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(54) **Wound characterization by tissue potential difference.**

(57) The invention provides a tissue contact unit for application on the human or animal tissue, the tissue contact unit comprising 4-10 electrodes, the tissue contact unit further comprising a reference point around which the electrodes are configured, wherein the electrodes have inter electrode distances of at least 0,25 cm, and wherein the electrodes have distances to the internal reference point in the range of 0,25-5 cm. With such tissue contact unit potential difference can be measured which can be translated by a control unit into geometric, deformation, discontinuity, or other parameters of the measured subcutaneous, surface, or other, tissue.

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Wound characterization by tissue potential difference

FIELD OF THE INVENTION

The invention relates to an analysis unit, amongst others for wound characterization and/or wound monitoring. The invention further relates to a tissue contact unit that can be part of such analysis unit.

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BACKGROUND OF THE INVENTION

In view of medical treatment of wounds and or characterization of wounds, it is desirable to be able to analyze and/or monitor wounds. US2001051774 describes e.g. a method and apparatus that use complex impedance measurements of tissue in human or animal bodies for the detection and characterization of medical pathologies. An analysis of the complex impedance measurements is performed by a trained evaluation system that uses a nonlinear continuum model to analyze the resistive, capacitive, and inductive measurements collected from a plurality of sensing electrodes. The analysis of the impedance measurements results in the construction of a multidimensional space that defines the tissue characteristics, which the trained evaluation system uses to detect and characterize pathologies. The method and apparatus are claimed to be sufficiently general to be applied to various types of human and animal tissues for the analysis of various types of medical pathologies.

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Amongst others, US2001051774 describes an apparatus for detection and characterization of one or more medical pathologies within an object under study comprising:

- (a) a current source adapted to provide current with a predetermined current waveform, said current source being disposed so as to be capable of electrically stimulating such object;
- (b) a plurality of electrodes being disposed relative to such object to receive current from such object, each of said plurality of electrodes being capable of measuring a voltage; (c)
- (d) means for controlling such current source and said plurality of electrodes to produce and receive current; and (d) a device coupled to said plurality of electrodes and configured to perform the steps of: (ii) calculating a plurality of complex impedances, each of said plurality of complex impedances corresponding to a current drive path defined by said current source and one of said plurality of electrodes; (ii) constructing a multidimensional representation of

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the electrical characteristics of a region within said object under study using said plurality of complex impedances; and (iii) detecting and characterizing such one or more medical pathologies within said object under study from said multidimensional representation.

5 SUMMARY OF THE INVENTION

Currently, it is not possible to measure tissue deformations, shape, depth, and characterize the chemical composition of a wound or a multi-layered wound simultaneously and in real-time, without the patient having to visit a diagnostic facility and undergo specialized, time consuming, and expensive diagnostic procedures. In practice, in case of complications in wound healing, including, but not limited to, infections, hernias, or necrosis of tissue, patients do not consult their physician until they start experiencing discomfort. Specifically, in the case of hernias: hernias take a lot of time to emerge, sometimes years. This exceeds the usual observation interval, which means that the patients will not visit the physician until they start experiencing discomfort, at which point the problem will have already manifested itself.

Moreover, it is currently not possible to know the variables described above for a multi-layered wound, i.e. the wound created from an abdominal operation, consisting sutured muscles (wound 1) and sutured skin on top (wound 2).

This diagnostic deficit also applies during surgery, where surgeons often have limited ability to be aware of wounds, exact locations of wounds (and much less their shape and depth) unless they are actually visible. This applies to wounds in organs, or any type of living tissue.

Finally, since these measurements are traditionally taken in hospital environments where patients are assumed to stay immobile during the tests, there is no smart device, to our knowledge, that can warn patients when they are moving their body in a way that will damage their wound.

Monitoring of wounds is generally limited to the time where the patient is still hospitalized. Afterwards, the doctor may check for abnormalities during regular checkups. It would be possible to use portable devices, for instance in the form of impedance sensors imbedded in the wound dressing, or digital optical measurements. These devices use the electrical impedance method, and may provide feedback on its healing progress by measuring the electrical impedance between the electrodes. However, this leads to a characterization of wounds as a whole, and it is coupled with changes in wound geometry. Also, present electrical impedance devices may not be able to provide separate information for more than

one wound, unless a second device is applied on the second wound, and so on. This inability in characterizing wounds of arbitrary shape with the detail described above, using electrical impedance, includes single or multi-layered wounds located on the skin, subcutaneous or in general internal wounds, or any combination of the above.

5 A common approach to decouple the impedance measurements from the geometry is use of optical means, such as a camera, or an optical examination from a physician. In case of a subcutaneous wound, this can be other imaging means, such as ultrasound. These approaches, however, cannot be real-time and usually involve spending time and money.

10 During surgery, doctors generally use imaging means before the operation in order to try and map the existing wounds, although this is often not practiced, especially for emergencies. Real-time imaging means include ultrasound and electrical impedance tomography (which is still highly experimental).

In the case of hernia detection, even nowadays it is usually accidental. Since
15 incisional hernias can take years to manifest, they are detected both because a patient experienced discomfort and, thus, underwent examinations, or because the doctor noticed it in an ultrasound (or similar) conducted for a different reason.

Finally, up to date there has been no smart device, to our knowledge, that can warn patients when they are moving their body in a way that will damage their wound.

20 Hence, it is an aspect of the invention to provide an alternative analysis unit and/or an alternative tissue contact unit as part of such alternative analysis unit, which preferably further at least partly obviate one or more of above-described drawbacks and/or which can provide one or more of the above defined desires.

In a first aspect, the invention provides an analysis unit comprising:

25 (a) a tissue contact unit for application on the human or animal tissue, the tissue contact unit comprising at least 3 electrodes, especially at least 4 electrodes, even more especially 4-10 electrodes, such as 5-8 electrodes, like 6-8 electrodes, the tissue contact unit further comprising a reference point around which the (at least 3, such as 4-10) electrodes are configured, wherein the (at least 3, such as 4-10) electrodes have inter electrode distances of
30 at least 0,15 cm, especially at least 0,25 cm, like up e.g. to 5 cm, such as up to 2 cm, and wherein the (at least 3, such as 4-10) electrodes have distances to the internal reference point in the range of 0,25-5 cm.

In this embodiment, the analysis unit comprises (only) the tissue contact unit; hence the tissue contact unit per se is also an aspect of the invention. Especially, the analysis

unit, or more precisely the tissue contact unit, comprises 6-10, such as especially 6-8 electrodes. It appears that with this number of electrodes, reliable measurements can be made, with one set for generating the (electrical) potential difference, and the other sets for measuring (electrical) potential differences. The fact that the tissue contact unit may have 6-10 electrodes, such as 5-8 electrodes, does not exclude devices with more than the indicated electrodes to be within the ambit of the claims.

In an embodiment, the first electrode and the second electrode have distances to the internal reference point in the range of 0,5-3 cm, and the other electrodes have larger distances to the internal reference point than the first electrode and the second electrode.

However, other configurations are possible as well. When using a set of reference electrodes, these may especially be configured at larger distances to the internal reference point than any of the other electrodes of the tissue contact unit.

The analysis unit can further optionally comprise:

(b) a voltage generator configured to generate a (electrical) potential difference between a first electrode and a second electrode.

The voltage generator may be configured to generate a difference in electrical potential (between the first and the second electrode). This voltage generator may be integrated in one single device, together with the tissue contact unit, such as being integrated in the tissue contact unit. However, the tissue contact unit and the voltage generator may also be two separate devices, which during use can be electrically connected. In principle, such is e.g. in hospital applications, the voltage generator may even wireless provide power to two (or optionally more) of the electrodes of the tissue contact unit. The first electrode or the second electrode will in general be grounded.

The analysis unit can further optionally comprise:

(c) a control unit, configured to measure a potential difference between one or more sets of two of the (at least 3, such as 4-10) electrodes, of which each set comprises the first or second electrode and one other electrode.

Again, this control unit may be integrated in one single device, together with the tissue contact unit, such as being integrated in the tissue contact unit. However, the tissue contact unit and the control unit may also be two separate devices, which during use can be electrically connected. The control unit may especially be configured to measure a (electrical) potential difference (potential difference method) between at least three sets of two of the (at least 3, such as 4-10) electrodes. The control unit may in an embodiment thus

not be a unit that is able to perform impedance measurements, as the invention especially relates to electrical potential difference measurements

This control unit may also control the voltage generator. Hence, the control unit can be configured to control the voltage generator. The potential difference that is

5 measured between the other electrodes and the first or the second electrode will in general be performed between a grounded electrode (first or second) and one or more of the other electrodes. The control unit may especially be configured to measure real-time potential differences between the first or the second electrode, and one or more of (or especially all) the other electrodes. Therefore, the term potential differences are applied, as this may relate
10 to a plurality of measurements in time as well between a plurality of other electrodes, or both.

Further, the control unit is especially configured to derive from the electrode signal(s) information about geometric and other tissue parameters of subcutaneous, surface, or other tissue. Hence, the control unit may further be configured to generate a sensor signal comprising information on the measured (electrical) potential difference(s).

