



(51) International Patent Classification:
A61F 13/00 (2006.01)

(21) International Application Number:
PCT/US2019/048812

(22) International Filing Date:
29 August 2019 (29.08.2019)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
62/726,006 31 August 2018 (31.08.2018) US

(71) Applicant: **KCI LICENSING, INC.** [US/US]; Legal Department Intellectual Property, P.O. Box 659508, San Antonio, TX 78265 (US).

(72) Inventors: **ALLEN, Diwi, L.**; 24538 Daisy Run, San Antonio, TX 78255 (US). **ROBINSON, Timothy, Mark**; 19 Wessex Avenue, Shillingstone DT11 0TG (GB). **KHARKAR, Prathamesh, Madhav**; 6203 Farinon Drive,

San Antonio, TX 78249 (US). **YOUNG, Nathaniel**; P.O. Box 659508, San Antonio, TX 78265-9508 (US).

(74) Agent: **FEI, Young et al.**; Harness, Dickey & Pierce, P.L.C., 5445 Corporate Drive, Suite 200, Troy, MI 48098 (US).

(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DJ, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JO, JP, KE, KG, KH, KN, KP, KR, KW, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

(84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ,

(54) Title: COOLING DRESSING FOR IMPROVED COMFORT

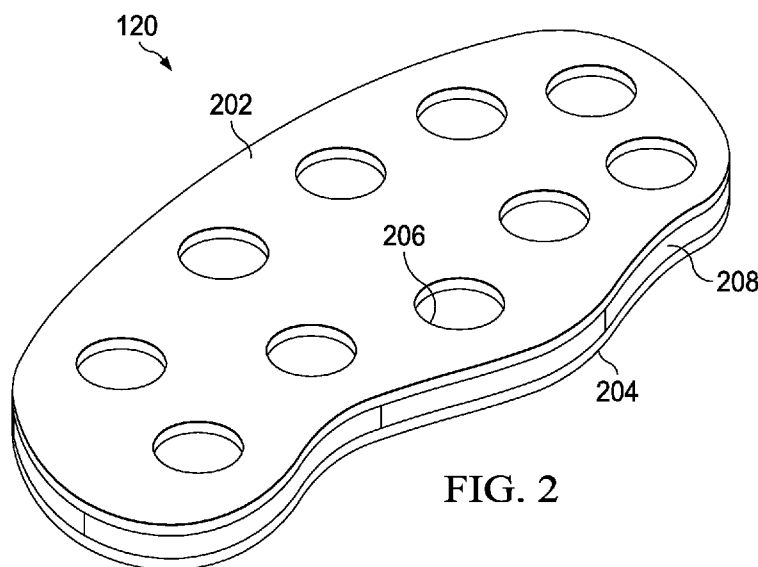


FIG. 2

(57) Abstract: Apparatuses and methods for treating a tissue site with dressing materials configured for improving comfort of the tissue site are disclosed. For example, an apparatus for treating a tissue site may comprise a manifold having a plurality of compartments containing substances adapted to react with each other to provide a cooling effect to the tissue site. In some examples, the apparatus may include a manifold having a first plurality of compartments containing a first substance, and a second plurality of compartments containing a second substance. The first plurality of compartments and the second plurality of compartments may be configured to allow mixing of the first substance and the second substance under the application of negative pressure to produce an endothermic reaction.



UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG).

Published:

— *with international search report (Art. 21(3))*

COOLING DRESSING FOR IMPROVED COMFORT

RELATED APPLICATIONS

[0001] The present application claims priority to U.S. Provisional Patent Application No. 62/726,006, entitled "Cooling Dressing for Improved Comfort," filed August 31, 2018, which is incorporated herein by reference for all purposes.

TECHNICAL FIELD

[0002] The invention set forth in the appended claims relates generally to tissue treatment systems and more particularly, but without limitation, to dressing materials for applying to a tissue site.

BACKGROUND

[0003] Clinical studies and practice have shown that reducing pressure in proximity to a tissue site can augment and accelerate growth of new tissue at the tissue site. The applications of this phenomenon are numerous, but it has proven particularly advantageous for treating wounds. Regardless of the etiology of a wound, whether trauma, surgery, or another cause, proper care of the wound is important to the outcome. Treatment of wounds or other tissue with reduced pressure may be commonly referred to as "negative-pressure therapy," but is also known by other names, including "negative-pressure wound therapy," "reduced-pressure therapy," "vacuum therapy," "vacuum-assisted closure," and "topical negative-pressure," for example. Negative-pressure therapy may provide a number of benefits, including migration of epithelial and subcutaneous tissues, improved blood flow, and micro-deformation of tissue at a wound site. Together, these benefits can increase development of granulation tissue and reduce healing times.

[0004] While the clinical benefits of negative-pressure therapy are widely known, improvements to therapy systems, components, and processes may benefit healthcare providers and patients.

BRIEF SUMMARY

[0005] New and useful systems, apparatuses, and methods for improving comfort to a tissue site in a negative-pressure therapy environment are set forth in the appended claims. Illustrative embodiments are also provided to enable a person skilled in the art to make and use the claimed subject matter.

[0006] For example, in some embodiments, an apparatus for treating a tissue site may include a manifold having a first side and a second side and a plurality of apertures extending through the manifold to allow for fluid communication between the first side and the second side. The apparatus may further include a first plurality of compartments contained by the manifold and containing a first substance, and a second plurality of compartments contained by the manifold and containing a second substance. The apparatus may be adapted so that, under the application of negative pressure, the first plurality of compartments and the second plurality of compartments are configured to allow mixing of the first substance and the second substance. In some instances, the mixing of the first substance and the second substance may produce an endothermic reaction.

[0007] In some additional embodiments, an apparatus for treating a tissue site may include a manifold having a first side, a second side, and a plurality of apertures adapted to fluidly connect the first side and the second side, and a first separator disposed within at least a portion of the manifold and adapted to provide a first compartment and a second compartment within the manifold. A first substance may be contained within the first compartment, and a second substance may be contained within the second compartment. The first separator may be configured to allow mixing of the first substance and the second substance to cause a chemical reaction upon application of a first amount of negative pressure to the manifold. In some instances, the chemical reaction may be an endothermic reaction for reducing the temperature of the apparatus. In some embodiments, the apparatus may further include a chamber adapted to encapsulate the first compartment and the second compartment within the manifold. In some additional embodiments, the apparatus may also include a second separator configured to allow mixing of the first substance and the second substance upon application of a second amount of negative pressure to the manifold.

[0008] In yet further embodiments, a method for treating a tissue site may include disposing a manifold proximate to the tissue site and supplying negative pressure to the manifold within a specified range. The manifold may include a first side, a second side, and a plurality of apertures extending through the manifold to allow for fluid communication

between the first side and the second side. The manifold may contain a chamber, and a separation layer may be disposed within the chamber in order to create a first compartment and a second compartment within the chamber, wherein the first compartment contains a first substance, the second compartment contains a second substance, and the separation layer is configured to break to allow mixing of the first substance and the second substance within the chamber upon application of negative pressure within the specified range. The mixing of the first substance and the second substance may generate an endothermic reaction. In some embodiments, the method may further comprise covering the manifold with a sealing member to form a sealed space around the tissue site.

[0009] In still further embodiments, an apparatus for treating a tissue site may include a first manifold layer, a second manifold layer, and a first active layer positioned between the first manifold layer and the second manifold layer. The first manifold layer may include a first plurality of apertures, and the second manifold layer may include a second plurality of apertures. The first active layer may comprise a first plurality of compartments containing a first active ingredient and a second plurality of compartments containing a second active ingredient. The apparatus may be adapted so that, under the application of negative pressure, at least a first portion of the first plurality of compartments and the second plurality of compartments are configured to breach to allow the first active ingredient and the second active ingredient to undergo an endothermic reaction.

[0010] Objectives, advantages, and a preferred mode of making and using the claimed subject matter may be understood best by reference to the accompanying drawings in conjunction with the following detailed description of illustrative embodiments.

BRIEF DESCRIPTION OF THE DRAWINGS

[0011] Figure 1 is a functional block diagram of an example embodiment of a therapy system that can provide negative-pressure treatment in accordance with this specification;

[0012] Figure 2 is a schematic, perspective view of an example of a tissue interface, illustrating additional details that may be associated with some example embodiments of the therapy system of Figure 1;

[0013] Figure 3 is an assembly view of an example of the tissue interface of Figure 2, illustrating some further details that may be associated with some example embodiments of the therapy system of Figure 1;

[0014] Figure 4 is a schematic, perspective view of an example configuration of a layer that may be associated with some embodiments of the tissue interface of Figure 3;

[0015] Figure 5 is a schematic, perspective view of an example configuration of an active component that may be associated with some embodiments of the tissue interface of Figure 3;

[0016] Figure 6 is a schematic, section view of a portion of an example configuration of an active component that may be associated with some embodiments of the tissue interface of Figure 3;

[0017] Figure 7 is a schematic, section view of a portion of an example configuration of an active component, illustrating additional details that may be associated with some embodiments of the active component of Figure 6;

[0018] Figure 8 is a schematic, perspective view of another example of an active component for use as part of the tissue interface of Figure 1, illustrating additional details that may be associated with some example embodiments;

[0019] Figure 9 is a section view illustrating additional details that may be associated with some embodiments of the active component of Figure 8;

[0020] Figure 10 is a section view illustrating additional details that may be associated with some additional embodiments of the active component of Figure 8;

[0021] Figure 11 is an assembly view of another example of an active component for use as part of the tissue interface of Figure 1, illustrating additional details that may be associated with some example embodiments; and

[0022] Figure 12 is an assembly view of another example embodiment of a tissue interface, illustrating additional details that may be associated with some example embodiments of the therapy system of Figure 1.

DESCRIPTION OF EXAMPLE EMBODIMENTS

[0023] The following description of example embodiments provides information that enables a person skilled in the art to make and use the subject matter set forth in the appended claims, but it may omit certain details already well-known in the art. The following detailed description is, therefore, to be taken as illustrative and not limiting.

[0024] The example embodiments may also be described herein with reference to spatial relationships between various elements or to the spatial orientation of various elements depicted in the attached drawings. In general, such relationships or orientation assume a frame of reference consistent with or relative to a patient in a position to receive treatment. However, as should be recognized by those skilled in the art, this frame of reference is merely a descriptive expedient rather than a strict prescription.

[0025] Figure 1 is a simplified functional block diagram of an example embodiment of a therapy system 100 that can provide negative-pressure therapy to a tissue site in accordance with this specification.

[0026] The term “tissue site” in this context broadly refers to a wound, defect, or other treatment target located on or within tissue, including, but not limited to, bone tissue, adipose tissue, muscle tissue, neural tissue, dermal tissue, vascular tissue, connective tissue, cartilage, tendons, or ligaments. A wound may include chronic, acute, traumatic, subacute, and dehiscent wounds, partial-thickness burns, ulcers (such as diabetic, pressure, or venous insufficiency ulcers), flaps, and grafts, for example. The term “tissue site” may also refer to areas of any tissue that are not necessarily wounded or defective, but are instead areas in which it may be desirable to add or promote the growth of additional tissue. For example, negative pressure may be applied to a tissue site to grow additional tissue that may be harvested and transplanted.

[0027] The therapy system 100 may include a source or supply of negative pressure, such as a negative-pressure source 105, and one or more distribution components. A distribution component is preferably detachable and may be disposable, reusable, or recyclable. A dressing, such as a dressing 110, and a fluid container, such as a container 115, are examples of distribution components that may be associated with some examples of the therapy system 100. As illustrated in the example of Figure 1, the dressing 110 may comprise or consist essentially of a tissue interface 120, a cover 125, or both in some embodiments.

[0028] A fluid conductor is another illustrative example of a distribution component. A “fluid conductor,” in this context, broadly includes a tube, pipe, hose, conduit, or other structure with one or more lumina or open pathways adapted to convey a fluid between two ends. Typically, a tube is an elongated, cylindrical structure with some flexibility, but the geometry and rigidity may vary. Moreover, some fluid conductors may be molded into or otherwise integrally combined with other components. Distribution components may also include or comprise interfaces or fluid ports to facilitate coupling and de-coupling other components. In some embodiments, for example, a dressing interface may facilitate coupling a fluid conductor to the dressing 110. For example, such a dressing interface may be a SENSAT.R.A.C.[™] Pad available from Kinetic Concepts, Inc. of San Antonio, Texas.

[0029] The therapy system 100 may also include a regulator or controller, such as a controller 130. Additionally, the therapy system 100 may include sensors to measure operating parameters and provide feedback signals to the controller 130 indicative of the operating parameters. As illustrated in Figure 1, for example, the therapy system 100 may include a first sensor 135 and a second sensor 140 coupled to the controller 130.

[0030] Some components of the therapy system 100 may be housed within or used in conjunction with other components, such as sensors, processing units, alarm indicators, memory, databases, software, display devices, or user interfaces that further facilitate therapy. For example, in some embodiments, the negative-pressure source 105 may be combined with the controller 130 and other components into a therapy unit.

