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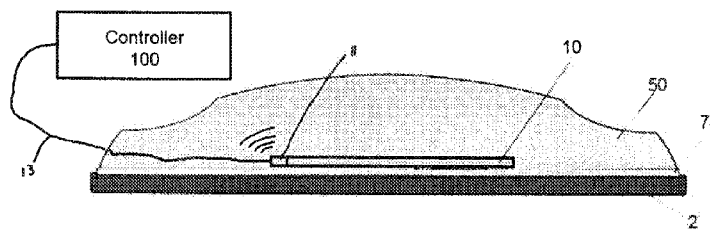


FIG. 2A

(57) Abstract: Skin graft harvesting systems and methods are disclosed that utilize sensors to automate the harvesting of skin grafts or assist a user in deciding when the skin graft is ready to be harvested. Such systems and methods can reduce the burden of visual observation and ensure greater reliability and consistency of the grafts. The invention is particularly useful with harvesters that rely upon suction and/or heating to raise a plurality of small or "micro" blisters simultaneously.

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SENSOR SYSTEMS FOR SKIN GRAFT HARVESTING

CROSS-REFERENCE TO RELATED APPLICATION

5 This application claims priority to U.S. Provisional Application No. 61/922,432, filed December 31, 2013. Prior application is incorporated herein by reference in its entirety.

FIELD OF THE INVENTION

10 The present invention generally relates to devices and methods for generating and harvesting skin grafts.

BACKGROUND

15 Skin is the largest organ of the human body, representing approximately 16% of a person's total body weight. Because it interfaces with the environment, skin has an important function in body defense, acting as an anatomical barrier from pathogens and other environmental substances. Skin also provides a semi-permeable barrier that prevents excessive fluid loss while ensuring that essential nutrients are not washed out of the body. Other functions of skin include insulation, temperature regulation, and sensation. Skin
20 tissue may be subject to many forms of damage, including burns, trauma, disease, and depigmentation (e.g., vitiligo).

 Skin grafts are often used to repair such skin damage. Skin grafting is a surgical procedure in which a section of skin is removed from one area of a person's body (autograft), removed from another human source (allograft), or removed from another
25 animal (xenograft), and transplanted to a recipient site of a patient, such as a wound site. Typically it is preferable to use an autograft instead of an allograft or a xenograft to reduce complications, such as graft failure and rejection of the skin graft.

30 [0005] A problem encountered when using an autograft is that skin is taken from another area of a person's body to produce the graft, resulting in trauma and wound generation at the donor site. Generally, the size of the graft matches the size of the recipient site, and thus a large recipient site requires removal of a large section of skin from a donor site, leading to increased pain and discomfort and longer healing time. Additionally, as the size

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of the section of skin removed from the donor site increases, so does the possibility of infection.

Techniques have been developed for harvesting a large number of smaller grafts, e.g., so-called micrografts, to reduce the trauma at the donor site. By removing only a fraction of the skin at a donor site and leaving regions of healthy skin surrounding the excised regions, a large amount of skin for transplantation can be obtained with less discomfort. Micrograft harvesting can also reduce the healing time and risk of infection at the donor site.

SUMMARY

Skin graft harvesting systems and methods are disclosed that utilize sensors to assist a user in deciding when the skin graft is ready to be harvested. Such systems and methods can reduce the burden of visual observation and ensure greater reliability and consistency of the grafts. The invention is particularly useful with harvesters that rely upon suction and/or heating to raise a plurality of small or “micro” blisters simultaneously.

In one embodiment, the sensor systems can include a matrix of proximity (non-contact) optical sensors, e.g., one or more light-emitters (e.g., laser, light-emitting diode or fiber light sources) and one or more detectors (e.g., photodetectors, photocells or photodiodes) arranged such that the path of light from the light-emitter to the detector is at least partially interrupted when a skin blister reaches a point suitable for harvesting.

The emitter can produce a signal that will be received by the detector. In certain embodiments, a single emitter can be paired with multiple sensors by directing the signal in multiple directions. Utilizing single emitters paired with multiple sensors can reduce complexity and cost by reducing the number of components in the system. The signal can be a continuous beam or a series of timed pulses to keep power consumption to a minimum (and reduce the heating effects due to irradiation of the harvested skin).

When a sensor does not receive an expected signal it can be assumed that the direct line of travel between the emitter and sensor has been broken and that therefore the blister has achieved a sufficient height ready for harvesting.

Due to the dynamic nature of blister formation, it may be advantageous to take repeated sensor readings before an alert is given that the site is ready for harvesting. In microblister systems it may also be desirable to set a threshold, e.g., when a pre-assigned

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number of sensors are in a 'ready' state, before giving an alert to the user that the site is ready for harvesting.

5 When the conditions have been met or a determination is otherwise made by the system that the skin is ready for harvesting, the device can instruct the user to do so. Alternatively, the system can be automatic, e.g., actuating the harvester to cleave the blisters as soon as certain conditions are met.

10 In one aspect of the invention, methods for preparing a skin graft can include the steps of applying a blister cutting device to a donor site on a subject's skin; applying a negative pressure within the device to thereby raise at least one blister at the donor site; and monitoring the formation of the blister with a sensor. The method can further include transmitting information from the sensor to alert the user when the blister has reached a state suitable for harvesting, e.g., by transmitting information from the sensor to a controller. Upon receipt of the information from the sensor to a controller reduce or
15 terminate the negative pressure, alert the user and/or activate the cutter device to cleave the blister.

In one embodiment, monitoring the formation of the blister within the device can further include deploying a sensor comprising at least one emitter-transmitter pair within the device and emitting a signal from the emitter and receiving the signal with the receiver.
20 The emitter can emit electromagnetic radiation or acoustic waves and the receiver is capable of detecting such radiation or acoustic wave. A disruption in the signal reception can thus indicate the presence of a skin blister.

In another embodiment, the sensor is disposable in close proximity to a growing blister and configured to sense the presence of a blister by detecting changes in electrical, magnetic or optical behavior of a sensor element. For example, the sensor can be a load
25 sensor disposable in close proximity to a growing blister and configured to sense the presence of a blister by a pressure the blister asserts on the load sensor. Alternatively, or in addition, the sensor can be a conductivity sensor disposable in close proximity to a growing blister and configured to sense the presence of a blister by a pressure the blister asserts on
30 the conductivity sensor.

In another embodiment, the sensor can be a color sensor and step of monitoring the formation of blisters within the device further comprises detecting changes in color within

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the device. For example, the sensor can be a colorimetric sensor capable of detecting changes in color in a plate having the holes through which the blisters will be raised.

