en outre, un actionneur axialement extensible (44) sur lequel sont fixés tous les pistons et grâce auquel les pistons peuvent être déplacés.

10. Cathéter selon l'une quelconque des revendications précédentes, comprenant, en outre :

une couche membraneuse (50) couvrant les poches (24), la couche membraneuse permettant au plasma sanguin de pénétrer dans les poches.

11. Cathéter selon l'une quelconque des revendications précédentes, dans lequel chaque échantillon discret est compris entre 10 μl et 50 μl.

12. Cathéter selon l'une quelconque des revendications précédentes, dans lequel le segment d'échantillonnage (6) comprend un membre échantillonneur axialement allongé (22) comprenant un matériau absorbant continu (46).

13. Cathéter selon l'une quelconque des revendications précédentes, comprenant une série d'orifices (26) axialement et radialement espacés le long d'une longueur du membre échantillonneur (22).

14. Système de cathéter incluant un cathéter selon l'une quelconque des revendications précédentes et un appareil pour analyser les échantillons sanguins discrets capturés par le cathéter, l'appareil étant disposé de manière à analyser le sang prélevé en une pluralité de positions le long de ladite longueur du vaisseau sanguin (4) et à fournir un profil des taux de concentration de l'un ou de plusieurs marqueur (s) pathologique(s) le long de ladite longueur du vaisseau sanguin.

15. Système de cathéter selon la revendication 14, dans lequel le marqueur est un marqueur inflammatoire.

16. Système de cathéter selon la revendication 14 ou 15, comprenant, en outre, un moyen de calculer, à partir du profil de la concentration, le taux de base du marqueur dans l'échantillon sanguin.

17. Système de cathéter selon l'une quelconque des revendications 13 à 16, dans lequel le profil est présenté sous la forme d'une carte des taux de concentration en 2D ou 3D pour l'un ou plusieurs marqueur (s) en la position située le long de la longueur du vaisseau sanguin.

18. Méthode d'élaboration d'un profil des données pour l'un ou plusieurs biomarqueur(s) en un point d'intérêt dans un vaisseau sanguin (4), ladite méthode comprenant l'analyse d'une pluralité d'échantillons sanguins discrets, espacés spatialement, qui ont été prélevés en des positions respectives le long d'une longueur du vaisseau sanguin, en mesurant la concentration du ou de plusieurs biomarqueur(s) dans chacun des échantillons et l'élaboration d'un profil des données relatives aux taux de concentration des biomarqueurs le long de la longueur dudit vaisseau sanguin.

19. Méthode selon la revendication 18, dans laquelle le nombre d'échantillons est d'au moins 3, de préférence d'au moins 5, plus préférablement d'au moins 20 et encore plus préférablement d'au moins 100.

20. Méthode selon la revendication 18 ou 19, dans laquelle les biomarqueurs testés incluent l'un ou plusieurs de ce qui suivent : CRP, PAPPA, myéloperoxydase, MMP 9, sCD40L, PLGF, néoptérine, P-sélectine soluble, SVCAM-1, sICAM-1, CD40L soluble, VCAM-1, ICAM-1, P-sélectine et E-sélectine.

21. Méthode selon l'une quelconque des revendications 18 à 20, dans laquelle les données sont présentées sous la forme d'une carte de l'un ou de plusieurs gradients de biomarqueurs le long de la longueur dudit vaisseau sanguin (4).

Fig.1(a).

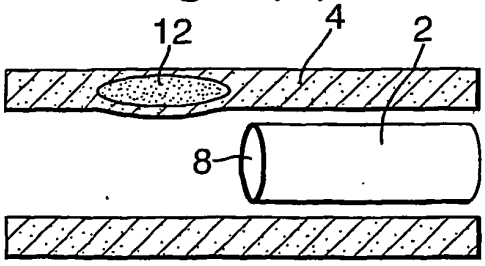


Fig.1(b).

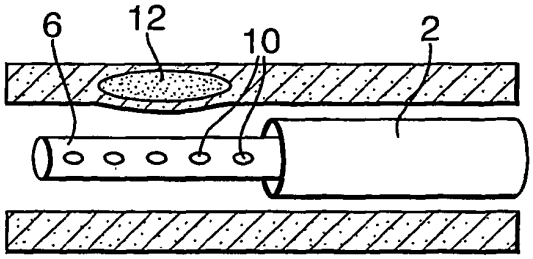


Fig.1(c).

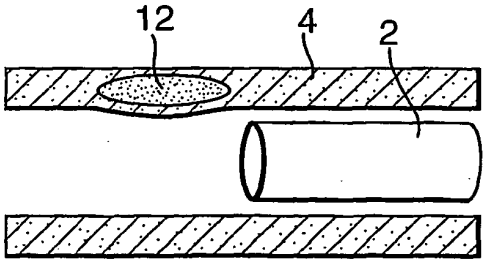


Fig.1(d).

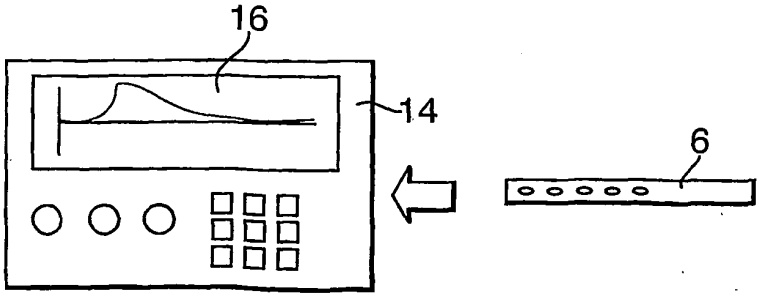


Fig.1(e).

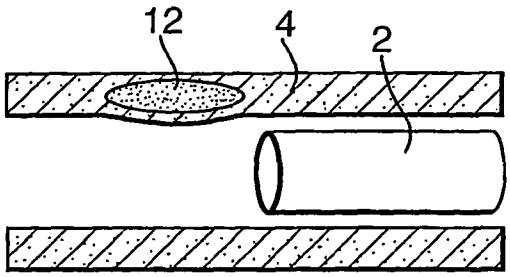


Fig.1(f).

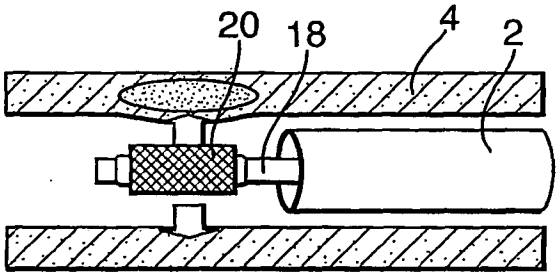
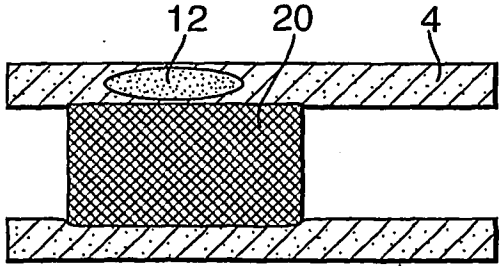


Fig.1(g).