[0031] In general, components of the therapy system 100 may be coupled directly or indirectly. For example, the negative-pressure source 105 may be directly coupled to the container 115 and may be indirectly coupled to the dressing 110 through the container 115. Coupling may include fluid, mechanical, thermal, electrical, or chemical coupling (such as a chemical bond), or some combination of coupling in some contexts. For example, the negative-pressure source 105 may be electrically coupled to the controller 130 and may be fluidly coupled to one or more distribution components to provide a fluid path to a tissue site. In some embodiments, components may also be coupled by virtue of physical proximity, being integral to a single structure, or being formed from the same piece of material.

[0032] A negative-pressure supply, such as the negative-pressure source 105, may be a reservoir of air at a negative pressure or may be a manual or electrically-powered device, such as a vacuum pump, a suction pump, a wall suction port available at many healthcare facilities, or a micro-pump, for example. “Negative pressure” generally refers to a pressure less than a local ambient pressure, such as the ambient pressure in a local environment

external to a sealed therapeutic environment. In many cases, the local ambient pressure may also be the atmospheric pressure at which a tissue site is located. Alternatively, the pressure may be less than a hydrostatic pressure associated with tissue at the tissue site. Unless otherwise indicated, values of pressure stated herein are gauge pressures. References to increases in negative pressure typically refer to a decrease in absolute pressure, while decreases in negative pressure typically refer to an increase in absolute pressure. While the amount and nature of negative pressure provided by the negative-pressure source 105 may vary according to therapeutic requirements, the pressure is generally a low vacuum, also commonly referred to as a rough vacuum, between -5 mm Hg (-667 Pa) and -500 mm Hg (-66.7 kPa). Common therapeutic ranges are between -50 mm Hg (-6.7 kPa) and -300 mm Hg (-39.9 kPa).

[0033] The container 115 is representative of a container, canister, pouch, or other storage component, which can be used to manage exudates and other fluids withdrawn from a tissue site. In many environments, a rigid container may be preferred or required for collecting, storing, and disposing of fluids. In other environments, fluids may be properly disposed of without rigid container storage, and a re-usable container could reduce waste and costs associated with negative-pressure therapy.

[0034] A controller, such as the controller 130, may be a microprocessor or computer programmed to operate one or more components of the therapy system 100, such as the negative-pressure source 105. In some embodiments, for example, the controller 130 may be a microcontroller, which generally comprises an integrated circuit containing a processor core and a memory programmed to directly or indirectly control one or more operating parameters of the therapy system 100. Operating parameters may include the power applied to the negative-pressure source 105, the pressure generated by the negative-pressure source 105, or the pressure distributed to the tissue interface 120, for example. The controller 130 is also preferably configured to receive one or more input signals, such as a feedback signal, and programmed to modify one or more operating parameters based on the input signals.

[0035] Sensors, such as the first sensor 135 and the second sensor 140, are generally known in the art as any apparatus operable to detect or measure a physical phenomenon or property, and generally provide a signal indicative of the phenomenon or property that is detected or measured. For example, the first sensor 135 and the second sensor 140 may be configured to measure one or more operating parameters of the therapy system 100. In some embodiments, the first sensor 135 may be a transducer configured to measure pressure in a pneumatic pathway and convert the measurement to a signal indicative of the pressure

measured. In some embodiments, for example, the first sensor 135 may be a piezo-resistive strain gauge. The second sensor 140 may optionally measure operating parameters of the negative-pressure source 105, such as a voltage or current, in some embodiments. Preferably, the signals from the first sensor 135 and the second sensor 140 are suitable as an input signal to the controller 130, but some signal conditioning may be appropriate in some embodiments. For example, the signal may need to be filtered or amplified before it can be processed by the controller 130. Typically, the signal is an electrical signal, but may be represented in other forms, such as an optical signal.

[0036] The tissue interface 120 can be generally adapted to partially or fully contact a tissue site. The tissue interface 120 may take many forms, and may have many sizes, shapes, or thicknesses, depending on a variety of factors, such as the type of treatment being implemented or the nature and size of a tissue site. For example, the size and shape of the tissue interface 120 may be adapted to the contours of deep and irregular shaped tissue sites. Any or all of the surfaces of the tissue interface 120 may have an uneven, coarse, or jagged profile.

[0037] In some embodiments, the tissue interface 120 may comprise or consist essentially of a manifold. A manifold in this context may comprise or consist essentially of a means for collecting or distributing fluid across the tissue interface 120 under pressure. For example, a manifold may be adapted to receive negative pressure from a source and distribute negative pressure through multiple apertures across the tissue interface 120, which may have the effect of collecting fluid from across a tissue site and drawing the fluid toward the source. In some embodiments, the fluid path may be reversed or a secondary fluid path may be provided to facilitate delivering fluid across a tissue site. In some illustrative embodiments, a manifold may comprise a plurality of pathways, which can be interconnected to improve distribution or collection of fluids. In some illustrative embodiments, a manifold may comprise or consist essentially of a porous material having interconnected fluid pathways. In some embodiments, a manifold may additionally or alternatively comprise projections that form interconnected fluid pathways. For example, a manifold may be molded to provide surface projections that define interconnected fluid pathways.

[0038] The thickness of the tissue interface 120 may also vary according to needs of a prescribed therapy. For example, the thickness of the tissue interface may be decreased to reduce tension on peripheral tissue. The thickness of the tissue interface 120 can also affect the conformability of the tissue interface 120. In some embodiments, a thickness in a range

of about 2 millimeters to 50 millimeters, or in some instances in a range of about 5 millimeters to 30 millimeters, may be suitable.

[0039] The tissue interface 120 may be either hydrophobic or hydrophilic. In an example in which the tissue interface 120 may be hydrophilic, the tissue interface 120 may also wick fluid away from a tissue site, while continuing to distribute negative pressure to the tissue site. The wicking properties of the tissue interface 120 may draw fluid away from a tissue site by capillary flow or other wicking mechanisms.

[0040] In some embodiments, the cover 125 may provide a bacterial barrier and protection from physical trauma. The cover 125 may also be constructed from a material that can reduce evaporative losses and provide a fluid seal between two components or two environments, such as between a therapeutic environment and a local external environment. The cover 125 may comprise or consist of, for example, an elastomeric film or membrane that can provide a seal adequate to maintain a negative pressure at a tissue site for a given negative-pressure source. The cover 125 may have a high moisture-vapor transmission rate (MVTR) in some applications. For example, the MVTR may be at least 250 grams per square meter per twenty-four hours in some embodiments, measured using an upright cup technique according to ASTM E96/E96M Upright Cup Method at 38°C and 10% relative humidity (RH). In some embodiments, an MVTR up to 5,000 grams per square meter per twenty-four hours may provide effective breathability and mechanical properties.

[0041] In some example embodiments, the cover 125 may be a polymer drape, such as a polyurethane film, that is permeable to water vapor but impermeable to liquid. Such drapes typically have a thickness in the range of 25-50 microns. For permeable materials, the permeability generally should be low enough that a desired negative pressure may be maintained. The cover 125 may comprise, for example, one or more of the following materials: polyurethane (PU), such as hydrophilic polyurethane; cellulotics; hydrophilic polyamides; polyvinyl alcohol; polyvinyl pyrrolidone; hydrophilic acrylics; silicones, such as hydrophilic silicone elastomers; natural rubbers; polyisoprene; styrene butadiene rubber; chloroprene rubber; polybutadiene; nitrile rubber; butyl rubber; ethylene propylene rubber; ethylene propylene diene monomer; chlorosulfonated polyethylene; polysulfide rubber; ethylene vinyl acetate (EVA); co-polyester; and polyether block polyimide copolymers. Such materials are commercially available as, for example, Tegaderm® drape, commercially available from 3M Company, Minneapolis Minnesota; polyurethane (PU) drape, commercially available from Avery Dennison Corporation, Pasadena, California; polyether block polyamide copolymer (PEBAX), for example, from Arkema S.A., Colombes, France;

and Inspire 2301 and Inspire 2327 polyurethane films, commercially available from Expopak Advanced Coatings, Wrexham, United Kingdom. In some embodiments, the cover 125 may comprise INSPIRE 2301 having an MVTR (upright cup technique) of 2600 g/m²/24 hours and a thickness of about 30 microns.

[0042] An attachment device may be used to attach the cover 125 to an attachment surface, such as undamaged epidermis, a gasket, or another cover. The attachment device may take many forms. For example, an attachment device may be a medically-acceptable, pressure-sensitive adhesive configured to bond the cover 125 to epidermis around a tissue site. In some embodiments, for example, some or all of the cover 125 may be coated with an adhesive, such as an acrylic adhesive, which may have a coating weight of about 25-65 grams per square meter (g.s.m.). Thicker adhesives, or combinations of adhesives, may be applied in some embodiments to improve the seal and reduce leaks. Other example embodiments of an attachment device may include a double-sided tape, paste, hydrocolloid, hydrogel, silicone gel, or organogel.

[0043] In operation, the tissue interface 120 may be placed within, over, on, or otherwise proximate to a tissue site. If the tissue site is a wound, for example, the tissue interface 120 may partially or completely fill the wound, or it may be placed over the wound. The cover 125 may be placed over the tissue interface 120 and sealed to an attachment surface near a tissue site. For example, the cover 125 may be sealed to undamaged epidermis peripheral to a tissue site. Thus, the dressing 110 can provide a sealed therapeutic environment proximate to a tissue site, substantially isolated from the external environment, and the negative-pressure source 105 can reduce pressure in the sealed therapeutic environment.

[0044] The fluid mechanics of using a negative-pressure source to reduce pressure in another component or location, such as within a sealed therapeutic environment, can be mathematically complex. However, the basic principles of fluid mechanics applicable to negative-pressure therapy are generally well-known to those skilled in the art, and the process of reducing pressure may be described illustratively herein as “delivering,” “distributing,” or “generating” negative pressure, for example.

[0045] In general, exudate and other fluid flow toward lower pressure along a fluid path. Thus, the term “downstream” typically implies something in a fluid path relatively closer to a source of negative pressure or further away from a source of positive pressure. Conversely, the term “upstream” implies something relatively further away from a source of negative pressure or closer to a source of positive pressure. Similarly, it may be convenient

to describe certain features in terms of fluid “inlet” or “outlet” in such a frame of reference. This orientation is generally presumed for purposes of describing various features and components herein. However, the fluid path may also be reversed in some applications, such as by substituting a positive-pressure source for a negative-pressure source, and this descriptive convention should not be construed as a limiting convention.

[0046] Negative pressure applied across the tissue site through the tissue interface 120 in the sealed therapeutic environment can induce macro-strain and micro-strain in the tissue site. Negative pressure can also remove exudate and other fluid from a tissue site, which can be collected in container 115.

[0047] In some embodiments, the controller 130 may receive and process data from one or more sensors, such as the first sensor 135. The controller 130 may also control the operation of one or more components of the therapy system 100 to manage the pressure delivered to the tissue interface 120. In some embodiments, controller 130 may include an input for receiving a desired target pressure and may be programmed for processing data relating to the setting and inputting of the target pressure to be applied to the tissue interface 120. In some example embodiments, the target pressure may be a fixed pressure value set by an operator as the target negative pressure desired for therapy at a tissue site and then provided as input to the controller 130. The target pressure may vary from tissue site to tissue site based on the type of tissue forming a tissue site, the type of injury or wound (if any), the medical condition of the patient, and the preference of the attending physician. After selecting a desired target pressure, the controller 130 can operate the negative-pressure source 105 in one or more control modes based on the target pressure and may receive feedback from one or more sensors to maintain the target pressure at the tissue interface 120.

[0048] Figure 2 is a schematic, perspective view of an example of the tissue interface 120 of Figure 1, illustrating additional details that may be associated with some embodiments. For example, the tissue interface 120 may include a first side 202 and a second side 204. In some embodiments, the tissue interface 120 may be at least partly, or substantially, formed from a non-foam material that is suitable for use with negative-pressure therapy. Additionally, the tissue interface 120 may be formed with a plurality of apertures 206, which may be positioned on either or both of the first side 202 and the second side 204 of the tissue interface 120, to allow fluid communication between the first side 202 and the second side 204 of the tissue interface 120. For example, the plurality of apertures 206 may be sized and adapted to allow for the transmission of negative pressure, as well as other fluids such as liquids, such as wound exudates, from the tissue site, through the tissue interface 120.

The tissue interface 120 may include or contain one or more materials, such as active component 208, which may be adapted to provide a cooling effect to an adjacent tissue site or surrounding materials. As shown in Figure 2, the active component 208 may be disposed or contained within the tissue interface 120.

