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(54) **METHOD AND DEVICE FOR SAMPLING AND ANALYZING INTERSTITIAL FLUID AND WHOLE BLOOD SAMPLES**

VERFAHREN UND GERÄT ZUR PROBENENTNAHME UND ANALYSE VON INTERSTITIELLER FLÜSSIGKEIT UND VOLLBLUT

PROCEDE ET DISPOSITIF POUR L'ECHANTILLONNAGE ET L'ANALYSE DE PRELEVEMENTS DE LIQUIDE INTERSTITIEL ET DE SANG ENTIER

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Description

Field of the Invention

[0001] The present invention relates to a method and device for combining the sampling and analyzing of interstitial fluid or whole blood samples which is suitable for hospital bedside and home use.

Background of the Invention

[0002] The management of many medical conditions requires the measurement and monitoring of a variety of analytes in bodily fluid. Historically, the measurement of analytes in blood has required an invasive technique, such as a venipuncture or finger puncture, to obtain blood for sampling purposes. An example of an analyte which is routinely tested by obtaining a blood sample through an invasive technique is glucose. In order to control their condition, diabetics must monitor their glucose levels on a regular basis. Invasive techniques used to obtain a blood sample for analysis have the disadvantage of being painful, which can reduce patient compliance in regular monitoring. Repeated testing, e.g., on a fingertip, can result in scar tissue build-up which makes obtaining a sample in that region more difficult. Moreover, invasive sampling procedures pose a risk of infection or disease transmission.

[0003] An alternative is to sample interstitial fluid rather than whole blood. Interstitial fluid is the fluid that fills the space between the connective tissue and cells of the dermal layer of the skin. An application where interstitial fluid has been shown to be an appropriate sampling substitute for plasma or whole blood is in the measurement of glucose concentration (J. Lab. Clin. Med. 1997, 130, 436-41).

[0004] In U.S. Pat. Nos. 5,879,367, 5,879,310, 5,820,570 and 5,582,184 are disclosed methods of sampling using a fine needle in conjunction with a device to limit the penetration depth to obtain small volumes of interstitial fluid for the purpose of glucose monitoring. However, there is no method disclosed for analyzing the drawn samples that is suitable for home use or hospital bedside use.

[0005] DE-3708031-A1 describes a puncturing device for determining metabolic states in blood, which acts to puncture the skin and drain blood into a collection chamber in the puncturing device.

Summary of the Invention

[0006] It is desirable to be able to measure the concentration of analytes in humans or other animals without having to draw a blood sample by conventional methods. It is further desirable to be able to do so with an inexpensive disposable device that is simple enough for home or hospital bedside use.

[0007] In view of the foregoing, the present invention is described in the appendant claims.

[0008] The invention provides a suitable alternative to conventional sampling devices and methods that is less invasive than traditional whole blood sampling techniques and that requires a considerably smaller sample volume than is required in the conventional venipuncture or finger puncture sampling methods. Because of the smaller sample volume required, a smaller wound is necessary to obtain the sample. In the conventional finger stick method, a drop of blood is formed on the tip of a finger, then the sensor sample entrance is wetted with the drop. Because the sample comes into contact with the skin surface, contamination of the sample by material on the skin surface is possible. The devices and methods disclosed herein do not require forming a blood drop on the surface of the skin, and therefore have less risk of sample contamination.

[0009] In one embodiment of the present invention, a fluid sampling device is provided which includes a body, the body including a dermal layer penetration probe having a penetrating end and a communicating end, and an analysis chamber having a proximal and distal end, the analysis chamber having a volume, wherein the penetration probe is in fluid communication with the analysis chamber such that fluid can flow from the penetration probe toward the analysis chamber. The analysis chamber can have at least one flexible wall which can be compressed to reduce the volume of the analysis chamber. The penetration probe can include, for example, a needle, a lancet, a tube, a channel, or a solid protrusion and can be constructed of a material such as carbon fiber, boron fiber, plastic, metal, glass, ceramic, a composite material, mixtures thereof, and combinations thereof. The penetration probe can include two sheets of material in substantial registration, having a protrusion on each sheet, wherein the sheets are spaced apart such that liquid can be drawn between the sheets by capillary action. The two sheets of material can extend into the device so as to form a pre-chamber. The penetration probe can be positioned within a recess in the proximal end of the device, and the recess can be configured to substantially align with a shape of a selected dermal surface.

[0010] The device further includes a pre-chamber having a volume and a first and second end, wherein the pre-chamber is interposed between the penetration probe and the analysis chamber such that the first end of the pre-chamber is adjacent the communicating end of the penetration probe and the second end of the pre-chamber is adjacent the proximal end of the analysis chamber. The volume of the pre-chamber is greater than the volume of the analysis chamber. The pre-chamber can have at least one flexible wall that can be compressed to reduce the volume of the pre-chamber. The pre-chamber can also include a valve at the first end capable of substantially sealing the pre-chamber from the penetration probe.

[0011] In another embodiment, the device further in-

cludes a compressible bladder in communication with the analysis chamber, the compressible bladder being capable of applying a positive or a negative pressure to the analysis chamber.

[0012] In yet another embodiment, the pre-chamber and the analysis chamber can be capable of exerting different capillary forces. The capillary force exerted by the analysis chamber can be greater than the capillary force exerted by the pre-chamber. The differential capillary force can be derived, at least in part, from a difference between the pre-chamber height and the analysis chamber height. In this embodiment, the interior surface of the pre-chamber can include at least first and second pre-chamber walls spaced apart at a first distance to define a pre-chamber height, and the interior surface of the analysis chamber can include at least first and second analysis chamber walls spaced apart at a second distance to define an analysis chamber height, wherein the height of the analysis chamber is less than the height of the pre-chamber.

[0013] In yet another further embodiment, at least one of the chambers can include a substance capable of enhancing or diminishing the capillary force exerted by the chamber. The substance can include, for example, a polymer, a resin, a powder, a mesh, a fibrous material, a crystalline material, or a porous material. Suitable substances include polyethylene glycol, polyvinylpyrrolidone, a surfactant, a hydrophilic block copolymer, and polyvinylacetate.

[0014] In a further embodiment, the device further includes a releasable actuator capable of supplying a force sufficient to cause the penetration probe to penetrate a dermal layer. The actuator can be external to or integral with the body, and upon release propels the body toward the dermal layer.

[0015] In a further embodiment, the analysis chamber can include an electrochemical cell including a working electrode and a counter/reference electrode and an interface for communication with a meter, wherein the interface communicates a voltage or a current.