15 Optionally, this control unit may be further be configured to process the measured potential differences between the one or more sets of two of electrodes (such as to provide said sensor signal (and/or warning signal, see below)). Therefore, the control unit may especially be configured to measure and process the potential differences between the first electrode or the second electrode, and one or more of the other electrodes. Thus, the
20 control unit may especially be configured to measure and process the potential differences between one or more sets of two of the (at least 3, such as 4-10) electrodes, of which each set comprises the first or the second electrode and one other electrode of the (at least 3, such as 4-10) electrodes. For instance, the difference in potential is applied between the first and the second electrode, and the differences in electrical potential between the set of the first
25 electrode and a third electrode, and a set of the first electrode and the fourth electrode, and a set of the first electrode and the fifth electrode may be measured. From these three measurements, tissue data can be derived.

Wireless technology, such as Bluetooth, can be used for communication (including control) between the control unit and the voltage generator, and/or between the
30 control unit and an external control and/or processing unit, such as in a control room of a hospital. Hence, the control unit may be configured to measure the above indicated potential difference(s) and send the thus obtained data (sensor signal) (wireless) to a remote control and/or processing unit (mother control unit, see below).

For instance, in a hospital application, or in a domestic application, wireless technology, like Bluetooth or another wireless technology, can be applied, by which the analysis unit can be configured or read out remotely. Optionally, the control unit is controlled (or is configured to be controlled) by an external (mother) control unit; the latter being

5 configured to control the control unit and/or process the obtained sensor signal. Again, wireless technology can be applied for communication. The external (mother) control unit may also be applied to process the data (sensor signal), though optionally the control unit of the analysis unit may process the data or partly process the data obtained by measuring the potential difference(s).

10 Hence, the term control unit may relate to a local control unit but optionally also to a plurality of communicating control units, with one main (dominant) control unit (which can also be indicated as mother control unit). The control unit may thus include one or more sensors to determine an electrical potential difference between sets of (two) electrodes.

15 The term control unit may relate to a plurality of control units, of which one or more may be subordinate to a main (mother) control unit.

Especially, the analysis unit comprises (a) the tissue contact unit, (b) the voltage generator, and (c) the control unit. In yet another embodiment, the analysis unit comprises (a) the tissue contact unit, (b) the voltage generator, and (c) the control unit,

20 wherein the latter is configured wireless from the tissue contact unit and the voltage generator. Hence, in a specific embodiment, the a) the tissue contact unit and (b) the voltage generator are a single unit, and the c) the control unit is a separate unit, which can be connected with electrical wires and/or wireless with the voltage generator and the tissue contact unit. During use, the control unit can even be remote (i.e. physically remote) from the

25 user wearing the tissue contact unit (on his/her/its tissue).

Through the use of the electrical potential difference method, we can estimate the geometry of a single-layered or multi-layered wound, by applying voltage, either AC or DC, and then measuring the electrical potentials on the surrounding tissue. This provides e.g. the user, and/or the user's physician, the capacity to measure tissue deformation, wound

30 shape, wound depth and chemical composition. This means that we can characterize changes in the topology, independently to tissue deformation (due to body motion or posture). This approach allows for a portable, inexpensive, and possibly non-invasive way to diagnose complications as early as possible. Another application is, of course, a measurement instrument for scientific research. Hence, in a specific embodiment, the control unit is

configured to derive from the potential difference data information about one or more of tissue deformation, wound shape, wound depth and chemical composition.

This technique can also be applied during surgery, in order to detect wounds in organs or, in general, living tissue, when these wounds cannot be spotted by optical means (such as when covered by blood or are located in a blind spot). This can, for instance, help the surgeons locate a source of bleeding during surgery.

Moreover, this technique can provide a portable device that can be used by the patients themselves to detect the possible existence of hernias, and alarm their physician if that is the case.

Finally, by measuring tissue deformations, the device can detect when a patient is moving in a way that may damage the wound, and give a warning signal.

Through the use of the potential difference method, we can estimate the geometry of a single-layered or multi-layered wound, by applying voltage, either AC or DC, and then measuring the electrical potentials on the surrounding tissue, or an overlaid conductive patch or superstrate (i.e. layer over the electrodes) (see also below).

Especially, DC voltages in the range of 0.2-12 V are applied, such as in the range of 0.5-1.5 V. Hence, in an embodiment the voltage generator is configured to generate a direct current. Thus, during use, the voltage generator may apply the indicated (DC) voltage (to the first and the second electrode).

Optionally, the voltage generator is configured to generate an AC voltage. In such instance, the voltage may be in the range of 0.2-20 V, and the frequency may be in the range of 20-10.000 Hz. Thus, during use, the voltage generator may apply the indicated (AC) voltage (to the first and the second electrode).

This may provide us the capacity to measure (real-time) tissue deformations, wound shape, depth and, in the first case, chemical composition. This means that we can characterize changes in the topology, independently to tissue deformation (due to body motion or posture). This approach allows for a portable, inexpensive, and possibly non-invasive way to diagnose complications as early as possible. Another application is, of course, a measurement instrument for scientific research.

Moreover, this technique can provide a portable device that can be used by the patients themselves to detect the possible existence of hernias, and alarm their physician if that is the case.

Finally, by measuring tissue deformations, the device may be able to detect when a patient is moving in a way that will damage the wound, and give warnings.

The method works by comparing potential differences (potential difference method, PDM) in a locally induced electrical field around the wound that we want to characterize. All electric potential differences are measured in respect to the same ground (such as the first or the second electrode), thus enabling the direct measurement of electric potentials. Any change on wound geometry or electrical properties (linked to its composition), induces changes upon the shape of the electric field. This deviation from the original (reference) situation is measured by electrodes at specific places. Then, the electric field is mathematically reconstructed using these measurements, and optionally compared to data from simulations, as well as the original (reference) data; these reference data can be measured remotely from the wound. Further, these reference data can be measured once, or can be measured several times, while the tissue contact unit is applied. For instance, each day one or more times reference values can be measured. Hence, in an embodiment, two electrodes are applied as reference electrodes (of which one is grounded). One or both, especially both, of these electrodes can be more remote from the reference point than the other electrodes.

This process allows us to match the changes in the measured electric potentials to the boundary of the wound and thus, estimate its geometry. Since the partial differential equations of our problem have a unique solution in a domain where all the boundaries have a Neumann or Dirichlet boundary condition attached, the field's shape is different for every possible configuration of parameters, geometrical or otherwise. By mathematically reconstructing the electric field, this fact is exploited in order to extract decoupled data on geometry of the wound's boundary, as well as the electrical properties of the domain contained within that boundary. Finally, based on the above, the method can also provide metrics for the deformation of tissue around the wound using the same principle, as well as take these deformations into account during the calculations.

An alternative (or supplementary) method for measuring deformations can be by applying a conductive patch over the wound and estimating the bi-axial strain field, applying the same method described above, only this time on the patch instead of through the tissue. A layer, such as a patch, over the electrodes implies in general that during use the electrodes are not in (physical) contact with the skin or penetrate the skin into the tissue.

This method can be embodied in a device that uses a plurality of electrodes which apply and measure electric potentials around a single-layered or multi-layered skin, subcutaneous, or internal wound. These can be applied by piercing the tissue, through means of an adhesive superstrate, wound bandage, wound coating, (patch) or otherwise.

In an embodiment, the analysis unit includes a bandage as means of adhesion to human or animal tissue. This bandage may be an adhesive bandage or a non-adhesive bandage. Hence, in an embodiment, the bandage is an adhesive bandage, comprising one or more adhesive regions. In an embodiment, the bandage is a textile bandage. In a further
 5 embodiment, the bandage is a polymeric foil. During use, the tissue contact may be between the bandage and the tissue, or the bandage may be between the tissue and the tissue contact unit. In the latter embodiment, the electrodes may penetrate the bandage and have physical contact with the tissue. Hence, the analysis unit, or especially the tissue contact unit, may include a (adhesive) bandage or other means of adhesion (for application on human or animal
 10 tissue).

Therefore, in an embodiment, the tissue contact unit includes a bandage or other means of adhesion (for application on human or animal tissue), and especially, the means of adhesion may comprise an adhesive bandage, comprising one or more adhesive regions (150).

15 The tissue contact unit may be integrated in the bandage, but the tissue contact unit may also be used on or below a bandage. The tissue contact unit may be thin foil like system, though other geometries may also be possible.

In an embodiment, the tissue contact unit can comprise a through hole around which the (at least 3, such as especially 4-10) electrodes (are configured. This through hole
 20 may be used by doctors to easily visually inspect the tissue. Hence, the reference point can be a virtual reference point, which will in general be somewhere in the through hole. Also, other types of tissue contact units may have such through hole. The through hole may have a cross-sectional area (in general in the plane of the tissue contact unit, such as in the plane of a bandage), in the range of 0,25-20 cm². The cross-sectional area can be dependent upon the
 25 dimensions of the wound at the skin.

