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(71) Applicant(s):
pSiMedica Ltd
(Incorporated in the United Kingdom)
Stephenson Harwood, LONDON,
EC4M 8SH, United Kingdom

(72) Inventor(s):
Nasrollah Torabi-Pour
Debbie Draeg
Roehieh Saffie
Leigh Trevor Canham

(74) Agent and/or Address for Service:
Qinetiq IP
Cody Technology Park,
A4 Building Room G016, Ively Road,
FARNBOROUGH, Hants, GU14 0LX,
United Kingdom

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(54) Abstract Title: **Device made of silicon and method for collecting mammary fluid**

(57) A mammary fluid collection device 11 comprises at least one silicon storage means 12 and a contact means which when in use causes and/or allows the or at least one of the silicon storage means 12 to contact at least part of a breast of a human subject. The silicon storage means 12 may comprise porous or partially oxidised silicon and may comprise a plurality of silicon needles or barbs. The device may comprise salicyclic acid. The silicon may be derivatised in such a manner that it binds to tumour markers. Also disclosed is a method of collection of mammary fluid. The device and method are for use in the detection of breast cancer.

Fig. 1

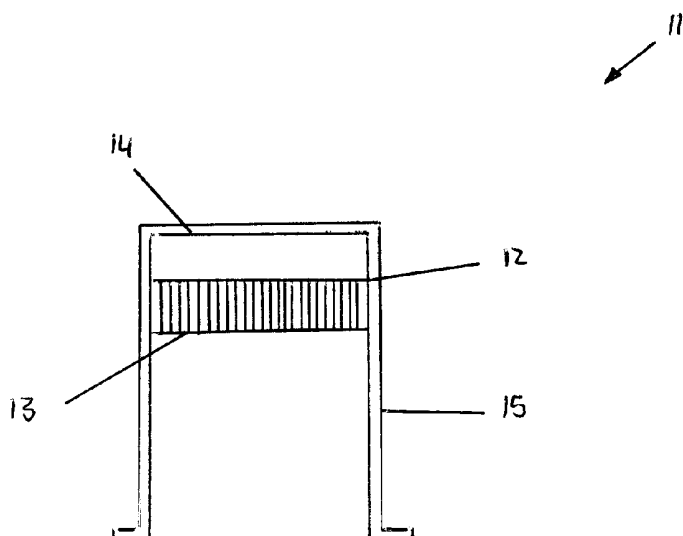
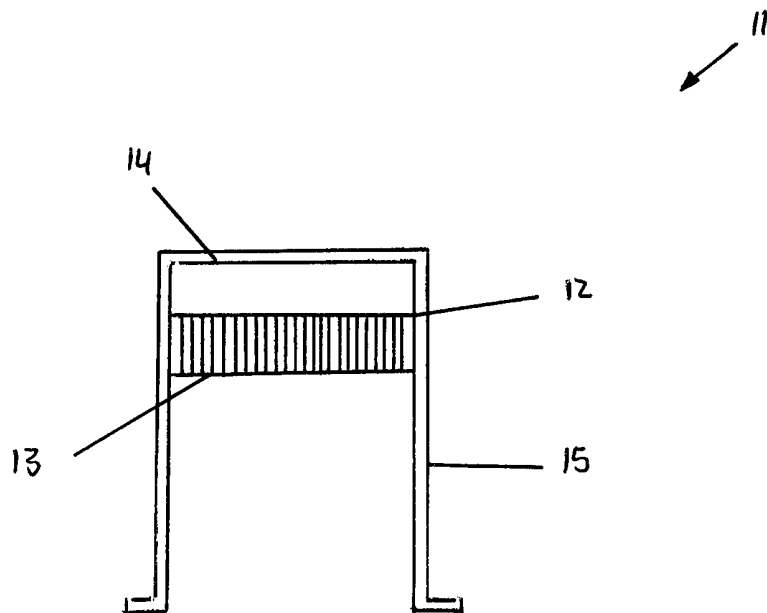


Fig. 1



Collection System

The present invention relates to a collection system. More specifically the invention relates to a collection and assay system. Yet more specifically the present invention relates to a collection and assay system for the detection of breast cancer and/or physiological conditions associated with breast cancer.