5 In yet another embodiment, the sensor can be an acoustic sensor and the step of monitoring the formation of blisters within the device further comprises detecting changes in the acoustics of the device. For example, the sensor can be an ultrasound sensor and the step of monitoring the formation of blisters within the device further comprises detecting changes in an acoustic signature or image obtained within the device.

10 In a further embodiment, the sensor can be a vacuum sensor and the step of monitoring the formation of blisters within the device further comprises detecting changes in a negative pressure within the device or by deducing volume changes within the device by measuring the time required to reach a negative pressure level within the device.

15 In another aspect of the invention, the method can employ a cutting device that includes at least one fixed plate and at least one movable cutter plate, each plate having a plurality of holes through which suction blisters can be raised when the holes of the fixed and movable plates are aligned, and the step of cleaving the blisters further comprises moving the cutter plate to disrupt alignment of the holes and thereby separate the blisters from remaining skin at the donor site. The method can further include delivering a warm hypotonic fluid to a chamber within the device such that skin exposed to the chamber via the plate holes can assimilate fluid before and/or after applying negative pressure to the chamber to pull skin into the chamber through the holes and thereby raise a plurality of blisters.

20 More specifically, the methods for preparing a skin graft according to the invention can be practiced with a device comprising a device body, a sealing head member, at least one fixed plate and at least one movable cutter plate, each plate comprising a plurality of holes and wherein as assembled the holes in the plates are aligned within the body, the method including the steps of: connecting the device to a donor site on a subject's skin; joining the sealing head member and body together to define a sealed chamber; applying negative pressure to the chamber to pull skin into the chamber through the holes and thereby raise a plurality of blisters; monitoring the formation of blisters with one or more sensors; detecting when the blisters are in a condition suitable for harvesting (e.g., based on a signal or loss of signal from a sensor); unsealing the chamber; applying an adhesive substrate to the exposed blisters within the chamber; actuating the movable cutter plate to

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disrupt the alignment of the holes and to cut the blisters; and removing the substrate together with the cleaved skin blisters.

5 In another aspect of the invention, devices are disclosed for obtaining a skin graft, the devices including a body that is disposable on a patient's skin; a head adapted for coupling to a cutting body, the head further comprising a sealing surface to engage with a mating surface on the cutting body such that, when the head is engaged with the body on a patient's skin, a sealed chamber is formed over a target region of skin; and a negative pressure conduit also connected to the chamber and adapted for applying negative pressure
10 within the chamber to raise at least one skin blister within the chamber; a sensor for monitoring the formation of the blister; and a cutter mechanism within the body for cleaving the blister after formation.

In some embodiments, the sensor is configured to alert the user when the blister has reached a state suitable for harvesting. Alternatively, the device can also include a
15 controller for receiving information from the sensor. The controller can be configured to reduce or terminate the negative pressure or to activate the cutter mechanism and cleave the blister based on information from the sensor.

In certain embodiments, the sensor can include at least one emitter-transmitter pair within the device such that the emitter is configured to emit a signal and the receiver is
20 configured to receive the signal, and wherein a disruption in the signal reception or a change in signal strength indicates the presence of a skin blister. Alternatively, the sensor is situated within the device such that it can be deployed in close proximity to a growing blister, and configured to sense the presence, e.g., the size and/or height of the blister by detecting changes in electrical, magnetic or optical behavior of a sensor element. In another
25 alternative embodiment, the sensor can be a load sensor disposable in close proximity to a growing blister and configured to sense the presence of a blister by a pressure the blister asserts on the load sensor. For example, the sensor can be a conductivity sensor disposable in close proximity to a growing blister and configured to sense the presence of a blister by a pressure the blister asserts on the conductivity sensor.

30 In other embodiments, the sensor can be a color sensor configured to detect the formation of blisters within the device based on detected changes in color within the device. For example, the sensor can be a colorimetric sensor capable of detecting changes in color in the plate having the holes through which the blisters will be raised.

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In another embodiment, the sensor can be an acoustic or ultrasound sensor capable of monitoring the formation of blisters within the device by detecting changes in the acoustics and/or an acoustic signature or image obtained within the device.

5 In yet another embodiment, the sensor can be a vacuum sensor capable of monitoring the formation of blisters within the device by detecting changes in a negative pressure within the device or by deducing volume changes within the device, e.g., by measuring the time required to reach a negative pressure level within the device.

10 In certain embodiments of the invention, a two part device for harvesting of skin microblisters is disclosed. The two parts are a harvester body that is adapted for attachment to a target region of skin and a harvester head, which delivers heat and/or negative pressure to at least portions of the skin engaged by the harvester body.

15 More specifically, the head is adapted for coupling to a cutting body ("harvester") that is disposable on a patient's skin and further adapted for coupling to a vacuum source, the head further providing a sealing surface to engage with a mating surface on the cutting body such that, when the head is engaged with the cutting body on a patient's skin, an evacuated chamber is formed over a target region of skin; and, preferably, the sensor system is disposed within the chamber to monitor that blisters as they are formed.

20 Optionally, in addition to defining at least a portion of a negative pressure chamber, the head can further include a heating element that is a resistive electrical heating element or a mechanism for infusing a heated fluid. In such systems, in addition to the blister-monitoring sensors, the head or harvester can also include at least one temperature measuring element, such as a thermistor, for measuring the temperature of the skin or evacuated chamber.

25 The harvester body is configured for placement on a target region of a patient's skin and further adapted to form a sealing engagement with a head and define the chamber for application of negative pressure. In one embodiment, the harvester body further includes at least one alignment plate having a plurality of holes through which skin blisters can be raised in the presence of negative pressure; and a cutting plate having at least one
30 cutting surface for cleaving skin blisters after they are formed within the chamber.

In another preferred embodiment, the harvester includes a top alignment plate and a bottom alignment plate and the cutting plate is disposed therebetween. The top and bottom alignment plates can be joined together by a plurality of vertical posts that pass through

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slots in the cutting plate to maintain the fixed position of the top and bottom plates relative to each other while permitting movement of cutting plate. The top plate, bottom plate and cutting plate can each have a plurality of holes that are adapted to be concentrically aligned to facilitate blister formation. In certain embodiments, the holes of the top plate are larger than the holes of the bottom plate.

The cutting plate can include a plurality of holes suitable for concentric alignment with holes in the alignment plate in a first position to facilitate blister formation and a plurality of cutting surfaces suitable for cleaving blisters in a second position. The harvester can further include an actuator for moving the cutting plate from the first position to the second position and the actuator can be configured to also at least partially retract the cutting plate following blister cleavage.

The sensor systems of the present invention can be disposed in proximity to the cutter mechanism (e.g., adjacent to, or incorporated into, the top plate or bottom plate to monitor blister formation). Signals from the sensor element(s) can be transmitted to a controller, e.g., a microprocessor or programmed logic unit, which can be disposed in the head, the harvester or in a remote console. Alternatively, the sensor elements can include a transmitter that wirelessly transmits information regarding blister formation to a remote terminal or controller.