[0049] Figure 3 is an assembly view of an example of the tissue interface 120 of Figure 1, illustrating additional details that may be associated with some embodiments in which the tissue interface 120 comprises multiple layers. Generally, the tissue interface 120 may include a component or section adapted to provide support and structure to the body of the tissue interface 120, such as structural component 302, and a component for providing a cooling or other therapeutic effect, such as active component 304. In some embodiments, each of the structural component 302 and the active component 304 of the tissue interface 120 may include one or more layers. For example, the structural component 302 of the tissue interface 120 may include a first structural layer 306 and a second structural layer 308. The first structural layer 306 may form a first side 307 of the tissue interface 120, and the second structural layer 308 may form a second side 309 of the tissue interface 120. Additionally, the active component 304 of the tissue interface 120 may include one or more layers positioned within the structural component 302, such as between multiple layers of the structural component 302, for example the first structural layer 306 and the second structural layer 308. For example, as illustrated in Figure 3, some embodiments of the tissue interface 120 may include an active component 304 comprising a stack of three layers, each containing a material adapted to provide a cooling effect, where the three layers are positioned between the first structural layer 306 and the second structural layer 308.

[0050] In some embodiments, the active component 304 may include a first active layer 310, a second active layer 312, and a third active layer 314, all of which may be positioned between the first structural layer 306 and the second structural layer 308 of the structural component 302. For example, the first structural layer 306, the first active layer 310, the second active layer 312, the third active layer 314, and the second structural layer 308 may be arranged in a stacked configuration, as depicted in Figure 3. Each of the first active layer 310, the second active layer 312, and the third active layer 314 may be bonded to the adjacent layer, with the first structural layer 306 bonded to the first active layer 310, and the second structural layer 308 bonded to the third active layer 314. Each of the layers of the structural component 302 and the active component 304 may be laminated or otherwise mechanically bonded to each other. In some alternative embodiments, the tissue interface 120 may include only one of the first structural layer 306 or second structural layer 308, and

the respective layer may form a sleeve or envelope around the one or more active layers, such as the first active layer 310, the second active layer 312, and the third active layer 314.

[0051] The structural component 302, which may include both the first structural layer 306 and the second structural layer 308, may comprise a material adapted to be placed in contact with a tissue site as well as communicate negative pressure to the tissue site. In some embodiments, the structural component 302 may comprise a filler material. In some embodiments, the structural component 302 may comprise a filler material in the form of a non-foam material. The structural component 302 may be suitable for communicating fluids, such as transferring negative pressure and/or wound exudates between the first side 307 of the tissue interface 120 and the second side 309 of the tissue interface 120. For example, the first structural layer 306 may include a first plurality of apertures 316, and the second structural layer 308 may include a second plurality of apertures 318, with the first plurality of apertures 316 and the second plurality of apertures 318 being sized and adapted to facilitate fluid communication through the tissue interface 120. For example, in some embodiments, the active component 304 may be sized so that at least some of the first plurality of apertures 316 of the first structural layer 306 may facilitate fluid communication with at least some of the second plurality of apertures 318 of the second structural layer 308 around the borders of the active component 304. Additionally or alternatively, the one or more layers of the structural component 302 may be formed from a porous material, which may allow for fluid transfer through the tissue interface 120. Additionally, the one or more layers of the structural component 302, such as the first structural layer 306 and the second structural layer 308, may provide a barrier between the active component 304 of the tissue interface 120 and a tissue site, so as to prevent direct physical contact between the active component 304 and the tissue site.

[0052] The one or more layers of the structural component 302 may be formed of a variety of materials, particularly materials that may require less force to be removed from a tissue site, such as a wound, even when potentially applied to the tissue site for a longer duration. For example, the one or more layers of the structural component 302 may comprise a polyethylene material, a polyurethane material, or a silicone or silicone-like material, among other possible materials. In some embodiments, for example, the first structural layer 306 and/or the second structural layer 308 may comprise or consist essentially of a hydrophobic polymer, such as a polyethylene film. The simple and inert structure of polyethylene can provide a surface that interacts little, if any, with biological tissues and fluids, providing a surface that may encourage the free flow of liquids and low adherence,

which can be particularly advantageous for many applications. Other suitable polymeric films may include polyurethanes, acrylics, polyolefin (such as cyclic olefin copolymers), polyacetates, polyamides, polyesters, copolyesters, PEBAX block copolymers, thermoplastic elastomers, thermoplastic vulcanizates, polyethers, polyvinyl alcohols, polypropylene, polymethylpentene, polycarbonate, styreneics, silicones, fluoropolymers, and acetates. More polar films suitable for laminating to a polyethylene film include polyamide, co-polyesters, ionomers, and acrylics. To aid in the bond between a polyethylene and polar film, tie layers may be used, such as ethylene vinyl acetate, or modified polyurethanes. In some embodiments, coextruded tie layers may be used, for example, where one layer is a polyethylene-compatible film and the other layer is a polyurethane-compatible film. In some additional or alternative embodiments, a polyethylene film may be surface treated, such as corona-treated or plasma-treated, to enhance its ability to bond to polar films. An ethyl methyl acrylate (EMA) film may also have suitable hydrophobic and welding properties for some configurations.

[0053] The one or more layers of the active component 304 of the tissue interface 120, such as the first active layer 310, the second active layer 312, and the third active layer 314, may comprise one or more active ingredients, such as one or more polymeric ingredients, which may be adapted to absorb a significant amount of heat in order to provide a local cooling effect. In some embodiments, one or more of the active layers of the active component 304 may include multiple active ingredients that may be contained separately from each other, such that when the active ingredients are allowed to mix, they may react according to an endothermic reaction to provide a cooling effect to the tissue interface 120. For example, the active component 304 may include two different active ingredients that may react with each other according to an endothermic reaction to provide a cooling effect to the environment surrounding the active component 304. For example, the one or more active ingredients may include ammonium nitrate, ammonium chloride, sodium chloride, potassium chloride, and nontoxic urea, among others. In some instances, the endothermic reaction may be achieved by mixing one or more of the above active ingredients with water. In some alternative embodiments, one or more different active ingredients, such as calcium chloride, sodium acetate, and magnesium sulfate may be selected for generating an exothermic reaction for providing a heating effect to the active component 304.

[0054] In some embodiments, the active ingredients of the one or more active layers may be separately contained within a plurality of separate compartments of each of the active layers of the tissue interface 120. For example, as shown in Figure 3, the first active layer

310 may include a first group of compartments 320, designated as the “A” compartments, which may contain a first active ingredient, and a second group of compartments 322 designated as the “B” compartments, which may contain a second active ingredient that is isolated from the first active ingredient. Similarly, the second active layer 312 may include a third group of compartments 324, designated as the “A” compartments containing the first active ingredient, and a fourth group of compartments 326, designated as the “B” compartments containing the second active ingredient. Likewise, the third active layer 314 may include a fifth group of compartments 328, designated as the “A” compartments containing the first active ingredient, and a sixth group of compartments 330, designated as the “B” compartments containing the second active ingredient. Accordingly, in some embodiments, each of the first active layer 310, the second active layer 312, and the third active layer 314 may include the same two active ingredients. Additional groups of compartments, such as compartments containing a third, fourth, or further additional active ingredients may also be included in one or more layers of the active component 304. In some embodiments, the active layers comprising multiple active compartments may be formed by a number of individual active compartments that are bonded together to form the one or more active layers. As will be described in further detail below, the different active ingredients may be kept separate or isolated from each other both within each active layer as well as between the one or more active layers of the active component 304 until a triggering event.

[0055] Additionally, although not shown in Figure 3, in some embodiments, each of the one or more layers of the active component 304 may individually include a material or chamber surrounding its respective compartments containing the active ingredients. Additionally or alternatively, in some embodiments, the active component 304 may include a single chamber surrounding and forming a fluid seal around the multiple active layers of the active component 304.

[0056] Figure 4 is a schematic, perspective view of an example active layer of the active component 304 of Figure 3, illustrating additional details that may be associated with some embodiments. For example, in Figure 4, the first active layer 310 of Figure 3 is shown as further including a first active chamber 402, which may provide a fluidly sealed container or barrier around the compartments of the first active layer 310 containing the active ingredients. For example, as shown in Figure 4, the first active chamber 402 may contain both the first group of compartments 320 and the second group of compartments 322. Each compartment of the first group of compartments 320 may contain a first active ingredient designated as the “A” ingredient, and each compartment of the second group of

compartments 322 may contain a second active ingredient designated as the “B” ingredient. The first active chamber 402 may be configured so as to contain the active ingredients of the first active layer 310 as they are released from their respective compartments, such as the first group of compartments 320 and the second group of compartments 322, and are allowed to mix and react. That is, as the walls of the individual compartments of the first group of compartments 320 and the second group of compartments 322 are breached or destructed during use of the first active layer 310, the active ingredients may still be contained by the structure of the first active chamber 402. The first active chamber 402 may therefore substantially prevent the active ingredients from escaping from the first active layer 310 and potentially coming into direct physical contact with a tissue site. The first active chamber 402 may be constructed from a variety of materials, however in some embodiments, may be substantially formed from one or more polymeric materials, such as thermoplastic polyurethanes, PEBAX, polyamides, ethylene-vinyl acetates, thermoplastic polyethylenes, and polyolefins.

[0057] Figure 5 is a schematic, perspective view of an example active component 304 of the tissue interface 120 of Figure 3, illustrating details that may be associated with some example embodiments. For example, the active component 304 may include a first active layer 310, a second active layer 312, and a third active layer 314, all of which may be contained within an active chamber 502 of the active component 304. The active chamber 502 may provide a sealed barrier or container around the active layers of the active component 304 in order to substantially prevent escape of the active ingredients of the active layers. In the arrangement of the active component 304 shown in Figure 5, the active ingredients of the first active layer 310, the second active layer 312, and the third active layer 314 may be free to mix and react with each other, while remaining contained within the active chamber 502. In additional or alternative embodiments, the active component 304 may include a lesser or greater number of active layers within the contained space of the active chamber 502, each of which may include one or more active ingredients that may react with active ingredients of the other active layers. In some additional or alternative embodiments, one or more of the active layers of the active component 304 may include only a single active ingredient. In such instances, the single active ingredient of one active layer may be released at the appropriate time to react with one or more active ingredients released by another one or more of the active layers, while remaining contained by the active chamber 502.

[0058] Figure 6 is a schematic, section view of an exemplary portion of the active component 304 of Figure 3 showing some additional details that may be associated with some embodiments. More specifically, Figure 6 illustrates how in assembled form, the multiple active layers of the active component 304, such as the first active layer 310, the second active layer 312, and the third active layer 314, may be positioned against one another so that the compartments containing the active ingredients of each of the active layers may be in close physical contact with compartments containing the active ingredients of the other active layers. As also shown in Figure 6, the active ingredients of each of the compartments of a single active layer, such as the first active layer 310, may be separated or isolated from the active ingredients of the adjacent compartments by first compartment walls 602. Additionally, the active ingredients of each compartment may be isolated from the active ingredients of the components of adjacent active layers by second compartment walls 604. In some embodiments, the compartment walls, such as the first compartment walls 602 and the second compartment walls 604 may be made from one or more of gelatin, starches, maltodextrins, alginates, chitosan, lipids, cellulose ethers, polyacrylates, polylactic acid or copolymers thereof, polysaccharides, cellulose, polyvinyl alcohol, or polyacrylates. In some embodiments, the first compartment walls 602 and/or the second compartment walls 604 may be formed as part of the individual compartments containing the active ingredients, and may form the enclosure or container of each of the individual active compartments.

[0059] In some alternative embodiments, the active component 304 may include multiple active layers containing the active ingredients, however the active component 304 may be formed as a single structure having only one divider layer or wall in place to separate the active ingredient of one layer from that of another. In other words, the active component 304 may be formed with multiple active layers, where each of the active layers includes a single compartment containing an active ingredient.

[0060] Figure 7 is a schematic of the exemplary portion of the active component 304 of Figure 6, illustrating some additional details associated with application or use of the active component 304. As shown in Figure 7, at the time of a triggering event, the walls or seals between groups of compartments containing different active ingredients may be broken, allowing the active ingredients to mix and undergo an endothermic reaction to provide a cooling effect to the tissue interface 120. For example, the compartments containing the active ingredients may be at least partially disrupted or breached so as to allow the individual active ingredients of each of the compartments to come into contact with each other to cause the desired reaction. In circumstances where the tissue interface 120 is used as part of the

dressings 110 as a component of the therapy system 100 for use in negative-pressure applications, the active component 304, as well as the overall tissue interface 120, may be compressed, squeezed, bent, or otherwise deformed from its original resting shape and position. Due to the compressive or bending forces applied to the active component 304 resulting from the application of negative pressure to the dressing 110, the walls or barriers of the individual compartments containing the active ingredients may be disrupted, breached, or broken, thus allowing the individual active ingredients to escape and come into contact with active ingredients also released from the other compartments. For example, as depicted in Figure 7, a first wall 702 separating a first active compartment 704 from a second active compartment 706 may be disrupted under compressive or bending forces due to the application of negative pressure to the dressing 110 and tissue interface 120, thus creating at least a first breach 708. As also depicted in Figure 7, the first breach 708 may allow the active ingredients previously contained within the second active compartment 706, or the active ingredient designated as the “B” active ingredient, to migrate into the space of the first active compartment 704 in order to react with the active ingredient designated as the “A” active ingredient, previously contained within the first active compartment 704. Similarly, the walls or barriers of the active compartments that are positioned on the surfaces of the active compartments between the active layers, such as the second wall 710 of the first active compartment 704 and a third wall 712 of a third active compartment 714, may be breached so as to allow mixing of the individual active ingredients between the multiple active layers of the active component 304. In some embodiments, the active ingredients of each of the individual compartments of the active component 304 may be allowed to mix and react with the active ingredients of some, if not all, of the other active compartments.