Breast cancer is the most common cause of cancer for women, affecting approximately one in nine females during their life, and is the main cause of death in women under 50.

Surgery and radiation therapy are the primary forms of treatment for breast cancer. Chemotherapy and biological therapy are promising additional treatments, but their effectiveness remains limited.

Early diagnosis of breast cancer is essential in order to optimise treatment. Early symptoms include: the formation of a new lump or node, swelling in part of the breast, skin irritation or dimpling, pain in the nipple or the nipple turning inward, redness or scaliness of one side of the nipple or breast skin, discharge of liquid other than breast milk. Methods of diagnosis include physical examination, X-ray analysis, and ultrasound (also known as sonography).

Ultrasound is not used for routine breast cancer screening because it does not consistently detect early signs of cancer such as micro-calcifications, which are clusters of calcium deposits in the breast that may indicate the presence of cancer.

Mass screening using mammography, although very effective in recent years, remains a costly and time intensive process. High quality mammography, which is an x-ray technique that provides images of the internal structure of the breast, is the most effective technology presently available for breast cancer screening. One problem with the present mammogram system is that the resulting images can be difficult to interpret.

A test that is inexpensive and convenient is therefore required, particularly for relatively high risk subjects including subjects at risk as a result of hereditary factors or because they have already been treated for cancer.

The majority of breast cancers originate in cells that line the inside of the milk ducts in the breasts. Changes in these cells, which are known as mammary epithelial cells have been associated with an increased risk of breast cancer.

- 5 There are a number of fluids generated in the breast and one of these, nipple aspirate fluid (NAF), contains exfoliated epithelial cells. It has been shown that assay of NAF may provide information about epithelial cells, and/or tumour markers. Tumour markers are typically proteins that are uniquely expressed by cancerous cells, or are expressed at measurably increased or decreased levels by cancerous cells compared to normal cells.
- 10 Other cancer markers can include specific DNA or RNA sequences marking deleterious genetic changes or alterations in the patterns or levels of gene expression associated with particular forms of cancer.

NAF may be secreted through the nipple of a breast; typically 15 to 20 lactiferous ducts supply each nipple, the lactiferous ducts merging at the nipple to result in 5 to 10 ducts that allow fluid to be expelled through the wrinkled tip of the nipple.

NAF is usually prevented from escaping from the nipple because the nipple ducts are occluded by constricting bands of smooth muscle, viscous and dried secretions, and by keratinized epithelium.

NAF differs from human milk both in composition and appearance. The colour of NAF may be clear, white, yellow, brown, green, or black.

- 25 There are several problems associated with existing assay techniques for NAF. The use of tools such as wide bore or fine needle aspiration may be painful or uncomfortable and are also prone to sampling errors.

- 30 Other techniques, such as the use of breast pumps, result in discharge of fluid for only a short interval of time. These techniques tend to be unsuitable for pre-menopausal women who produce relatively small amounts of NAF.

It is an objective of the present invention to solve at least some of the above mentioned problems.

According to one aspect, the invention provides a mammary fluid collection device comprising: (a) at least one silicon storage means, and (b) a contact means which, when in use, causes and/or allows the or at least one of the silicon storage means to contact at least part of a breast of a human subject.

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The or at least one of the silicon storage means may be used to collect mammary fluid secreted from a breast of a subject. By placing the or at least one of the silicon storage means in fluid communication with at least part of a breast of a human subject, fluid can pass into and/or onto the or at least one of the silicon storage means.

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The mammary fluid may be one or more of nipple aspirate fluid, human milk, and colostrum milk.

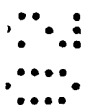
Preferably the collection device may be used to collect nipple aspirate fluid.

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Once a sufficient quantity of fluid has been collected from the breast, the sample may be assayed by a suitable assay technique. The assay may be performed in situ, or it may be performed after the collection is complete.

20



The collection device may further comprise an assay means for assaying at least part of the mammary fluid. The assay means may comprise an assay electronic circuit. The assay means may comprise an assay electronic circuit and an assay electrical power supply.

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The contact between the or at least one of the silicon storage means and a breast may be intermittent contact.