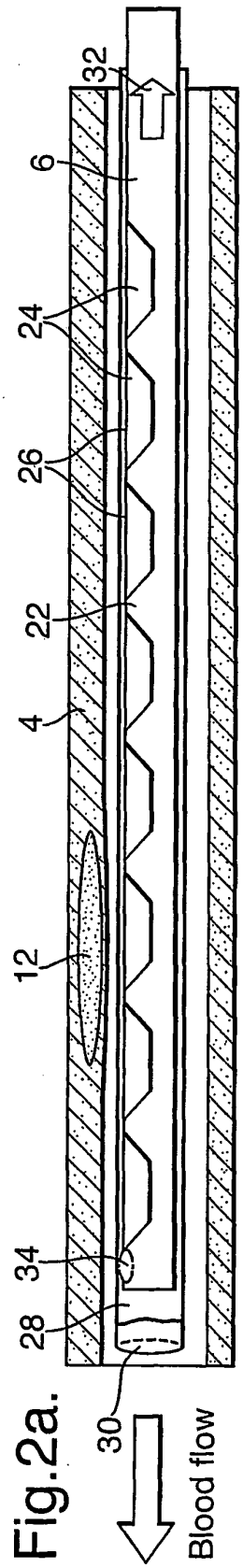


Fig.2a.

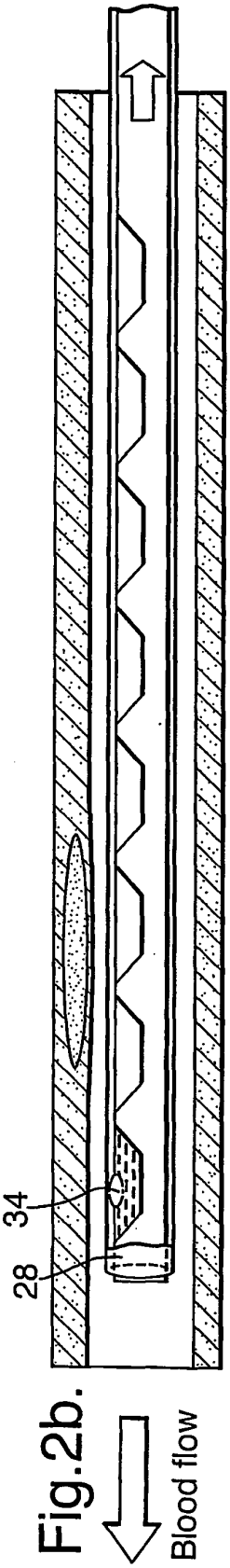


Fig.2b.

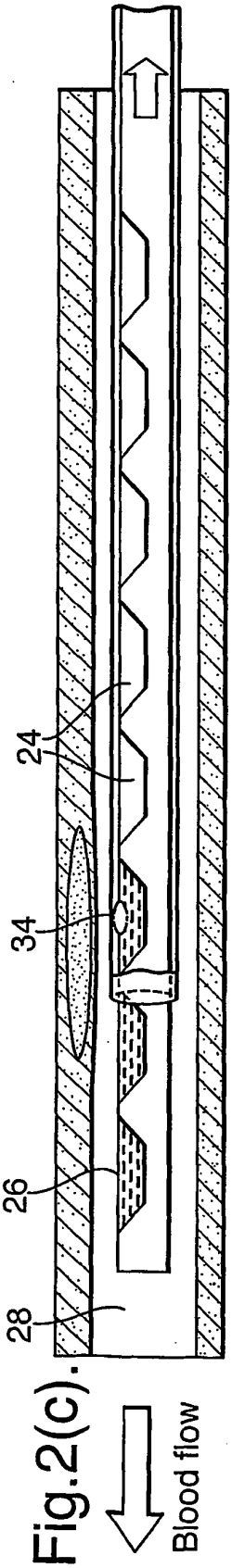


Fig.2(c).

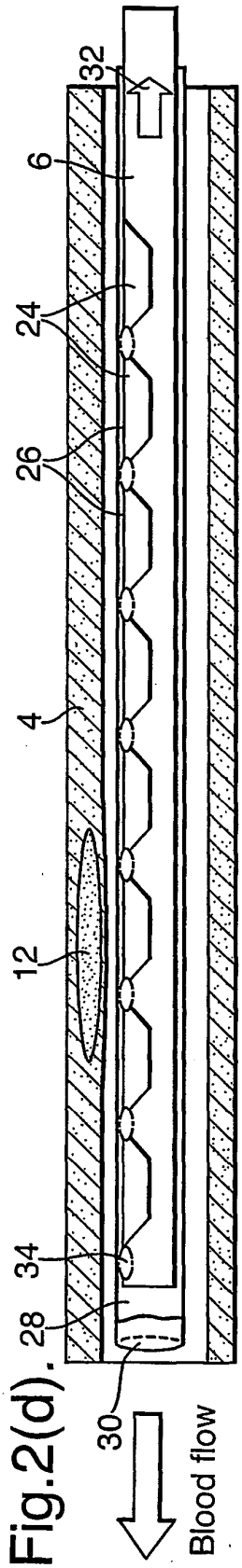


Fig.2(d).

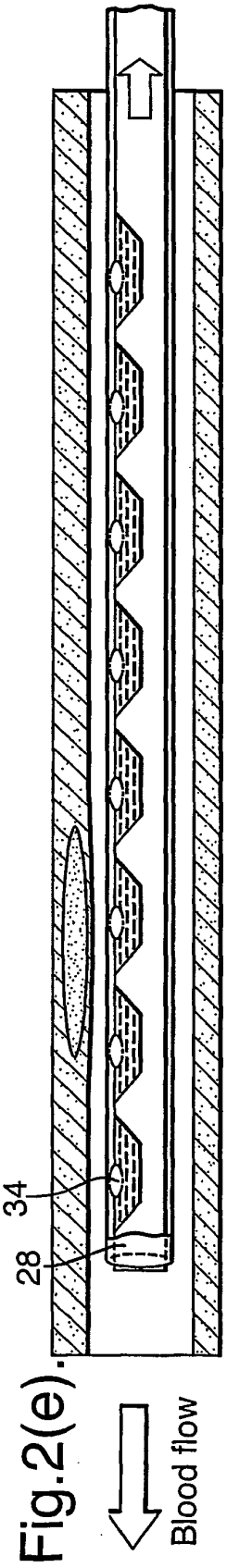


Fig.2(e).

Fig.3.

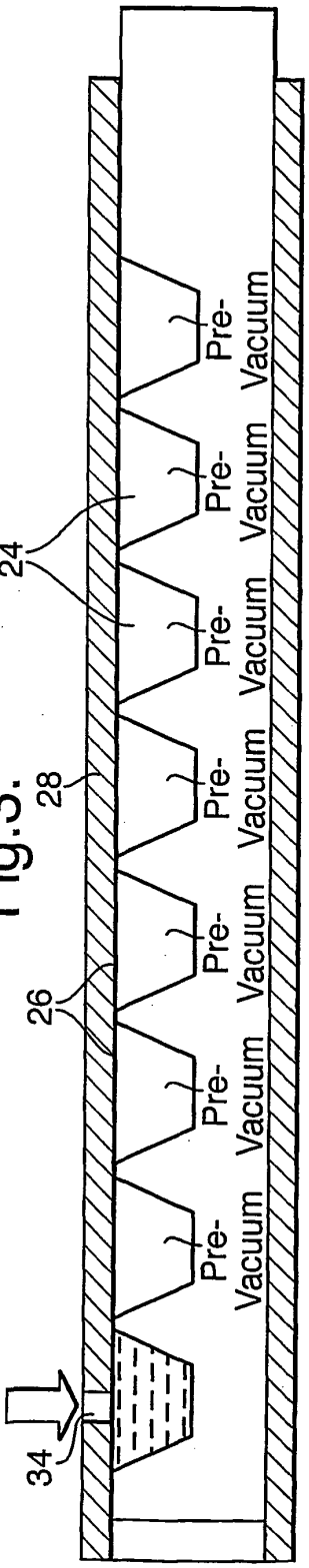


Fig.4.