[0061] In some additional embodiments, tissue interface 120 may include an active component, such as active component 304, that responds to differential pressure to provide multiple stimuli of cooling or heating effects. For example, the walls or dividers separating the active ingredients in the different active compartments from each other may breach at different amounts of force caused by application of negative pressure of different magnitudes. In some embodiments, one or more of the separators, such as first wall 702, may break under negative pressure in a first range of approximately -80mmHg to -120mmHg that is applied to the tissue interface 120, while a second group of the separators, such as second wall 710, may break under the application of negative pressure in a second range of approximately -100mmHg to -150mmHg. In some embodiments, approximately 50% of the separators between active compartments may break at a first level of applied negative pressure, such as

approximately -100mmHg negative pressure, and the remaining separators may break at a second level of applied negative pressure, such as at approximately -125mmHg negative pressure.

[0062] Figure 8 is a schematic, perspective view of another example of an active component 208, for use as part of the tissue interface 120, illustrating additional details that may be associated with some example embodiments. The active component 208 of Figure 8 may include one or more layers, with each layer having multiple compartments, or bubbles, for containing the one or more active ingredients of the active component 208. The active ingredient in one of the compartments, or bubbles, may remain isolated from the active ingredients of the neighboring compartments, or bubbles, until a time where it is desirable for the active ingredients to be allowed to come into contact with each other in order to react to provide the cooling effect to the tissue interface 120.

[0063] In some embodiments, the active component 208 may include a first active layer 802, which may be formed from a first sheet 806 and a second sheet 808. For example, each of the first sheet 806 and the second sheet 808 may comprise or consist essentially of a non-porous polymer film, having inner surfaces coupled to each other to form a sealed region 810 defining a plurality of bubbles in the form of closed cells 812. The inner surfaces of the first sheet 806 and the second sheet 808 may be coupled to each other to form closed cells 812 that are substantially airtight to inhibit premature collapsing of the closed cells 812 or escape of the active ingredients contained within each of the closed cells 812.

[0064] The two sheets of non-porous, polymeric film, first sheet 806 and second sheet 808, may be in the form of a single sheet of material having two laminae or two separate sheets that are coupled together to form the closed cells 812. The sheets of non-porous, polymeric film may initially be separate sheets that are brought into superposition and sealed or they may be formed by folding a single sheet unto itself with a heat sealable surface facing inward. Each sheet of the non-porous polymeric film may also be a monolayer or multilayer structure depending on the desired structure of the closed cells 812.

[0065] The sheets of non-porous, polymeric film may comprise any flexible material that can be manipulated to enclose closed cells. For example, the first active layer 802 may be formed of two welded layers of polyolefin film that may encapsulate air, the active ingredients, and potentially other substances, in pockets. Additionally or alternatively, various thermoplastic materials may be used for producing the film layers of the first active layer 802. Non-limiting examples of suitable thermoplastic polymers include polyethylene homopolymers, such as low density polyethylene (LDPE) and high density polyethylene

(HDPE), and polyethylene copolymers, such as, ionomers, EVA, EMA, heterogeneous (Ziegler-Natta catalyzed) ethylene/alpha-olefin copolymers, and homogeneous (metallocene, single-site catalyzed) ethylene/alpha-olefin copolymers. Ethylene/alpha-olefin copolymers are copolymers of ethylene with one or more comonomers selected from C₃ to C₂₀ alpha-olefins, such as 1-butene, 1-pentene, 1-hexene, 1-octene, and methyl pentene, in which the polymer molecules comprise long chains with relatively few side chain branches, including linear low-density polyethylene (LLDPE), linear medium-density polyethylene (LMDPE), very low-density polyethylene (VLDPE), and ultra-low-density polyethylene (ULDPE). Various other materials are also suitable such as, polypropylene homopolymer or polypropylene copolymer (e.g., propylene/ethylene copolymer), polyesters, polystyrenes, polyamides, polycarbonates, etc.

[0066] In some example embodiments, the sealed region 810 may be formed by a heat seal between the inner surfaces of the first sheet 806 and the second sheet 808. Additionally or alternatively, the sealed region 810 may be formed by adhesion between the first sheet 806 and the second sheet 808. The first sheet 806 and the second sheet 808 may also be adhesively bonded to each other. The closed cells 812 may be substantially airtight when formed and have an internal pressure that is substantially an ambient pressure. In other embodiments, in addition to being at least partially filled with active ingredients, the closed cells 812 may be inflated with air or other suitable gas, such as, for example, carbon dioxide or nitrogen. The closed cells 812 may be inflated to have an internal pressure greater than the atmospheric pressure to maintain their shape and resistance to premature collapsing or perforating under pressure. For example, the closed cells 812 may be inflated to a pressure up to about 25 psi above the atmospheric pressure so that they do not collapse before the desired time of releasing the active ingredients.

[0067] The sealed region 810 may comprise sealed segments between the closed cells 812 that may be flexible enough so that the first active layer 802 is sufficiently flexible to conform to the shape of a tissue site when in use. The sealed segments may be sufficiently flexible or sized so that the first active layer 802 may be folded into two or more layers. The sealed segments of the sealed region 810 may also be perforated to provide pathways for fluid to flow through the first active layer 802. In some example embodiments, the sealed region 810 may include a plurality of apertures 814 between the closed cells 812 in the sealed region 810 and extending through both the first sheet 806 and the second sheet 808 to permit fluid to flow through the first active layer 802. The number of apertures 814 may vary, depending on the particular intended application of the first active layer 802 and tissue

interface 120. The apertures 814 may have different shapes, such as, for example, circular, elliptical, rectangular, or other irregular shape. Such apertures 814 may have a diameter, major axis, or length between about 0.5 mm and 1.5 mm. In other example embodiments, the apertures 814 may be formed by perforating or cutting the segments of the sealed region 810. In some embodiments, the sealed segments between the closed cells of the sealed region 810 may provide areas for allowing the active component 208 to be perforated and/or act for sizing purposes.

[0068] As illustrated in the example of Figure 8, the sealed region 810 may define the base or the cross-sectional shape of each of the closed cells 812 as generally circular. Additionally or alternatively, the base of one or more of the closed cells 812 may have other shapes, such as rectangular, triangular, or hexagonal. The closed cells 812 may be formed with a three-dimensional shape corresponding to the cross-sectional shape of the closed cells 812. For example, the closed cells 812 may be generally hemispherical or spherical in shape, as shown in Figure 8. In other example embodiments, the closed cells 812 may be formed with a volumetric shape that is generally conical, cylindrical, tubular having a flattened or hemispherical end, or geodesic shape. The closed cells 812 that are generally hemispherical or spherical in shape may have a diameter between about 0.5 mm and 10 mm. The closed cells 812 may also have a pitch, i.e., the center to center distance between each of the closed cells 812, between about 1.5 mm and 15 mm. Because the sealed region 810 defines the base of the closed cells 812 including the diameter of a circular base and the pitch of adjacent closed cells 812, the surface area of the first active layer 802 covered by the closed cells 812 may also be determined as a percentage, i.e., the cell coverage percentage. In one example embodiment wherein the diameter of the closed cells 812 is about 1.0 mm and the pitch is about 2.0 mm, the cell coverage percentage is about 22% of the surface area of the first active layer 802. In other example embodiments, wherein the diameter of the closed cells 812 is about 2.0 mm and the pitch is about 5.0 mm, the cell coverage percentage is about 14% of the surface area of the first active layer 802. In yet another example embodiment wherein the diameter of the closed cells 812 is about 1.0 mm and the pitch is about 1.5 mm, the cell coverage percentage is about 30% of the surface area of the first active layer 802. In still another example embodiment, wherein the diameter of the closed cells 812 is about 1.5 mm, the pitch is about 2.0 mm, and the closed cells 812 are more tightly arranged such that there are about 28.5 cells in a 10 mm² section of the first active layer, the cell coverage percentage is about 51% of the surface area of the first active layer 802. Depending on the diameter, pitch, and arrangement of the closed cells 812, the cell coverage percentage may range

between about 10% and about 55% of the surface area of the first active layer 802. Closed cells 812 having other base shapes or three-dimensional shapes also may have a cell coverage percentage in generally the same range.

[0069] Some embodiments of the closed cells 812 may have three-dimensional shapes, including hemispherical shapes, spherical shapes, conical shapes, cylindrical shapes, or tubular shapes formed with a flattened or hemispherical end. These shapes may be formed in one or both of the first sheet 806 and the second sheet 808, such as the single hemispherical shape shown in Figure 9 and the two hemispherical shapes that are aligned with one another to form a spherical shape as shown in Figure 10. The closed cells 812 may have a height between about 0.25 mm and about 5 mm, e.g., about half the diameter of closed cells 812 having a hemispherical shape as described in the examples above. In some embodiments, the closed cells 812 may measure about 10 mm in diameter and about 3 mm in height. In other example embodiments, the closed cells 812 may have a generally tubular shape formed with generally parallel walls extending from the sealed region 810 to a hemispherical end. In yet other example embodiments, closed cells 812 having a tubular shape may have a diameter of about 1.5 mm and an average height in a range between about 2.0 mm and 4.0 mm.

[0070] Still referring primarily to Figure 8, the first sheet 806 and the second sheet 808 may each have a thickness of about 5 μm to 500 μm , and the sealed region 810 may have a thickness of between about 10 μm and 1000 μm . The walls of the closed cells 812 after being formed by coupling the first sheet 806 and the second sheet 808 together may have a thickness relative to the thickness of the first sheet 806 and the second sheet 808 defined by a draw ratio, which is the ratio of the average height of the closed cells 812 to the average thickness of the first sheet 806 and the second sheet 808. In one example embodiment where the closed cells 812 have a generally tubular shape, the first sheet 806 and the second sheet 808 may have an average thickness of 250 μm and the closed cells 812 may have an average height in a range between about 2.0 mm and 4.0 mm with a diameter of about 1.5 mm. Consequently, the closed cells 812 have a draw ratio ranging from about 8:1 to about 16:1 for heights of 2.0 and 4.0 mm, respectively. In another example embodiment, the first sheet 806 and the second sheet 808 may have an average thickness of 100 μm and the closed cells 812 may have an average height in a range between about 2.0 mm and 4.0 mm with a diameter of about 1.5 mm. Consequently, the closed cells 812 have a draw ratio ranging from about 20:1 to about 40:1 for heights of 2.0 and 4.0 mm, respectively. In yet other example embodiments, it is desirable that the draw ratio be greater than about 16:1 where the thickness

of the first sheet 806 and the second sheet 808 is less than about 250 μm . The first sheet 806 and the second sheet 808 may each have the same or different thicknesses and flexibilities.

[0071] Figure 9 is a section view of an example of the first active layer 802, illustrating additional details that may be associated with some embodiments. For example, the first active layer 802 of Figure 9 may be configured so that the closed cells extend from only one side of the sealed region of the first active layer 802, such as closed cells 812 having a hemispherical shape. More specifically, the first active layer 802 may comprise two sheets of polymeric film, the first sheet 806 and the second sheet 808, having inner surfaces coupled to each other in a pattern defining a plurality of the closed cells 812. The first sheet 806 and the second sheet 808 may be sealed to each other in the sealed region 810 that defines the closed cells 812 that are generally hemispherical in shape. The closed cells 812 may project from only one side of the first active layer 802, as shown in Figure 9, by using sheets of polymeric film having a different thickness or flexibility for each of the first sheet 806 and the second sheet 808 when forming the first active layer 802. For example, the closed cells 812 may be formed in the first sheet 806 by applying a vacuum to the first sheet 806 where the second sheet 808 is sufficiently thicker than the first sheet 806 to withstand the vacuum being applied and to retain a generally planar shape. The closed cells 812 having other shapes may be formed to extend from only one side of the sealed region 810 of the first active layer 802 and may be formed by using a variety of different methods. For example, the shape of the closed cells 812 may be formed separately in the first sheet 806, which can be subsequently coupled to the second sheet 808 to complete the encapsulation of the closed cells 812. The second sheet 808 may have the same thickness as the first sheet 806 so that the sealed region 810 remains thin and flexible.