The contact means may, when in use, cause and/or allow the or at least one of the silicon storage means to contact at least part of a nipple of a human subject. The contact means may cause and/or allow the or at least one of the silicon storage means to contact at least part of an areola of the human subject.

30

One advantage of using a silicon storage means, which is placed in fluid communication with at least part of the breast of a subject, is that it may be used as part of a non-invasive or minimally invasive technique for sampling mammary fluid.

35

The silicon, from which the silicon storage means is at least partly formed, may also be fabricated in highly pure forms, using standard silicon fabrication processes, allowing very sensitive assay techniques to be used.

- 5 Preferably the or each silicon storage means comprises one or more of porous silicon, polycrystalline silicon, bulk crystalline silicon, and amorphous silicon.

Preferably the silicon storage means comprises porous silicon.

- 10 The use of porous silicon is advantageous for the collection of fluid secreted by a breast of a subject for several reasons. Porous silicon has a high surface area on which the mammary fluid or components of the mammary fluid may be collected. Because of its porous nature, the use of porous silicon may also allow the application of a reduced pressure to the part of the breast that is in fluid communication with the porous silicon. In
 15 other words, the reduced pressure may be transmitted through the pores of the porous silicon.

The or each silicon storage means may comprise semiconductor silicon.

- 20 The or each silicon storage means may comprise derivatised silicon. The or each silicon storage means may comprise derivatised porous silicon. For the purposes of this specification derivatised silicon is silicon comprising a monomolecular or monatomic layer that is covalently bonded to at least part of the surface of the silicon. The covalent bond may be one or more of Si-H bond, Si-C bond, a Si-O bond, and a Si-O-C bond.

- 25 Preferably the derivatized silicon is derivatised in such a manner that it binds to a tumour marker. Preferably the derivatized silicon is derivatised in a such a manner that it binds to one or more of the following tumour markers: carcino embryonic antigen, prostate specific antigen, carbohydrate antigen, carbohydrate antigen - 15-3, carbohydrate antigen 19-9,
 30 carbohydrate antigen - 125, carbohydrate antigen - 27-29, carbohydrate antigen - 549.

The or at least one of the storage means may comprise silicon oxide. The or at least one of the storage means may comprise porous silicon oxide.

- 35 Preferably the silicon oxide has the chemical formula SiO_x where $0.1 \leq x \leq 2$.

Advantageously the or at least one of the silicon storage means comprises a sample of porous silicon that has been partially oxidised.

For the avoidance of doubt the term “partially oxidised” is used, in the specification, to describe a material that has been oxidised in such a manner that part of the material remains completely unoxidised. Therefore a sample of silicon that had been partially oxidised would comprise silicon in a completely unoxidised state.

The or at least one of the silicon storage means may comprise a sample of porous silicon, the sample of porous silicon being partially oxidised in such a manner that between 0.1% and 99% of the porous silicon atoms are bonded to oxygen. The or at least one of the silicon storage means may comprise a sample of porous silicon, the sample of porous silicon being partially oxidised in such a manner that between 0.1% and 10% of the porous silicon atoms are bonded to oxygen. The or at least one of the silicon storage means comprises a sample of porous silicon, the sample of porous silicon being partially oxidised in such a manner that between 0.1% and 50% of the porous silicon atoms are bonded to oxygen.

Preferably the collection device comprises a first silicon storage means and a second silicon storage means. The contact means may, when in use, cause the first sample of silicon to contact at least part of one breast of the subject and the second sample of silicon to contact the other breast of the subject.

Significant differences, between the NAF secreted by each breast, in the composition and/or volume of nipple aspirate fluid (NAF) is one indication of breast disease. Therefore application of samples of silicon to both breasts may be advantageous, since it could allow such an indication to be obtained.

The contact means may comprise a nipple attachment means. The nipple attachment means may have a shape and size such that it capable of fitting over a nipple. The nipple attachment means may comprise: a cup, sleeve, or teat.

The nipple attachment means may comprise: a resiliently flexible teat, a resiliently flexible cup, or a resiliently flexible sleeve.

The nipple attachment means may comprise a resiliently flexible material such as a silicone material.

The contact means may comprise a cup having a shape and size such that it is capable of fitting over a breast. The cup may comprise a flexible material. The cup may comprise a plastic material.