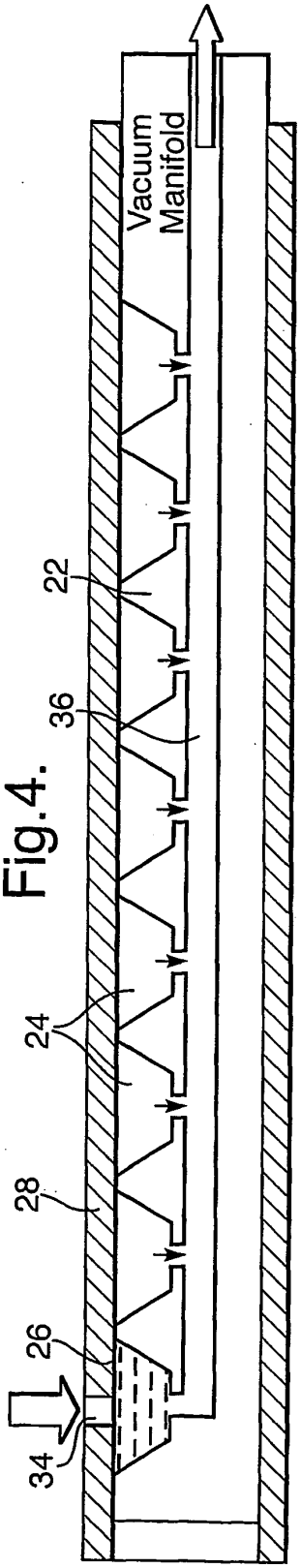


Fig.5.

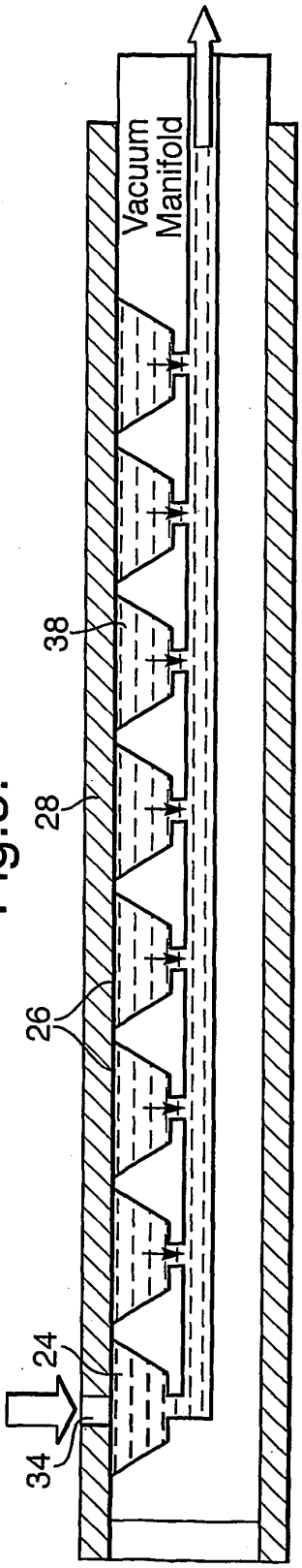


Fig.6(a).

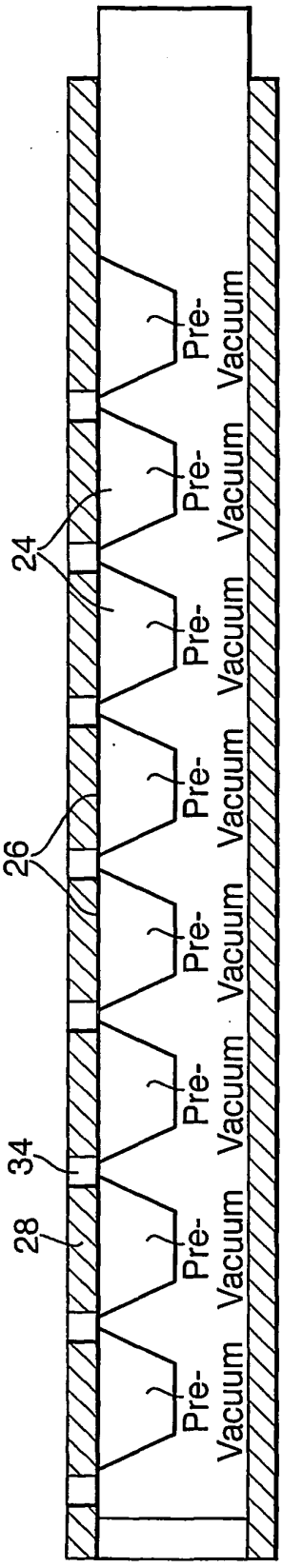
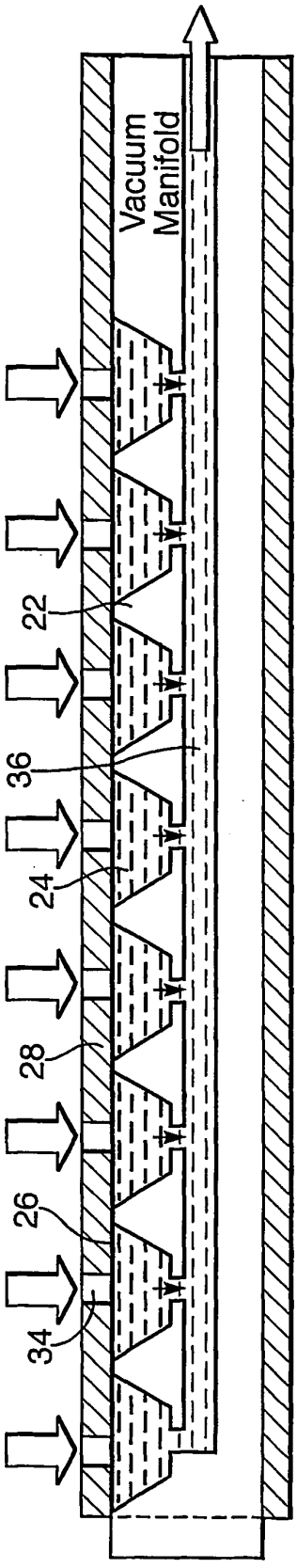


Fig.6(b).