[0016] A method for determining a presence or an absence of an analyte in a fluid sample is provided including the steps of providing a fluid sampling device as described above; penetrating a dermal layer with the penetration probe; substantially filling the analysis chamber with a fluid sample by allowing the sample to flow from the penetration probe toward the analysis chamber; and detecting a presence or an absence of the analyte within the analysis chamber. The sample can include, for example, interstitial fluid and whole blood. A qualitative or quantitative measurement of a characteristic of the sample can be obtained in the detecting step. The characteristic of the sample can include, for example, a reaction product of the analyte, such as a color indicator, an electric current, an electric potential, an acid, a base, a reduced species, a precipitate, and a gas. The analyte can include, for example, an ion such as potassium, an element, a sugar, an alcohol such as ethanol, a hormone, a protein, an enzyme, a cofactor, a nucleic acid sequence, a lipid, a pharmaceutical, and a drug. Cholesterol and lactate are examples of substances that can be analyzed.

[0017] In a further embodiment, the flow of sample toward the analysis chamber can be driven by a driving force, e.g., capillary force or a pressure differential. Where the analysis chamber has a flexible wall, the wall can be compressed to reduce the volume of the analysis chamber prior to penetrating the dermal, then the compression released to form a partial vacuum in the analysis chamber. Where the fluid sampling device further includes a compressible bladder, the bladder can be compressed to reduce its volume, then after penetration of the dermal layer the compression can be released to form a partial vacuum in the compressible bladder and analysis chamber.

Brief Description of the Drawings

[0018]

FIG. 1 shows a top view (not to scale) of one embodiment of a sampling device illustrating an arrangement of the penetration probe, pre-chamber, and analysis chamber.

FIG. 2 shows a cross section (not to scale) along the line A-A' of FIG. 1.

FIG. 3 shows a top view (not to scale) of one embodiment of a sampling device illustrating an arrangement of the penetration probe, pre-chamber, and analysis chamber wherein the proximal edge of the device forms a recess.

FIG. 4 shows a top view (not to scale) of one embodiment of a sampling device illustrating an arrangement of the penetration probe, pre-chamber, and analysis chamber.

FIG. 5 shows a cross section (not to scale) along the line B-B' of FIG. 4.

FIGS. 6a and 6b (not to scale) depict an embodiment of the invention wherein the device is loaded in a releasable actuator to facilitate penetration of a dermal layer by the penetration probe. Fig. 6a depicts the device loaded in the actuator, wherein the actuator is in the cocked position, ready to be triggered. FIG. 6b depicts the device and actuator after triggering.

Detailed Description of the Preferred Embodiments

Introduction

[0019] The following description and examples illustrate various embodiments of the present invention in detail. Those of skill in the art will recognize that there are numerous variations and modifications of this invention that are encompassed by its scope. Accordingly, the description of a preferred embodiment should not be

deemed to limit the scope of the present invention. Methods and devices for optimizing sampling of fluid samples are discussed further in copending U.S. patent no. 6,571,651, filed on even date herewith, entitled "METHOD OF PREVENTING SHORT SAMPLING OF A CAPILLARY OR WICKING FILL DEVICE".

[0020] The invention disclosed in this application is a device for combining the sampling and analyzing of a fluid sample from sub-dermal tissue in a device suitable for hospital bedside and home use. The fluid sample can comprise, but is not limited to, interstitial fluid or whole blood samples obtained from an animal. Any fluid sample obtained from sub-dermal tissue of a plant or an animal can be sampled and analyzed, thus the invention has broad application in the fields of human medicine, veterinary medicine, and horticultural science. The device is applicable to any analyte that exists in a usefully representative concentration in the fluid sample. For clarity, the present disclosure will discuss the application to glucose monitoring. However, it is to be understood that the invention is not limited to the monitoring of glucose, and that other analytes, as discussed below, can also be measured.

[0021] A method utilizes an integrated sampling and analyzing device 10 incorporating a penetration probe 12 capable of penetrating a patient's dermal layers to extract an interstitial fluid or whole blood sample, and for transferring the sample from the penetration probe 12 to the analysis chamber 20. In one embodiment, the device 12 can be a one-shot disposable device which can be inserted into a meter which communicates with the analysis chamber 20 to perform the analysis of the sample and present and optionally store the result.

[0022] In the device 10, a penetration probe 12 for penetrating the subject's dermal layers to collect an interstitial fluid or whole blood sample is integrated with an analysis chamber 20. A property of sampling interstitial fluid is that it can take from several to tens of seconds to collect sufficient sample to analyze. This is often not desirable for an analysis chamber 20 wherein the analyte undergoes a reaction as part of the analysis process, as it can be difficult to obtain an accurate start time for the test as well as achieve an even reacting reagent distribution in the sample. A method is disclosed for collecting the sample in a pre-chamber 14 and, when full, transferring the sample quickly to an analysis chamber 20.

[0023] In this disclosure, unless a different meaning is clear from the context of its usage, "proximal" refers to a region or structure of the device situated toward or adjacent to the dermal surface to be penetrated, and "distal" refers a region or structure of the device situated toward the opposite (non-proximal) end of the device. For example, the penetration probe **12** is at the proximal end of the device.

The Penetration Probe

[0024] The penetration probe 12 can be any device capable of penetrating the patient's dermal layers to the desired extent and capable of transporting a sample to a pre-chamber **14** or analysis chamber **20**. The penetration probe **12** comprises two ends, as illustrated in FIG. 1. The penetrating end **11** of the penetration probe **12** is the end inserted into the dermal layer. The communicating end **13** of the penetration probe **12** is the end which is in communication with either the pre-chamber **14** or the analysis chamber **20**.

[0025] One or more protrusions **12** with at least one sharp edge or point are suitable as the penetration probe **12**. The penetration probe **12** can be fabricated from materials including plastic, metal, glass, ceramic, a composite material (e.g., a composite of ceramic and metal particles), or mixtures and combinations of these materials. The penetration probe **12** can be in the form of a solid protrusion, a needle, a lancet, a tube or a channel. The channel can optionally be open along one or more of its elongated sides. As illustrated in FIG. 2, a preferred embodiment of the penetration probe **12** is two sheets **30** of material formed so as to have a sharply pointed protrusion **12** on each sheet **30** in substantial registration, with the sheets **30** spaced apart such that liquid can be drawn between the sheets **30** by capillary action. In a particularly preferred embodiment, the two sheets **30** of material extend to and overlap with the analysis chamber **20** to form a pre-chamber **14** for sample collection.

