US006939312B2

(12) **United States Patent**
Hodges et al.

(10) **Patent No.: US 6,939,312 B2**
(45) **Date of Patent: Sep. 6, 2005**

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

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(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 56 days.

(21) Appl. No.: **10/166,487**

(22) Filed: **Jun. 10, 2002**

(65) **Prior Publication Data**

US 2002/0177788 A1 Nov. 28, 2002

Related U.S. Application Data

(63) Continuation of application No. 09/536,235, filed on Mar. 27, 2000, now Pat. No. 6,612,111.

(51) **Int. Cl.**[7] **A61B 5/00**
(52) **U.S. Cl.** **600/583**; 600/584; 73/864.01
(58) **Field of Search** 600/309, 322, 600/345, 347, 365, 576, 578, 580, 582, 584; 606/181; 435/4, 7.1, 14, 69.6; 422/50, 55, 68.1, 101, 102; 436/68; 204/403; 73/863, 864.01, 864.02, 864.51, 864.62

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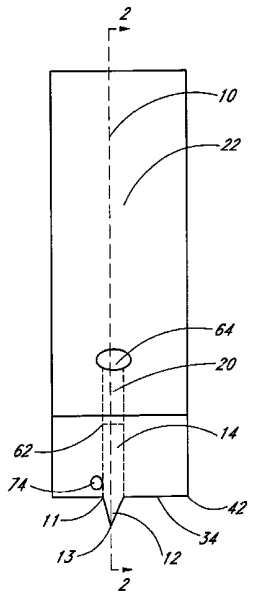
(57) **ABSTRACT**

The invention disclosed in this application is a method and device for combining the sampling and analyzing of subdermal fluid samples, e.g., interstitial fluid or whole blood, in a device suitable for hospital bedside and home use. It is applicable to any analyte that exists in a usefully representative concentration in the fluid, and is especially suited to the monitoring of glucose.

12 Claims, 6 Drawing Sheets



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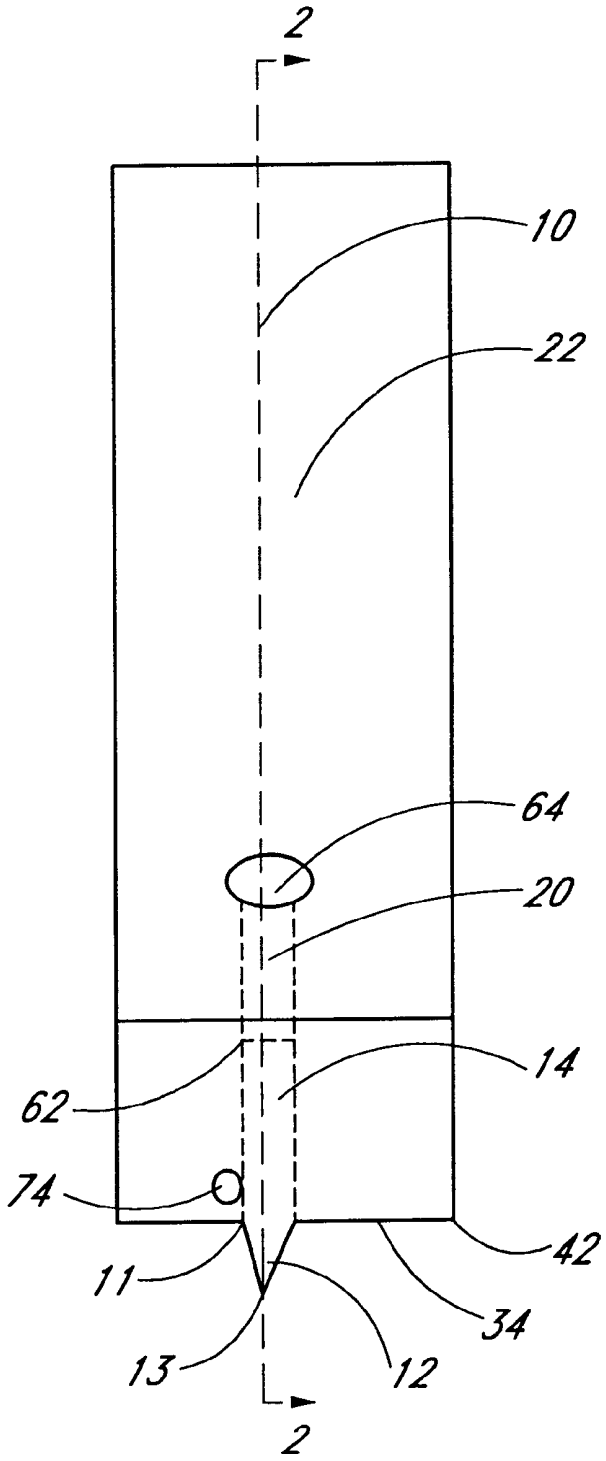