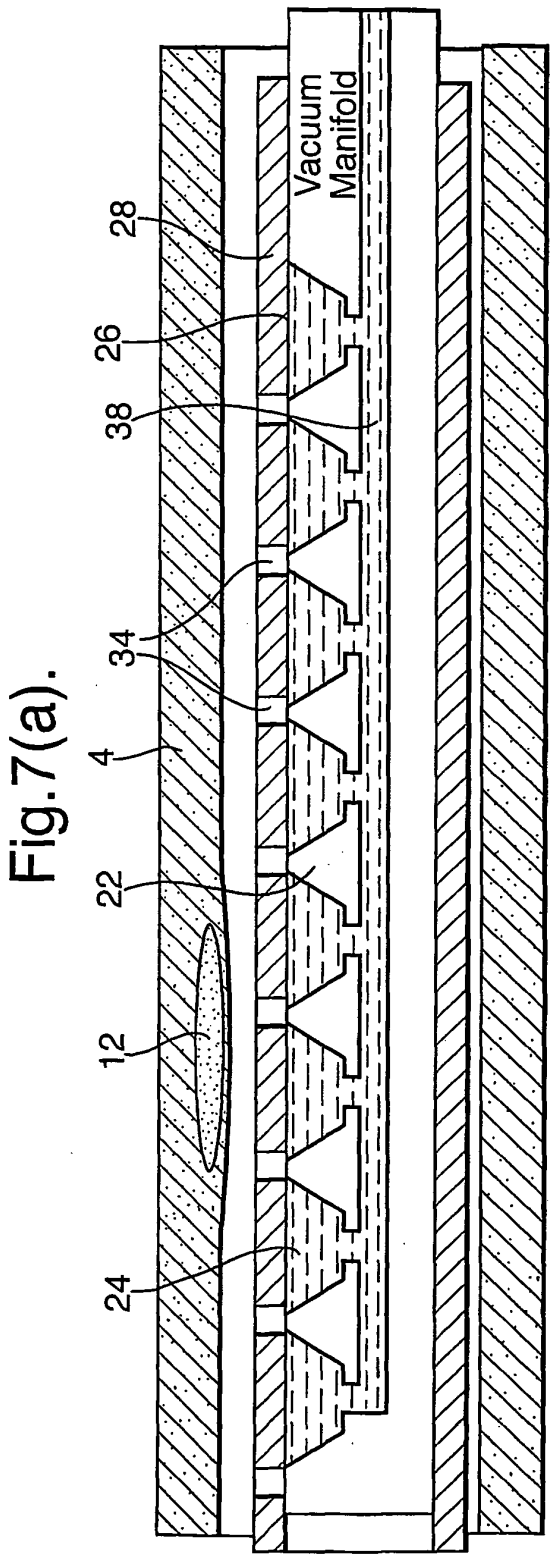


Fig.7(a).

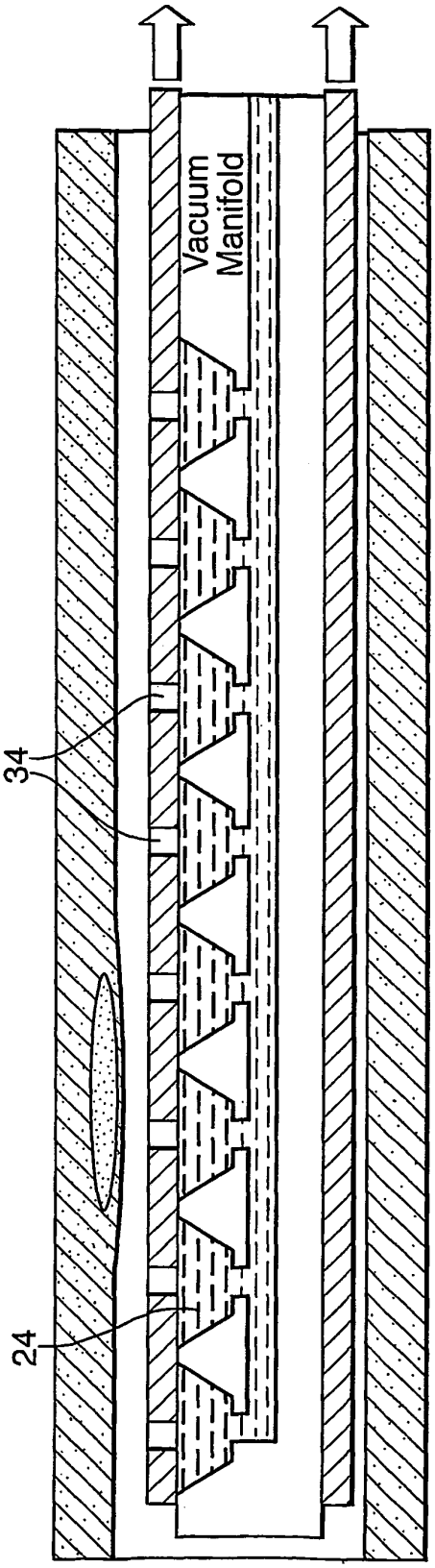


Fig.7(b).

Fig.8(a).

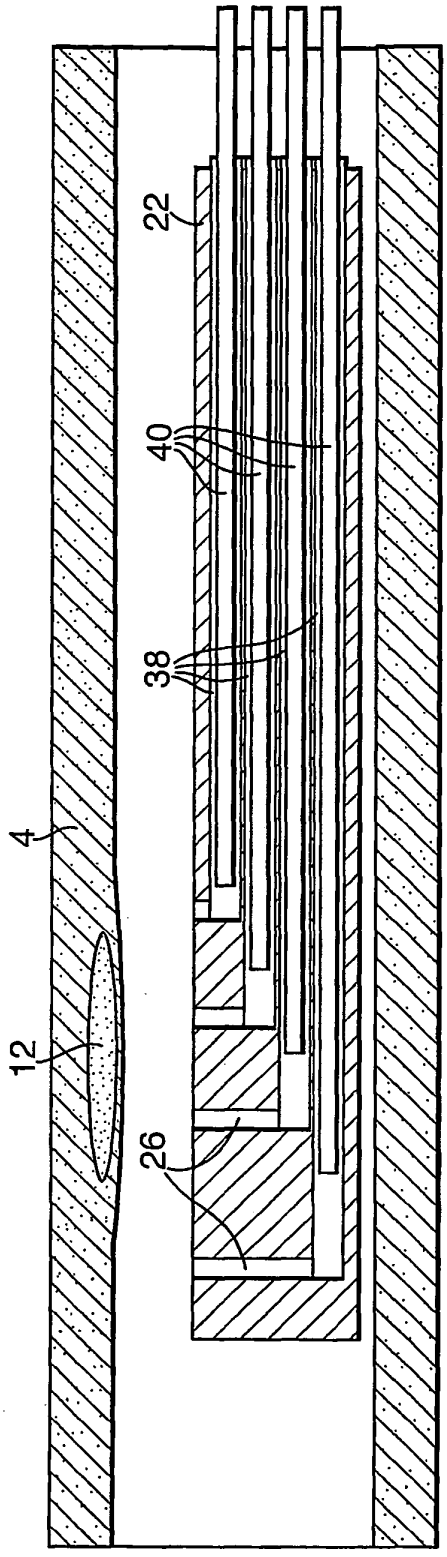
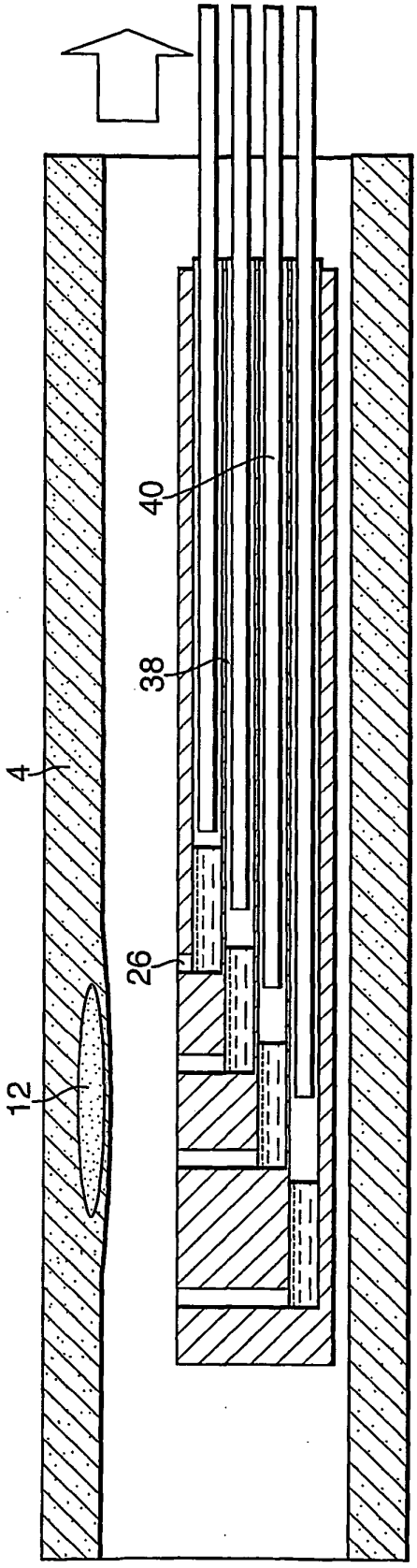


Fig.8(b).