[0026] When interstitial fluid is sampled, the penetration depth can be controlled by limiting the length the penetration probe **12** protrudes from the proximal surface **34** of the sampling device **10** to less than the thickness of the dermal layer. In a preferred embodiment, the length of the protrusion **12** will be less than 2 to 3 mm, more preferably about 1.5 mm. After penetration to a suitable depth corresponding to the length of the protrusion **12**, contact between the surface of the dermal layer and the surface **34** of the analyzing device prevents further penetration. For other uses, such as in sampling interstitial fluid from regions having a thick dermal layer, or for veterinary uses, it can be desirable for the length of the protrusion **12** to be greater than 3 mm. Accordingly, the invention contemplates protrusions **12** of any length, wherein the length is sufficient to sample interstitial fluid. When whole blood is sampled, a slightly longer penetration probe **12** should be used, i.e., one having a length greater than 2 to 3 mm.

[0027] The diameter or width of the penetration probe **12** depends upon the design of the penetration probe **12**. Suitable diameters or widths are those which provide sufficient sample flow. In the case of a protrusion **12** forming a sharp edge or point, or a tube or channel, the minimum diameter or width is typically greater than about 10μm. When the penetrating means **12** comprises two sheets **30** in substantial registration, each having a

sharply pointed protrusion **12**, the two protrusions **12** are typically spaced from 1 mm to 10 μm apart.

[0028] The penetration probe **12** can be located on any suitable part of the test strip **10**, i.e., an edge **34**, a corner **42**, or one of the flat surfaces **44**. Protection can be provided to the penetration probe **12** by locating it within a recess formed in the distal edge **34** of the test strip **10**, as shown in FIG. 3, or in a depression on the surface **44** of the test strip 10. In a preferred embodiment, the recess in the distal edge 34 of the test strip 10 can be configured to substantially align with the shape of a selected dermal surface, e.g., a fingertip. However, the recess can be configured in other suitable shapes, e.g., a square recess, a V-shaped recess, a curved recess, a polygonal recess, and the like. In a preferred embodiment, the penetration probe 12 does not protrude past the proximal-most portion of the proximal edge 34 or surface 44 of the device 10, but when pressed against the skin, the skin deforms into the recess and is punctured by the penetration probe 12. Such an arrangement aids sampling by compressing the area of the skin around the sampling point. The penetration probe 12 can form an integral part of another component of the test strip 10, e.g., a side of the pre-chamber 54, as shown in FIG. 2. Alternatively, the penetration probe 12 can comprise a separate part which is attached to or incorporated into the test strip 10 by any suitable means, e.g., adhesive, thermal bonding, interlocking parts, pressure, and the like. The penetration probe 12 can be retractable or non-retractable.

[0029] Penetration itself can be accomplished by any suitable means, including inserting the penetration device 12 manually or by means of a releasable actuator 84 such as, for example, a spring-loaded mechanism 84 as depicted in FIGS. 6a and 6b. Such a spring-loaded mechanism 84 incorporates a spring 86 which is compressed and held in place by a trigger (not shown) which can release the force compressing the spring 86 when the triggering mechanism is activated. The trigger can be activated manually, or the device 84 can incorporate a pressure sensor which indicates that sufficient pressure has been applied to obtain the sample, thereby activating the trigger. In one embodiment, the distal end of the device 10 is placed in the spring-loaded mechanism 84 such that when the force compressing the spring 86 is released by activating the trigger, force is transferred to the device 10, which is ejected from the mechanism 84, thereby inserting the penetrating probe 12 into the dermal layer.

[0030] Any suitable body part can be used for sampling. In a preferred embodiment, the sampling area is one which does not have a high density of nerve endings, e.g., the forearm. Typically, 5 to 15 seconds is required to obtain sufficient sample. Application of pressure to the sampling area can be needed to extract interstitial fluid or whole blood. To facilitate the appropriate amount of pressure being applied, a pressure sensor can be incorporated into the device 10 which indicates when sufficient pressure has been applied. Sample acquisition time can be improved by applying increased pressure to the area surrounding the direct sampling area. Some of the factors that can affect interstitial fluid or whole blood sample acquisition include the patient's age, skin thickness, temperature, and hydration. The amount of interstitial or whole blood sample collected for testing can preferably be about 0.02 μl or greater, more preferably 0.1 μl or greater, and most preferably about 0.5 μl or greater.

[0031] In one preferred embodiment, the device 10 can be inserted into a meter prior to sample acquisition. In such an embodiment, the meter serves multiple functions, including supporting the device 10, providing an automated means of initiating sample acquisition, and indicating when sample acquisition is complete.

Transfer of Sample from Penetration Probe to Analysis Chamber

[0032] In a preferred embodiment of the sampling device 10, the device comprises a penetration probe 12 an analysis chamber 20 and illustrated in FIGS. 1 and 2, the device 10 comprises a pre-chamber **14.** The pre-chamber **14** can then be integrated with or can be interfaced to the analysis chamber **20.**

[0033] In a further embodiment, the analysis chamber **20** is integrated with or can be interfaced to a means for facilitating filling of the analysis chamber **20.** This means can comprise a collapsible or compressible bladder **22,** as shown in FIGS. 3 and 4, which can be used to apply a positive or negative pressure (i.e., partial vacuum) to the analysis chamber **20**. The compressible bladder **22** can comprise any chamber with flexible walls that can be compressed to reduce the volume of the chamber. When the force compressing the compressible bladder 22 is released, a partial vacuum is formed which draws sample into the analysis chamber **20.** In a preferred embodiment, the volume of the compressible bladder **22** is sufficiently large so that when the bladder **22** is substantially fully compressed, the reduction in volume of the bladder **22** is larger than or equal to the total volume of the analysis chamber **20,** thereby ensuring that the analysis chamber **20** is substantially filled. However, a compressible bladder **22** with a smaller volume than the analysis chamber **20** can also be effective in assisting the filling of the analysis chamber **20**.

[0034] Alternatively, the analysis chamber **20** itself can be collapsible or compressible. In such an embodiment, a piston or other compressing agent, such as a patient's or clinician's fingers, can first compress then release the analysis chamber **20**, thereby forming a partial vacuum. When the compressing force is released, the partial vacuum causes the sample to flow from the penetration probe toward the analysis chamber.