The contact means may comprise a tape and/or sheet and/or fabric and/or plastic material and/or patch. The contact means may comprise an adhesive and/or flexible band and/or flexible garment. The contact means may comprise a resiliently flexible band and/or resiliently flexible garment. The garment may be designed to fit around part of a human subject, for example the garment may be a brassiere. The garment may comprise a means for heating one or both breasts of the subject.

The contact means may result in the silicon storage means being in contact with the breast for the whole time of collection, or it may result in the silicon storage means being in contact with the breast intermittently during collection.

The collection device may comprise a heating means. The heating means may comprise polycrystalline silicon. The heating means may comprise a polycrystalline resistive heater.

The collection device may further comprise a heater power supply for applying a potential difference across the polycrystalline resistive heater.

The heater power supply may have a construction such that, when in use, the potential difference applied across the polycrystalline resistive heater varies sinusoidally with time.

The collection device may further comprise a temperature control means. The temperature control means may comprise a temperature sensor and a heating means. The temperature sensor may comprise a thermocouple.

When in use the temperature sensor may be in contact with the surface of at least part of a breast of the subject.

The temperature control means may have a construction such that, when in use, the temperature of the breast in the region of the collection device is maintained in the range 37 C to 45 C.

The heating means may allow the breast to be heated thereby promoting the secretion of NAF.

5 The collection device may further comprise means for applying an external expression agent to part of the breast. The means for applying the external expression agent may be a reservoir for containing the expression agent. The expression agent may comprise salicylic acid. The expression agent may comprise an aqueous solution of salicylic acid.

10 The use of salicylic acid is advantageous since it is capable of dissolving the keratin plugs that block the lactiferous ducts.

The collection device may comprise a pump for reducing the pressure on at least part of a breast of a subject. The pump may have a construction such that it is capable of a reducing the pressure in the evacuated region by between 50 to 200 mm Hg relative to the pressure of the non-evacuated region of the breast.

15 The collection device may further comprise a collection power source for applying a potential difference between the silicon storage means and at least part of the breast of the subject.

20 The application of a potential difference between the silicon storage means and the breast may facilitate the collection of the cancer markers from the fluid expressed from the breast.

25 The or at least one of the silicon storage means may comprise a plurality of silicon needles and/or barbs. The or at least one of the silicon storage means may comprise a plurality of silicon needles and/or barbs each silicon needle and/or barb comprising porous silicon.

The or at least one of the silicon storage means may comprise between 10 and 1000 needles and/or barbs. Preferably the or at least one of the silicon storage means may comprise between 10 and 100 needles and/or barbs.

The or at least one of the silicon storage means may comprise a plurality of silicon needles and/or barbs, each needle and/or barb having a tip diameter between 1 and 50 microns.

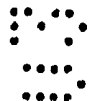
The or at least one of the silicon storage means may comprise a plurality of the silicon needles and/or barbs, each needle and/or barb having a base width between 200 and 500 microns.

- 5 The or at least one of the silicon storage means may comprise a plurality of silicon needles and/or barbs, each needle and/or barb having a height between 50 microns and 5 mm.

The or at least one of the silicon storage means may comprise a plurality of silicon needles and/or barbs, each needle and/or barb having a height between 150 microns and 2 mm.

- 10 The or at least one of the silicon storage means may comprise a plurality of silicon needles and/or barbs, each needle and/or barb having a height between 50 microns and 600 microns. The or at least one of the silicon storage means may comprise a plurality of silicon needles and/or barbs, each needle and/or barb having a height between 200 microns and 600 microns.

- 15 The silicon collection means may comprise a plurality of silicon needles, each needle having a duct passing from the tip, and through the body of, the needle.



The mammary fluid collection device may comprise a silicon storage means, the storage means comprising a plurality of silicon needles and/or barbs each silicon needle and/or



- 20 barb being integral with a substrate. The spacing between any two nearest adjacent needles and/or barbs, measured along the surface of the substrate, may be between 100 and 1000 microns. Preferably the spacing between any two nearest adjacent needles and/or barbs, measured along the surface of the substrate, may be between 100 and 300 microns.



25

The mammary fluid collection device may comprise a plurality of silicon needles and/or barbs each silicon needle and/or barb being integral with at least one silicon substrate. The or at least one of the silicon substrates may comprise bulk crystalline silicon.