Various other sensor mechanisms for monitoring blister formations can be used in lieu of an optical emitter-detector system. For example, distance sensing can be employed using laser, sonar or ultrasound techniques. In such embodiments, emitters and receivers can sit above the openings through which the blisters are pulled in the system. By recording the time it takes for the signal to return, the distance from the emitter and the top of the blister can be calculated. When this distance is reduced to be equal or less than a predetermined value, the skin is ready for harvesting. The controller can then shut off the blister forming elements of the harvester or alert the user that the blisters can be harvested.

In a further embodiment, ultrasound can also be used to produce a volume representation of the cavity in which the blisters are being pulled within the system. This can then be used to calculate the volume of the blisters by subtracting the measured volume from the start volume. Again, when a predetermined value is reached, the device can alert the user that the skin is ready for harvesting or automatically shut off the blister forming elements of the harvester.

Alternatively, contact-based systems and methods can also be used in the invention. For example, load sensors can be placed above each harvest orifice (or at predetermined sites to reduce cost). When the blister contacts the load sensor the device can shut off or alert the user that the skin is ready for harvesting. In another embodiment, the system can periodically lower and retract the load sensors (so that the load sensor does not inhibit the blister from rising further or otherwise interfere with the application of negative pressure to the orifices).

In yet another embodiment, conductive systems and methods can be employed. For example, since skin is conductive, a touch panel can be placed within the harvester (or at predetermined positions). Once in contact with the skin in an acceptable number of locations or total area, the device can shut off or alert the user that the skin is ready for harvesting. As with the load sensor method, the capacitive sensor may need to be periodically lowered.

In yet another embodiment, changes in the volume of the chamber can be measured (e.g., by deadspace leak detection). For example, when a vacuum source is used to exert negative pressure on the internal chamber of the harvester, the chamber in which the blisters are being formed can be periodically vented. If the volume of the chamber is known, then the time it takes for the chamber pressure to reach a predetermined threshold (e.g., a specific negative pressure level) can be used to calculate the volume of the blisters that are protruding through the harvester and terminate the harvesting process or alert the user that the skin is ready for harvesting.

In yet another embodiment the sensor can be a colorimetric sensor capable of detecting changes in color, e.g., in a plate having the holes through which the blisters will be raised. When a sufficient portion of the sensor's field of view registers one or more colors associated with the skin or blister, a controller associated with the sensor can alert the user that the skin graft(s) are ready for harvesting – or automatically initiate steps to cut the blister(s).

The potential advantages of this invention in the context of suction blister devices can include (a) reducing the burden on the caregiver in terms of monitoring and constant visual checking, (b) providing more accurate determinations of when the blisters are in condition for harvesting, (c) reducing the time for harvesting since the system will alert the care giver as soon as the site is ready and/or (d) reducing discomfort for patient as system is

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currently monitored manually by removing the top of the device if the user cannot judge the state of blisters through the viewing window.

5 These and other aspects of the devices of the invention are described in the figures, description and claims that follow. While several improved design features have been individually described, such features are not mutually exclusive of each other. Any combination of design features disclosed herein can be used integrated into the devices of the invention. These design features and other aspects of the devices of the invention are described in the figures, description and claims that follow.

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BRIEF DESCRIPTION OF THE DRAWINGS

FIG. 1A is a schematic perspective view of a skin blister harvesting device according to the invention;

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FIG. 1B is a schematic perspective view of a base portion of the skin blister harvesting device of FIG. 1A;

FIG. 2A is a schematic side view of a harvester device with a sensor system according to one embodiment of the invention; FIG. 2B is a schematic cross-sectional view of the harvester device of FIG. 2A;

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FIG. 3 is a schematic illustration of a sensor system employing a transmitter and receivers prior to blister formation;

FIG. 4 is a schematic illustration of the sensor system of FIG. 3 detecting the formation of a blister;

FIG. 5 is a schematic illustration of a pattern of transmitter and receiver elements that can reduce the number of transmitters;

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FIG. 6 is a schematic illustration of an alternative pattern of transmitters; and

FIG. 7 is a schematic illustration of only the transmitter elements in the pattern of FIG. 5;

FIGS. 8 and 9 are schematic illustrations of an alternative sensor system based on load sensing;

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FIG. 8 illustrates the load sensor prior to blister formation;

FIG. 9 is a schematic illustration of a load sensor detecting the formation of a blister;

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FIGS. 10 and 11 are schematic illustrations of an alternative sensor system based on distance sensing;

FIG. 10 illustrates the distance sensor prior to blister formation;

5 FIG. 11 is a schematic illustration of a distance sensor detecting the presence of a blister;

FIG. 12 is a schematic illustration of a color sensor detecting the presence of a blister;

10 FIG. 13A is a schematic illustration of a controller display showing a user interface for selecting a desired blister height;

FIG. 13B is a schematic illustration of a controller display showing a user interface for selecting a desired blister fill factor; and

FIG. 13C is a schematic illustration of a controller display showing a user interface
| for showing progress in successful blister formation.

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DETAILED DESCRIPTION

The present invention generally relates to sensor systems for use in devices that can raise a blister (e.g., a suction blister) and cut the raised blister, i.e., a blister raising device integrated with a cutting member. Such devices are useful for harvesting skin grafts. In particular the devices and systems are adapted to infuse a fluid into skin at a donor site to enhance blister formation.

20 In certain embodiments, the devices according to the invention include a head portion that can be removably coupled to a harvester body that is positioned at the donor site of a subject's skin. The head portion and the body portion define a sealed chamber therebetween so that a fluid can be instilled and removed, and so that negative pressure can be applied to skin following fluid infusion. Although shown and described as part of the head portion, it should be clear that the coupler or conduit for fluid delivery and evacuation of the chamber can be part of either the head portion or the body portion and that the fluid and negative pressure can be applied separately via multiple couplings or via a single
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30 conduit as illustrated.

FIG. 1A is a schematic view of a skin graft harvester 50 for use in accordance with various aspects of the present teachings. In this illustrative embodiment, the harvest 50 includes a detachable head portion 52 and harvester body 54. The harvester body 54 is

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adapted for placement on a patient's skin at a donor site where skin grafts are to be obtained, e.g., on the inner thigh, and secured in place, for example, with strap 56 (shown in phantom). The head 52 can further include a heater (not shown) powered via a coupler 60 adapted to couple with a power source in a base unit (not shown). The head 52 further includes a seal 63 which permits a reduced pressure chamber to be formed when the head 52 and body 54 are joined together and the harvester 50 is coupled to a vacuum pump or other source of reduced pressure, e.g., via coupler 60 connecting the harvester 50 to its base unit. The head 52 can further include one or more windows 58 for observation of skin blisters being formed within the chamber by application of reduced pressure, heat or both. Once the blisters have been formed, the head 52 can be removed, e.g., by deactivating the source of reduced pressure and by actuation of release levers 62, which break the seal 63 and allow the head 52 to be lifted off the harvester body 54.