[0072] Figure 10 is a section view of another example of the first active layer 802, illustrating additional details that may be associated with some embodiments. For example, the first active layer 802 of Figure 10 may include portions of closed cells 812 that are formed in both of the two sheets of the first active layer 802, so that the portions of closed cells 812 extend from both sides of the sealed region 810 of the first active layer 802. More specifically, the first active layer 802 may comprise two sheets of polymeric film, the first sheet 806 and the second sheet 808, having inner surfaces coupled to each other in a pattern defining the plurality of closed cells 812. For example, the portions of closed cells 812 formed in each of the first sheet 806 and the second sheet 808 may be hemispherical in shape, such as open cell 1002 and open cell 1004. The open cell 1002 and the open cell 1004 may then be aligned to form the single closed cell 812 having a generally spherical shape. In other

words, each of the single closed cells 812 comprises two open cells, open cell 1002 and open cell 1004, formed in the first sheet 806 and the second sheet 808, respectively. The first sheet 806 and the second sheet 808 may be sealed to each other in the sealed region 810 that defines the closed cells 812 that are generally spherical in shape. In other example embodiments, the open cells, such as open cell 1002 and open cell 1004, in each sheet, such as the first sheet 806 and the second sheet 808, may not be aligned with each other, but rather are overlapped or aligned with the sealed portions of the opposite sheet. In some embodiments, the closed cells 812 may be formed on both sides of the sealed region 810 by using sheets of polymeric film having a different thickness or flexibility. For example, the shape of the closed cells 812 may be asymmetric when the first sheet 806 and the second sheet 808 have different thicknesses or flexibilities from each other. However, when the first sheet 806 and the second sheet 808 have substantially identical thickness or flexibility, the shape of the closed cells 812 may be substantially spherical, as shown in Figure 10.

[0073] Figure 11 is a schematic, assembly view of an active component 208 for use as part of the tissue interface 120, illustrating additional details that may be associated with some additional example embodiments. The active component 208 of Figure 11 may be similar to the embodiment of the active component 208 illustrated in Figure 8, however may include multiple layers, with each layer having multiple compartments, or bubbles, for containing the one or more active ingredients of the active component 208. For example, the active component 208 may include a first active layer 1102 and a second active layer 1104. In some embodiments, the first active layer 1102 may include a first plurality of closed cells 1108, and the second active layer 1104 may include a second plurality of closed cells 1110. For example, the first plurality of closed cells 1108 may contain a first active ingredient, and the second plurality of closed cells 1110 may contain a second active ingredient. Each of the first plurality of closed cells 1108 and the second plurality of closed cells 1110 may be configured to contain the first active ingredient and the second active ingredient, respectively, until the appropriate time for allowing the first active ingredient and the second active ingredient to come into contact with each other to react in order to provide the cooling effect of the active component 208. For example, the active component 208 may be subjected to compression or apposition forces due to the application of negative-pressure therapy to the tissue interface 120, of which the active component 208 may be a component. Each of the first plurality of closed cells 1108 and the second plurality of closed cells 1110 may be configured to perforate or break under an applicable compression or apposition force that may correspond to the typical force experienced due to the application of the negative-

pressure therapy. In some additional or alternative embodiments, the first plurality of closed cells 1108 and the second plurality of closed cells 1110 may be configured to be ruptured or torn open due to a manual compressive, twisting, bending, or tearing force applied by a user. Upon rupturing of at least some of both the first plurality of closed cells 1108 and the second plurality of closed cells 1110, the different active ingredients, such as a first active ingredient and a second active ingredient, may come into contact with each other and react to provide the cooling effect of the active component 208.

[0074] In some additional or alternative embodiments, a first subset of the first plurality of closed cells 1108 may include a first active ingredient, while a second subset of the first plurality of closed cells 1108 may include a second active ingredient. Similarly, additional active ingredients may also be include in each of the first active layer 1102 or the second active layer 1104, as third or fourth subsets of either or both of the first plurality of closed cells 1108 and the second plurality of closed cells 1110. In some additional embodiments, the active component 208 may include additional active layers, such as a third active layer, a fourth active layer, etc. Additionally, although not shown in Figure 8 or 11, the example embodiments of the active component 208 may be surrounded or encased by an active chamber, so as to contain the active ingredients once released from the closed cells and to prevent the active ingredients from coming into direct contact with the tissue site.

[0075] Figure 12 is an assembly view of another example embodiment of the tissue interface 120 of Figure 1, illustrating additional details that may be associated with some further embodiments in which the tissue interface 120 comprises multiple layers. In the example embodiment depicted in Figure 12, the tissue interface 120 may include a structural component 1202, which may be in the form of a single layer adapted to provide support and structure to the tissue interface 120. As shown in Figure 12, the single layer of the structural component 1202 may be positioned on a top side of the tissue interface 120. In some additional or alternative embodiments, the structural component 1202 may further include a second layer adapted to be positioned on a bottom side of the tissue interface 120. The tissue interface 120 of Figure 12 may further include active component 1204, which may include a stack of one or more layers, such as the first active layer 1206 and the second active layer 1208, each of which may contain a material, such as active ingredients, adapted to react to provide a cooling effect. Additionally, the tissue interface 120 of Figure 12 may include a contact layer 1210, which may be adapted to be positioned between the one or more layers of the active component 1204 and a bottom surface of the tissue interface 120 that may be adapted to be placed in contact with a tissue site. In some embodiments, the contact layer

1210 may comprise a mixture of collagen and oxidized regenerated cellulose (ORC). In some instances, by including a collagen/ORC component as part of the contact layer 1210, the tissue interface 120 may be able to more rapidly mitigate inflammation and swelling of a tissue site. For example, a collagen/ORC material of the contact layer 1210 may provide a sacrificial matrix metalloprotease (MMP) substrate at the tissue site, as well as offer a pH-balancing effect at the tissue site. While normal endogenous levels of MMPs are essential for tissue remodeling during wound healing, in excess, MMPs may continually break down the new tissue being formed, which may lead to a sustained state of inflammation and a wound that does not heal quickly. The inclusion of a sacrificial MMP substrate, such as collagen, may provide a substrate for the excess MMPs to break down, as opposed to solely the new tissue being formed. The relative amounts of the collagen and ORC in the material of the contact layer 1210 may vary, however the material of the contact layer 1210 may comprise between 0.5% and 99% collagen and between 0.5% and 95% ORC. Additionally, the collagen component of the contact layer 1210 may induce faster granulation of a tissue site. Additional therapeutic ingredients may also be included in the contact layer 1210. For example, silver, copper, zinc polyhexamethylene biguanide (PHMB), as well as other antimicrobial and ingredients could be incorporated into the contact layer 1210 which may help treat tissue sites that may benefit from tissue dressings with such antimicrobial properties. In general, the additional therapeutic ingredients may comprise between about 0.05% and 10% of the material of the contact layer 1210.

[0076] In some embodiments, the contact layer 1210 may be in the form of a collagen/ORC sheet included in the tissue interface 120. Additionally or alternatively, the contact layer 1210 may be in the form of a collagen/ORC mixture that is spray-coated onto a bottom surface of the tissue interface 120 that is for being placed in contact with a tissue site. For example, the contact layer 1210 may be spray-coated on a bottom surface of the second active layer 1208 of the active component 1204 of Figure 12. In some additional embodiments, a collagen and/or collagen/ORC material may be incorporated with the active component 208 of Figure 8, described above. For example, the sealed segments of the sealed region 810 may be coated with a layer of collagen or collagen/ORC, or additionally or alternatively, the surfaces of the closed cells 812 may be coated with such a collagen or collagen/ORC material.

[0077] Some additional embodiments of the tissue interface 120 may incorporate additional features for providing therapeutic benefits to a tissue site. For example, the tissue interface 120 may further include a heating element, so as to be able to provide a heating

effect to the tissue interface 120. In some embodiments, the tissue interface 120 may include one or more layers of a conductive textile material, which may be electrically connected through leads to an electrical power source. A control button or activation switch that is separate from the tissue interface 120 and dressing 110, for example as part of the electrical power source, may be engaged to cause the electrical power source to provide a prescribed voltage to the conductive textile material in order to heat the tissue interface 120. The one or more layers of conductive textile material may be insulated from the surrounding layers and the external borders of the tissue interface 120 so as not to come into direct contact with a tissue site. The tissue interface 120 may therefore offer the multiple capabilities and benefits of being able to provide both heating and cooling effects to a tissue site, for example, in an alternating fashion. Such alternating warm and cold therapy may be particularly advantageous in sports medicine applications. The alternating warm and cold therapy may be applied during the administration of negative-pressure therapy.

[0078] The systems, apparatuses, and methods described herein may provide significant advantages. For example, including the therapeutic cooling benefits, as well as in some embodiments the heating benefits, offered by the tissue interface 120 may provide significant comfort benefits during the administration of negative-pressure therapy to a tissue site. Improving patient comfort by incorporating the therapeutic and/or soothing benefits offered by the tissue interface 120 will result in improved patient compliance with therapy regimens and protocols. Additionally, the comfort benefits offered by the tissue interface 120 may reduce or eliminate any potential need for administering separate pain relief medication during the application of negative-pressure therapy, as well as upon dressing removal. The incorporation of the tissue interface 120 including the pain-reducing cooling benefits may allow for the application of negative-pressure therapy to tissue sites involving wounds that are especially painful to treat, and in cases where negative-pressure therapy may not otherwise have been considered. Furthermore, the cooling benefits of the tissue interface 120 may offer anti-inflammatory and/or pain-relief benefits without the administration of medication that would require a prescription and possibly take time to administer, as well as potentially have a delayed effect following the administration.

[0079] The therapeutic and/or soothing effects of the tissue interface 120 may also allow for an increased use of intermittent negative-pressure therapy. Thus, the beneficial effects of the tissue interface 120 may allow for an increased use of intermittent or dynamic negative-pressure therapy options, as opposed to in some cases having to suspend negative-pressure therapy in order to provide a break or reprieve to the patient during a therapy

regimen. Furthermore, including the cooling aspects of the tissue interface 120 may offer the same or similar pain-reduction benefits as other solutions that require the instillation of pain-reducing agents or medicaments such as lidocaine. The pain-reducing cooling aspects of the tissue interface 120 may also improve comfort during dressing removal, therefore also potentially reducing or eliminating the need to inject a soaking solution, such as saline solution, into a dressing upon dressing removal. The cooling features of the tissue interface 120 may therefore offer time-saving as well as more economical pain-relief solutions during both the application of negative-pressure therapy as well as during other stages of wound treatment, such as dressing removal.

[0080] The cooling features of the disclosed dressing components may also be used in numerous applications outside of the negative-pressure therapy context. For example, the cooling features may be included in the form of a standalone dressing for use in treatment of wounds or other tissue injuries. For example, some embodiments of the tissue interface 120 may be used for treatment of incision wounds to alleviate swelling or inflammation. Additionally, the cooling features may be incorporated in a tissue wrap or compression sleeve that may be used in sports-medicine-related applications, particularly over intact skin injuries requiring assistance with swelling or inflammation. In at least some of the latter applications, the cooling functionality may be manually initiated by a user twisting, bending, squeezing, or compressing the dressing, bandage, or wrap to allow the inner active ingredients to come into contact with each other and react to provide the cooling benefits.

[0081] While shown in a few illustrative embodiments, a person having ordinary skill in the art will recognize that the systems, apparatuses, and methods described herein are susceptible to various changes and modifications that fall within the scope of the appended claims. Moreover, descriptions of various alternatives using terms such as “or” do not require mutual exclusivity unless clearly required by the context, and the indefinite articles “a” or “an” do not limit the subject to a single instance unless clearly required by the context. Components may also be combined or eliminated in various configurations for purposes of sale, manufacture, assembly, or use. For example, in some configurations the dressing 110, the container 115, or both may be eliminated or separated from other components for manufacture or sale. In other example configurations, the controller 130 may also be manufactured, configured, assembled, or sold independently of other components.

[0082] The appended claims set forth novel and inventive aspects of the subject matter described above, but the claims may also encompass additional subject matter not specifically recited in detail. For example, certain features, elements, or aspects may be

omitted from the claims if not necessary to distinguish the novel and inventive features from what is already known to a person having ordinary skill in the art. Features, elements, and aspects described in the context of some embodiments may also be omitted, combined, or replaced by alternative features serving the same, equivalent, or similar purpose without departing from the scope of the invention defined by the appended claims.