- 30 The mammary fluid collection device may comprise a plurality of silicon needles and/or barbs each of the needles and/or barbs being integral with a silicon substrate having a planar substrate surface. At least some of the silicon needles and/or barbs may be non-perpendicular to the substrate surface.

The use of silicon needles and/or barbs may be of value in puncturing the keratin plugs that block the lactiferous ducts through which fluid is expressed. The use of porous silicon needles and/or barbs may allow the mammary fluid to pass into the pores of the porous silicon once the blocked ducts have been opened.

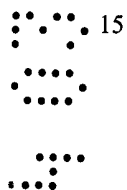
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If the dimensions of the needles and/or barbs are sufficiently small, there should be no or minimal discomfort caused to the human subject by their use.

The use of a relatively large number of closely spaced silicon needles and/or barbs markedly increases the chances of obtaining samples of mammary fluid from each of the lactiferous ducts, thereby increasing the chances of detecting any abnormality.

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The number, position, and orientation of each needle and/or barb may be such that there is a high probability of puncturing the keratin plugs when the collection device is in use.



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A further advantage of silicon is that the electrical and mechanical components, such as pumps, heaters, and needles and/or barbs, may all be fabricated at least partly from silicon.



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The or at least one of the silicon storage means may comprise a silicon particulate product, the silicon particulate product comprising a multiplicity of silicon particles, each silicon particle comprising one or more of: bulk crystalline silicon, porous silicon, polycrystalline silicon, and amorphous silicon. At least some of the silicon particles may be partially oxidised.

The mean particle size of the silicon particulate product may be between 1 micron and 1 mm. The mean particle size of the silicon particulate product may be between 10 microns and 100 microns.

25

Advantageously the silicon storage means comprises porous silicon having a porosity between 1% and 99%, more advantageously the porous silicon has a porosity between 10% and 80%, even more advantageously the porous silicon has a porosity between 10% and 60%.

30

The silicon storage means may comprise microporous silicon, having a pore diameter between 1.0 and 2.0 nm.


35


The silicon storage means may comprise mesoporous silicon, having a pore diameter between 2.0 and 50 nm.


5 The silicon storage means may comprise macroporous silicon, having a pore diameter between 50 nm and 5 microns.

10 The collection device may further comprise a backing layer. The backing layer may be constructed in such a manner that it forms a receptacle for the or at least one of the silicon storage means. At least part of the backing layer may form at least part of said contact means. The backing layer may be permeable or impermeable.

The backing layer may comprise silicon, the backing layer may comprise bulk crystalline silicon.

15  The backing layer may serve to isolate the or at least one of the silicon storage means from the environment surrounding the attachable collection device, including neighbouring areas of skin. The backing layer may be permeable to allow water vapour to escape from the mammary fluid collection device.

20  The mammary fluid collection device may further comprise a semipermeable membrane.

 The semipermeable membrane may form a barrier through which, when in the collection device is in use, the mammary fluid passes before collection in and/or on the silicon storage means.

25 The use of a semipermeable membrane may prevent unwanted material, such as particles of skin, passing into or onto the silicon storage means.

30 The body fluid collection device may comprise at least one reference storage means and at least one derivatised storage means. The or each reference storage means comprising silicon. The or each derivatised storage means comprising derivatised silicon, the derivatisation being selected such that, when brought into contact with mammary fluid, the derivatised silicon binds to a component of the mammary fluid.

The use of reference and derivatised storage means may be advantageous. Analysis of both the reference and derivatised storage means may allow comparison of the two types of storage means to determine whether binding to a tumour marker has occurred.

- 5 The or at least one of the silicon storage means may comprise at least one first storage means and at least one second storage means. The or at least one of said first storage means may comprise a first type of derivatised silicon, which is derivatised in such a manner that, when brought into contact with mammary fluid, the first type of derivatised silicon binds to a first component of the mammary fluid. The or at least one of said second
- 10 silicon storage means may comprise a second type of derivatised silicon, which is derivatised in such a manner that, when brought into contact with mammary fluid, the second type of derivatised silicon binds to a second component of the mammary fluid.

