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(54) Title: PERFORATED TISSUE MATRIX

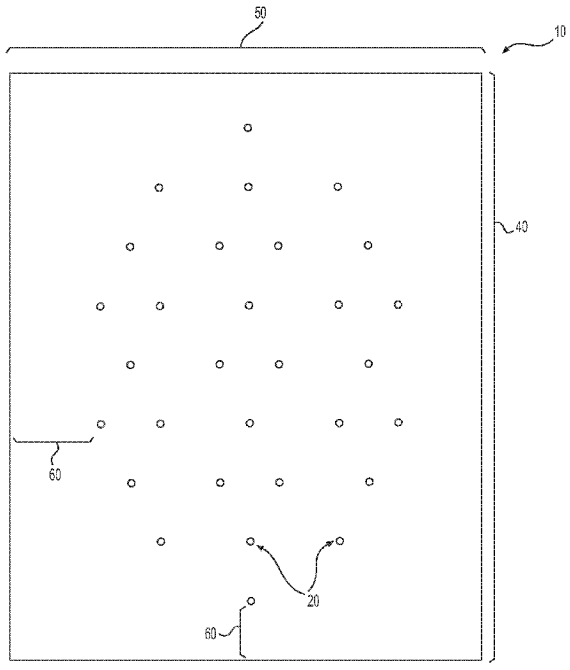

FIG. 2A

(57) Abstract: The present disclosure relates to tissue matrix products. The products can includes tissue matrices (10) that have holes or perforations (20) located at certain positions to improve certain in vivo functions without substantial loss of strength or other important properties.

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— *as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii))*

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PERFORATED TISSUE MATRIX

[0001] This application claims priority to United States Provisional Patent Application 62/217,353, filed September 11, 2015 and incorporated herein by reference in its entirety.

[0002] The present disclosure relates generally to acellular tissue matrix products, including tissue matrix products having perforations or holes at certain locations.

[0003] Surgeons currently use acellular tissue matrix products such as ALLODERM® and STRATTICE™, both dermal acellular matrices produced by LIFECELL® CORPORATION (Branchburg, NJ), for treatment of a variety of different structural defects. For example, such products can be useful in abdominal wall repair (e.g., complex hernia repair), breast reconstruction, orthopedic surgery, and neurosurgical applications.

[0004] Such tissue matrix products are often provided as flexible sheets of material that can replace, augment, or alter existing tissues. For some applications, however, it may be desirable to include holes or openings in the sheets, for example, to permit more rapid fluid flow across the sheets or to provide sites for securing surgical anchors such as sutures, clips, or staples.

[0005] Accordingly, the present application provides tissue matrix products having preformed holes or perforations. The holes or perforations are provided in a configuration that provides the desired functionality without sacrificing other properties such as strength and suture retention.

[0006] According to certain embodiments, a tissue matrix product is provided. The product can include a flexible sheet comprising a tissue matrix,

wherein the flexible sheet includes a group of holes passing through the tissue matrix, wherein the holes are formed in a pattern comprised of a repeating motif of five holes.

[0007] In other embodiments, a tissue matrix comprising a flexible sheet comprising a tissue matrix is provided. The flexible sheet includes a group of between 10 and 80 holes passing through the tissue matrix, wherein the flexible sheet comprises a rectangular shape having a width between 10 cm and 30 cm and a length between 10 cm and 30 cm, and the holes have a maximum dimension between about 1.5 mm and 2.5 mm, and wherein the holes are arranged in a pattern such that a uniaxial tensile strength measured in any direction along the sheet is at least 60% of the uniaxial tensile strength of the sheet without the group of holes.

[0008] In other embodiments, a tissue matrix including a flexible sheet comprising a tissue matrix is provided. The flexible sheet includes a group of between 10 and 80 holes passing through the tissue matrix, wherein the flexible sheet comprises a rectangular shape having a width between 10 cm and 30 cm and a length between 10 cm and 30 cm, and the holes have a maximum dimension between about 1.5 mm and 2.5 mm, and wherein the holes are arranged in a pattern such that a straight line drawn obliquely across a top or bottom surface of the tissue matrix can pass through no more than three of the holes.

[0009] Also provided are methods of treatment including the disclosed products.

BRIEF DESCRIPTION OF THE DRAWINGS

[0010] Reference will now be made to exemplary embodiments, examples of which are illustrated in the accompanying drawings. Wherever possible, the same

reference numbers will be used throughout the drawings to refer to the same or like parts. The drawings are not necessarily to scale.

[0011] Fig. 1 illustrates methods of treatment of an abdominal wall using tissue matrix products of the present application.

[0012] Fig. 2A illustrates a tissue matrix product including holes or perforations, according to certain embodiments.

[0013] Fig. 2B illustrates the tissue matrix product of Fig. 2A with various features highlighted, according to certain embodiments.

[0014] Fig. 2C illustrates the tissue matrix product of Fig. 2A with various features highlighted, according to certain embodiments.

[0015] Fig. 3 illustrates a tissue matrix product including holes or perforations, according to certain embodiments.

[0016] Fig. 4 illustrates a tissue matrix product including holes or perforations, according to certain embodiments.