As indicated above, it may be desirable to penetrate with the electrodes the tissue. Hence, in an embodiment the electrodes, especially their tips, touch the tissue. In yet another embodiment, the electrodes are configured to penetrate the tissue. Therefore, in an embodiment the tissue contact unit comprises needle like electrodes extending from a first
 30 face of the tissue contact unit, and configured to be able to penetrate the tissue. In an embodiment, one or more of the electrodes are configured to penetrate the tissue and one or more of the other electrodes are not configured to penetrate the tissue.

In a further embodiment, at least 3, such as 4-10 electrodes comprise electrode tips, wherein the tissue contact unit further comprises a conductive patch (further also

indicated as “patch”) over which the electrode tips are placed, wherein the conductive patch especially has an electric resistivity in the range of 0.01-100 k Ω .cm, especially in the range of 0.01-5 k Ω .cm.

The patch can e.g. be used to detect two-dimensional deformation of the tissue, as the patch may be – during use- in direct contact with a part of the tissue. Hence, the control unit may be configured to determine from the sensor signal a bi-axial deformation, by applying the potential difference method on the patch instead of the tissue. The patch may also comprise the above indicated through hole. The main advantage of the patch is that it can be made of a much more predictable and reliable material for measurements than tissue is. Also, the electrodes do not need to contact the tissue (or even penetrate the tissue), but the patch is in (physical) contact with the tissue. During use, the patch is thus configured between the electrodes and the tissue of the user.

All potential differences may be measured with respect to a common ground, thus enabling the direct measurement of electric potentials. This tissue contact unit may be coupled with a processing setup, which may be part of the control unit and/or an external control (and processing) unit. The measured potentials can be processed in the control unit which uses an algorithm that may compare them with reference measurements, as well as optionally with simulation data. Deviations among all this data provide metrics on how the electric field and, thus, wound geometry and electrical properties change over time, as well as deformation of surrounding tissue.

The control unit may need to be able to know the position of the electrodes in respect to an original, reference measurement (see also above on reference electrodes). This can be accomplished either through the computational model, or through other means of measuring electrode position, such as an overlaid conductive patch, strain gages, potentiometers, or otherwise.

The mathematical calculations performed in the device may have low computational cost, which enables measurement and processing in real time and, thus, real-time feedback. This feedback can be fed to the patient or the physician, and can be an early alarm for possible complications during wound healing, such as infections, inflammations, ischemia, danger of overstretching, or rupture of the wound. This can be accomplished in real-time through a wire or by using any wireless technology. Hence, in an embodiment the control unit is configured to send a warning signal when the tissue parameter approaches a reference value or exceeds a reference value.

To this end the analysis unit may comprise a warning unit, which may be part of the analysis unit. In another embodiment, this may be an external unit, which may optionally be addressed wireless. In an embodiment, the analysis unit may comprise such warning unit and optionally in addition, an external warning unit is available, for instance in a control center in a hospital. The warning unit may be configured to translate the warning signal of the control unit into one or more of a vibration, a sound or a light signal. Hence, the control unit may be configured to generate one or more of a vibration, a sound or a light signal, either directly or via an (external) warning unit. This warning signal can be given when the estimated deformation field of the tissue, which is estimated through processing the measurements of the potential difference(s) between the electrodes, indicates impending tissue rupture or suture failure. These failure thresholds are estimated through a combination of data libraries and real-time calculations. The warning unit may in an embodiment be part of the control unit (of the analysis unit).

As indicated above, the analysis unit may be used in e.g. real time measurement of tissue deformation. Especially, the analysis unit can be used wherein (during use) a direct current is applied between the first electrode and the second electrode.

The term “substantially” herein will be understood by the person skilled in the art. The term “substantially” may also include embodiments with “entirely”, “completely”, “all”, etc. Hence, in embodiments the adjective substantially may also be removed. Where applicable, the term “substantially” may also relate to 90% or higher, such as 95% or higher, especially 99% or higher, even more especially 99.5% or higher, including 100%. The term “comprise” includes also embodiments wherein the term “comprises” means “consists of”.

Furthermore, the terms first, second, third and the like in the description and in the claims, are used for distinguishing between similar elements and not necessarily for describing a sequential or chronological order. It is to be understood that the terms so used are interchangeable under appropriate circumstances and that the embodiments of the invention described herein are capable of operation in other sequences than described or illustrated herein.

The devices herein are amongst others described during operation. As will be clear to the person skilled in the art, the invention is not limited to methods of operation or devices in operation.

It should be noted that the above-mentioned embodiments illustrate rather than limit the invention, and that those skilled in the art will be able to design many alternative embodiments without departing from the scope of the appended claims. In the claims, any

reference signs placed between parentheses shall not be construed as limiting the claim. Use of the verb "to comprise" and its conjugations does not exclude the presence of elements or steps other than those stated in a claim. The article "a" or "an" preceding an element does not exclude the presence of a plurality of such elements. The invention may be implemented by means of hardware comprising several distinct elements, and by means of a suitably programmed computer. In the device claim enumerating several means, several of these means may be embodied by one and the same item of hardware. The mere fact that certain measures are recited in mutually different dependent claims does not indicate that a combination of these measures cannot be used to advantage.

The invention further applies to a device comprising one or more of the characterizing features described in the description and/or shown in the attached drawings. The invention further pertains to a method or process comprising one or more of the characterising features described in the description and/or shown in the attached drawings.

The various aspects discussed in this patent can be combined in order to provide additional advantages. Furthermore, some of the features can form the basis for one or more divisional applications.

Specific embodiments are describe below:

1. An analysis unit (1) comprising:

(a) a tissue contact unit (2) for application on human or animal tissue, the tissue contact unit (2) comprising 4-10 electrodes (111, 112, 113, 114, ...), the tissue contact unit (2) further comprising a reference point (101) around which the 4-10 electrodes (111, 112, 113, 114, ...) are configured, wherein the 4-10 electrodes (111, 112, 113, 114, ...) have inter electrode distances (d1) of at least 0,25 cm, and wherein the 4-10 electrodes (111, 112, 113, 114, ...) have distances (d2) to the internal reference point (101) in the range of 0,25-5 cm,

(b) a voltage generator (50) configured to generate a potential difference between a first electrode (111) and a second electrode (112),

(c) a control unit (60), configured to measure and process potential differences between one or more sets of two of the electrodes, of which each set comprises the first or the second electrode and one other electrode of the 4-10 electrodes (111, 112, 113, 114, ...).

2. The analysis unit (1) according to embodiment 1, wherein the voltage generator (50) is configured to generate an alternating current (AC).

3. The analysis unit (1) according to any one of the preceding embodiments, wherein the tissue contact unit (2) includes a bandage (100) or other means of adhesion, for application on human or animal tissue.

4. The analysis unit (1) according to embodiment 3, wherein the means of adhesion comprises an adhesive bandage, comprising one or more adhesive regions (150).

5. The analysis unit (1) according to any one of the preceding embodiments 3-4, wherein the tissue contact unit (2) comprises a through hole (125) around which 4-10 electrodes (111, 112, 113, 114, ...) are configured.

6. The analysis unit (1) according to any one of the preceding embodiments, wherein the tissue contact unit (2) comprises needle like electrodes (111a, 112a, 113a, 114a, ...) extending from a first face (11) of the tissue contact unit (2), and configured to be able to penetrate the tissue.

7. The analysis unit (1) according to any one of the preceding embodiments, wherein the 4-10 electrodes (111, 112, 113, 114, ...) comprise electrode tips (7), wherein the tissue contact unit (2) further comprises a conductive patch over the electrode tips (7), wherein the conductive patch (200) has an electric resistivity in the range of 0.01-100 k Ω .cm.

8. The analysis unit (1) according to embodiment 7, wherein the control unit (60) is configured to determine from the electrode measurements an electric potential map of the underlying domain from which a deformation field or a discontinuity field can be inferred.

9. The analysis unit (1) according to any one of the preceding embodiments, wherein the control unit (60) is configured to send a warning signal when the tissue parameter approaches a reference value or exceeds a reference value.

10. The analysis unit (1) according to embodiment 9, further comprising a warning unit (90), configured to translate the warning signal of the processing and control unit (60) into one or more of a vibration, a sound or a light signal.

11. The analysis unit (1) according to any one of the preceding embodiments, comprising 6-8 electrodes (111, 112, 113, 114, ...).

12. The analysis unit (1) according to any one of the preceding embodiments, wherein the first electrode (111) and the second electrode (112) have distances (d2) to the internal reference point (101) in the range of 0,5-3 cm, and wherein the other electrodes have larger distances (d2) to the internal reference point than the first electrode (111) and the second electrode (112).

13. Use of the analysis unit (1) according to any one of the preceding embodiments, in real time measurement of tissue bi-axial deformation and discontinuity field.

14. Use of the analysis unit (1) according to any one of embodiments 1-12, in real time detection and measurement of tissue rupture.

15. Use according to any one of embodiments 13-14, wherein an alternating current is applied between the first electrode (111) and the second electrode (112).

16. A tissue contact unit (2) for application on human or animal tissue, the tissue contact unit (2) comprising 4-10 electrodes (111, 112, 113, 114, ...), the tissue contact unit (2) further comprising a reference point (101) around which the 4-10 electrodes (111, 112, 113, 114, ...) are configured, wherein the 4-10 electrodes (111, 112, 113, 114, ...) have inter electrode distances (d1) of at least 0,25 cm, and wherein the 4-10 electrodes (111, 112, 113, 114, ...) have distances (d2) to the internal reference point (101) in the range of 0,25-5 cm.