The use of two types of derivatisation allows the detection of more than one component of the mammary fluid. The presence of cancer in a subject may be indicated by more than one component in the mammary fluid. Measurement of the relative concentrations of the first and second components of the mammary fluid may also provide an indication of the presence of cancer in the subject.

- 20 The collection device may further comprise at least one antibody. The collection device may comprise at least one antibody and the or at least one of the silicon storage samples may comprise a sample of porous silicon, the antibody being disposed in and/or on at least part of the sample of porous silicon.

- 25 The collection device may comprise a radiolabelled antibody or an antibody comprising a fluorescent group.

- The or at least one of the silicon storage means may comprise a sample of porous silicon in and/or on which a radiolabelled antibody is disposed or an antibody comprising a
- 30 fluorescent group is disposed.

According to a second aspect the invention provides a method of collecting mammary fluid and/or a component of mammary fluid from a human subject, the method comprising the steps:

- (a) placing at least one silicon storage means in fluid communication with at least part of a breast of a subject;
- (b) allowing and/or causing the breast to secrete mammary fluid; and
- (c) collecting the mammary fluid and/or a component of the mammary fluid, secreted by the breast, in and/or on the or at least one of the silicon storage means.

The step (b) may comprise the step of allowing and/or causing the breast to secrete one or more of: nipple aspirate fluid, human milk, and colostrum milk.

- Preferably the step (b) comprises the step of allowing and/or causing the breast to secrete nipple aspirate fluid.

The or at least one of the silicon storage means may comprise one or more of porous silicon, polycrystalline silicon, bulk crystalline silicon, and amorphous silicon.

The or at least one of the silicon storage means may comprise a sample of silicon that has been partially oxidised.

The step (a) may comprise the step of causing the or at least one of the silicon storage means to contact at least part of the breast of the subject.

The step (a) may comprise the step of placing the or at least one of the silicon storage means in fluid communication with one or both of the breasts of the subject.

The step (a) may comprise the step of placing the or at least one of the silicon storage means in contact with at least part of a nipple of a human subject.

The step (a) may comprise the step of placing the or at least one of the silicon storage means in contact with at least part of an areola of a human subject.

The method may further comprise the step (d) of assaying the mammary fluid and/or a component of the mammary fluid that has been collected on and/or in at least part of the or at least one of the silicon storage means.

The step (d) may be performed after step (c) or during step (c).

The step (d) may comprise the step of assaying the mammary fluid for the presence and/or quantity of one or more of the following substances: carcino embryonic antigen, prostate specific antigen, carbohydrate antigen, carbohydrate antigen - 15-3, carbohydrate antigen 19-9, carbohydrate antigen - 125, carbohydrate antigen - 27-29, carbohydrate antigen - 549. Other antigens for which an assay may be performed are given in US 6,063,029 which is herein incorporated by reference.

The or at least one of the silicon storage means may comprise a sample of porous silicon in and/or on which at least one antibody is disposed. The method may further comprise the step of reacting the or at least one the antibodies with one or more tumour marker antigens. The or each tumour marker antigen may be present in the secreted mammary fluid. The step (d) may comprise the step of analysing a component of the mammary fluid using a conventional immunoassay such as horse raddish peroxide, or alkaline phosphatase.

The step (d) may comprise the step of assaying the mammary fluid using one or more of the following techniques: Laser Induced Mass Analysis, Mass Assisted Laser Desorption ionisation, Gel Electrophoresis, Capillary Electrophoresis, RadiolImmunoAssay, and Chemiluminescent Assay, ELISA immunoassay, Immunoprecipitation Assay, and Affinity Purification Assay.

The method may further comprise the step of administering a systemic expression agent to the subject. The expression agent may comprise one or more of the following substances: salicyclic acid, nasal oxytocin, salagen, and prolactin.

The use of a systemic expression agent promotes the expression of NAF, for example by inducing hormonal changes within the subject.

The step (c) may comprise the step of collecting between 30 and 500 micro litres of mammary fluid.

The method may comprise the further step of separating the mammary fluid from at least part of the or at least one of the silicon storage means.

The method may comprise the step of separating the mammary fluid collected on the or at least one of the silicon storage means by immersing the or at least one of the silicon

storage means in a solvent; the solvent may be selected from one or more of: water, ethanol, acetone, and acetonitrile.