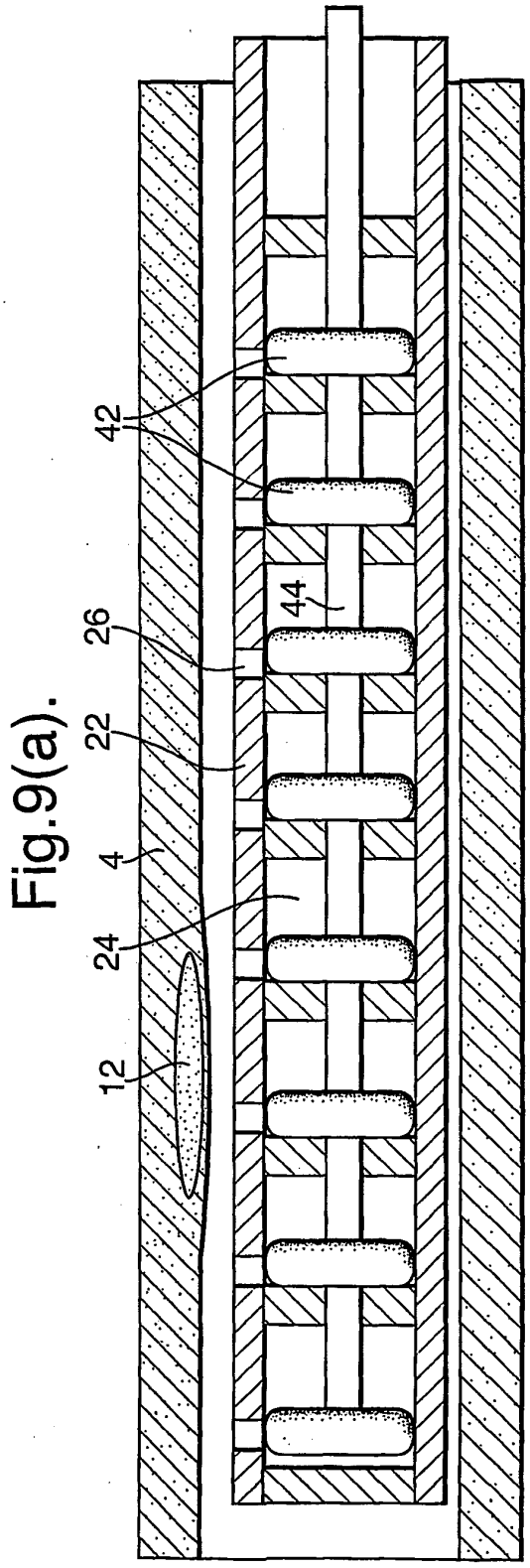


Fig.9(a).

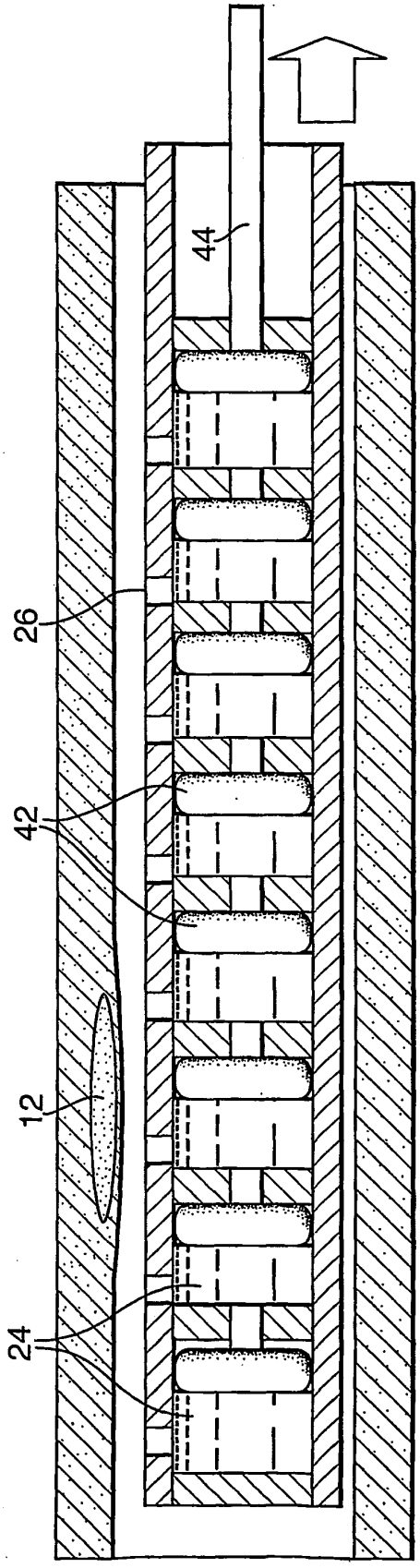


Fig.9(b).

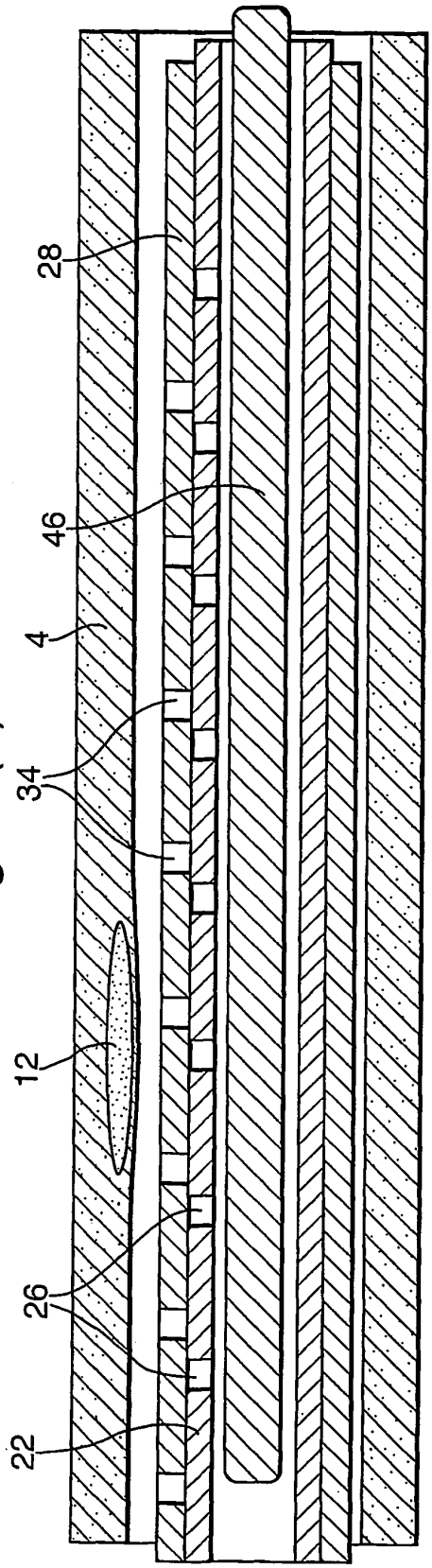


Fig.10(a).