Pre-chamber

[0035] In a preferred embodiment, as illustrated in FIGS. 1 and 2, a pre-chamber **14** is provided in the integrated sampling and testing device **10** for accumulation and storage of the collected sample prior to its being transferred to the analysis chamber **20.** A pre-chamber **14** is useful when using an analysis method which requires that the sample fill the analysis chamber **20** in a short period of time to return accurate results, i.e., a time shorter than that required to draw sufficient sample from the dermal layer. In a preferred embodiment, the volume of the pre-chamber **14** is larger than that of the analysis chamber **20**, thus ensuring that once the pre-chamber **14** is filled, sufficient sample has been collected to completely fill the analysis chamber **20**.

[0036] In a preferred embodiment, as illustrated in FIGS. 1 and 2, the penetration probe **12** opens into the pre-chamber **14** at a first end, and at the second end the pre-chamber **14** opens to the analysis chamber **20.** The pre-chamber **14** can be free of reagents or other substances, or can optionally contain one or more substances to enhance or diminish the capillary force exerted by the walls of the pre-chamber **14** or to pre-treat the sample prior to analysis. These substances can include, for example, polymers, resins, powders, meshes, fibrous materials, crystalline materials, porous materials, or a mixture or combination thereof. To facilitate effective filling of the analysis chamber **20**, a preferred embodiment utilizes a pre-chamber **14** and analysis chamber **20** of different heights, as shown in FIG. 2. Where the analysis chamber **20** is formed so that its height (typically referring to the smallest chamber dimension) is smaller than the height of the pre-chamber **14**, a capillary force is generated that is capable of drawing fluid out of the pre-chamber **14** and into the analysis chamber **20.** A first air vent **64** can be formed at the end **70** of the analysis chamber **20** opposite the opening **62** to the pre-chamber **14**, facilitating the filling of the analysis chamber **20** by allowing air to be displaced from the analysis chamber **20** as sample enters. Optionally, a second vent **74** can be formed opening into the pre-chamber **14** at the substantially opposite and **60** of the pre-chamber **14** to where the penetration probe **12** opens into the pre-chamber **14**. This vent **74** provides air to the pre-chamber 14 to replace the sample as it is transferred from the pre-chamber **14** to the analysis chamber **20**. The vent **74** can be placed in any suitable position on the test strip **10**. In a preferred embodiment, the vent **74** incorporates a sharp corner, e.g., at a 90° angle, which functions as a "capillary stop" to prevent sample from exiting the device **10** through the vent **74**.

[0037] In another embodiment, the pre-chamber **14** consists of a tube, or other shaped chamber, with flexible walls, attached to the penetration probe **12**. In this embodiment, the pre-chamber **14** is either permanently fixed to the analysis chamber **20** or is placed next to and aligned with a port to the analysis chamber **20.** Such alignment can occur during use by suitable placement in an external device such as the measurement meter. In one aspect of this embodiment, the pre-chamber **14** further comprises a valve, defined as a device to control the flow of fluid sample between the penetration probe **12** and the pre-chamber **14**. The valve can comprise one or more rollers, pistons, or squeezing devices capable of simultaneously dosing off the first end **60** of the pre-chamber **14**, and compressing the pre-chamber **14** such that the fluid in the pre-chamber **14** is forced towards the second end **62** of the pre-chamber **14** and subsequently into the analysis chamber **20**.

[0038] Alternatively, the analysis chamber **20** consists of a tube, or other shaped chamber, with flexible walls, attached to the penetration probe **12**. In one aspect of this embodiment, the analysis chamber **20**, prior to penetration, is compressed by one or more rollers, pistons, or other squeezing devices. After the penetration probe **12** is inserted, the compression is released, forming a vacuum which pulls sample into the analysis chamber **20**. In such an embodiment, the pre-chamber **14** can not be necessary if sufficient vacuum is generated for rapid sample acquisition. In such an embodiment, the device **10** can not require a vent **64**, **74** if such would interfere with forming a vacuum.

[0039] In another embodiment, illustrated in FIGS. 3 and 4, a pre-chamber **14** of suitable size is formed which opens to the penetration probe **12** on one end **60** and to the analysis chamber **20** on the other end **62**. The end **70** of the analysis chamber **20** opposite to that opening to the pre-chamber **14** opens to a compressible bladder **22.** The bladder **22** can be formed separately and attached to the end **70** of the analysis chamber **20.** Alternatively, it can be formed by removing a section on the middle laminate **82** in the test strip **10**, similar to those described in WO97/00441, as illustrated in FIGS. 3 and 4.

[0040] In use, the bladder **22** in the strip **10** is compressed by suitable means prior to the penetration probe **12** being inserted into the patient. Insertion of the penetration probe **12** can be confirmed by use of a sensor, such as a pressure sensor, or the patient can confirm that the penetration probe **12** is inserted either visually or by touch. In the iatter case, the patient sensing can signal the meter, such as by pushing a button. At this point, the means compressing the bladder **22** is withdrawn to a halfway position to draw sample into the pre-chamber **14**. When the pre-chamber **14** is full, as indicated by a suitable sensor, the meter indicates to the patient to withdraw the penetration probe **12.** The compressing means then moves to its fully withdrawn position and so draws the sample from the pre-chamber **14** into the analysis chamber **20.** In the case where the initial suction from the bladder **22** causes the sample to be accumulated with sufficient speed, the pre-chamber **14** can be dispensed with and the bladder **22** used to draw sample through the penetration probe **12** directly into the analysis chamber **20.** A vent **64, 74** which would

interfere with forming a vacuum need not be incorporated into the device in some embodiments.

Analysis Chamber

[0041] In a preferred embodiment, the analysis chamber **20** is contained in an analyzing device **10** comprising a disposable analysis strip similar to that disclosed in WO97/00441. The analysis strip of WO97/00441 contains a biosensor for determining the concentration of an analyte in a carrier, e.g., the concentration of glucose in a fluid sample. The electrochemical analysis cell **20** in this strip has an effective volume of 1.5µl or less, and can comprise a porous membrane, a working electrode on one side of the membrane, and a counter/reference electrode on the other side. In a preferred embodiment, an analysis cell **20** having an effective volume of about 0.02µl or greater is used. More preferably, the cell **20** has a volume ranging from about 0.1µl to about 0.5µl.