The method may comprise the step of separating the mammary fluid collected on the or at least one of the silicon storage means by immersing the or at least one of the silicon storage means in a solvent and applying a bias to the or at least one of the silicon storage means; the solvent may be selected from one or more of water, ethanol, and acetone.

The step (b) may comprise the step of heating at least part of the breast to a temperature in the range from 37 C to 45 C.

The invention will now be described, by way of example only, with reference to the following diagram:

Figure 1 shows a schematic diagram of a collection device according to the invention.

Figure 1 shows a schematic diagram of a mammary fluid collection device, generally indicated by 11, according to the invention. The collection device 11 comprises a silicon storage means 12, and an attachment means 15. The silicon storage means 12 comprises a sample of porous silicon 13, and a portion of bulk crystalline silicon 14. Anodisation of bulk crystalline silicon by a standard technique such as that described in US 5, 348, 618, which is herein incorporated by reference results in the formation of the sample of porous silicon 13 which is connected to the remaining portion of bulk crystalline silicon 14. The attachment means 15 maintains the storage means in contact with at least part of a breast of the subject, which in this case is a nipple of a human subject.

The attachment means 15 comprises a resiliently flexible cup that is formed from a silicone material.

Once the sample of porous silicon 13 has been in contact with the nipple of a human subject for an appropriate interval, under conditions which cause the area of the nipple in contact with the storage sample to secrete a sample of mammary fluid, it is removed from the nipple and assayed by one of the following techniques: MALDI, SIMS, and SEM. The sample of mammary fluid may also be analysed by one of: photoluminescence spectroscopy, reflectivity spectroscopy, absorbance spectroscopy, and fluorescence spectroscopy. MALDI may be used to determine the uptake of molecules contained in the mammary fluid sample,

SIMS may be used to determine the uptake of elements contained in the mammary fluid sample. The spectroscopic analysis may be used to determine the presence of a mammary fluid sample on and/or in the storage sample of porous silicon 13.

- 5 The collection device may further comprise an antibody. The antibody may incorporated into the sample of porous silicon by incubating the sample of porous silicon in a solution of the antibody at 37 C to 56 C for 1 to 24 hours.

10 The surface of a (100) oriented Si wafer may be processed into an array of needles by standard wet etching techniques such as those described in IEEE Transactions in Biomedical Engineering Vol 38, No 8, August 1991, p 758 to 768, which is hereby incorporated by reference. For example, two sets of deep (200 micron) orthogonal cuts may be made into a 380 micron thick wafer. The wafer is rotated by 90 degrees between the first set of n cuts in one direction, and the second set of m cuts in the orthogonal direction. This sawing does not cut through the wafer at any point but creates an array of n x m square columns having an aspect ratio determined by the spacing of the cuts. The subsequent etching processes to define dart-like shapes then involves two further steps. A first chemical etch removes saw damage, isotropically reducing the width of the columns and rounding the edges at the base of the columns. It utilizes an HF: HNO₃ etch (eg 5% to 95%) that is conducted with vigorous agitation. A second chemical etch may be performed under static conditions that promote preferential attack of the top of the columns to create pointed tips and a tapered shaft.

25 In this way an array of needles may be fabricated, each needle having a tip diameter between 1 and 50 microns, a base width between 200 and 500 microns, and being separated from the nearest adjacent needle by between 100 and 300 microns.

The needles may be porosified by standard stain etch or anodisation techniques.

- 30 The array of needles may be applied to a nipple of a human subject in such a manner that at least some of the needles enter the ducts located in the tip of the nipple. NAF may then pass into the pores of the porosified needles. After an interval of time the array of needles is removed from the human subject, and assayed for tumour markers. The small dimensions of the needles should ensure that there is no or minimal discomfort caused to the human subject.
- 35

Claims

1. A mammary fluid collection device comprising: (a) at least one silicon storage means,
and (b) a contact means which, when in use, causes and/or allows the or at least one of
5 the silicon storage means to contact at least part of a breast of a human subject.

2. A collection device according to claim 1 characterised in that the silicon storage means
comprises porous silicon.

10 3. A collection device according to claim 1 characterised in that the silicon storage means
comprises partially oxidised silicon.