BRIEF DESCRIPTION OF THE DRAWINGS

Embodiments of the invention will now be described, by way of example only, with reference to the accompanying schematic drawings in which corresponding reference symbols indicate corresponding parts, and in which:

Figs. 1a-1i schematically depicts some aspects of the invention.

The drawings are not necessarily to scale.

DETAILED DESCRIPTION OF THE EMBODIMENTS

In this section a simple, special case of application of the method is described, which serves both as demonstration and proof of concept.

The problem that this case addresses is the real-time measurement of the length and width of an ellipse-shaped, non-conductive discontinuity in soft tissue.

The potential difference method (PDM) is based on applying a voltage between two points in a continuum, and measuring the fluctuation of electric potential in fixed points along the continuum while changes in the geometry of the material are taking place. The method is most effective when the change in geometry is taking place on a plane that is perpendicular to the imaginary line that connects the two electrodes, because of large gradients in the electric field formed. For this reason, the electrodes may be placed in such a way that they encompass the discontinuity.

It is assumed that the surface is infinitely large (a reasonable assumption considering the inverse square law of electric intensity). The electrical resistivity of the samples examined was not found to be significantly anisotropic, thus the surface is also assumed to have isotropic resistivity. Since the experiment is performed using samples composed of the same type of tissue, it can be assumed that the material has homogenous electrical properties at a macro-scale.

In contrast to Mode I cracks in metals, a discontinuity in soft tissue can cause significant contraction along the x-axis, therefore it cannot be considered to be an infinitely thin, or fixed-width discontinuity. It is inferred, both from observation and the good match between theoretical and experimental results, that approximating the discontinuity's shape by an ellipse is a good fit to the problem.

This shape is expected because of the elastic properties of the material. Moreover, as the simulations demonstrate, the semi-axes of the ellipse are the dominant variables that affect the potentials.

The problem can be considered to be symmetrical along the x and y axes, and was non-dimensionalised by defining a source voltage $V \in [0,1]$, and dividing every distance by the distance between the point (0,0) and the ground electrode.

Measurements are taken by 4 electrodes (in addition to two electrodes that were used to apply the potential difference to), at fixed distances from each other. These are referred to by using their coordinates, as shown in the adjoining figure.

The problem is considered to be symmetrical. Therefore, the choice of points 1-4 in a circle around the centre of the ellipse presents certain advantages. Due to the symmetry, the measurements of electrodes 1-2 and 3-4 can be averaged in order to reduce experimental error.

Numerical solution

All simulations were performed using finite element code written in MATLAB. The code is verified to yield accurate results by comparing its output to experimental data, as well as to problems that possess an analytical solution. Furthermore, the use of an adaptive mesh was employed, in order to minimize numerical error.

The problem can be described by defining a square domain with dimensions 20 times the non-dimensionalisation distance. The use of domain boundaries so far from the point of interest effectively reproduces the assumption of an infinite surface. The governing equation of the problem is Laplace's equation for electric potential:

$$\nabla^2 V(x, y) = 0 \quad (1.1.)$$

On the boundaries of the domain, we imposed Neumann boundary conditions:

$$\nabla V(x, y) \cdot \vec{n} = 0 \quad (1.2.)$$

5

where $\vec{n}$ is the vector normal to the boundary. The same Neumann boundary conditions are imposed on the boundary of the discontinuity. The problem was non-dimensionalised using source voltage $V \in [0, 1]$. Thus, we imposed two Dirichlet boundary conditions where the voltage is applied:

10

$$V(x_{ground}, y_{ground}) = 0, \quad V(x_{High\ potential}, y_{High\ potential}) = 1 \quad (1.3.)$$

The electric current flowing through the surface is calculated by defining a contour around the ground electrode (taking care that it does not conflict with the ellipse) and calculating the line integral of the current density across the circumference, as follows:

$$I = \sigma \int_c \vec{J} \cdot \hat{n} dl \quad (1.4.)$$

15

Where $\vec{J}$ is the current density vector along the contour c , and $\hat{n}$ is the normal unit vector of the contour, and l being the arc length. For the purposes of this simulation, the conductivity σ is assumed to be 1. As it is a constant, it is straightforward to generalize this result to any homogenous material with isotropic conductivity.

20 **Numerical Results**

Due to the x-y symmetry of the problem, $V(-1, 1)$ and $V(-1, -1)$ as well as $V(1, 1)$ and $V(1, -1)$ coincide in pairs as expected. The two resulting curves that were obtained are mirrored around the mean value (0.5) of the provided voltage. As the length of the discontinuity grows, so does the potential difference, and, thus, the resistance between the corresponding points. In order to keep the following figures concise, only one of the coinciding curves will hereby be presented, denoted as V_{high} (proximal to the source) and V_{low} (proximal to the ground).

25

In contrast to cracks in metals where width is seldom of interest, the discontinuity width is expected to be significant enough to alter the potentials at the points of interest.

It appears that for any given length, an increase in width increases the potential difference between the measurement points. This also results in an increase in measurement sensitivity, since the obtained curves become steeper.

Because of the geometry of the problem, when the length of the discontinuity is very small, the equipotential lines are almost perpendicular to the boundary, even with substantial width. This state is very similar to the state without a discontinuity. However, the choice of an ellipse as the best fit theoretically guarantees that there will always be a distortion in the field. Experimental practice suggests that in this case, for better sensitivity, it is preferable to place the source electrodes along the y-axis instead of the x-axis. When the axes of symmetry are interchanged, the results are identical to the length case. However, the types of discontinuities that are studied in this paper are expected to have sufficiently large width. Thus, the width can be measured without rotating the device.

Our goal is to estimate the length and width of the ellipse by using the averaged potential measurements V_{high} and V_{low} . Given this set of 4 measurements, the exact combination of length and width cannot be estimated using the potentials alone. In order to overcome this obstacle, another quantity that is bijectively correlated to length and width is necessary. This quantity is the electric current flowing through the circuit.

Experimental investigation

Test Rig

The simulations were verified through the use of a custom test rig. Electrodes were placed on a supporting head. A PROXXON XYZ positioning table was used for accurate positioning (measured positioning precision ± 0.1 mm).

The accuracy in positioning the needle tips was measured to be within 0.05 mm of specifications. The data was transmitted to a Grant Squirrel 2020 data logger, measuring at a time interval of 0.1 seconds. All potential differences recorded by the data logger share a common ground, enabling the direct measurement of the potential field along the sample.

Power was provided to the circuit through a Delta Electronica ES 075-2 power supply. The elliptical discontinuity geometries were reproduced with accuracy using 3D

printed elliptical parts made out of polylactide, measured to be within 0.02mm of the specifications.

Experimental Protocol

A discontinuity was created in fresh (less than two hours) porcine tissue using a scalpel, and the samples were subsequently placed on the elliptical extrusion. The length of the discontinuity was equal to half the perimeter of the elliptical extrusion. The needles were then lowered, piercing all the way through the sample, and power was turned and kept on for 10 seconds. The samples were between 15-18 mm, thus sufficiently thick in order to justify neglecting the edge effects and reducing the problem to two dimensional. This process was repeated for numerous configurations of ellipse dimensions, as shown in the following plots. Great care was taken that every surface in contact with the sample or the electrodes was insulated.

Experimental Results and Discussion

It appears that there is a good much between measured and predicted values. The curves that were obtained representing the potentials close to the ground and high voltage are almost identical, which is expected because of the x-symmetry of the problem. As discussed above, there is also symmetry around the central value (0.5), which is due to the y-symmetry. Interestingly, the difference in potentials as the length of the discontinuity deviates no more than 5% from the reference state (where there is no discontinuity at all), which gives a good estimate of the necessary accuracy of the measuring equipment for various cases. This fact, along with the shape of the curves obtained, indicates that small discontinuities are much more difficult to measure at the same level of accuracy. However, the predictive power of the method is evident. Since the curves are bijective, any 4-tuple of electrode measurements can be matched to a unique length.

There appears to be a very good match between the expected and measured results, where the measurements have been non-dimensionalised by dividing with a measured tissue conductivity of 0.05 S/m.

This demonstrates the feasibility of using the PDM in order to estimate the dimensions of a soft tissue discontinuity. This method has proven to be effective in measuring two-parametrical tissue discontinuities.

Fig. 1a schematically depicts a tissue contact unit 2 for application on human or animal tissue, the tissue contact unit comprising 4-10 electrodes 111, 112, 113, 114, ...;

here, schematically 10 electrodes are depicted. The electrodes are arranged in an electrode configuration 3.

The phrase “the electrodes 111, 112, 113, 114, ...”, and similar phrases, indicate a plurality of electrodes which are for the sake of understanding numbers. Assuming
 5 that there would only be three electrodes, this would give “the electrodes 111, 112, 113”; likewise, when there would be eight electrodes, this would give “the electrodes 111, 112, 113, 114, 115, 116, 117, 118”, etc.