CLAIMS

What is claimed is:

1. An apparatus for treating a tissue site, comprising:
 - a manifold having a first side, a second side configured to be placed adjacent to a tissue site, and a plurality of apertures configured to allow for fluid communication between the first side and the second side;
 - a first plurality of compartments contained by the manifold and containing a first substance; and
 - a second plurality of compartments contained by the manifold and containing a second substance;wherein the first plurality of compartments and the second plurality of compartments are configured to allow mixing of the first substance and the second substance.
2. The apparatus of claim 1, wherein the mixing of the first substance and the second substance produces an endothermic reaction.
3. The apparatus of claim 1, wherein the first substance is water and the second substance produces an endothermic reaction upon mixing with water.
4. The apparatus of claim 1, wherein the first substance is water and the second substance is selected from the group consisting of ammonium nitrate, ammonium chloride, sodium chloride, and sodium thiosulfate.
5. The apparatus of claim 1, wherein the mixing of the first substance and the second substance produces an exothermic reaction.
6. The apparatus of claim 1, wherein the second side of the manifold comprises a polyethylene film.
7. The apparatus of claim 1, wherein the second side of the manifold comprises a polyurethane film.
8. The apparatus of claim 1, wherein the manifold comprises a silicone gel.

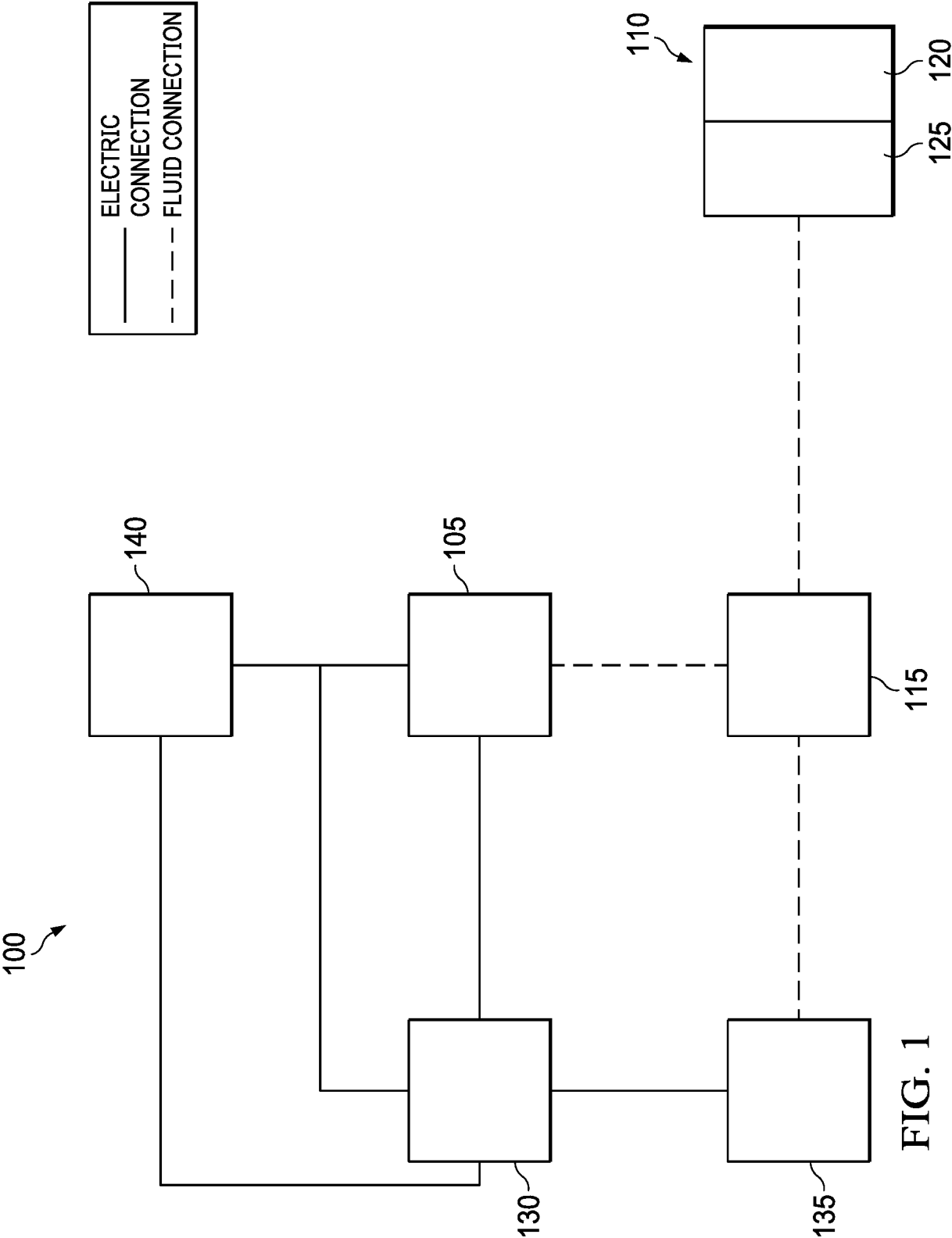
9. The apparatus of claim 1, further comprising a contact layer positioned adjacent the second side of the manifold, wherein the contact layer comprises collagen and oxidized regenerated cellulose.
10. The apparatus of claim 9, wherein the collagen and oxidized regenerated cellulose are spray coated onto the second side of the manifold.
11. The apparatus of claim 1, further comprising an antimicrobial agent incorporated within the manifold.
12. The apparatus of claim 1, wherein the manifold is adapted to be compressed under the application of negative pressure to cause the first substance to be released from at least one of the plurality of first compartments and the second substance to be released from at least one of the plurality of second compartments.
13. The apparatus of claim 1, wherein the first substance and the second substance are adapted to form hydroxyethyl cellulose when mixed.
14. The apparatus of claim 1, wherein the first substance and the second substance are adapted to form sodium polyacrylate gel when mixed.
15. The apparatus of claim 1, wherein the first substance and the second substance are adapted to form polyethylene glycol when mixed.
16. The apparatus of claim 1, wherein at least a first portion of the first plurality of compartments and the second plurality of compartments are formed as part of a first active layer.
17. The apparatus of claim 16, further comprising a second active layer, wherein at least a second portion of the first plurality of compartments and the second plurality of compartments are formed as part of the second active layer.
18. The apparatus of claim 1, further comprising a heating layer comprising a conductive textile material adapted to receive an electrical charge from a source of electricity.
19. The apparatus of claim 18, wherein the heating layer is contained within the manifold.

20. An apparatus for treating a tissue site, comprising:
- a manifold having a first side, a second side, and a plurality of apertures adapted to fluidly connect the first side and the second side;
 - a first separator disposed within at least a portion of the manifold and adapted to provide a first compartment and a second compartment within the manifold;
 - a first substance contained within the first compartment; and
 - a second substance contained within the second compartment;
- wherein the first separator is configured to allow mixing of the first substance and the second substance to cause a chemical reaction upon application of a first amount of negative pressure to the manifold.
21. The apparatus of claim 20, wherein the chemical reaction is an endothermic reaction for reducing the temperature of the apparatus.
22. The apparatus of claim 20, further comprising a chamber adapted to encapsulate the first compartment and the second compartment within the manifold.
23. The apparatus of claim 20, further comprising:
- a second separator configured to allow mixing of the first substance and the second substance upon application of a second amount of negative pressure to the manifold.
24. The apparatus of claim 20, wherein the first amount of negative pressure is in a range of -80mmHg to -120mmHg.
25. The apparatus of claim 23, wherein:
- the first amount of negative pressure is in a first range of -80mmHg to -120mmHg;
 - and
 - the second amount of negative pressure is in a second range of -100mmHg to -150mmHg.
26. The apparatus of claim 20, wherein the manifold is adapted to bend under the application of the first amount of negative pressure to cause the first separator to fracture and allow mixing of the first substance and the second substance between the first compartment and the second compartment.

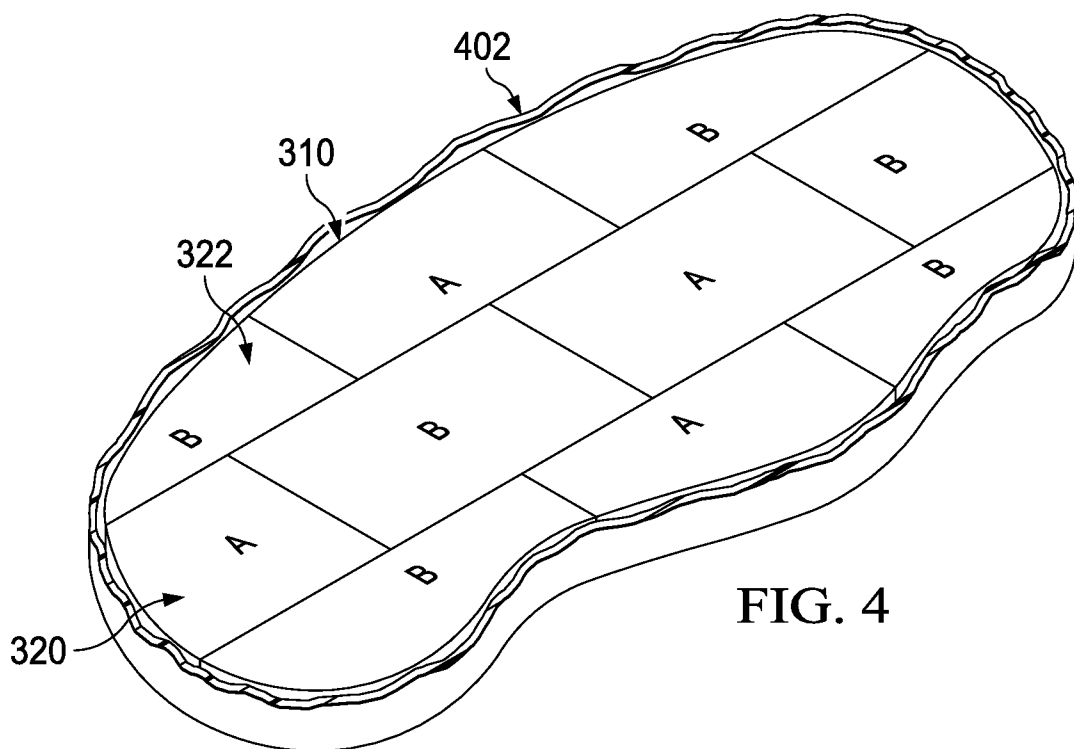
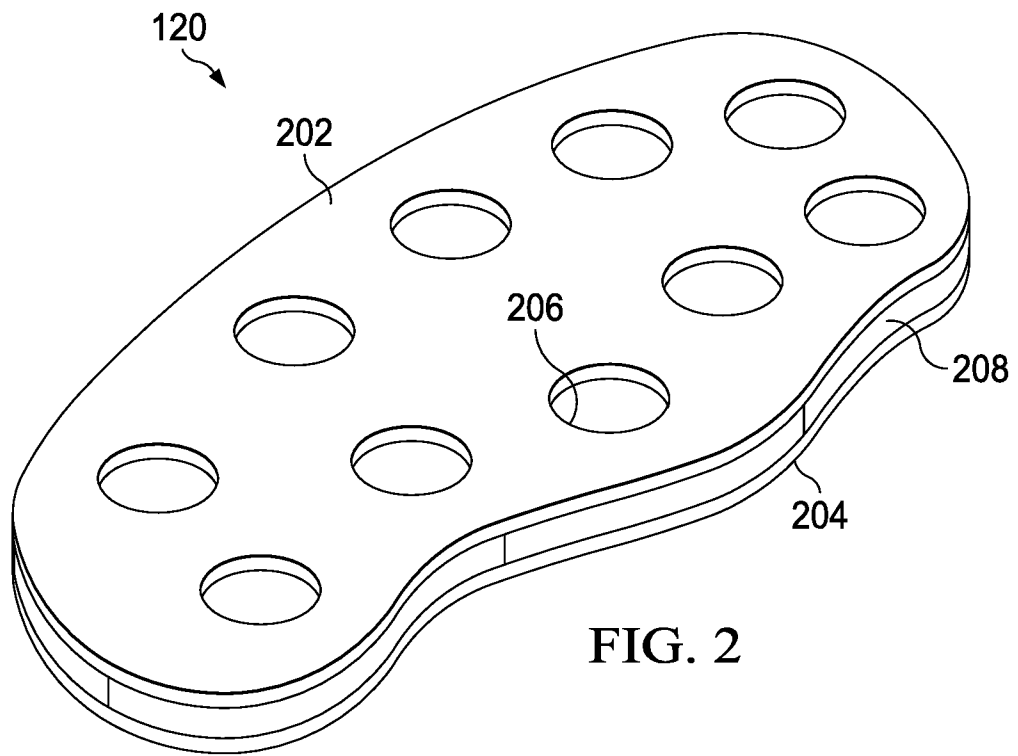
27. A method for treating a tissue site, comprising:
- disposing a manifold proximate to the tissue site, wherein the manifold comprises:
 - a first side, a second side, and a plurality of apertures to allow for fluid communication between the first side and the second side,
 - a chamber contained within the manifold,
 - a separation layer disposed within the chamber in order to create a first compartment and a second compartment within the chamber, wherein the first compartment contains a first substance, the second compartment contains a second substance, and the separation layer is configured to break to allow mixing of the first substance and the second substance within the chamber upon application of negative pressure within a specified range; and
 - wherein the mixing of the first substance and the second substance generates an endothermic reaction; and
 - supplying negative pressure within the specified range to the manifold.
28. The method of claim 27, wherein the first substance is water and the second substance is a chemical that produces an endothermic reaction upon mixing with water.
29. The method of claim 27, wherein the first substance is water and the second substance is a chemical selected from the group consisting of ammonium nitrate, ammonium chloride, sodium chloride, and sodium thiosulfate.
30. The method of claim 27, further comprising covering the manifold with a sealing member to form a sealed space around the tissue site.