4. A collection device according to claim 1 characterised in that the device further comprises
a temperature control means that has a construction such that, when in use, the
15 temperature of the breast in the region of the collection device is maintained in the range
37 C to 45 C.

5. A collection device according to claim 1 characterised in that the device comprises
salicyclic acid.

20 6. A collection device according to claim 1 characterised in that the device comprises a
pump.

7. A collection device according to claim 1 characterised in that the or at least one of the
25 silicon storage means comprises a plurality of silicon needles and/or barbs.

8. A collection device according to claim 7 characterised in that each of the silicon needles
and/or barbs is integral with a substrate having a substantially planar substrate surface.

30 9. A collection device according to claim 8 characterised in that the smallest angle between
the axis of at least one of the needles and/or barbs and the planar substrate surface is
between 89 degrees and 10 degrees.

10. A collection device according to claim 9 characterised in that the smallest angle
35 between the axis of at least one of the needles and/or barbs and the planar substrate
surface is between 85 degrees and 30 degrees.

11. A collection device according to claim 1 characterised in that the silicon storage means comprises derivatized silicon, the silicon being derivatised in such a manner that it binds to one or more of the following tumour markers: prostate specific antigen, Carcino Embryonic Antigen, Carbohydrate Antigen -15-3, Carbohydrate Antigen 19-9, Carbohydrate Antigen 125, Carbohydrate Antigen 27-29, Carbohydrate Antigen 549.

12. A collection device according to claim 1 characterised in that the device further comprises at least one antibody.

13. A collection device according to claim 1 characterised in that the or at least one of the silicon storage means comprises a sample of porous silicon, and in that the antibody is disposed in and/or on the sample of porous silicon.

14. A method of collecting mammary fluid or a component of mammary fluid from a human subject, the method comprising the steps:

- (a) placing at least one silicon storage means in fluid communication with a breast of a subject;
- (b) allowing and/or causing the breast to secrete mammary fluid; and
- (c) collecting the mammary fluid, secreted from the breast, in and/or on the or at least one of the silicon storage means.

15. A method according to claim 14 characterised in that the step (b) comprises the step of allowing and/or causing the breast to secrete nipple aspirate fluid.

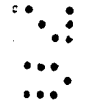
16. A method according to claim 14 characterised in that the method comprises a further step (d) of assaying the mammary fluid for the presence and/or quantity of one or more of the following substances: prostate specific antigen, CEA, CA-15-3, CA 19-9, CA 125, CA27-29, CA 549.

17. A method according to claim 16 characterised in that the method comprises the further step (d) of assaying the mammary fluid using one or more of the following techniques: laser induced mass analysis, mass assisted laser desorption ionisation, enzyme ImmunoAssay, Gel Electrophoresis, Capillary Electrophoresis, RadioImmunoAssay, and Chemiluminescent Assay.

18. A method according to claim 14 characterised in that the method further comprises the step of administering one or more of: salicyclic acid, nasal oxytocin, salagen, and prolactin to the human subject.

5

19. A method according to claim 14 characterised in that step (b) comprises that step of collecting mammary fluid from both breasts of a subject.





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Application No: GB 0307453.1
Claims searched: 1-19

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Date of search: 26 November 2003

Patents Act 1977 : Search Report under Section 17

Documents considered to be relevant:

Category	Relevant to claims	Identity of document and passage or figure of particular relevance	
A		US 6221622 B1	Love
A		US 3786801	Sartorius
A		WO 02/083005 A3	Hung
A		US 2002/0013539 A1	Hung

Categories:

X Document indicating lack of novelty or inventive step	A Document indicating technological background and/or state of the art.
Y Document indicating lack of inventive step if combined with one or more other documents of same category.	P Document published on or after the declared priority date but before the filing date of this invention.
& Member of the same patent family	E Patent document published on or after, but with priority date earlier than, the filing date of this application.

Field of Search:

Search of GB, EP, WO & US patent documents classified in the following areas of the UKC^V:

A5R, G1B

Worldwide search of patent documents classified in the following areas of the IPC⁷:

A61B, A61M, G01N

The following online and other databases have been used in the preparation of this search report:

JAPIO, WPI, EPODOC