The tissue contact unit further comprising a reference point 101 around which the electrodes 111, 112, 113, 114, ... are configured, wherein the electrodes 111, 112, 113,
 10 114, ... have inter electrode distances d_1 of preferably at least 0,25 cm, and wherein the electrodes 111, 112, 113, 114, ... have distances d_2 to the internal reference point in the range of 0,25-5 cm.

Reference 125 indicates a possible through hole. The tissue contact unit 2, here includes, by way of example, a bandage 100, may have a first face 11, opposite thereof a
 15 second face 12, and edges 13,14. The through hole 125 is a hole from the first face 11 to the second face 12. Here, the electrodes are at the first face 11 or extend thereof (see also below).

The tissue contact unit 2 may comprise one or more adhesive regions 150, for sticking the tissue contact unit to the skin of a user.

In addition to the tissue contact unit 2, the analysis unit may further comprise
 20 one or more of a voltage generator 50, a control unit 60, and a warning unit 90.

Electrodes 111,112, or electrodes 119,120 may e.g. be used to apply a potential difference. In this drawing, electrodes 111,112 are used to apply the potential difference to (with the voltage generator 50).

The control unit is especially configured to measure (and process) electrical
 25 potential differences between one or more sets of two of the electrodes, of which each set comprises the first or the second electrode and one other electrode of the 4-10 electrodes 111, 112, 113, 114, ... Hence, the control unit can be configured to measure (and process) electrical potential differences between (on the one hand) electrode 111 or 112, and (on the other hand) one or more of the other electrodes (111, 112, 113, 114, ...). Therefore, the
 30 control unit is especially configured to measure (and process) electrical potential differences between one or more sets of two of the (at least 3, such as 4-10) electrodes, of which each set comprises the first or the second electrode and one other electrode of the (at least 3, such as 4-10) electrodes.

Fig. 1b schematically depicts a perspective view of the tissue contact unit 2. Reference 7 indicates the tip(s) of the electrodes. Reference 11, the first face, indicates the face that is seen; reference 12 the second face, is the opposite face. The electrodes are at the first face. When applying the first face 11 to a skin or tissue, the electrodes will be in physical contact therewith.

Fig. 1c schematically depicts an alternative embodiment of the tissue contact unit and analysis device respectively. Here, only six electrodes are applied, with electrodes 111, 112 again being used to generate a potential difference, and the other electrodes being used to measure other potential differences.

Figs. 1d and 1e schematically depict different embodiments of the electrodes, wherein in fig. 1d the electrodes may have tips 7 which do not substantially (or only slightly) protrude from the tissue contact unit 2, and wherein in fig. 1e the electrodes have tips 7 which are sharp and may protrude from the tissue contact unit. The former electrodes can be in (physical) contact with the top of the tissue; the latter electrodes can be used to penetrate the tissue. Needle like electrodes are indicated with references 111a, 112a, 113a, 114a, etc. The needle length is indicated with reference L; the needle thickness is indicated with reference d3, which may be in the range of about 0.1-2mm. Note that in fig. 1d the electrodes are extending slightly from the tissue contact unit. However, they may also be at the same height as first face 11 (or second face 12). Note that the thickness of the electrodes in fig. 1d may be very small, such that first face 11 and the electrodes at this first face are substantially at the same height. In an embodiment, the electrode tips are at the same level of the first surface (i.e. a substantially flat surface).

Fig. 1f and 1g schematically depict embodiment wherein a patch is shown.

Here, the tissue contact unit 2 further comprises a conductive patch 200 over the electrode tips 7. The conductive patch 200 may have an electric resistivity in the range of 0.01-100 k Ω .cm.

The patch may have a thickness d4 in the range of about 6 - 10.000 μ m. Reference 230 indicates a layer, which may be used to position/hold the electrode arrangement. Alternatively, the electrodes are integrated in the patch 200, and no further layer 230 is necessary. The patch may have a patch first face 11 and a patch second face 212. The patch 200 may (also) have one or more adhesive regions 150 for attachment to human or animal tissue, here indicated with reference 211.

Fig 1h schematically depicts a configuration of the tissue contact unit 2 including a conductive patch on a tissue (here indicated with reference 92), with in fig. 1h,

the tissue contact unit being attached to the surface tissue 91 (such as skin). In fig. 1h, the electrodes 111,112, ... do not penetrate the tissue, though this may also be possible. The bandage 100 may be configured to keep the tissue contact unit in physical contact with the tissue.

5 In fig. 1i, the bandage 100 is in between the body contact unit 2 and the tissue 92. Here, the electrodes may penetrate the bandage 100 and touch or penetrate (as depicted) the tissue 92.

Referring to especially figs. 1h and 1i, optionally, tissue contact unit 2 can be interpreted as the analysis unit (including the voltage generator and the control unit).

CONCLUSIES:

- 5 1. Een analyse-inrichting (1) omvattende:
 - (a) een weefselcontacteenheid (2) voor toepassing op menselijk of dierlijk weefsel, de weefselcontacteenheid (2) omvattende 4-10 elektroden (111, 112, 113, 114, ...), de weefselcontacteenheid (2) verder omvattende een referentiepunt (101) waaromheen de 4-10 elektroden (111, 112, 113, 114, ...) geconfigureerd zijn, waarbij de 4-10 elektroden (111, 10 112, 113, 114, ...) inter-elektrode afstanden (d1) van ten minste 0,25 cm hebben, en waarbij de 4-10 elektroden (111, 112, 113, 114, ...) afstanden (d2) tot het interne referentiepunt (101) in het bereik van 0,25-5 cm bezitten,
 - (b) een spanningsgenerator (50) geconfigureerd om een potentiaalverschil tussen een eerste elektrode (111) en een tweede elektrode (112) te genereren,
 - 15 (c) een besturingseenheid (60) geconfigureerd om potentiaalverschillen tussen een of meer sets van twee elektroden te meten en te verwerken, waarbij elk set bestaat uit de eerste of de tweede elektrode en een andere elektrode van de 4-10 elektroden (111, 112, 113, 114, ...).
- 20 2. De analyse-inrichting (1) volgens conclusie 1, waarbij de spanningsgenerator (50) geconfigureerd is om een wisselstroom (AC) genereren.
3. De analyse-inrichting (1) volgens een der voorgaande conclusies, waarbij de weefselcontacteenheid (2) een verband (100) omvat of andere hechtmiddelen, voor
 25 toepassing op menselijk of dierlijk weefsel.
4. De analyse-inrichting (1) volgens conclusie 3, waarbij het hechtmiddel een pleister omvat, omvattende een of meer lijmgebieden.
- 30 5. De analyse-inrichting (1) volgens een van de conclusies 3-4, waarbij de weefselcontacteenheid (2) een gat (125) omvat, waaromheen de 4-10 elektroden (111, 112, 113, 114, ...) zijn geconfigureerd.

6. De analyse-inrichting (1) volgens een der voorgaande conclusies, waarbij de weefselcontacteenheid (2) naaldachtige elektroden (111a, 112a, 113a, 114a, ...) omvat welke zich uitstrekken vanuit een eerste vlak (11) van de weefselcontacteenheid (2) en welke geconfigureerd zijn om weefsel binnen te dringen.

5

7. De analyse-inrichting (1) volgens een der voorgaande conclusies, waarbij de 4-10 elektroden (111, 112, 113, 114, ...) elektrodetoppen (7) omvatten, waarbij de weefselcontacteenheid (2) verder een geleidende patch omvat over de elektrodetoppen (7), waarbij de geleidende patch (200) een elektrische weerstand in het bereik van 0,01-100 k Ω .cm.

10

8. De analyse-inrichting (1) volgens conclusie 7, waarbij de besturingseenheid (60) geconfigureerd is om van de elektrodemetingen een elektrische potentiaalkaart te bepalen van een onderliggend domein, waarvan een vervormingsveld of discontinuïteitsveld kan worden afgeleid.

15

9. De analyse-inrichting (1) volgens een der voorgaande conclusies, waarbij de besturingseenheid (60) is geconfigureerd om een waarschuwingssignaal te geven wanneer de weefselparameter een referentiewaarde nadert of een referentiewaarde overstijgt.

20

10. De analyse-inrichting (1) volgens conclusie 9, verder omvattende een waarschuwingseenheid (90) geconfigureerd om een waarschuwingssignaal van de verwerkings- en stuureenheid (60) te vertalen tot een of meer van een trilling, geluid of een lichtsignaal.

25

11. De analyse-inrichting (1) volgens een der voorgaande conclusies, omvattende 6-8 elektroden (111, 112, 113, 114, ...).

12. De analyse-inrichting (1) volgens een der voorgaande conclusies, waarbij de eerste elektrode (111) en de tweede elektrode (112) afstanden (d2) tot het interne referentiepunt (101) hebben in het bereik van 0,5 - 3 cm, en waarbij de andere elektroden grotere afstanden (d2) tot het interne referentiepunt hebben dan de eerste elektrode (111) en de tweede elektrode (112) hebben.

30

13. Gebruik van de analyse apparaat (1) volgens een der voorgaande conclusies, voor het real-time meten van bi-axiale weefselvervorming en een discontinuïteitveld.