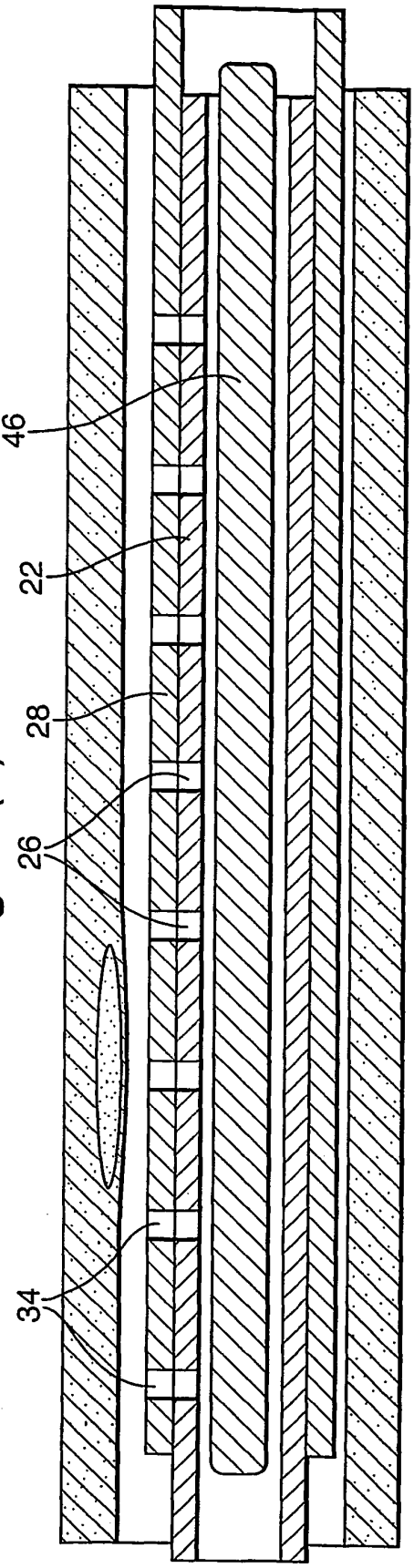


Fig.10(b).

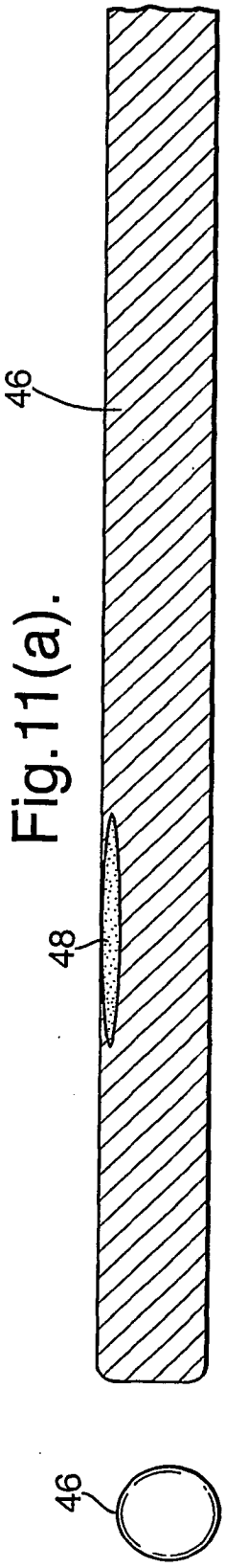


Fig.11(a).

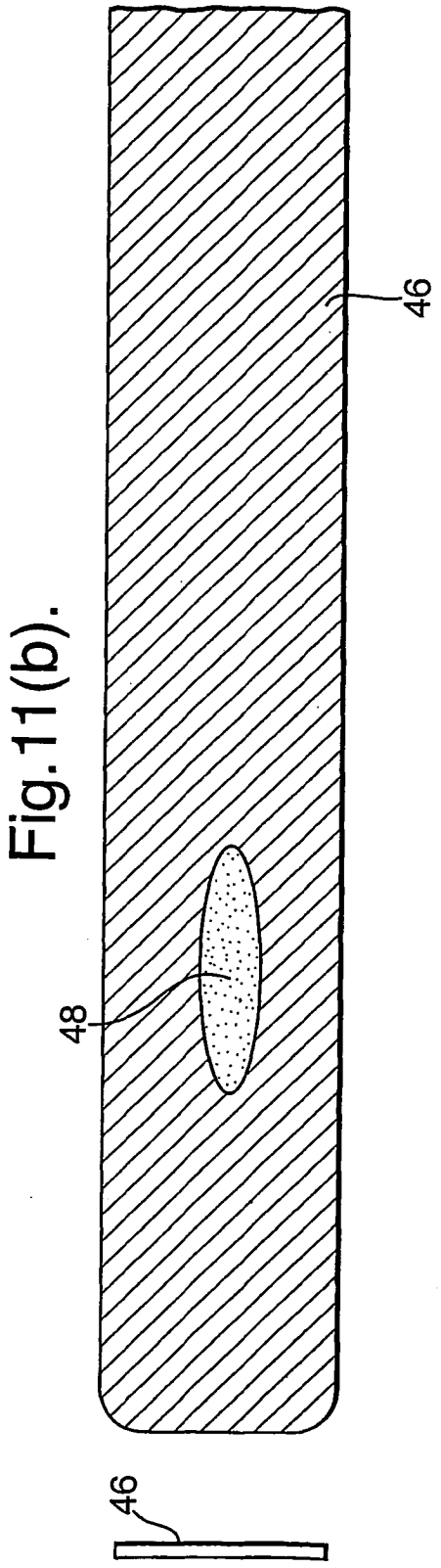
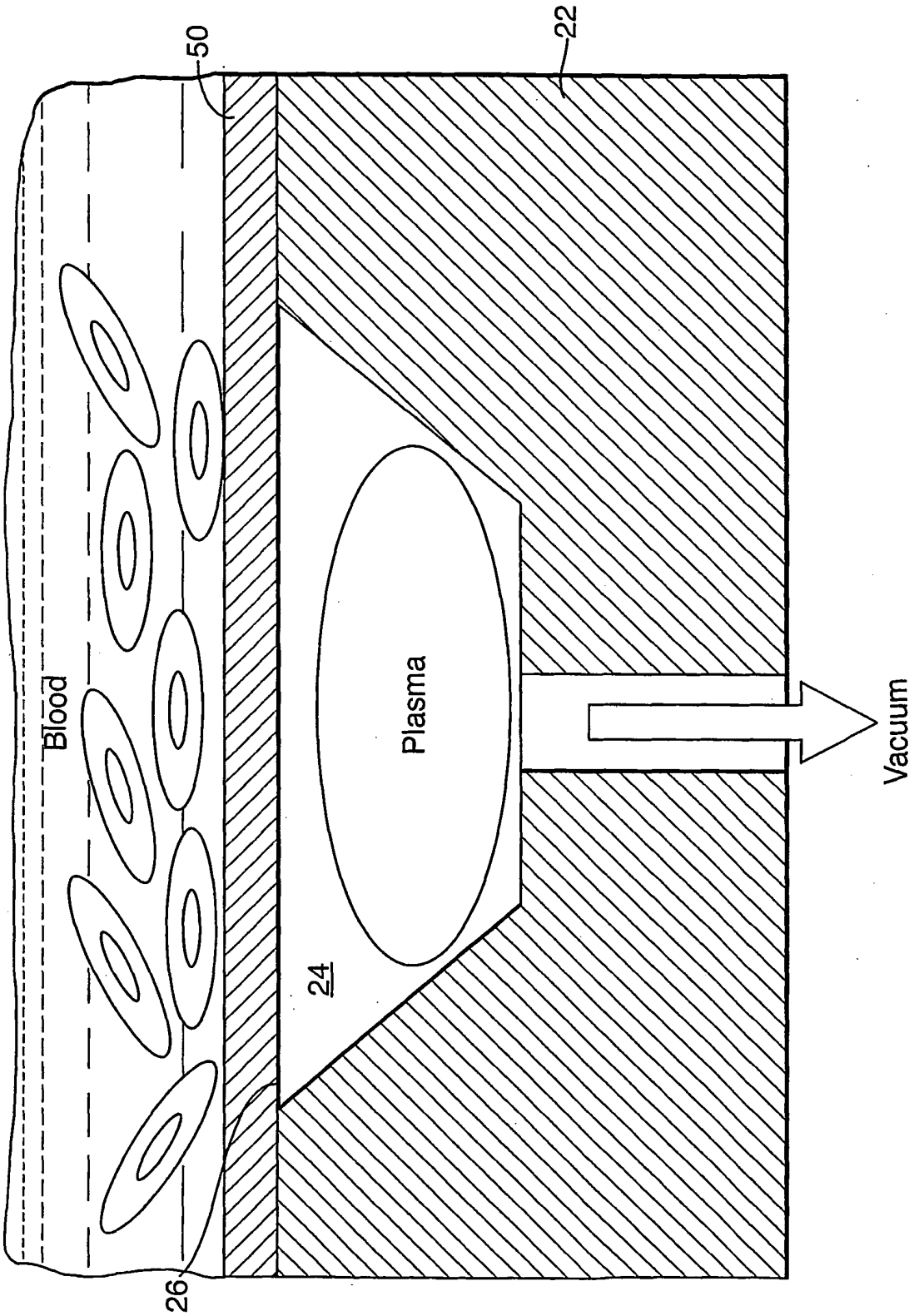