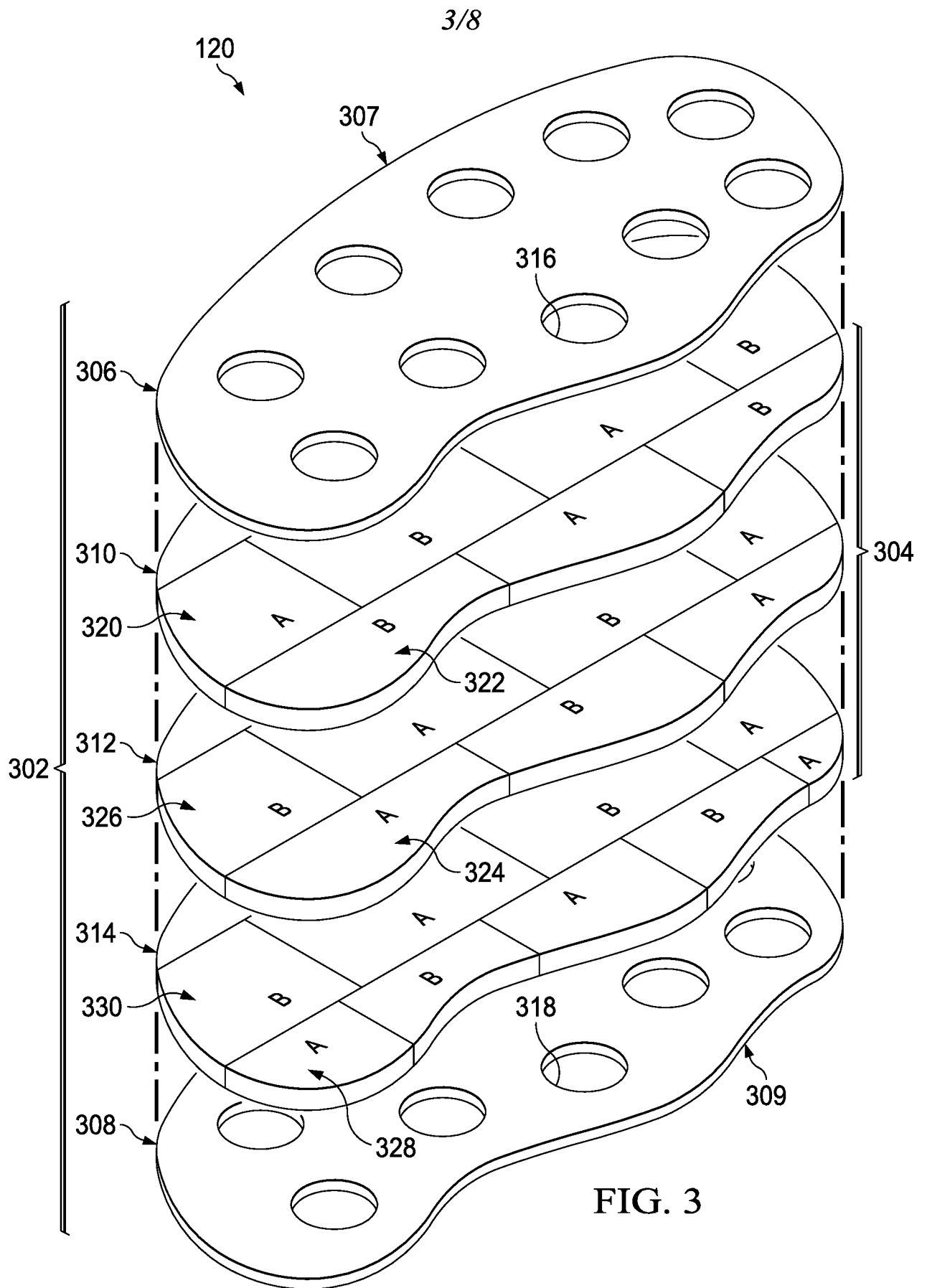
31. An apparatus for treating a tissue site, comprising:
- a first manifold layer comprising a first plurality of apertures;
 - a second manifold layer comprising a second plurality of apertures; and
 - a first active layer positioned between the first manifold layer and the second manifold layer and comprising:
 - a first plurality of compartments containing a first active ingredient, and
 - a second plurality of compartments containing a second active ingredient;
- wherein, under the application of negative pressure, at least a first portion of the first plurality of compartments and the second plurality of compartments are configured to breach to allow the first active ingredient and the second active ingredient to undergo an endothermic reaction.
32. The apparatus of claim 31, further comprising a second active layer positioned between the first manifold layer and the second manifold layer, and comprising:
- a third plurality of compartments containing the first active ingredient; and
 - a fourth plurality of compartments containing the second active ingredient.
33. The apparatus of claim 32, further comprising a third active layer positioned between the first manifold layer and the second manifold layer, and comprising:
- a fifth plurality of compartments containing the first active ingredient; and
 - a sixth plurality of compartments containing the second active ingredient.
34. The apparatus of claim 31, wherein:
- the first plurality of compartments comprises a first plurality of closed cells; and
 - the second plurality of compartments comprises a second plurality of closed cells.
35. The apparatus of claim 34, wherein the first active layer further comprises a plurality of perforations positioned between the first plurality of closed cells and the second plurality of closed cells.
36. The apparatus of claim 31, further comprising a chamber configured to contain the first active layer.
37. The apparatus of claim 32, further comprising a chamber configured to contain the first active layer and the second active layer.

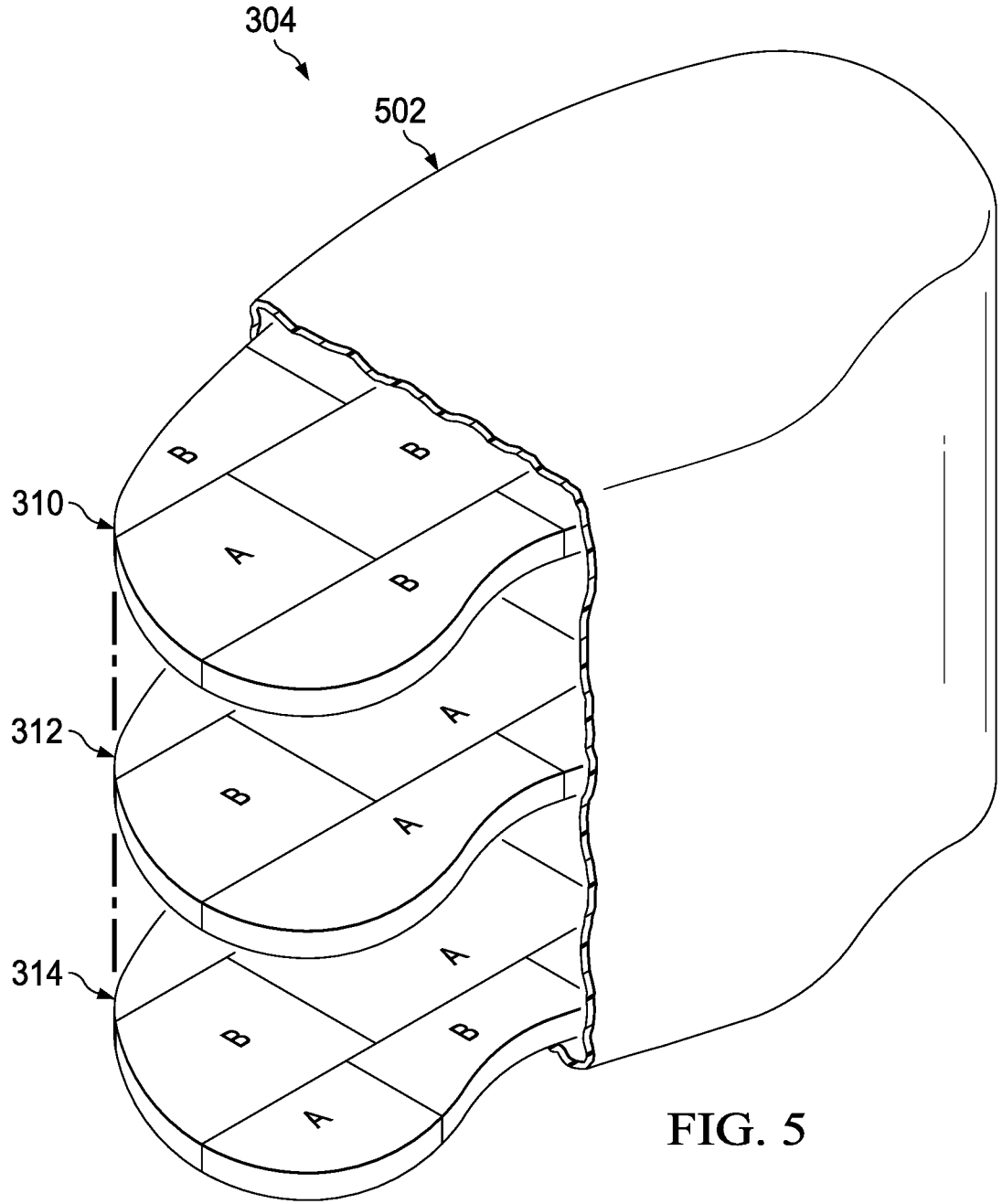
38. The systems, apparatuses, and methods substantially as described herein.



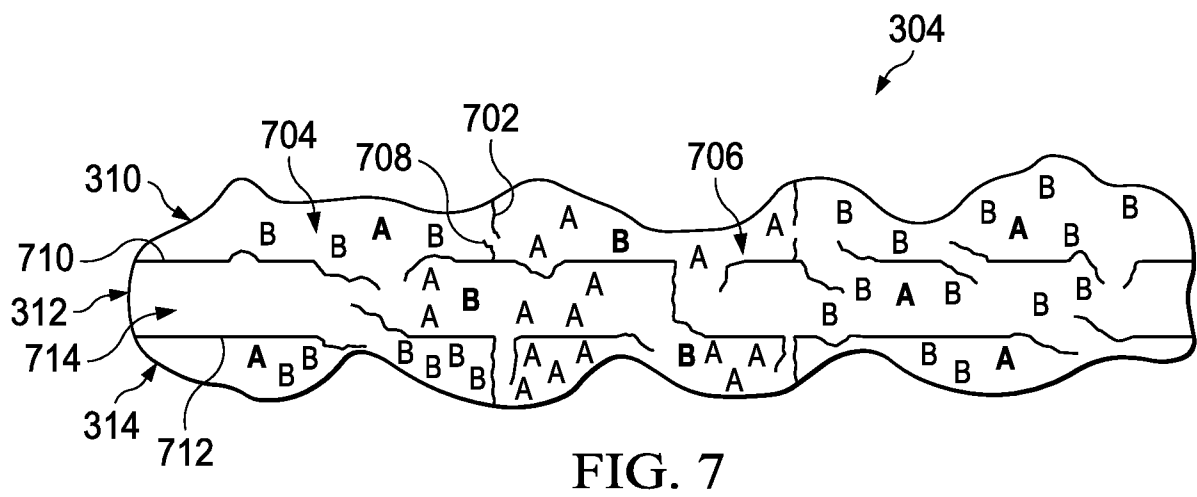
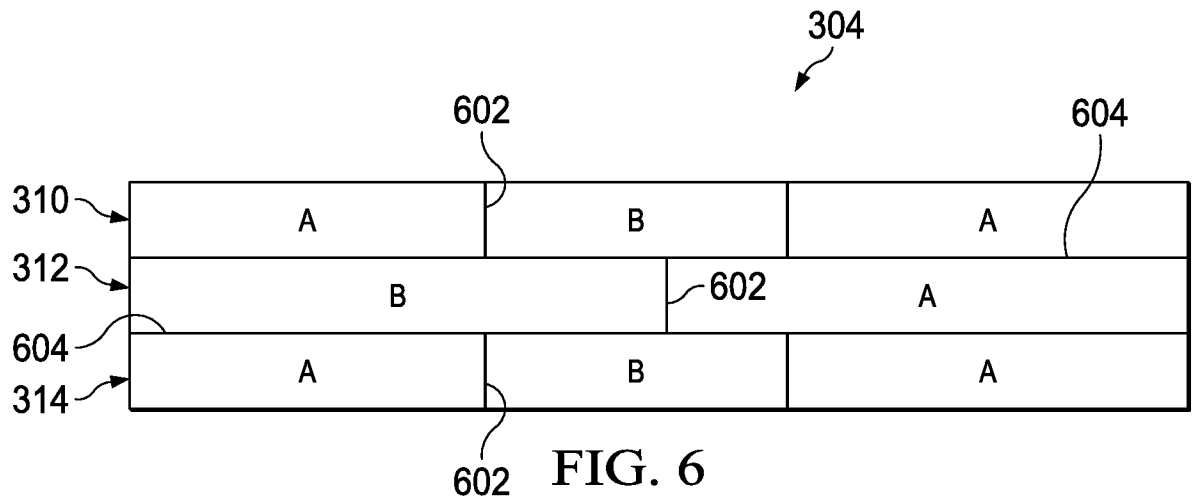
2/8