Additional details on harvesters useful in connection with the present invention can be found in U.S. Patent Application No. 13/839,518 filed March 15, 2013; U.S. Patent Application No. 13/346,329 filed January 9, 2012; U.S. Patent Application No. 13/436,318 also filed January 9, 2012; U.S. Patent Application Ser. No. 13/014,737 filed January 27, 2011; U.S. Patent Application Ser. No. 12/851,656 filed August 6, 2010; U.S. Patent Application Ser. No. 12/851,621 filed August 6, 2010; U.S. Patent Application Ser. No. 12/851,703 filed August 6, 2010; and U.S. Patent Application Ser. No. 12/851,682 filed August 6, 2010. The contents of each of the above-referenced related applications are herein incorporated by reference in their entireties.

FIG. 1B is a schematic view of the skin graft harvester 50 of FIG. 1A with the head 52 removed and the cutting mechanism 74 exposed. The harvester body 54 can include a base portion 70, a sled 72, and actuator handle 80. The cutting mechanism 74 can include a plurality of plates with initially aligned holes through which skin blisters are drawn by heat and/or application of suction when the head 52 is joined to the harvester body 54 and activated. Once the blisters are formed, they can be cleaved by the cutting mechanism 74. For example, below the top plate depicted in FIG. 8, one or more additional plates, e.g., a cutter plate and a bottom plate can be deployed with aligned holes. By actuation (e.g., pulling up) of handle 80, the sled 72 is caused to move horizontally such that one of the plates below the top plate, e.g., the "cutter plate" (not shown) also moves (because of its

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linkage to the sled 72), thereby occluding the alignment of holes 78 and cleaving the raised blisters from the donor's skin.

As explained in more detail below, the sensor systems of the present invention can be incorporated into either the harvester head 52 or harvester body 54 – or both.

FIG. 2A and 2B are schematic illustrations of harvester device 50 having a cutter mechanism 74 in contact with a donor site of a patient's skin 2 and equipped with a non-contact blister sensor 10 to reduce burden and variability in deciding when a skin graft is ready to be harvested. The sensor is connected (e.g., by a wired connection 13 or wireless path via transceiver 11) to a controller 100 which can be part of the harvester or situated remotely (e.g., as part of the console that provides a source of negative pressure and/or current to heater elements (not shown) within the harvester. The controller 100 can be a dedicated device or a software application on general purpose computer, laptop, tablet or smart phone type device. The wireless connection can operate via a Bluetooth or other communication protocol.

As shown in the cross-sectional schematic view of FIG. 2B, The sensor 10 can be constructed of a matrix of non-contact proximity sensor elements (e.g., utilizing technology such as infrared or laser optics). The sensor elements can include emitters 12 and receivers 14. The sensor elements are disposed above or integrated into the cutting mechanism 74. When initially deployed the cutter mechanism has a plurality of align holes, through which skin blisters will be drawn by suction, heating or other manner.

As shown in FIGS. 3 and 4, each emitter 12 produces a signal 16 that can be received by a receiver 14. If emitter 12 emits multidirectional signal, it can be paired with multiple sensors, e.g., receivers 14A and 14B. (Possible emitter and receiver combinations arranged around holes 78 on the top plate 82 of a cutter mechanism can be seen in Fig 5 - 7 with the receivers omitted from Fig 6 & 7 for simplicity).

When receiver 14A does not receive an expected signal (Fig 4) it can be assumed that the direct line of travel between the emitter 12 and receiver 14A has been broken and that therefore the blister 4 has achieved a sufficient height to be ready for harvesting.

By using multidirectional or omnidirectional emitters paired with multiple sensors, as shown in Fig 5-7, the complexity and cost is lessened by reducing the number of components in the system. The signal can be a continuous beam or a series of timed pulses

to reduce power consumption (and also limit irradiation of skin as well as the graft to be harvested).

5 Due to the dynamic nature of some intended donor sites, it may be necessary to take repeated readings for each emitter and receiver arrangement before an alert is given that the site is ready for harvesting. In certain embodiments, the system can be configured to ensure that a pre-assigned number of paired sensor arrangements (emitter and receiver) are in a 'ready' state before giving an alert to the user that the site is ready for harvesting.

10 When the conditions have been met and the system is sure that the skin is ready for harvesting, the device can instruct the user of this status. Depending on the complexity of the device, the system may even indicate the next steps in the process.

In an alternative embodiment, the sensors can be contact sensors. For example, load sensors can be placed above each harvest orifice (Fig 8); or at predetermined sites to minimize cost. When the blister contacts the load sensor 92 the device can alert the user that the skin is ready for harvesting. The system may need to periodically raise and lower the load sensors (Fig 9) to avoid interference with blister formation during the application of negative pressure within the chamber. Moreover, conductivity sensors can be used in lieu of (or in conjunction with) load sensors. As skin is conductive, the sensor can be a conduction touch panel that can be placed within the harvester (or at predetermined positions). Once in contact with the skin in an acceptable number of locations or total area, the device can alert the user that the skin is ready for harvesting. As with the load sensor method, the capacitive sensor may need to be periodically raised and lowered.

20 In another alternative embodiment, the sensors can be distance sensing sensors. Utilizing laser, sonar or ultrasound techniques, a sensor (e.g., an emitter and receiver pair) can sit above the openings through which the blisters are pulled in the system. By recording the time it takes for the signal to return to the distance sensor 94 (Fig 10), the distance from the emitter and the top of the blister 4 can be calculated. When this hits a predetermined time, the skin is ready for harvesting (Fig 11). In some embodiments, a single emitter and multiple receivers can be employed. Alternatively, multiple emitters and a single receiver can be used. The signals from the receiver(s) can be multiplexed or averaged to determine when a sufficient number of holes have been filled with blisters ready for harvesting.

30 In yet another embodiment, the sensor can employ "volume sensing" techniques. For example, ultrasound can be used to produce a volume representation of the cavity in

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which the blisters are being pulled within the system. This can then be used to calculate the volume of the blisters by subtracting the measured volume from the start volume. When the ultrasound signal reaches a predetermined threshold the device can alert the user that the skin is ready for harvesting. Alternatively, changes in the volume of the chamber can be determined by dead-space leak detection. By utilizing the vacuum source, the cavity in which the blisters are being formed can periodically be vented. If the leak within the cavity is known, then utilizing the time it takes for the cavity pressure to hit a predetermined threshold the system can calculate the volume of the blisters that are protruding through the harvester and alert the user the skin is ready for harvesting.