[0042] In one aspect of this embodiment, the penetration probe **12** is a small needle integrated into the analysis strip **10** by being inserted through a wall of the analysis chamber **20** such that one end of the needle **12** opens into the strip analysis chamber **20**. In using a device **10** having this arrangement to obtain and analyze a sample of interstitial fluid, the needle **12** is inserted into the patient's dermal layer and sample is drawn into the needle **12** via capillary action. The sample is then transferred from the needle **12** into the analysis chamber **20** by capillary action whereupon the sample is analyzed. An opening **64** in the analysis chamber **20** to atmosphere, remote from the point where the needle **12** opens into the chamber, acts as a vent **64** to allow the escape of displaced air as the analysis chamber **20** fills with sample. Analysis devices of the type disclosed in WO97/00441 are particularly suited for use with this arrangement because of their ability to utilize the very small volumes of sample typically available with interstitial fluid sampling.

[0043] The analysis chamber **20** can contain one or more substances to enhance or diminish the capillary force exerted by the walls of analysis chamber **20.** Such materials can include polymers, resins, powders, meshes, fibrous materials, crystalline materials, porous materials, or a mixture or combination thereof, as can also be used in the pre-chamber, discussed above. For example, the walls **24** of the analysis chamber **20** can be coated with a hydrophilic material to encourage the flow of fluid sample into the analysis chamber. Suitable hydrophilic materials include polyethylene glycol, polyvinylpyrrolidone, a surfactant, a hydrophilic block copolymer, and polyacrylic acid. The analysis chamber **20** can also contain reagents capable of reacting with the analyte or other substances present in the sample. Such other substances can include substances which interfere in determining the presence or absence of the analyte. In such cases, the reagent will react with the substance so that it no longer interferes with the analysis.

[0044] Any analyte present in a fluid sample in a detectable amount can be analyzed using the device **10.** A typical analytes can include, but is not limited to, an ion, an element, a sugar, an alcohol, a hormone, a protein, an enzyme, a cofactor, a nucleic acid sequence, a lipid, and a drug. In a preferred embodiment, glucose is the analyte to be tested. Typical analytes could include, but are not limited to, ethanol, potassium ion, pharmaceuticals, drugs, cholesterol, and lactate.

[0045] The presence or absence of the analyte can be determined directly. Alternatively, the analyte can be determined by reacting the analyte with one or more reagents present in the analysis chamber. The product of that reaction, indicative of the presence or absence of the analyte, would then be detected. Suitable reaction products include, but are not limited to, a color indicator, an electric current, an electric potential, an acid, a base, a precipitate, or a gas.

[0046] Any suitable analytical method can be used for determining the presence or absence of the analyte or a reaction product of the analyte. Suitable analytical methods include, but are not limited to, electrochemical methods, photoabsorption detection methods, photoemission detection methods, and the measurement of magnetic susceptibility. In the case of a reaction product having a different color than the analyte, or the formation of a precipitate or a gas, a visual determination can be a suitable method for determining the presence or absence of the analyte.

Display/Storage of Measurement Data

[0047] In a preferred embodiment, an analysis strip as described above or another embodiment of the sampling device 10 is integrated with a measuring device, e.g., a meter, which can display, store or record test data, optionally in computer-readable format. In such an embodiment, the test strip 10 comprises an interface for communicating with the meter, e.g., conductive leads from the electrodes of the electrochemical cell 20. In the case of obtaining an electrochemical measurement, the interface communicates a voltage or a current to the electrochemical cell 20.

[0048] The above description discloses several materials of the present invention. This invention is susceptible to modifications in the methods and materials, as well as alterations in the fabrication methods and equipment. Such modifications will become apparent to those skilled in the art from a consideration of this disclosure or practice of the invention disclosed herein. Consequently, it is not intended that this invention be limited to the specific embodiments disclosed herein, but that it cover all modifications and alternatives coming within the true scope of the invention as embodied in the attached claims.

Claims

1. A fluid sampling device (10) comprising a body, the body comprising a dermal layer penetration probe (12) having a penetrating end and a communicating end, and an analysis chamber (20) having a proximal and distal end, the analysis chamber (20) having a volume, the sampling device (10) further comprising a pre-chamber (14) having a volume and a first and second end, wherein the pre-chamber (14) is interposed between the penetration probe (12) and the analysis chamber (20) such that the first end of the pre-chamber (14) is adjacent the communicating end of the penetration probe (12) and the second end of the pre-chamber (14) is adjacent the proximal end of the analysis chamber (20), wherein the volume of the pre-chamber (14) is greater than the volume of the analysis chamber (20), and wherein the penetration probe (12) is in fluid communication with the analysis chamber (20) such that fluid can flow from the penetration probe (12) toward the analysis chamber (20).

2. The device (10) of claim 1, wherein the analysis chamber (20) has at least one flexible wall and wherein upon compression of the chamber at the flexible wall the volume of the analysis chamber (20) is reduced.

3. The device (10) of claim 2, wherein the pre-chamber (14) has at least one flexible wall and wherein upon compression of the chamber at the flexible wall the volume of the pre-chamber (14) is reduced.

4. The device (10) of claim 3, wherein the pre-chamber (14) is capable of exerting a first capillary force and the analysis chamber (20) is capable of exerting a second capillary force and wherein a differential exists between the first and the second capillary forces.

5. The device (10) of claim 4, wherein the capillary force exerted by the analysis chamber (20) is greater than the capillary force exerted by the pre-chamber (14).

6. The device (10) of claim 5, wherein an interior surface of the pre-chamber (14) comprises at least first and second pre-chamber (14) walls spaced apart at a first distance to define a pre-chamber (14) height, and wherein an interior surface of the analysis chamber (20) comprises at least first and second analysis chamber (20) walls spaced apart at a second distance to define an analysis chamber (20) height, wherein the height of the analysis chamber (20) is less than the height of the pre-chamber (14), and wherein the differential capillary force derives at least in part from a difference between the pre-chamber (14) height and the analysis chamber (20) height

7. The device (10) of claim 6, wherein at least one of the chambers comprises a substance capable of enhancing or diminishing the capillary force exerted by the chamber.

8. The device (10) of claim 7, wherein the substance is selected from the group consisting of a polymer, a resin, a powder, a mesh, a fibrous material, a crystalline material, a porous material, or a combination thereof.

9. The device (10) of claim 7, wherein the substance is selected from the group consisting of polyethylene glycol, polyvinylpyrrolidone, a surfactant, a hydrophilic block copolymer, and polyvinylacetate.

10. The device (10) of claim 1, wherein the pre-chamber (14) comprises a first pre-chamber (14) wall and a second pre-chamber (14) wall and wherein the analysis chamber (20) comprises a first analysis chamber (20) wall and a second analysis chamber (20) wall, and wherein the distance between the pre- chamber walls is greater than the distance between the analysis chamber (20) walls.

11. The device (10) of claim 1, wherein the penetration probe (12) is selected from the group consisting of a needle, a lancet, a tube, a channel, and a solid protrusion.