FIG. 1

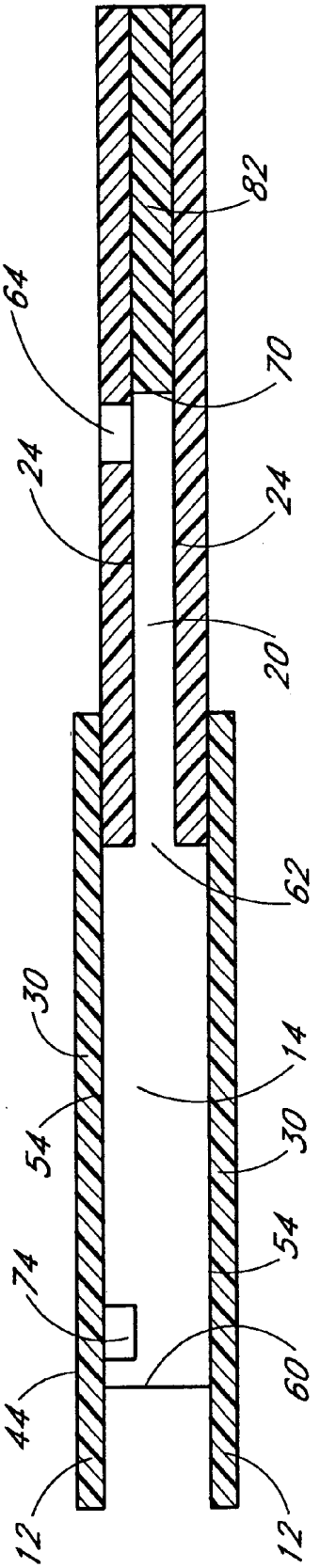

FIG. 2

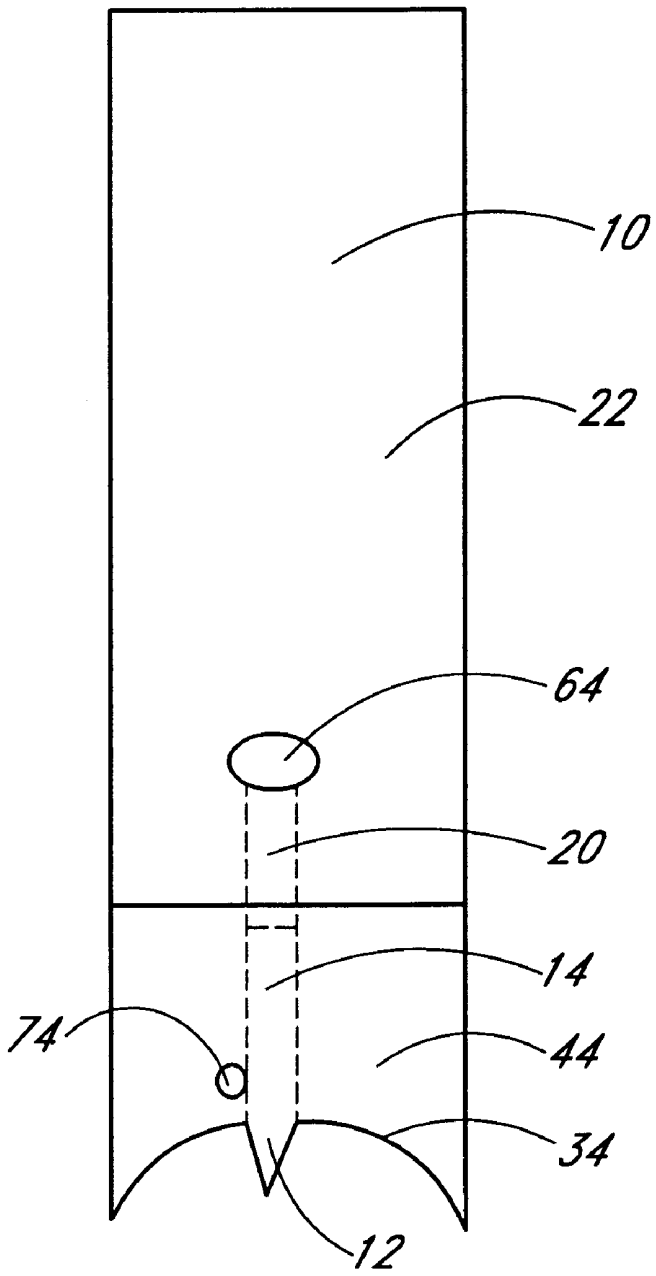

FIG. 3

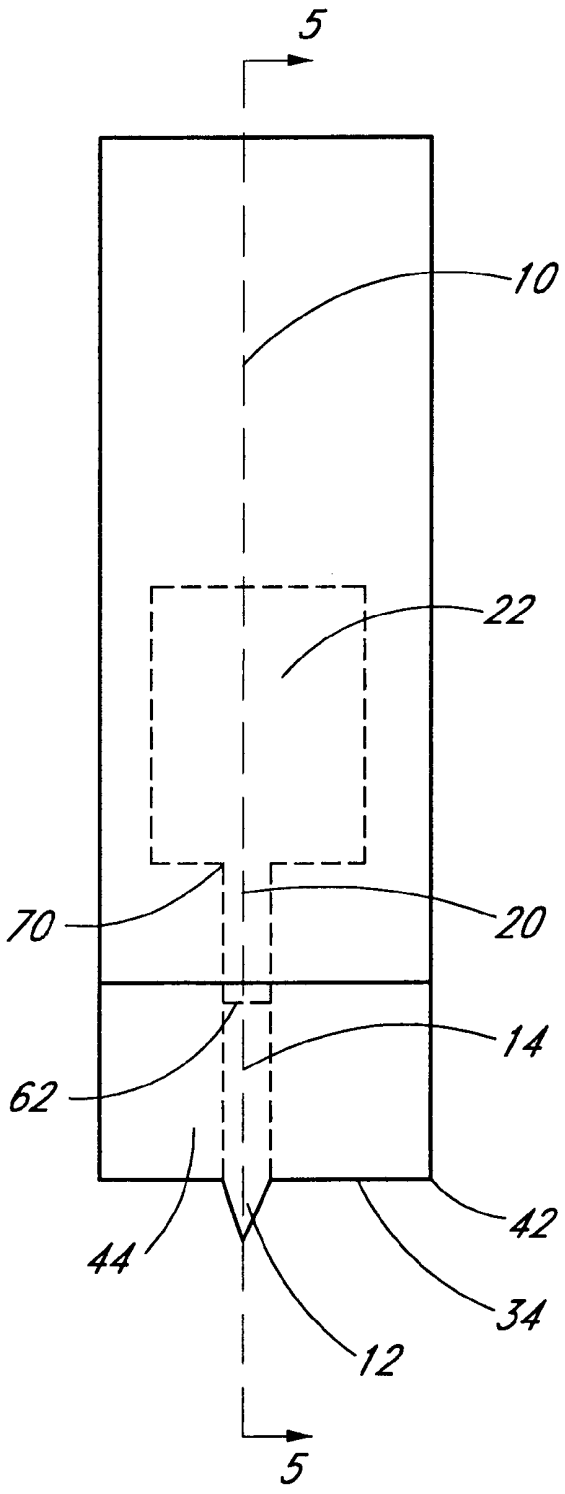

FIG. 4

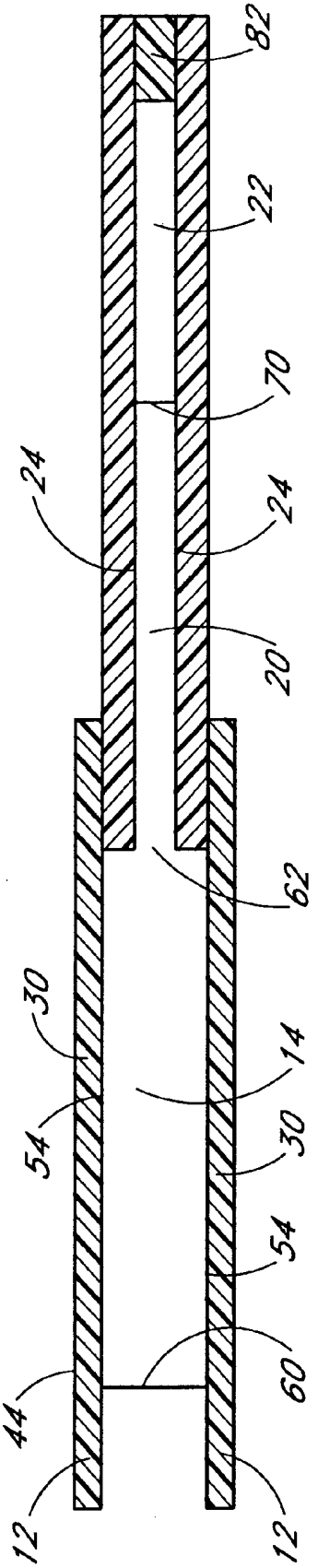

FIG. 5

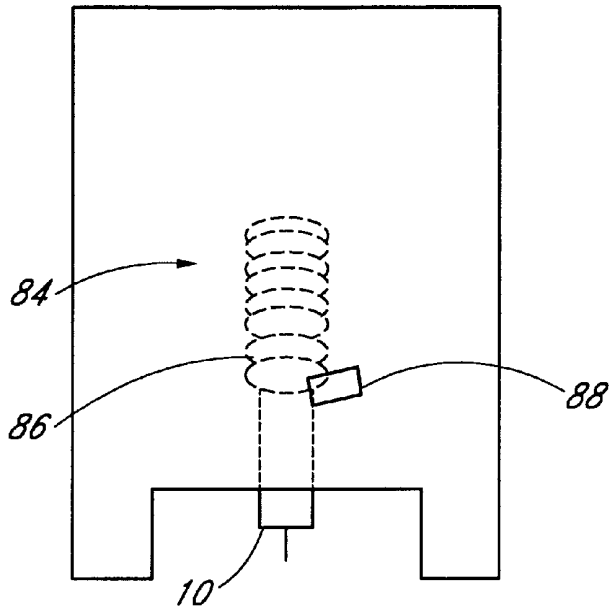

FIG. 6A

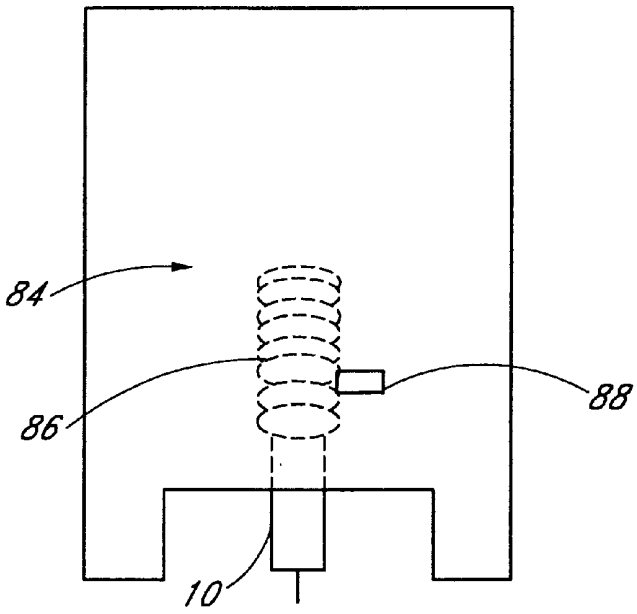

FIG. 6B

METHOD AND DEVICE FOR SAMPLING AND ANALYZING INTERSTITIAL FLUID AND WHOLE BLOOD SAMPLES

RELATED APPLICATION

This application is a continuation of U.S. application Ser. No. 09/536,235, filed Mar. 27, 2000 now U.S. Pat. No. 6,612,111.

FIELD OF THE INVENTION

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

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.

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).

In the patents U.S. Pat. No. 5,879,367, U.S. Pat. No. 5,879,310, U.S. Pat. No. 5,820,570 and U.S. Pat. No. 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.

SUMMARY OF THE INVENTION

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.

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.

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.

In a further embodiment, the device can further include 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 can be greater than or equal to 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.

In another embodiment, the device further includes 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.

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.

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.

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.

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.

In yet another embodiment of the present invention, 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.

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

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. **6***a* and **6***b* (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. **6***a* depicts the device loaded in the actuator, wherein the actuator is in the cocked position, ready to be triggered. FIG. **6***b* depicts the device and actuator after triggering.

DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENTS

Introduction

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 application Ser. No. 09/536,234, filed on Mar. 27, 2000, entitled "METHOD OF PREVENTING SHORT SAMPLING OF A CAPILLARY OR WICKING FILL DEVICE," which is incorporated herein by reference in its entirety.