In yet another embodiment, as shown in FIG. 12 the sensor can be a colorimetric sensor 120 capable of detecting changes in color, e.g., in a plate having the holes through which the blisters will be raised. The sensor can include a color photo detector 122 (or an array of such detectors) and an optional lens 124 (for widening the view of view). When a sufficient portion of the sensors field of view registers one or more colors associated with the skin or blister, a controller associate with the sensor can alert the user that the skin graft(s) are ready for harvesting – or automatically initiate steps to cut the blister(s). The colorimeter can further include filters 126 to preferentially pass colors associated with skin tones (or skin components such as melanin). The detector can be deployed within the device's chamber. Alternatively, light from the chamber can be collected via a waveguide or optical fiber (or fiber bundle) and transmitted to a detector outside of the device.

The device/sensor can be configured to allow the user to define the blister height before initiating graft formation. This can be done mechanically by adjusting the space between the sensor and the forming hole, or electronically by adjusting the calibration of the sensor for proximity, pressure, reflection, time to receive a sound wave, etc. For example, as shown in FIG. 13A, the controller 100, e.g., a smartphone app, can communicate with the sensor to select a desired height.

The device/sensor can also be configured to allow the user to define the minimal number of successfully formed grafts that need to be formed before alerting the clinician that the grafts are ready (50%, 70%, 100%). In addition, the device can count the number of grafts formed and either display as a total, a percentage of the total, or in a light grid pattern (one light for each graft, changing from red to green when formed). This allows the user to decide if they have enough grafts and in the pattern/orientation suitable for them.

- 15 -

For example, as shown in FIG. 13B, the controller 100, e.g., a smartphone app, can communicate with the sensor to select a desired fill factor to be obtained or, as shown in FIG. 13C, the controller 100 can monitor and display the progress of blister formation so
5 that the user can determine when to initiate graft formation.

The term “load sensor,” as used herein, is intended to encompass pressure transducers, touch sensors, piezometers and other piezoelectric devices, force sensors, force sensing variable resistors and/or capacitors and like devices which can determine pressure or contact based on changes in force or electrical or magnetic behavior.

10 The term “conductivity sensor,” as used herein, is intended to encompass devices that can measure or determine changes in light, electrical resistance, capacitance and/or impedance, associated with the presence of skin within or near a target site.

The term “in proximity” encompasses situations wherein objects are close to each other as well situations where objects are in contact with each other. Closeness is not
15 absolute quantity but rather denotes a distance wherein an object, e.g., a sensor, can perform its intended function.

References and citations to other documents, such as patents, patent applications, patent publications, journals, books, papers, web contents, have been made throughout this disclosure. All such documents are hereby incorporated herein by reference in their entirety
20 for all purposes.

The invention may be embodied in other specific forms without departing from the spirit or essential characteristics thereof. The foregoing embodiments are therefore to be considered in all respects illustrative rather than limiting on the invention described herein. Scope of the invention is thus indicated by the appended claims rather than by the foregoing
25 description, and all changes which come within the meaning and range of equivalency of the claims are therefore intended to be embraced therein.

CLAIMS

1. A device for obtaining a skin graft, the device comprising:
5 a body that is disposable on a patient's skin;
a head adapted for coupling to the cutting body, the head further comprising a sealing surface to engage with a mating surface on the cutting body such that, when the head is engaged with the body on a patient's skin, a sealed chamber is formed over a target region of skin; and
10 a negative pressure conduit also connected to the chamber and adapted for applying negative pressure within the chamber to raise at least one skin blister within the chamber; a sensor for monitoring the formation of the blister; and
a cutter mechanism within the body for cleaving the blister after formation.
- 15 2. The device of claim 1 wherein the sensor is configured to alert the user when the blister has reached a state suitable for harvesting.
3. The device of claim 1 wherein the device further comprises a controller for receiving information from the sensor.
20
4. The device of claim 1 wherein the controller is configured to reduce or terminate the negative pressure based on information from the sensor.
5. The device of claim 1 wherein the controller is configured to activate the cutter
25 mechanism and cleave the blister based on information from the sensor.
6. The device of claim 1 wherein the sensor comprises at least one emitter-transmitter pair within the device such that the emitter is configured to emit a signal and the receiver is configured to receive the signal with the receiver, and wherein a disruption in the signal
30 reception indicates the presence of a skin blister.

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7. The device of claim 1 wherein the sensor is a sensor disposable in close proximity to a growing blister and configured to sense the presence of a blister by detecting changes in electrical, magnetic or optical behavior of a sensor element.

5

8. The device of claim 1 wherein the sensor is a load sensor disposable in close proximity to a growing blister and configured to sense the presence of a blister by a pressure it asserts on the load sensor.

10

9. The device of claim 1 wherein the sensor is a conductivity sensor disposable in close proximity to a growing blister and configured to sense the presence of a blister.

10. The device of claim 1 wherein the sensor is a color sensor configured to detect the formation of blisters within the device based on detected changes in color within the device.

15

11. The device of claim 1 wherein the sensor is a colorimetric sensor capable of detecting changes in color in the plate having the holes through which the blisters will be raised.

20

12. The device of claim 1 wherein the sensor is an acoustic sensor capable of monitoring the formation of blisters within the device by detecting changes acoustics of the device.

25

13. The device of claim 1 wherein the sensor is an ultrasound sensor capable of monitoring the formation of blisters within the device by detecting changes in an acoustic signature or image obtained within the device.

30

14. The device of claim 1 wherein the sensor is a vacuum sensor capable of monitoring the formation of blisters within the device by detecting changes in a negative pressure within the device.

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15. The device of claim 1 wherein the sensor is a vacuum sensor capable of monitoring the formation of blisters within the device by deducing volume changes within the device by measuring the time required to reach a negative pressure level within the device.

5

16. The device of claim 1 wherein the controller and sensor communicate via a wireless communication protocol.

10

17. The device of claim 1 wherein the controller permits a user to select at least one parameter needed to initiate graft formation, the parameter selected from the group of a desired blister height, a desired number of blisters, a desired percentage of successfully formed blisters, a visualization of the progress in graft formation.

15

18. A method for preparing a skin graft, the method comprising the steps of:
applying a blister cutting device to a donor site on a subject's skin;
applying a negative pressure within the device to thereby raise at least one blister at the donor site;
monitoring the formation of the blister with a sensor.

20

19. The method of claim 18 wherein the method further comprises transmitting information from the sensor to alert the user when the blister has reached a state suitable for harvesting.

25

20. The method of claim 18 wherein the method further comprises transmitting information from the sensor to a controller.