12. The device (10) of claim 1, wherein the penetration probe (12) comprises a material selected from the group consisting of carbon fiber, boron fiber, plastic, metal, glass, ceramic, a composite material, mixtures thereof, and combinations thereof.

13. The device (10) of claim 1, wherein the penetration probe (12) comprises two sheets of material in substantial registration, having a protrusion on each sheet, wherein the sheets are spaced apart such that liquid can be drawn between the sheets by capillary action.

14. The device (10) of claim 13, wherein the two sheets of material extend into the device (10) so as to form a pre-chamber (14) adjacent the analysis chamber (20) and in fluid communication therewith.

15. The device (10) of claim 1, wherein the device (10) has a proximal edge, the edge comprising a recess, wherein the penetration probe (12) is positioned within the recess.

16. The device (10) of claim 15, wherein the recess is configured to substantially align with a shape of a

selected dermal surface.

17. The device (10) of claim 1, wherein the analysis chamber (20) comprises an electrochemical cell, the cell comprising a working electrode and a counter/reference electrode.

18. The device (10) of claim 1, further comprising an interface for communication with a meter.

19. The device (10) of claim 18, wherein the interface communicates a voltage or a current.

Patentansprüche

1. Vorrichtung zur Probenahme von Flüssigkeit (10), umfassend einen Körper, wobei der Körper eine Hautschicht-durchdringende Sonde umfasst (12), die ein Durchdringungsende und ein kommunizierendes Ende aufweist, und eine Analysenkammer (20), die ein proximales und distales Ende aufweist, wobei die Analysenkammer (20) ein Volumen aufweist, wobei die Vorrichtung zur Probenahme (10) weiter eine Vor-Kammer (14) umfaßt, die ein Volumen und ein erstes und zweites Ende aufweist, wobei die Vor-Kammer (14) zwischen der Durchdringungssonde (12) und der Analysenkammer (20) geschaltet ist, so daß das erste Ende der Vor-Kammer (14) an das kommunizierende Ende der Durchdringungsprobe (12) angrenzt und das zweite Ende der Vor-Kammer (14) an das proximale Ende der Analysenkammer angrenzt (20), wobei die Durchdringungssonde (12) in Flüssigkeits-Verbindung mit der Analysenkammer (20) steht, so daß die Flüssigkeit von der Penetrationssonde (12) in Richtung der Analysenkammer (20) fließen kann.

2. Vorrichtung (10) nach Anspruch 1, wobei die Analysenkammer (20) wenigstens eine flexible Wand aufweist und wobei nach Kompression der Kammer der flexiblen Wand auf das Volumen der Analysenkammer (20) reduziert ist.

3. Vorrichtung (10) nach Anspruch 2, wobei die Vor-Kammer (14) wenigstens eine flexible Wand aufweist und wobei nach Kompression der Kammer der flexiblen Wand auf das Volumen der Vor-Kammer (14) reduziert ist.

4. Vorrichtung (10) nach Anspruch 3, wobei die Vor-Kammer (14) geeignet ist, um eine erste Kapillarkraft auszuüben und die Analysenkammer (20) geeignet ist, um eine zweite Kapillarkraft auszuüben und wobei ein Unterschied zwischen der ersten und der zweiten Kapillarkraft besteht.

5. Vorrichtung (10) nach Anspruch 4, wobei die Kapillarkraft, die durch die Analysenkammer (20) ausgeübt wird, größer ist als die Kapillarkraft, die durch die Vor-Kammer (14) ausgeübt wird.

6. Vorrichtung (10) nach Anspruch 5, wobei eine innere Oberfläche der Vor-Kammer (14) wenigstens eine erste und zweite Vor-Kammerwand (14) umfaßt, die in einem ersten Abstand beabstandet sind, um eine Höhe der Vor-Kammer (14) zu definieren, und wobei eine innere Oberfläche der Analysenkammer (20) wenigstens eine erste und zweite Analysenkammerwand umfaßt, die in einem zweiten Abstand beabstandet sind, um die Höhe der Analysenkammer (20) zu definieren, wobei die Höhe der Analysenkammer (20) weniger als die Höhe der Vor-Kammer (14) ist und wobei die unterschiedlichen Kapillarkräfte zum Teil durch den Unterschied zwischen der Höhe der Vor-Kammer (14) und der Höhe der Analysenkammer (20) erreicht werden.

7. Vorrichtung (10) nach Anspruch 6, wobei wenigstens eine der Kammern einen Stoff umfaßt, der geeignet ist, um die Kapillarkraft, die durch die Kammer ausgeübt wird, zu verstärken oder zu vermindern.

8. Vorrichtung (10) nach Anspruch 7, wobei der Stoff ausgewählt ist aus der Gruppe bestehend aus einem Polymer, einem Harz, einem Pulver, einem Netz, einem faserigen Material, einem kristallinen Material, einem porösen Material oder eine Kombination davon.

9. Vorrichtung (10) nach Anspruch 7, wobei der Stoff ausgewählt ist aus der Gruppe bestehend aus Polyethylenglycol, Polyvinylpyrrolidon, einem grenzflächenaktiven Stoff, einem hydrophilen Blockcopolymer und Polyvinylacetat.

10. Vorrichtung (10) nach Anspruch 1, wobei die Vor-Kammer (14) eine erste Vor-Kammerwand (14) und eine zweite Vor-Kammerwand (14) umfaßt, und wobei die Analysenkammer (20) eine erste Analysenkammerwand (20) und eine zweite Analysenkammerwand (20) umfaßt, und wobei der Abstand zwischen den Vor-Kammerwänden größer ist als der Abstand zwischen den Analysenkammerwänden (20).

11. Vorrichtung (10) nach Anspruch 1, wobei die Durchdringungssonde (12) ausgewählt ist aus der Gruppe bestehend aus einer Nadel, einer Lanzette, einer Tube, einem Kanal, und einem festen Vorsprung.

12. Vorrichtung (10) nach Anspruch 1, wobei die Durchdringungssonde (12) einen Stoff umfaßt ausgewählt aus der Gruppe bestehend aus Kohlefaser, Borfaser, Plastik, Metall, Glas, Keramik, einen Ver-

bundstoff, Mischungen davon und Kombinationen davon.

13. Vorrichtung (10) nach Anspruch 1, wobei die Durchdringungssonde (12) zwei Lagen an Material umfaßt, die aus im wesentlichen genau zusammenpassen, die einen Vorsprung auf jeder Lage aufweisen, wobei die Lagen beabstandet verteilt sind, so daß Flüssigkeit durch Kapillarwirkung zwischen die Lagen gesaugt werden kann.