Fig.11(b).

Fig.12.



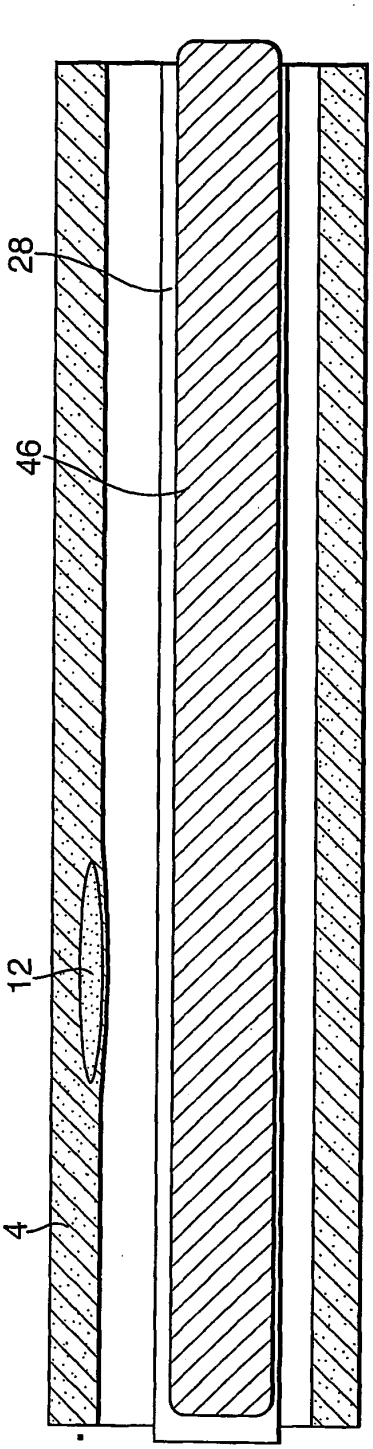
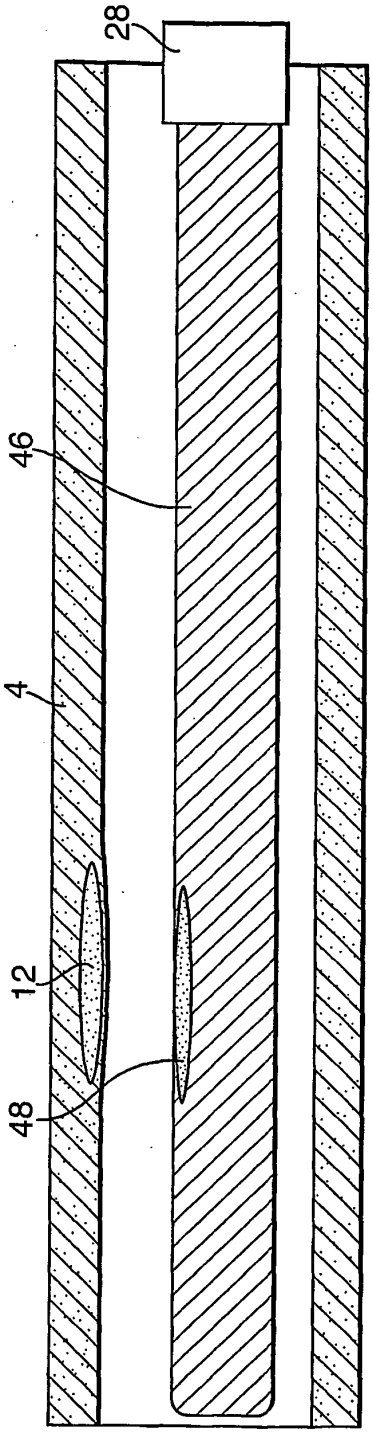


Fig.13(a).



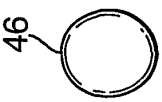


Fig.13(b).

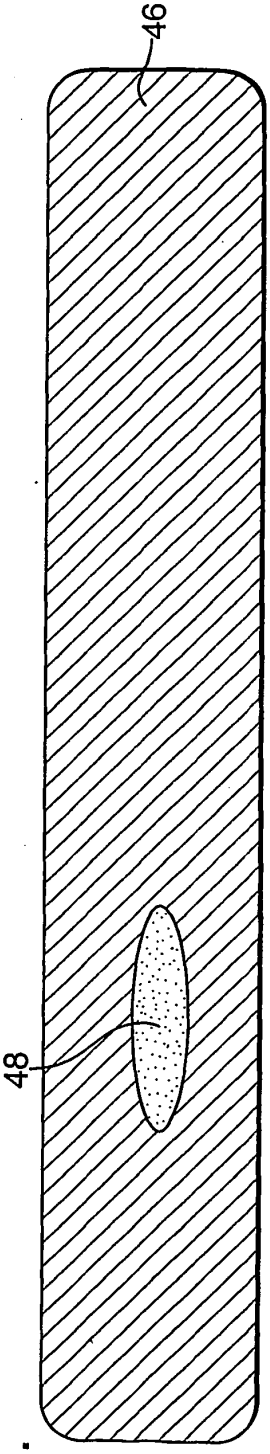


Fig.13(c).