5 14. Gebruik van de analyse apparaat (1) volgens een der conclusies 1-12, voor het real-time detecteren en meten van weefselbreuk.

15. Toepassing volgens een der conclusies 13-14, waarbij een wisselstroom wordt toegepast tussen de eerste elektrode (111) en de tweede elektrode (112).

10 16. Een weefselcontacteenheid (2) voor toepassing op menselijk of dierlijk weefsel, de weefselcontacteenheid (2) omvattende 4-10 elektroden (111, 112, 113, 114, ...), de weefselcontacteenheid (2) verder omvattende een referentiepunt (101) waaromheen de 4-10 elektroden (111, 112, 113, 114, ...) geconfigureerd zijn, waarbij de 4-10 elektroden (111, 112, 113, 114, ...) inter-elektrode afstanden (d_1) van ten minste 0,25 cm hebben, en waarbij
15 de 4-10 elektroden (111, 112, 113, 114, ...) afstanden (d_2) tot het interne referentiepunt (101) in het bereik van 0,25 - 5 cm bezitten.

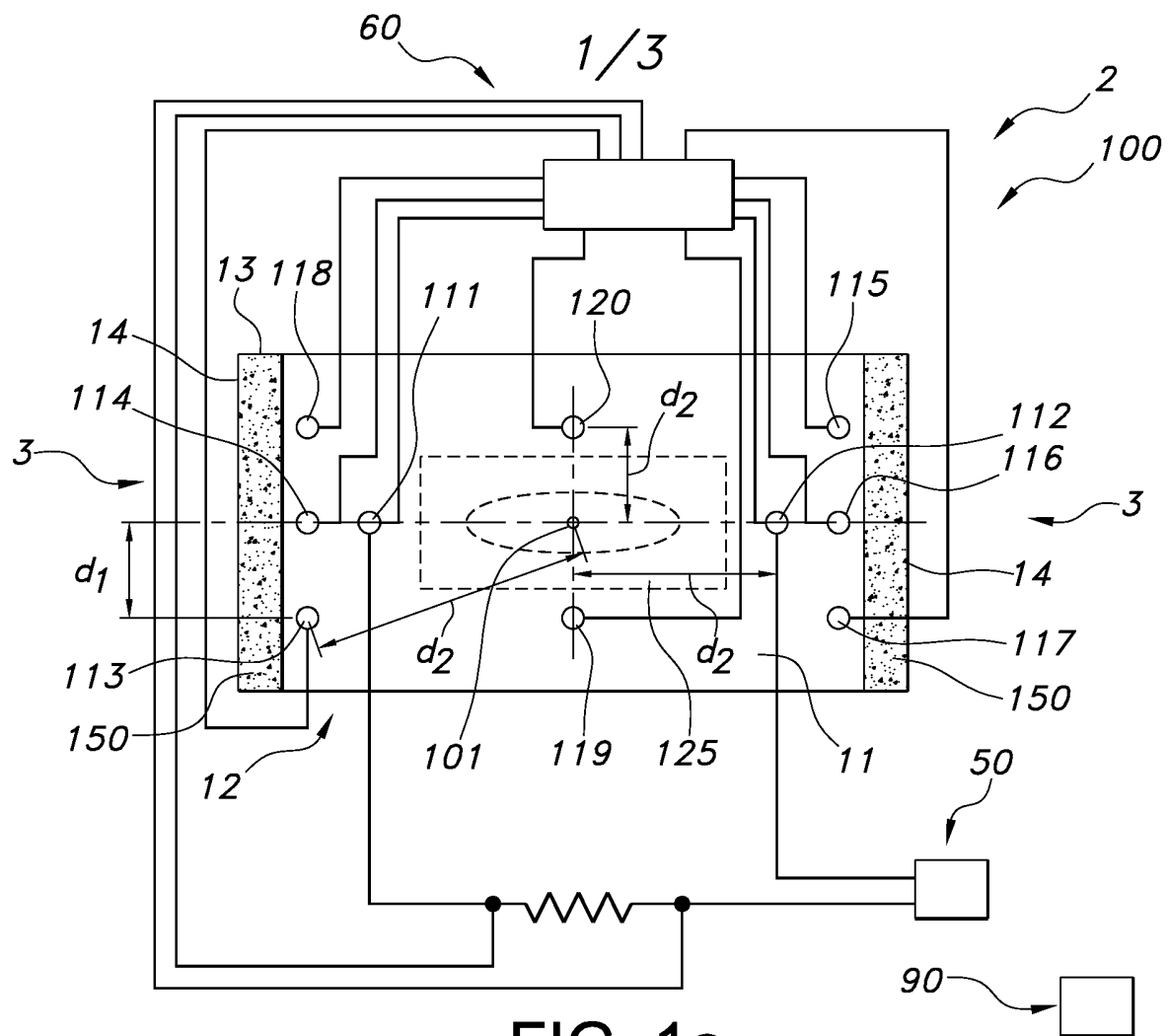


FIG. 1a

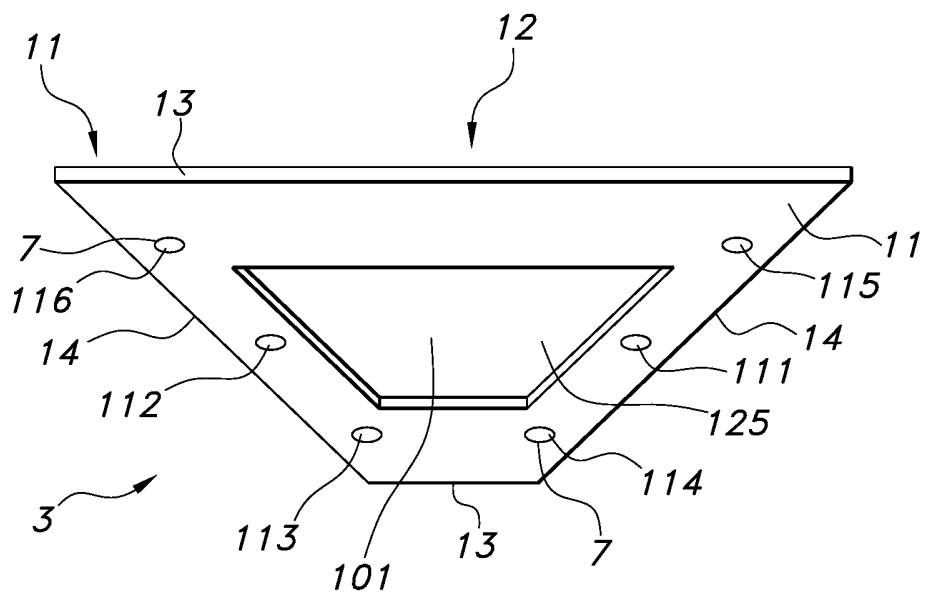


FIG. 1b

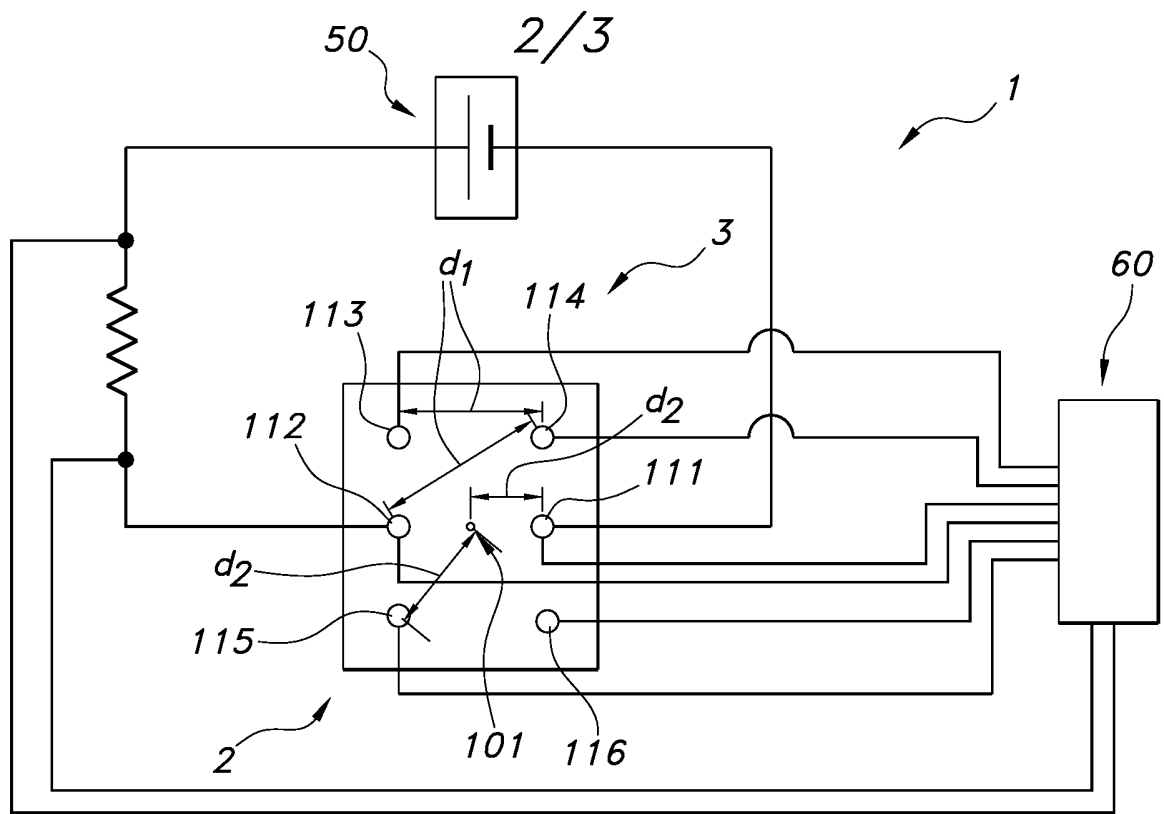


FIG. 1c

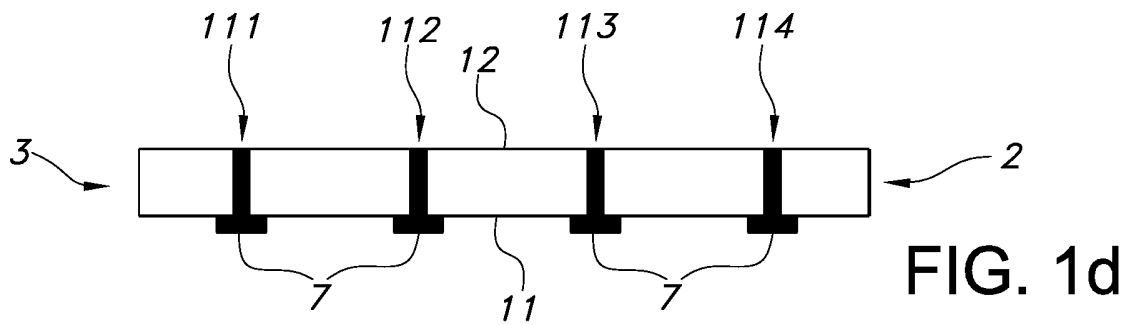


FIG. 1d

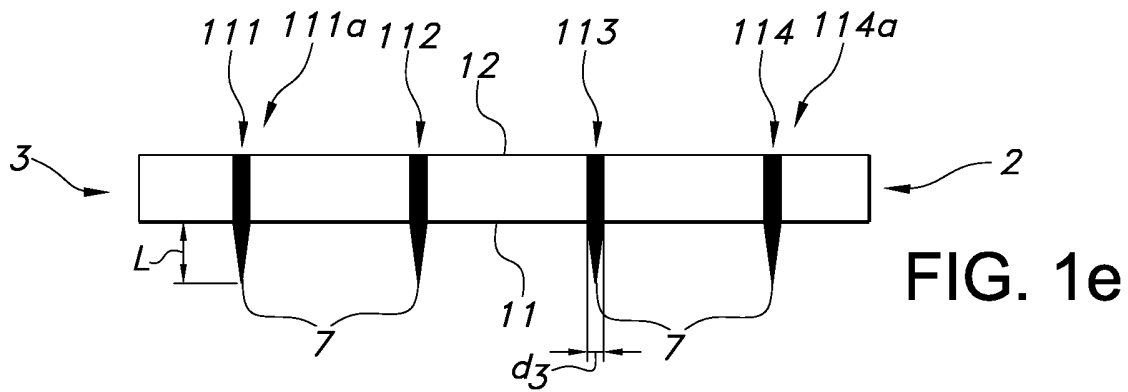


FIG. 1e

3/3

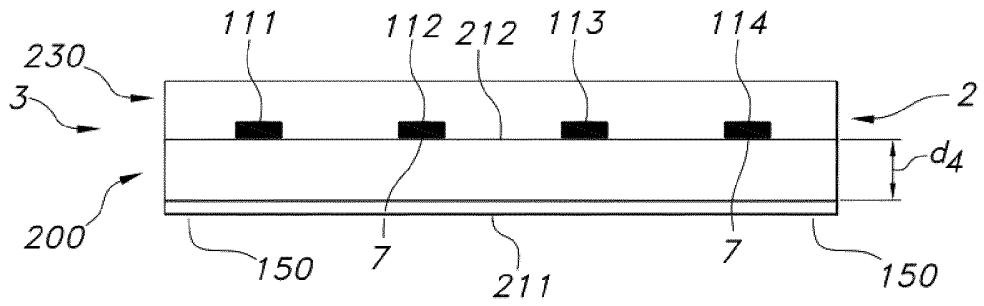


FIG. 1f

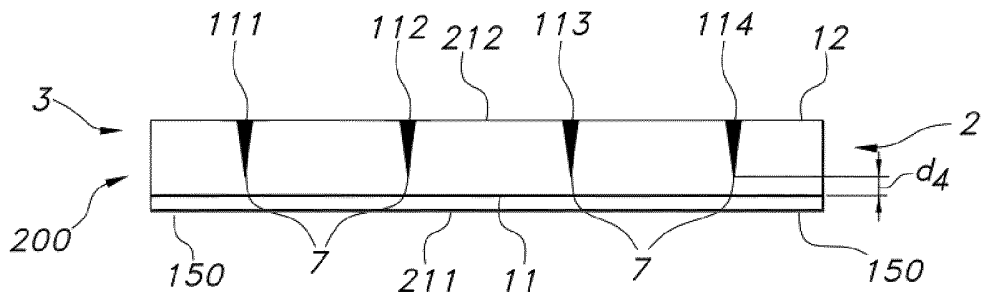


FIG. 1g

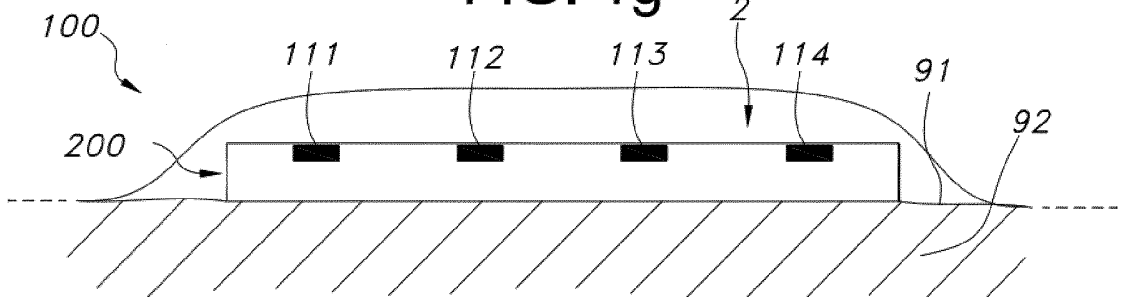


FIG. 1h

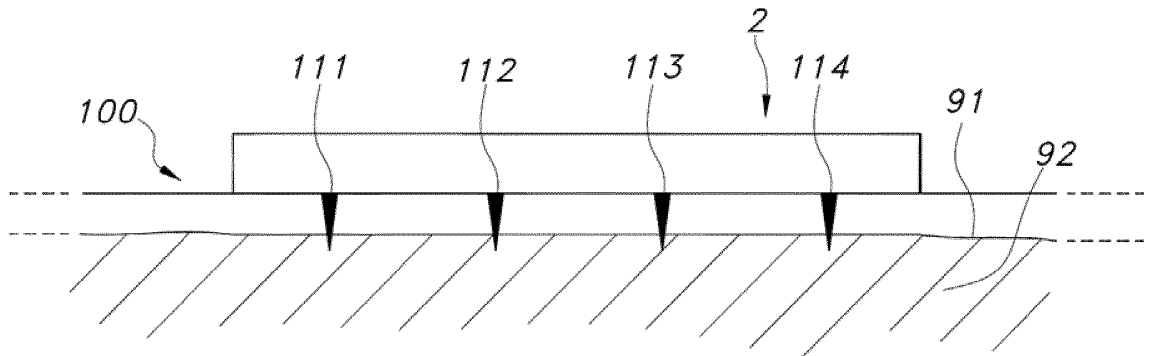


FIG. 1i

SAMENWERKINGSVERDRAG (PCT)

RAPPORT BETREFFENDE NIEUWHEIDSONDERZOEK VAN INTERNATIONAAL TYPE