14. Vorrichtung (10) nach Anspruch 13, wobei sich die zwei Lagen aus Material in die Vorrichtung erstrekken, so daß eine Vor-Kammer (14) geformt wird, die an die Analysenkammer (20) angrenzt und in flüssiger Verbindung damit steht.

15. Vorrichtung (10) nach Anspruch 1, wobei die Vorrichtung (10) eine proximale Grenze aufweist, die Grenze eine Einbuchtung umfaßt, wobei die Durchdringungssonde (12) innerhalb der Einbuchtung angeordnet ist.

16. Vorrichtung (10) nach Anspruch 15, wobei die Einbuchtung so konfiguriert ist, sich im wesentlichen der Form einer ausgewählten Hautoberfläche anzupassen.

17. Vorrichtung (10) nach Anspruch 1, wobei die Analysenkammer (20) eine elektrochemische Zelle umfaßt, wobei die Zelle eine Arbeits-Elektrode und eine Gegen-Referenz- Elektrode umfaßt.

18. Vorrichtung (10) nach Anspruch 1, weiter umfassend eine Schnittstelle zur Kommunikation mit dem Meßgerät.

19. Vorrichtung (10) nach Anspruch 18, wobei die Schnittstelle eine Spannung oder einen Strom vermittelt.

Revendications

1. Dispositif d'échantillonnage d'un fluide (10) comportant un corps, le corps comportant une sonde de pénétration de couche dermique (12) ayant une extrémité de pénétration et une extrémité de communication, et une chambre d'analyse (20) ayant une extrémité proximale et une extrémité distale, la chambre d'analyse (20) ayant un volume, le dispositif d'échantillonnage (10) comportant de plus une préchambre (14) ayant un volume et une première et une seconde extrémité, dans lequel la préchambre (14) est interposée entre la sonde de pénétration (12) et la chambre d'analyse (20) de telle sorte que la première extrémité de la préchambre (14) est adjacente à l'extrémité de communication de la sonde de pénétration (12) et la seconde extrémité de la préchambre (14) est adjacente à l'extrémité proximale de la chambre d'analyse (20), dans lequel le volume de la préchambre (14) est plus grand que le volume de la chambre d'analyse (20), et dans lequel la sonde de pénétration (12) est en communication hydraulique avec la chambre d'analyse (20) de telle sorte qu'un fluide peut s'écouler depuis la sonde de pénétration (12) en direction de la chambre d'analyse (20).

2. Dispositif (10) selon la revendication 1, dans lequel la chambre d'analyse (20) a au moins une paroi souple et dans lequel lors d'une compression de la chambre au niveau de la paroi souple le volume de la chambre d'analyse (20) est réduit.

3. Dispositif (10) selon la revendication 2, dans lequel la préchambre (14) a au moins une paroi souple et dans lequel lors d'une compression de la chambre au niveau de la paroi souple le volume de la préchambre (14) est réduit.

4. Dispositif (10) selon la revendication 3, dans lequel la préchambre (14) est capable d'exercer une première force capillaire et la chambre d'analyse (20) est capable d'exercer une seconde force capillaire et dans lequel un différentiel existe entre les première et seconde forces capillaires.

5. Dispositif (10) selon la revendication 4, dans lequel la force capillaire exercée par la chambre d'analyse (20) est plus grande que la force capillaire exercée par la préchambre (14).

6. Dispositif (10) selon la revendication 5, dans lequel une surface intérieure de la préchambre (14) comporte au moins une première et une seconde paroi de préchambre (14) espacées à une première distance pour définir une hauteur de préchambre (14), et dans lequel une surface intérieure de la chambre d'analyse (20) comporte au moins une première et une seconde paroi de chambre d'analyse (20) espacées d'une seconde distance pour définir une hauteur de chambre d'analyse (20), dans lequel la hauteur de la chambre d'analyse (20) est plus petite que la hauteur de la préchambre (14) et dans lequel la force capillaire différentielle dérive au moins en partie de la différence entre la hauteur de la préchambre (14) et la hauteur de la chambre d'analyse (20).

7. Dispositif (10) selon la revendication 6, dans lequel au moins une des chambres est constituée d'une substance capable de renforcer ou de diminuer la force capillaire exercée par la chambre.

8. Dispositif (10) selon la revendication 7, dans lequel

la substance est sélectionnée parmi le groupe constitué d'un polymère, une résine, une poudre, une maille, un matériau fibreux, un matériau cristallin, un matériau poreux, ou d'une combinaison de ceux-ci.

9. Dispositif (10) selon la revendication 7, dans lequel la substance est sélectionnée parmi le groupe constitué de polyéthylèneglycol, polyvinylpyrrolidone, un tensioactif, un copolymère bloc hydrophile, et de l'acétate de polyvinyle.

10. Dispositif (10) selon la revendication 1, dans lequel la préchambre (14) comporte une première paroi de préchambre (14) et une seconde paroi de préchambre (14) et dans lequel la chambre d'analyse (20) comporte une première paroi de chambre d'analyse (20) et une seconde paroi de chambre d'analyse (20), et dans lequel la distance entre les parois de préchambre est plus grande que la distance entre les parois de chambre d'analyse (20).

11. Dispositif (10) selon la revendication 1, dans lequel la sonde de pénétration (12) est sélectionnée parmi le groupe constitué d'une aiguille, d'une lancette, d'un tube, d'un canal et d'une saillie solide.

12. Dispositif (10) selon la revendication 1, dans lequel la sonde de pénétration (12) est constituée d'un matériau sélectionné parmi le groupe constitué d'une fibre de carbone, une fibre de bore, une matière plastique, un métal, un verre, une céramique, un matériau composite, des mélanges de ceux-ci et des combinaisons de ceux-ci.

13. Dispositif (10) selon la revendication 1, dans lequel la sonde de pénétration (12) est constituée de deux feuilles de matériau sensiblement calées, ayant une saillie sur chaque feuille, les feuilles étant espacées de telle sorte que du liquide peut être attiré entre les feuilles par action capillaire.

14. Dispositif (10) selon la revendication 13, dans lequel les deux feuilles de matériau s'étendent dans le dispositif (10) de manière à former une préchambre (14) adjacente à la chambre d'analyse (20) et en communication hydraulique avec celle-ci.