The invention disclosed in this application is a method and 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 sampled and analyzed, thus the invention has broad application in the fields of human medicine, veterinary medicine, and horticultural science. The device and method are 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.

The 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 a method 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.

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. In a second aspect of the current invention 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**.

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

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**.

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.

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.

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 10 μm. 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.

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.

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. **6***a* and **6***b*. Such a spring-loaded mechanism **84** incorporates a spring **86** which is compressed and held in place by a trigger **88** which can release the force compressing the spring **86** when the triggering mechanism is activated. The trigger **88** 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 **88**. 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 **88**, force is transferred to the device **10**, which is ejected from the mechanism **84**, thereby inserting the penetrating probe **12** into the dermal layer.

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.

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

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

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**.

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

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**.

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 end **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**.

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 closing 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**.

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.

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 (incorporated wherein by reference in its entirety), as illustrated in FIGS. **3** and **4**.

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 latter 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

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 1.5 μl 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 0.02 μl or greater is used. More preferably, the cell **20** has a volume ranging from about 0.1 μl to about 0.5 μl.

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.

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.

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.

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.

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

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**.

The above description discloses several methods and 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 and spirit of the invention as embodied in the attached claims.

What is claimed is:

1. A fluid sampling device, said fluid sampling device comprising:

a test strip comprising:

a penetration probe having a penetrating end and a communicating end;

an electrochemical analysis chamber having a first volume, said electrochemical analysis chamber further comprising a working electrode and a counter/reference electrode;

a pre-chamber integrated between said communication penetration probe and said analysis chamber, said pre-chamber having a second volume, wherein said second volume is larger than said first volume such that said analysis chamber exerts a greater capillary force than said pre-chamber;

a releasable actuator adapted to receive said test strip, wherein said releasable actuator is capable of supplying a force sufficient to cause said penetration probe to penetrate a dermal layer of a user' skin; and

an interface for communication with a meter.

2. A fluid sampling device according to claim **1** wherein said fluid sampling device is adapted to limit the penetration of said penetrating end into said dermal layer to a depth of less than approximately 2 mm.

3. A fluid sampling device according to claim **2** wherein said fluid sampling device is adapted to limit the penetration of said penetrating end into said dermal layer to a depth of approximately 1.5 mm.

4. A fluid sampling device according to claim **1** wherein said penetrating end of said penetration probe comprises two sheets in substantial registration, wherein each of said sheets has a sharply pointed protrusion.

5. A fluid sampling device according to claim **4** wherein said two sheets are separated by a distance of between 10 micrometers and 1 millimeter.

6. A fluid sampling device according to claim 1 wherein said first volume is less than 1.5 microliters.

7. A fluid sampling device according to claim 6 wherein said first volume is between 0.02 microliters and 1.5 microliters.

8. A fluid sampling device according to claim 7 wherein said first volume is between 0.1 microliters and 0.5 microliters.

9. A fluid sampling device according to claim 1 wherein said analysis chamber includes at least one material adapted to increase the capillary force exerted by said analysis chamber.

10. A fluid sampling device according to claim 9 wherein one or more walls of said analysis chamber is coated with a hydrophilic material to encourage the flow of fluid sample into the analysis chamber.

11. The method of claim 10, wherein the hydrophilic material is selected from the group consisting of: polyethylene glycol, polyvinylpyrrolidone, a surfactant, a hydrophilic block copolymer, and polyacrylic acid.

12. A fluid sampling device according to claim 1 wherein one or more walls of said analysis chamber is coated with a reagent material to react with interfering substances.

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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	US6939312	公开(公告)日	2005-09-06
申请号	US10/166487	申请日	2002-06-10
[标]申请(专利权)人(译)	HODGES ALASTAIR 查德里RON 钱伯斯GARRY		
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IPC分类号	A61B5/15 A61B5/00 A61B10/00 G01N33/48 G01N33/49		
CPC分类号	A61B5/1411 A61B5/14514 A61B5/14532 A61B5/14546 A61B5/14865 A61B2010/008 A61B2562/0295 A61B5/150022 A61B5/150213 A61B5/150221 A61B5/150358 A61B5/150389 A61B5/150503 A61B5/150755 A61B5/15105 A61B5/15113 A61B5/15117 A61B5/15142 A61B5/1519		
其他公开文献	US20020177788A1		
外部链接	Espacenet USPTO		

摘要(译)

本申请中公开的发明是一种用于将皮下液体样品（例如组织间液或全血）的取样和分析组合在适于医院床边和家庭使用的装置中的方法和装置。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。