IDENTIFICATIE VAN DE NATIONALE AANVRAGE		KENMERK VAN DE AANVRAGER OF VAN DE GEMACHTIGDE	
		P100087NL01	
Nederlands aanvraag nr. 2009123		Indieningsdatum 04-07-2012	
		Ingeroepen voorrangsdatum	
Aanvrager (Naam) Technische Universiteit Delft			
Datum van het verzoek voor een onderzoek van internationaal type 25-08-2012		Door de Instantie voor Internationaal Onderzoek aan het verzoek voor een onderzoek van internationaal type toegekend nr. SN 58750	
I. CLASSIFICATIE VAN HET ONDERWERP (bij toepassing van verschillende classificaties, alle classificatiesymbolen opgeven)			
Volgens de internationale classificatie (IPC)			
A61B5/053		G01N27/02	
II. ONDERZOCHE GEBIEDEN VAN DE TECHNIEK			
Onderzochte minimumdocumentatie			
Classificatiesysteem	Classificatiesymbolen		
IPC	A61B	G01B	G01N
Onderzochte andere documentatie dan de minimum documentatie, voor zover dergelijke documenten in de onderzochte gebieden zijn opgenomen			
III.	☐ GEEN ONDERZOEK MOGELIJK VOOR BEPAALDE CONCLUSIES (opmerkingen op aanvullingsblad)		
IV.	☐ GEBREK AAN EENHEID VAN UITVINDING (opmerkingen op aanvullingsblad)		

**ONDERZOEKSRAPPORT BETREFFENDE HET
RESULTAAT VAN HET ONDERZOEK NAAR DE STAND
VAN DE TECHNIEK VAN HET INTERNATIONALE TYPE**

Nummer van het verzoek om een onderzoek naar
de stand van de techniek

NL 2009123

A. CLASSIFICATIE VAN HET ONDERWERP
INV. A61B5/053 G01N27/02
ADD.

Volgens de Internationale Classificatie van octrooien (IPC) of zowel volgens de nationale classificatie als volgens de IPC.