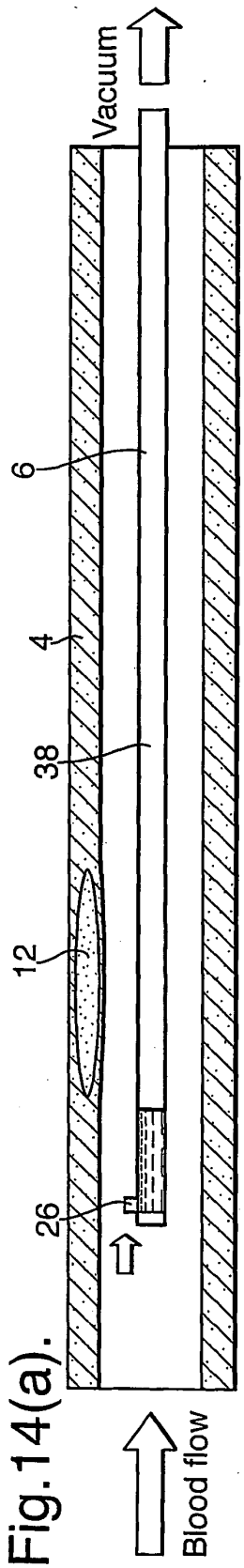


Fig.14(a).

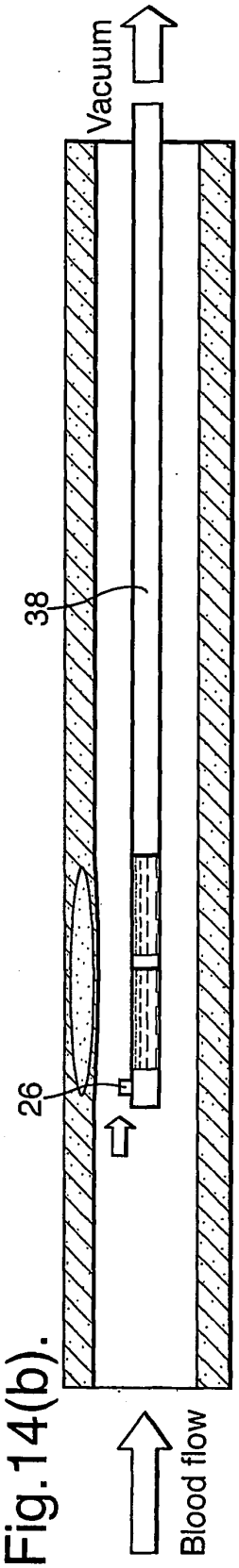


Fig.14(b).

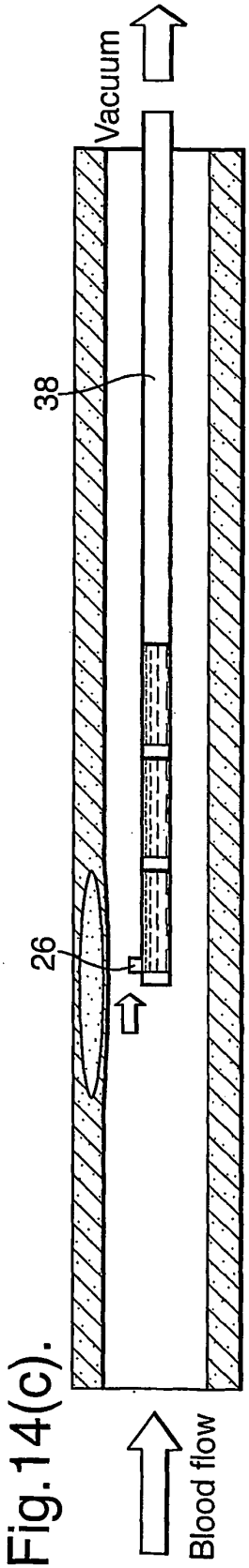


Fig.14(c).

Fig.15.

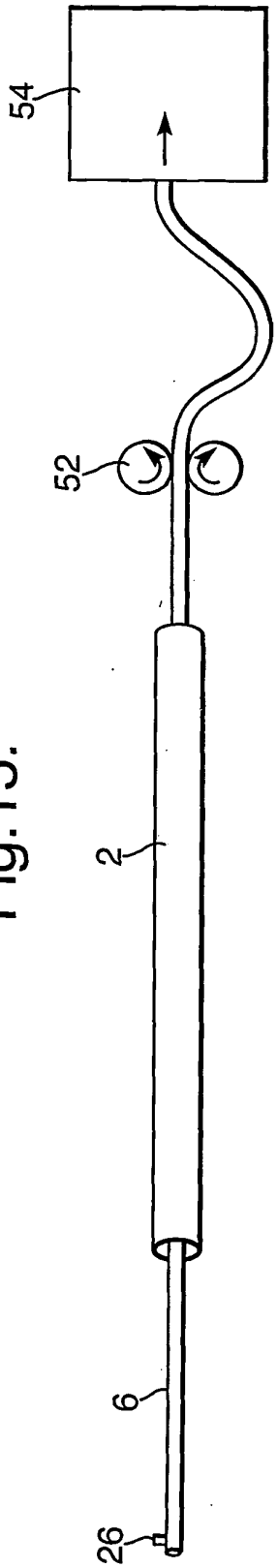
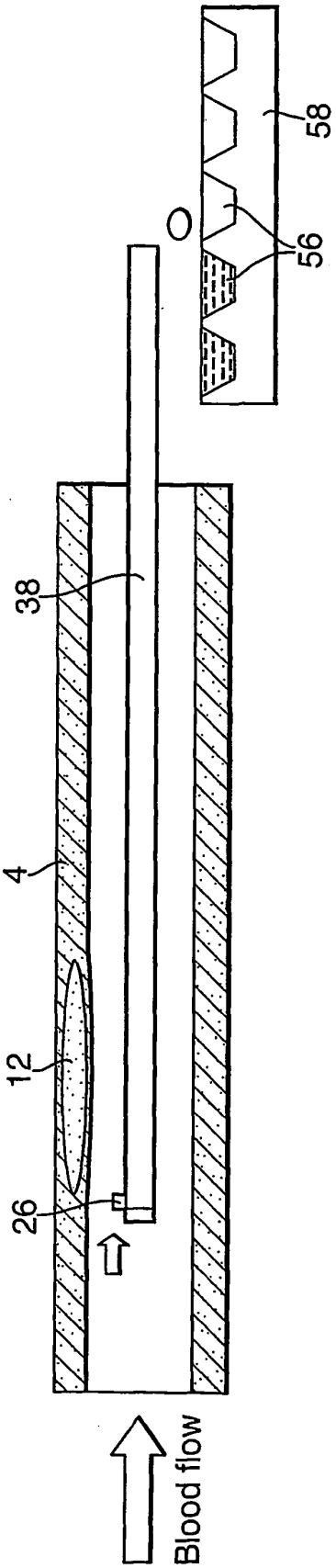


Fig.16.



REFERENCES CITED IN THE DESCRIPTION

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- US 5533516 A **[0003]**
- GB 1405556 A **[0004]**
- WO 2004010874 A **[0005]**

专利名称(译)	采血导管		
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当前申请(专利权)人(译)	PLAQUETEC有限公司		
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IPC分类号	A61B5/00 A61B10/00 A61B5/155		
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外部链接	Espacenet		

摘要(译)

一种用于插入血管的导管，该导管具有采样部分（6），该采样部分（6）布置成沿着血管的长度在多个位置处捕获血液样本，并且该装置布置成分析从多个位置采集的血液。血管的长度并提供沿血管长度的浓度水平的分布。