[0017] Fig. 5 illustrates a motif for use in creating a hole or perforation pattern, according to certain embodiments.

Description of Exemplary Embodiments

[0018] Reference will now be made in detail to various embodiments of the disclosed devices and methods, examples of which are illustrated in the accompanying drawings. Wherever possible, the same reference numbers will be used throughout the drawings to refer to the same or like parts.

[0019] In this application, the use of the singular includes the plural unless specifically stated otherwise. In this application, the use of “or” means “and/or”

unless stated otherwise. Furthermore, the use of the term "including", as well as other forms, such as "includes" and "included", is not limiting. Any range described herein will be understood to include the endpoints and all values between the endpoints.

[0020] The section headings used herein are for organizational purposes only and are not to be construed as limiting the subject matter described. All documents, or portions of documents, cited in this application, including but not limited to patents, patent applications, articles, books, and treatises, are hereby expressly incorporated by reference in their entirety for any purpose.

[0021] The present disclosure relates generally to devices for surgical procedures and systems and methods relating to such devices. The devices can be used for tissue augmentation, repair or regeneration of damaged tissue, and/or correction of tissue defects. As such, the devices and methods discussed herein can be suitable for a wide range of surgical applications, such as, for example, abdominal wall repair, prophylactic treatment of post-operative complications (e.g., to prevent hernia, dehiscence, or other post-operative abdominal complications), hernia treatment (e.g., any abdominal or visceral hernia, such as a hiatal hernia, inguinal hernia, parastomal hernia, or midline abdominal hernia). The devices disclosed herein can also be used to treat other tissue sites, including, for example, breasts, connective tissue (tendons, ligaments, or fascia), and to assist in any structural defect correction or prevention.

[0022] The devices and associated methods discussed herein can include a flexible sheet of biologic material, such as an acellular tissue matrix. Such tissue matrix materials are used for a variety of surgical applications and have become an important tool for treating or preventing many problems associated with trauma,

post-operative complications, and/or structural defects due to aging, disease, congenital or acquired defects, or iatrogenic problems.

[0023] For some surgical procedures, it may be desirable to include holes or openings in the tissue matrix. For example, in some cases, it is desirable to place a drainage tube near a surgical site to allow drainage of fluids, e.g., to prevent formation of seromas or other fluid accumulations. Drainage of fluid from opposite sides of implantable tissue matrices, however, can be improved by providing holes or fluid passages through the matrices so that a drainage device located on one side will collect fluids from both sides of the device.

[0024] In addition, properly designed holes or openings can be useful for securing the tissue matrices. For example, some tissue matrix materials are designed to be strong and potentially relatively thick. Accordingly, fixation of such devices to surrounding tissues using conventional means such as sutures, staples, or clips, can sometimes be challenging and/or time consuming. Therefore, tissue matrices with preformed holes that can be used for fixation using sutures or other means are desirable.

[0025] On the other hand, holes or openings in tissue matrices should be configured to prevent unacceptable changes in other materials properties. For example, a group of holes in a flexible sheet of tissue matrix must be sized, shaped, and positioned such that the tissue matrix does not experience an unacceptable degradation in important mechanical properties such as tensile strength, elasticity, burst strength, and/or suture retention strength. Accordingly, the present application provides improved tissue matrix products that include a group of holes or perforations that are specially configured to provide the aforementioned advantages without causing unacceptable alterations in other material properties. As used

herein, “holes” and “perforations” are used interchangeably and will generally refer to any opening that passes through a flexible sheet of material from one side to the other.

[0026] According to certain embodiments, the present application provides tissue products for use in surgical procedures. The tissue products can include a flexible sheet 10 (Figs. 2A-C) comprising a tissue matrix, wherein the flexible sheet includes a group of holes 20 passing through the tissue matrix 10. The holes 20 can be placed on the sheet in a specifically designed pattern. In one embodiment, the holes are placed using a repeating motif 30 (Fig. 2B).

[0027] As used herein “motif” will be understood to refer to any repeatable pattern of holes. Further, the motif need not be repeated exactly, but can be varied (e.g., by changing dimension of holes or spacing of holes), so long as one or all of the goals discussed herein are met.

[0028] According to other embodiments, the present application provides tissue products including a flexible sheet 10 comprising a tissue matrix and a group of holes 20. The holes 20 are sized and positioned on the flexible sheet of tissue matrix 10 to maintain a desired tensile strength of the sheet, as compared to a sheet without the group of holes 20.

[0029] According to other embodiments, the present application provides tissue products including a flexible sheet 10 comprising a tissue matrix and a group of holes 20. The group of holes are positioned such that the number of holes that are aligned along an oblique axis of the sheet is minimized or kept below a certain level. For example, in one embodiment, the holes 20 are arranged in a pattern such that a

straight line 80, 81 (Fig. 2C) drawn obliquely across a top or bottom surface of the tissue matrix can pass through no more than three of the holes 20.