15. Dispositif (10) selon la revendication 1, dans lequel le dispositif (10) a un bord proximal, le bord comportant un évidement, la sonde de pénétration (12) étant positionnée dans l'évidement.

16. Dispositif (10) selon la revendication 15, dans lequel l'évidement est configuré pour être sensiblement aligné avec une forme d'une surface dermique sélectionnée.

17. Dispositif (10) selon la revendication 1, dans lequel la chambre d'analyse (20) comporte une cellule électrochimique, la cellule comportant une électrode active et une électrode auxiliaire/de référence.

18. Dispositif (10) selon la revendication 1, comportant de plus une interface pour communiquer avec un dispositif de mesure.

19. Dispositif (10) selon la revendication 18, dans lequel l'interface communique une tension ou un courant.

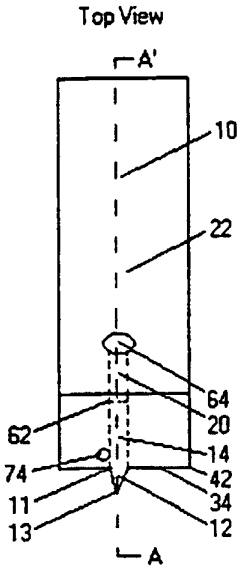

FIG. 1

Cross Section Along A-A' of FIG. 1

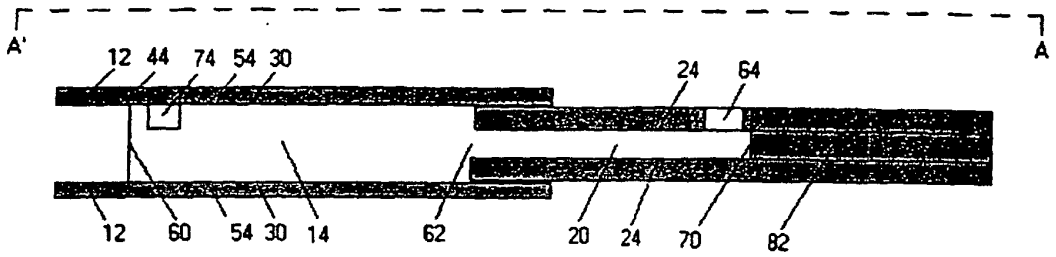

FIG. 2

Top View

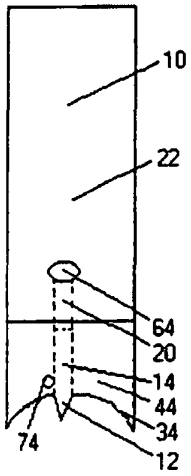

FIG.3

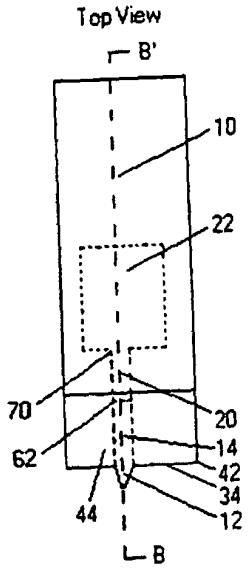

FIG. 4

Cross Section Along Line B-B' of FIG. 4

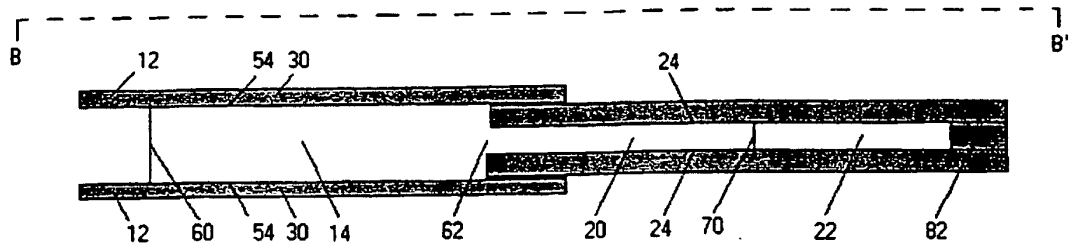

FIG. 5

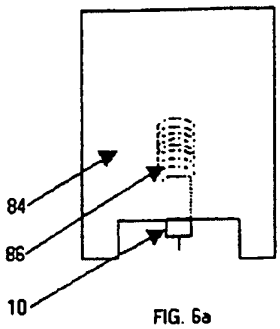

FIG. 6a

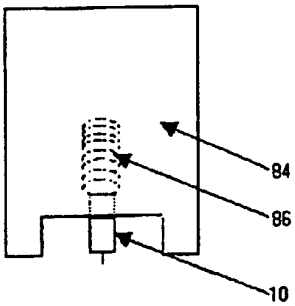

FIG. 6b

专利名称(译)	用于采样和分析组织间液和全血样品的方法和装置		
公开(公告)号	EP1276412B1	公开(公告)日	2005-12-28
申请号	EP2001922697	申请日	2001-03-26
[标]申请(专利权)人(译)	USF过滤分离集团公司		
申请(专利权)人(译)	USF过滤和离职集团公司.		
当前申请(专利权)人(译)	LIFESCAN INC.		
[标]发明人	HODGES ALASTAIR MCINDOE CHATELIER RON CHAMBERS GARRY		
发明人	HODGES, ALASTAIR, MCINDOE CHATELIER, RON CHAMBERS, GARRY		
IPC分类号	G01N33/48 A61B5/00 A61B5/15 A61B10/00 G01N33/49		
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代理机构(译)	FISHER，ADRIAN JOHN		
优先权	09/536235 2000-03-27 US		
其他公开文献	EP1276412A1		
外部链接	Espacenet		

摘要(译)

本申请中公开的发明是一种方法和装置（10），用于将皮下流体样品（例如组织间液或全血）的采样和分析组合在适于医院床边和家庭使用的装置中。该装置包括与分析室（20）流体连通的真皮层穿透探针（12）。它适用于在流体中以有用的代表性浓度存在的任何分析物，并且特别适用于监测葡萄糖。

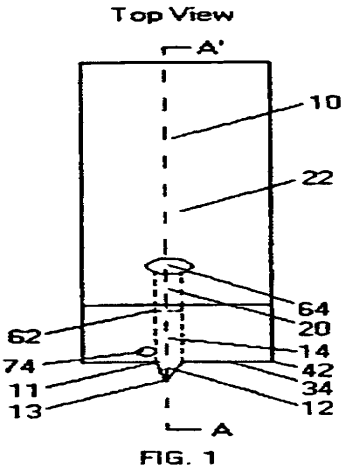

FIG. 1