30

21. The method of claim 18 wherein the method further comprises transmitting information from the sensor to a controller to reduce or terminate the negative pressure.

22. The method of claim 18 wherein the method further comprises transmitting information from the sensor to a controller to activate the cutter device and cleave the blister.

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23. The method of claim 18 wherein the step of monitoring the formation of the blister within the device further comprises deploying a sensor comprising at least one emitter-transmitter pair within the device and emitting a signal from the emitter and receiving the signal with the receiver.

5

24. The method of claim 23 wherein the emitter emits electromagnetic radiation or acoustic waves and the receiver is capable of detecting said radiation or acoustic wave and wherein a disruption in the signal reception indicates the presence of a skin blister.

10

25. The method of claim 18 wherein the sensor is a sensor disposable in close proximity to a growing blister and configured to sense the presence of a blister by detecting changes in electrical, magnetic or optical behavior of a sensor element.

15

26. The method of claim 18 wherein the sensor is a load sensor disposable in close proximity to a growing blister and configured to sense the presence of a blister by a pressure it asserts on the load sensor.

20

27. The method of claim 18 wherein the sensor is a conductivity sensor disposable in close proximity to a growing blister and configured to sense the presence of a blister.

28. The method of claim 18 wherein the sensor is a color sensor and step of monitoring the formation of blisters within the device further comprises detecting changes in color within the device.

25

29. The method of claim 18 wherein the sensor is a colorimetric sensor capable of detecting changes in color in a plate having the holes through which the blisters will be raised.

30

30. The method of claim 18 wherein the sensor is an acoustic sensor and step of monitoring the formation of blisters within the device further comprises detecting changes in the acoustics within the device.

- 20 -

31. The method of claim 18 wherein the sensor is an ultrasound sensor and step of monitoring the formation of blisters within the device further comprises detecting changes in an acoustic signature or image within the device.

5

32. The method of claim 18 wherein the sensor is a vacuum sensor and step of monitoring the formation of blisters within the device further comprises detecting changes in a negative pressure within the device.

10

33. The method of claim 18 wherein the sensor is an vacuum sensor and step of monitoring the formation of blisters within the device further comprises deducing volume changes within the device by measuring the time required to reach a negative pressure level within the device.

15

34. The method of claim 18 further comprising the steps of applying an adhesive substrate to the blister prior to cleavage and harvesting the skin graft by removal of the substrate from cutting device following blister cleavage.

20

35. The method of claim 18 wherein the cutting device comprises at least one fixed plate and at least one movable cutter plate, each plate having a plurality of holes through which suction blisters can be raised when the holes of the fixed and movable plates are aligned, and the step of cleaving the blisters further comprises moving the cutter plate to disrupt alignment of the holes and thereby separate the blisters from remaining skin at the donor site.

25

36. The method of claim 18 wherein the device further comprises a plate with holes through which blisters can be raised and the method further comprises delivering a warm hypotonic fluid to a chamber within the device such that skin exposed to the chamber via the plate holes can assimilate fluid before and/or after applying negative pressure to the chamber to pull skin into the chamber through the holes and thereby raise a plurality of blisters.

30

- 21 -

37. A method for preparing a skin graft with a device comprising a device body, a sealing head member, at least one fixed plate and at least one movable cutter plate, each plate comprising a plurality of holes and wherein as assembled the holes in the plates are aligned within the body, the method comprising the steps of:
- 5 aligned within the body, the method comprising the steps of:
- connecting the device to a donor site on a subject's skin;
 - joining the sealing head member and body together to define a sealed chamber;
 - applying negative pressure to the chamber to pull skin into the chamber through the holes and thereby raise a plurality of blisters;
 - 10 monitoring the formation of blisters with sensor;
 - detecting when the blisters are in a condition suitable for harvesting;
 - unsealing the chamber;
 - applying an adhesive substrate to the exposed blisters within the chamber;
 - actuating the movable cutter plate to disrupt the alignment of the holes and to cut the
 - 15 blisters; and
 - removing the substrate together with the cleaved skin blisters.