B. ONDERZOCHETE GEBIEDEN VAN DE TECHNIEK

Onderzochte minimum documentatie (classificatie gevolgd door classificatiesymbolen)
A61B G01B G01N

Onderzochte andere documentatie dan de minimum documentatie, voor dergelijke documenten, voor zover dergelijke documenten in de onderzochte gebieden zijn opgenomen

Tijdens het onderzoek geraadpleegde elektronische gegevensbestanden (naam van de gegevensbestanden en, waar uitvoerbaar, gebruikte trefwoorden)

EPO-Internal

C. VAN BELANG GEACHTE DOCUMENTEN

Categorie °	Geciteerde documenten, eventueel met aanduiding van speciaal van belang zijnde passages	Van belang voor conclusie nr.
X	US 2006/052678 A1 (DRINAN DARREL D [US] ET AL) 9 maart 2006 (2006-03-09) * alineas [0004], [0005], [0017], [0025] - [0029], [0036] - [0043], [0066] *	1-6, 9-11, 14-16
A	----- WEBER S A ET AL: "Remote Wound Monitoring of Chronic Ulcers", IEEE TRANSACTIONS ON INFORMATION TECHNOLOGY IN BIOMEDICINE, IEEE SERVICE CENTER, LOS ALAMITOS, CA, US, deel 14, nr. 2, 1 maart 2010 (2010-03-01), bladzijden 371-377, XP011327674, ISSN: 1089-7771, DOI: 10.1109/TITB.2010.2042605 * het gehele document * -----	1-16



Verdere documenten worden vermeld in het vervolg van vak C.



Leden van dezelfde octrooifamilie zijn vermeld in een bijlage

° Speciale categorieën van aangehaalde documenten

"A" niet tot de categorie X of Y behorende literatuur die de stand van de techniek beschrijft

"D" in de octrooiaanvraag vermeld

"E" eerdere octrooi(aanvraag), gepubliceerd op of na de indieningsdatum, waarin dezelfde uitvinding wordt beschreven

"L" om andere redenen vermelde literatuur

"O" niet-schriftelijke stand van de techniek

"P" tussen de voorrangsdatum en de indieningsdatum gepubliceerde literatuur

"T" na de indieningsdatum of de voorrangsdatum gepubliceerde literatuur die niet bezwarend is voor de octrooiaanvraag, maar wordt vermeld ter verheldering van de theorie of het principe dat ten grondslag ligt aan de uitvinding

"X" de conclusie wordt als niet nieuw of niet inventief beschouwd ten opzichte van deze literatuur

"Y" de conclusie wordt als niet inventief beschouwd ten opzichte van de combinatie van deze literatuur met andere geciteerde literatuur van dezelfde categorie, waarbij de combinatie voor de vakman voor de hand liggend wordt geacht

"&" lid van dezelfde octrooifamilie of overeenkomstige octrooipublicatie

Datum waarop het onderzoek naar de stand van de techniek van internationaal type werd voltooid

19 maart 2013

Verzenddatum van het rapport van het onderzoek naar de stand van de techniek van internationaal type

Naam en adres van de instantie

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De bevoegde ambtenaar

Manschet, Jan

**ONDERZOEKSRAPPORT BETREFFENDE HET
RESULTAAT VAN HET ONDERZOEK NAAR DE STAND
VAN DE TECHNIEK VAN HET INTERNATIONALE TYPE**

Informatie over leden van dezelfde octrooifamilie

Nummer van het verzoek om een onderzoek naar
de stand van de techniek

NL 2009123

In het rapport genoemd octrooigeschrift		Datum van publicatie	Overeenkomend(e) geschrift(en)		Datum van publicatie
US 2006052678	A1	09-03-2006	US 2006052678	A1	09-03-2006
			US 2006058593	A1	16-03-2006
			US 2010268111	A1	21-10-2010
			WO 2006029034	A2	16-03-2006
			WO 2006029035	A1	16-03-2006

WRITTEN OPINION

File No. SN58750	Filing date (<i>day/month/year</i>) 04.07.2012	Priority date (<i>day/month/year</i>)	Application No. NL2009123
International Patent Classification (IPC) INV. A61B5/053 G01N27/02			
Applicant Technische Universiteit Delft			

This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the application
- ☒ Box No. VIII Certain observations on the application

	Examiner Manschot, Jan
--	-------------------------------

WRITTEN OPINION

Application number
NL2009123

Box No. I Basis of this opinion

1. This opinion has been established on the basis of the latest set of claims filed before the start of the search.
2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the application and necessary to the claimed invention, this opinion has been established on the basis of:
 - a. type of material:
 - ☐ a sequence listing
 - ☐ table(s) related to the sequence listing
 - b. format of material:
 - ☐ on paper
 - ☐ in electronic form
 - c. time of filing/furnishing:
 - ☐ contained in the application as filed.
 - ☐ filed together with the application in electronic form.
 - ☐ furnished subsequently for the purposes of search.
3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
4. Additional comments:

Box No. V Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty	Yes: Claims	7, 8, 12, 13
	No: Claims	1-6, 9-11, 14-16
Inventive step	Yes: Claims	7, 8
	No: Claims	1-6, 9-16
Industrial applicability	Yes: Claims	1-16
	No: Claims	

2. Citations and explanations

see separate sheet

WRITTEN OPINION

Application number
NL2009123

Box No. VIII Certain observations on the application

see separate sheet

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

- 1 Reference is made to the following document:

D1 US 2006/052678 A1 (DRINAN DARREL D [US] ET AL) 9 maart 2006 (2006-03-09)
- 2 The present application does not meet the criteria of patentability, because the subject-matter of claims 1 and 16 is not new.
- 3 In particular, from document D1 (Figure 3A) is known: a tissue contact unit (300) for application on human or animal tissue, the tissue contact unit (300) comprising 4-10 (e.g. 8) electrodes (245, 250, 255, 260), the tissue contact unit (2) further comprising a reference point (a virtual point in the center of the frame) around which the 4-10 electrodes are configured (Figure 3A; paragraph 38), wherein the 4-10 electrodes (240, 250, 255, 260) have inter electrode distances of at least 0,25 cm (more than 2.5 mm; paragraph 29) , and wherein the 4-10 electrodes have distances (d2) to the internal reference point (101) in the range of 0,25-5 cm (since inter-electrode distance is more than 2.5 mm, the electrode distance to the center of the Figure 3A configuration, must more than 2.5 mm).

Consequently, the subject-matter of present claim 16 is known from D1.
- 4 Document D1 further discloses that the tissue contact unit is part of an analysis unit comprising: a generator (210) configured to generate a potential difference between a first electrode (245) and a second electrode (250); a control unit (220, 225, 235), configured to measure and process potential differences between one or more sets of two of the electrodes, of which each set comprises the first or the second electrode and one other electrode of the 4-10 electrodes (paragraphs 5, 36, 38 (various pairs of electrodes may be used)).

Consequently, the subject-matter of claim 1 is anticipated by D1.
- 5 Document D1 further discloses the following features of the following dependent claims:

claim 2: the generator (50) is configured to generate an alternating current (AC) (paragraphs 25, 36);

claims 3 and 4: adhesive bandage (300) (paragraphs 41,42);

claim 5: the gaze (320) is only optional (paragraph 43). Hence, omitting the gaze leaves a hole;

claim 6: needle electrodes (paragraph 28);

claims 9 and 10: sound alert (paragraphs 17, 66, 74); and

claim 14: used for detecting tissue rupture (healing interruption; paragraphs 17, 38).

Re Item VIII

Certain observations on the application

- 1 Although claims 1 and 16 have been drafted as separate independent claims, they appear to relate effectively to the same subject-matter (claim 1 repeats claim 16) and to differ from each other only with regard to the definition of the subject-matter for which protection is sought. The aforementioned claims therefore lack conciseness.
- 2 The subject-matter described on pages 3-5 does not (completely) fall within the scope of the claims, as the description includes a tissue contact unit with at least 3 electrodes, whereas the independent claims define at least 4 electrodes. This inconsistency between the claims and the description leads to doubt concerning the matter for which protection is sought, thereby rendering the claims unclear.