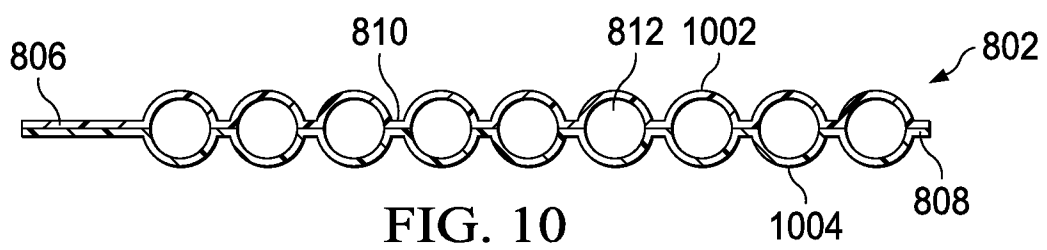
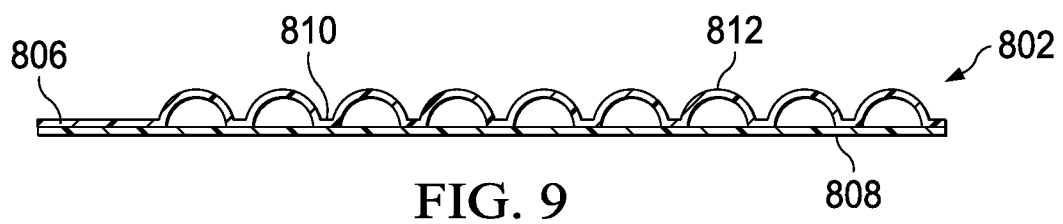
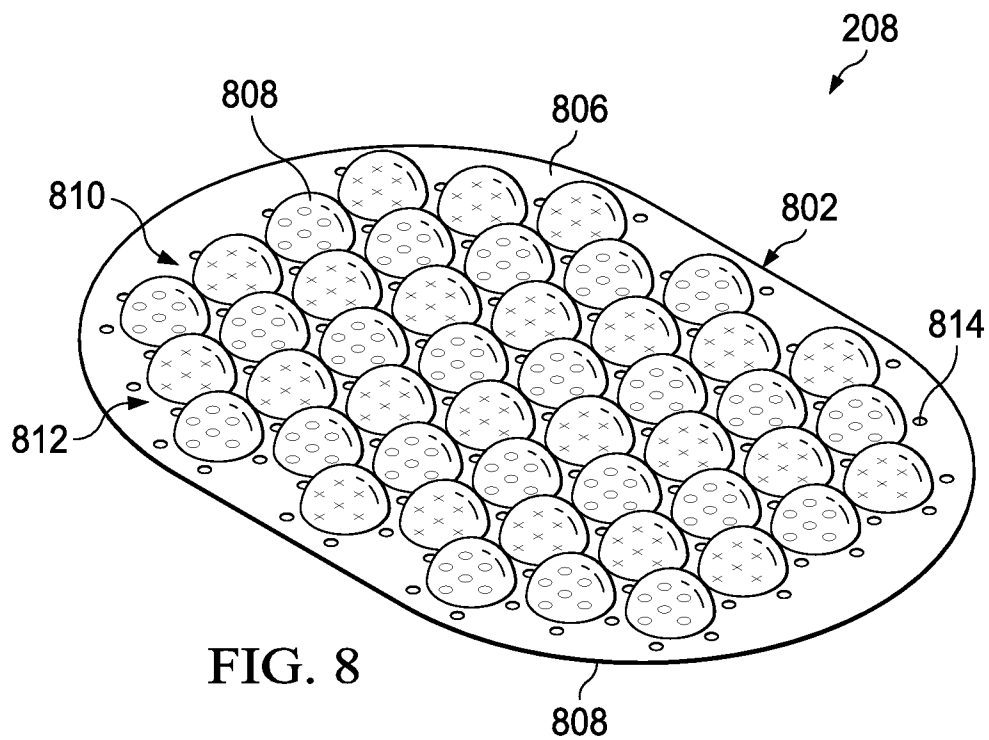


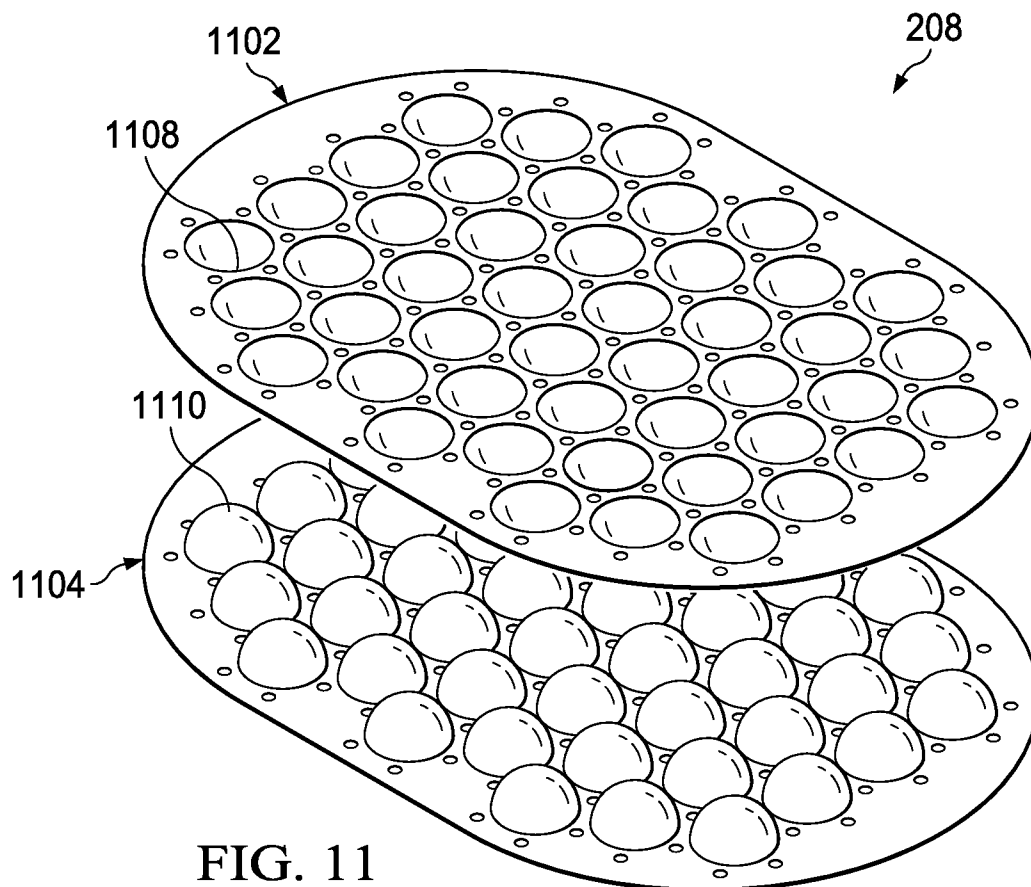


5/8



6/8





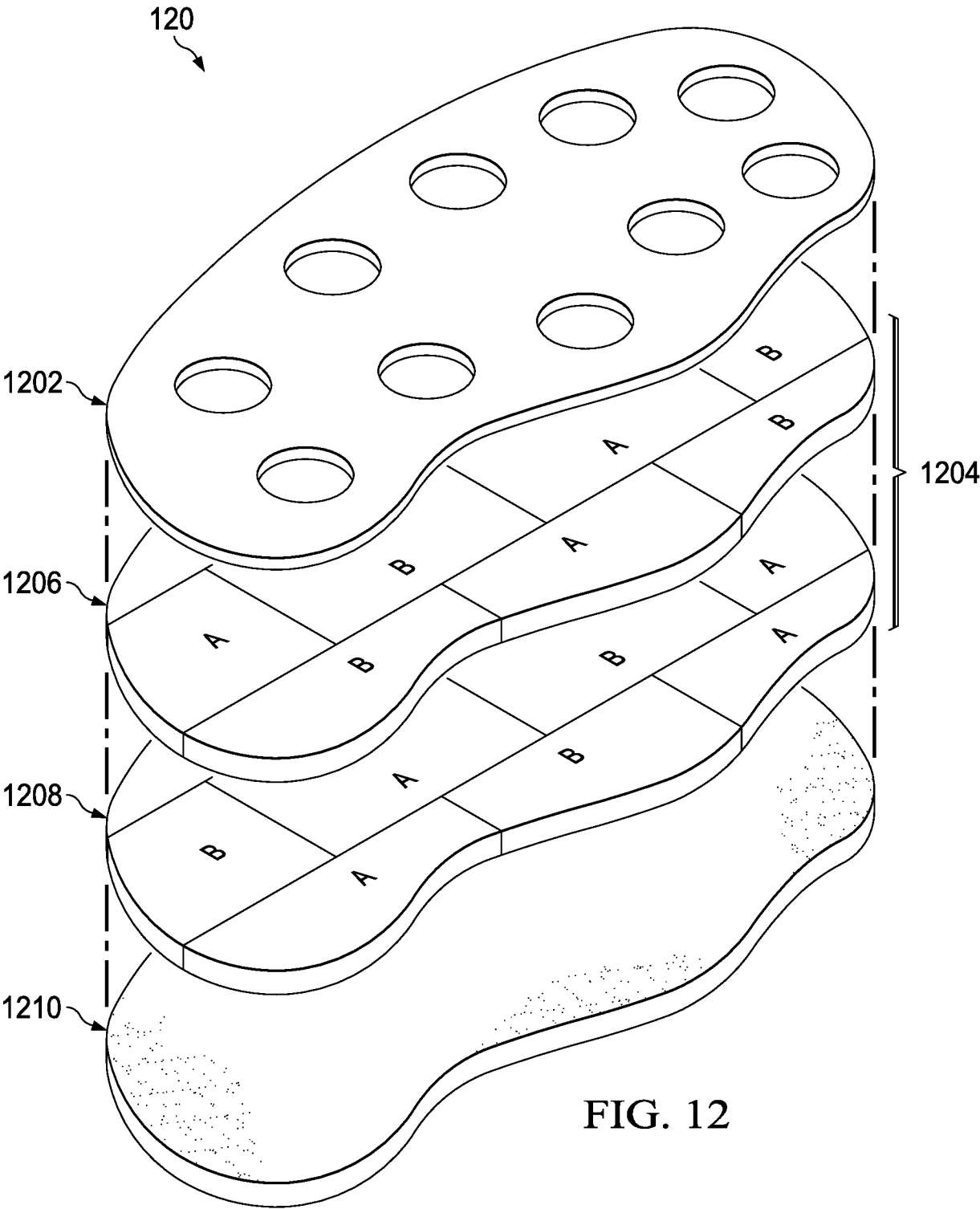


FIG. 12

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2019/048812

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.: 27-30
because they relate to subject matter not required to be searched by this Authority, namely:
claims 27-30: Rule 39.1(iv) PCT - Method for treatment of the human or animal body by therapy
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

International application No
PCT/US2019/048812

A. CLASSIFICATION OF SUBJECT MATTER
INV. A61F13/00
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)
A61F

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.
X	US 2003/195448 A1 (JENSEN JEFFREY L [US]) 16 October 2003 (2003-10-16) paragraphs [0029] - [0039]; claims; figures -----	1-26, 31-38
X	US 2015/080827 A1 (FOGG MICHELLE LYNN [US]) 19 March 2015 (2015-03-19) paragraphs [0025] - [0032]; figures -----	1-26, 31-38
X	WO 2015/030536 A1 (SKINDAUM CO LTD [KR]) 5 March 2015 (2015-03-05) abstract; figures -----	1-26, 31-38
X	US 2008/184456 A1 (FONTANEZ PEDRO J [US]) 7 August 2008 (2008-08-07) paragraphs [0063] - [0074]; claims; figures -----	1-26, 31-38



Further documents are listed in the continuation of Box C.



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

29 October 2019

Date of mailing of the international search report

11/11/2019

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

Boccignone, Magda

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/US2019/048812

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 2003195448	A1	16-10-2003	NONE
US 2015080827	A1	19-03-2015	NONE
WO 2015030536	A1	05-03-2015	CN 105208983 A 30-12-2015 KR 101416443 B1 10-07-2014 WO 2015030536 A1 05-03-2015
US 2008184456	A1	07-08-2008	NONE