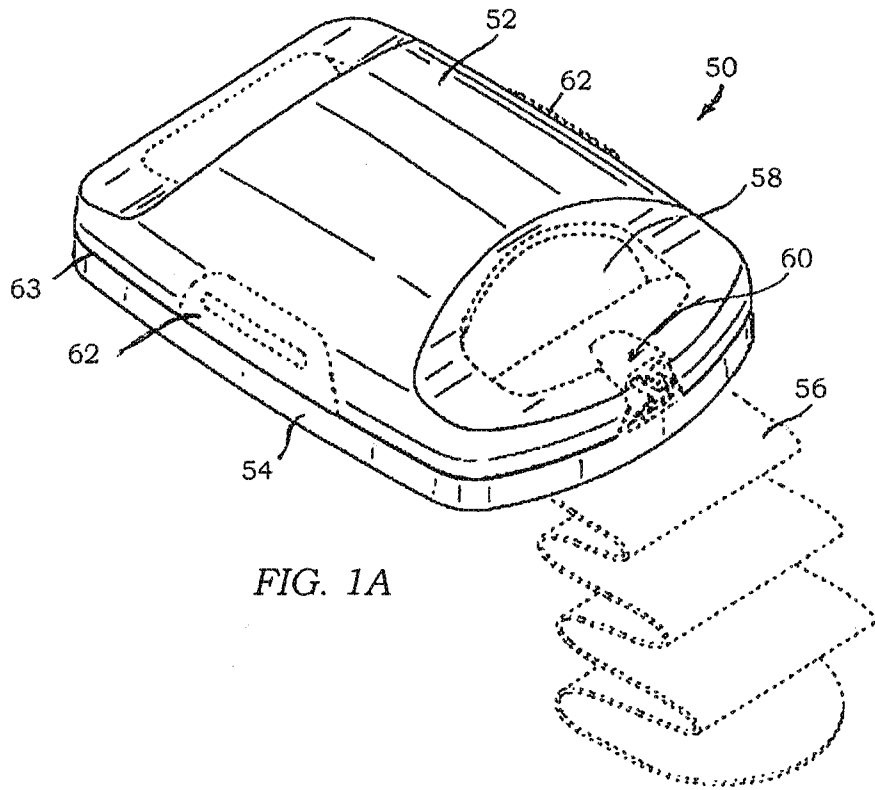


FIG. 1A

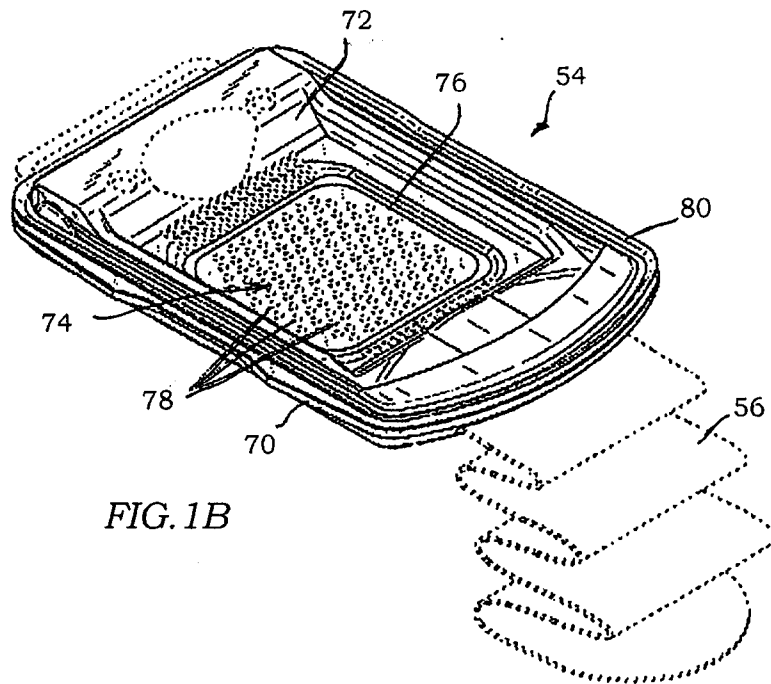


FIG. 1B

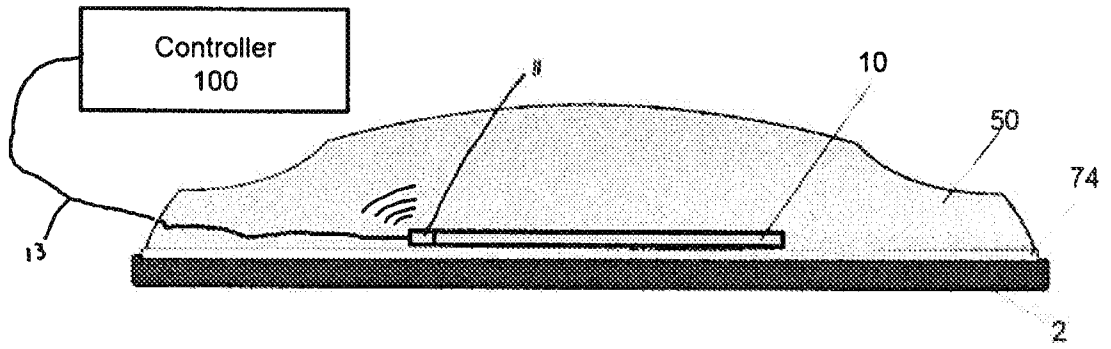


FIG. 2A

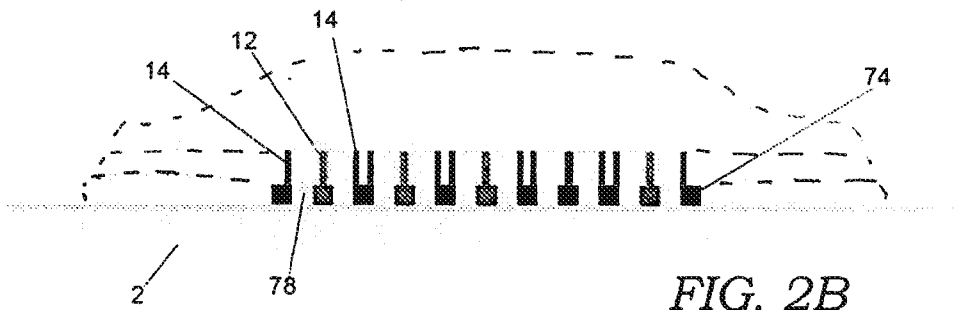


FIG. 2B

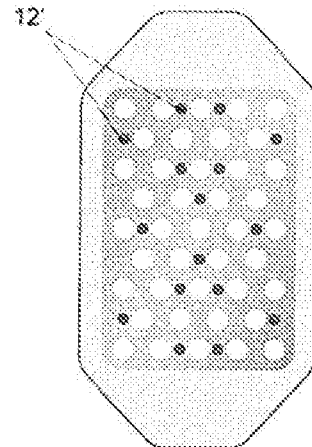
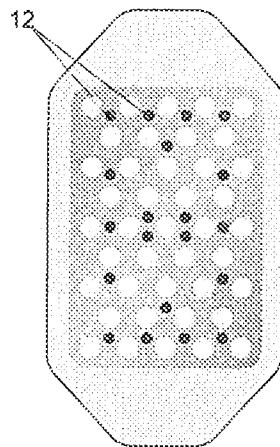
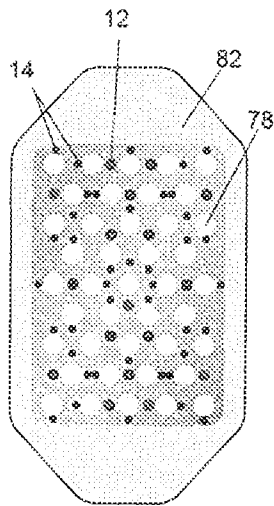
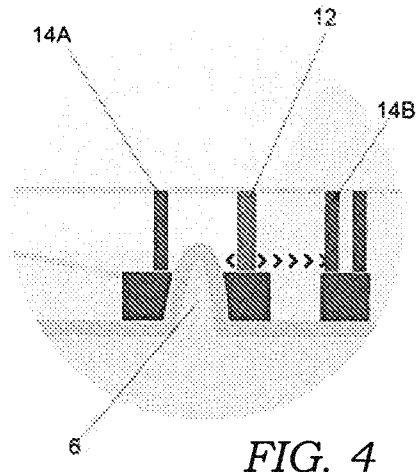
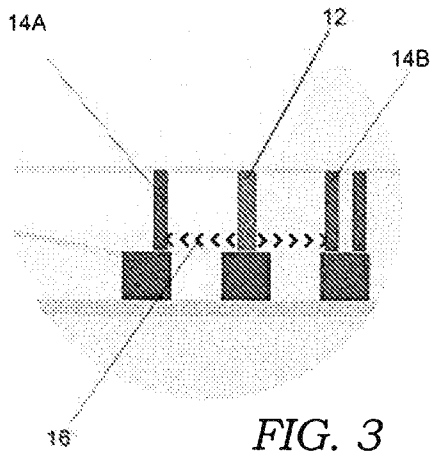


FIG. 5

FIG. 6

FIG. 7

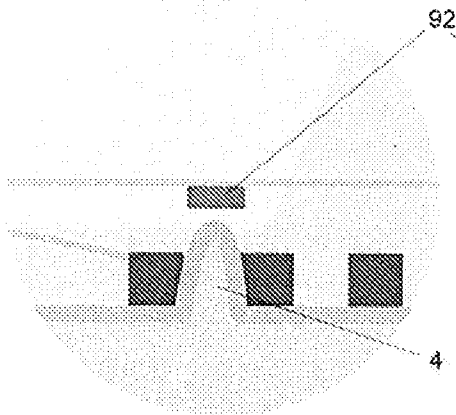


FIG. 8

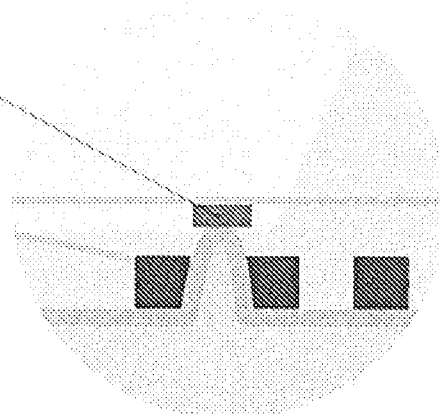


FIG. 9

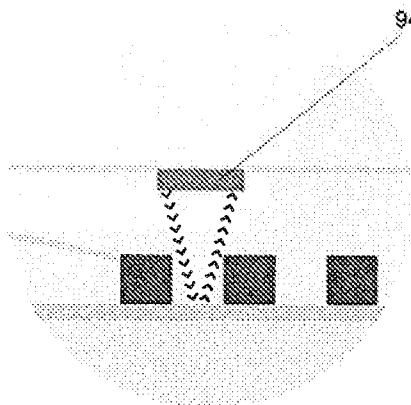


FIG. 10

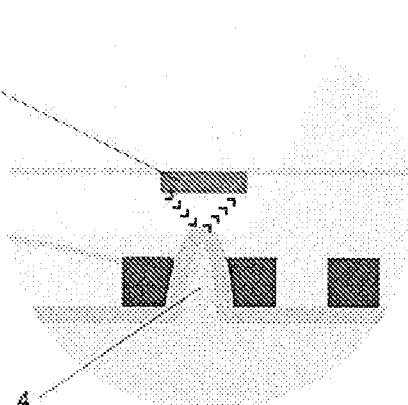


FIG. 11

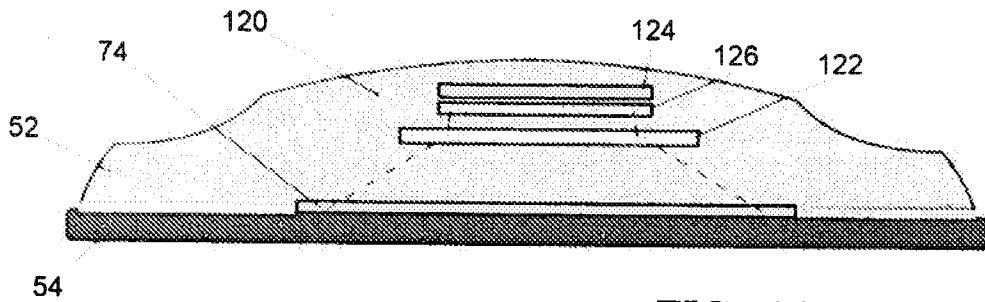


FIG. 12

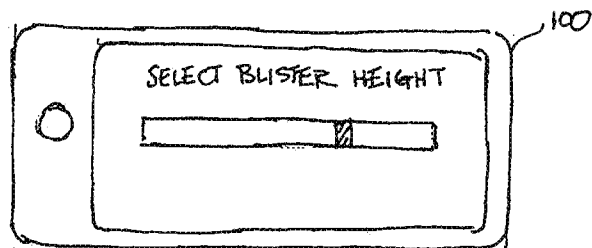


FIG. 13A

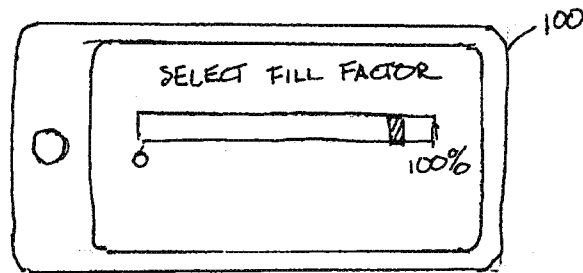


FIG 13B

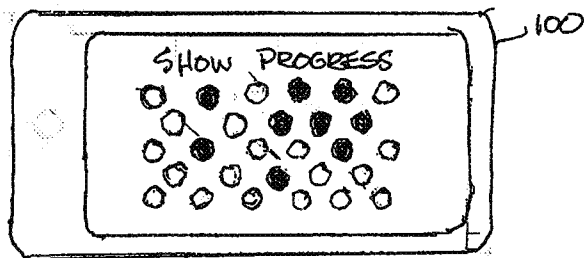


FIG 13C

INTERNATIONAL SEARCH REPORT

International application No PCT/US2014/072180

A. CLASSIFICATION OF SUBJECT MATTER INV. A61B17/322 ADD.		
According to International Patent Classification (IPC) or to both national classification and IPC		
B. FIELDS SEARCHED		
Minimum documentation searched (classification system followed by classification symbols) A61B		
Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched		
Electronic data base consulted during the international search (name of data base and, where practicable, search terms used) EPO-Internal, WPI Data		
C. DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 2013/204273 A1 (SABIR SAMEER AHMED [US] ET AL) 8 August 2013 (2013-08-08) abstract; figures 1-13 claim 1 -----	1
A	CN 101 053 528 A (ZHANG LEI [CN]) 17 October 2007 (2007-10-17) abstract; figure 1 -----	1
<input type="checkbox"/> Further documents are listed in the continuation of Box C.		
<input checked="" type="checkbox"/> See patent family annex.		
* Special categories of cited documents :		
"A" document defining the general state of the art which is not considered to be of particular relevance "E" earlier application or patent but published on or after the international filing date "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) "O" document referring to an oral disclosure, use, exhibition or other means "P" document published prior to the international filing date but later than the priority date claimed	"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art "&" document member of the same patent family	
Date of the actual completion of the international search	Date of mailing of the international search report	
13 March 2015	20/03/2015	
Name and mailing address of the ISA/ European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016	Authorized officer Moers, Roelof	

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2014/072180

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. Claims Nos.: **18-37**
because they relate to subject matter not required to be searched by this Authority, namely:
Rule 39.1(iv) PCT - Method for treatment of the human or animal body by surgery
2. Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
3. Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. As all searchable claims could be searched without effort justifying an additional fees, this Authority did not invite payment of additional fees.
3. As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.
- The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.
- No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/US2014/072180

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 2013204273	A1	08-08-2013	NONE

CN 101053528	A	17-10-2007	NONE