[0030] The devices disclosed herein can be used for treating a variety of different anatomic sites. For example, Fig. 1 illustrates methods of treatment of an abdominal wall using tissue matrix products 10 of the present application. The methods of treatment are described in more detail below, but in general, the device 10 can be used to treat portions of the abdominal wall 150, while using the group of holes 20 to allow fluid flow through the devices or to provide a site for fixation using sutures or other fixation means. Furthermore, as discussed below, the devices 10 can be implanted at a variety of different locations to support various anatomic structures and/or treat a variety of different conditions.

[0031] Figs. 2A-2C illustrate an exemplary tissue matrix product 10 including holes or perforations, according to certain embodiments. The products 10 illustrated in each of Figs. 2A-2C are identical but include different reference numerals and markings to facilitate discussion of various features of the product 10.

[0032] The tissue matrix product 10 is illustrated as a two-dimensional view of a flexible sheet of material. Accordingly, it should be appreciated that the flexible sheet will have a length 40 and width 50, and a thickness (not shown). The length 40, width 50, and thickness can be selected based on the desired surgical indication, e.g., to provide a sufficient surface area (measured in terms of the length 40 and width 50) and structural stability (e.g., based on strength, tensile properties, suture retention, burst strength, etc.). For dermal tissue matrix materials, the thickness can vary, but may be between, for example, 0.75mm to 4mm, 0.75mm to 1.25mm, or 1.05mm to 1.55mm.

[0033] The tissue matrices used to produce the products 10 described herein can include a variety of different materials. For example, an acellular tissue matrix or other tissue product can be selected to allow tissue ingrowth and remodeling to assist in regeneration of tissue normally found at the site where the matrix is implanted. For example, an acellular tissue matrix, when implanted on or into subdermal tissue, fascia, mammary tissue, or other tissue, may be selected to allow regeneration of the tissue without excessive fibrosis or scar formation. In certain embodiments, the devices can be formed from ALLODERM® or STRATTICE™ (LIFECELL® CORPORATION, BRANCHBURG, NJ) which are human and porcine acellular dermal matrices, respectively. Alternatively, other suitable acellular tissue matrices can be used. For example, a number of biological scaffold materials as described by Badylak et al., or any other similar materials, can be used. Badylak et al., "Extracellular Matrix as a Biological Scaffold Material: Structure and Function," *Acta Biomaterialia* (2008), doi:10.1016/j.actbio.2008.09.013. The devices described herein can be produced from a variety of different human or animal tissues including human, porcine, ovine, bovine, or other animals tissues.

[0034] As stated above, the products 10 can include a group of holes 20 that can be sized and positioned to provide a number of desired properties. As illustrated in Fig. 2A, the product 10 includes a total of thirty holes, but a range in the number of holes can be used, as discussed further below. Further, as shown in Fig. 2A, the holes 20 can be positioned such that a perimeter region 60 is formed in which no holes 20 are present. The perimeter region 60 can be sized to allow an area for passage of sutures or other connection devices and/or to provide a non-perforated section for fixation to tissue such as fascia. Suitable sizes may include

1.5–3 cm, 2–2.5 cm, about 2 cm, 1.5–2.5 cm, or values in between. Larger or smaller perimeter regions 60 can be used.

[0035] To provide the desired functional properties, the group of holes 20 can be positioned in specialized patterns. For example, in one embodiment, the group of holes 20 are positioned using a repeating motif 30. The motif 30 can be selected to allow formation of a desired number of holes 20 without unacceptable changes in certain material properties such as strength or elasticity.

[0036] A suitable motif 30 is illustrated in Figs. 2B, 3, 4, and 5. As shown, the motif 30 can include five holes 20. In one embodiment the motif 30 has a rectangular shape with a hole 31 positioned at each corner of the rectangle and one hole 32 positioned at the center of the rectangle. Further, as illustrated in Fig. 5, the rectangular shape can have a range of suitable sizes, including a width 35 and a length 34 (the length being double the distance 33 measured along an edge of the rectangle from a corner hole 31 to the center hole 32). In various embodiment the width can be between about 2 and 4 cm, or between about 2.5 and 3.5 cm; the length between about 3 and 5 cm, between about 3.5 and 4.5 cm; and the distance 33 between about 1.5 and 2.5 cm. In one embodiment, the width is about 3 cm and the length 34 about 4 cm, but the width and length can be varied (e.g., scaled at the same ratio or otherwise varied in accordance with the goals described herein).

[0037] The motif 30 can be distributed across the sheet of tissue matrix 10 in a variety of patterns. For example, as shown, the motif 30 may be arranged in multiple columns 1, 2, 3, and in rows 11, 12, and, 13. The number of columns 1, 2, 3, and rows may be varied based on the size of the product 10 and the specific number of holes 20 desired. For example, the device of Fig. 2B includes three columns, but suitable devices may include between 1 and 10 columns, or any specific number in

between. In addition, each column or row need not include all five holes of a motif. For example, as shown in Fig. 2B, the motifs at some positions, e.g., column 1, rows 11 and 13, have four holes of the motif 30, and the motif at the top and bottom of column 2 have only three holes (holes 23 and 22 are not part of the motif 30 and are discussed below).

[0038] The distances between each column 1, 2, 3, and rows 11, 12, 13 can be selected to produce desired hole spacing. For example, in one embodiment, the distance between two columns and the size of the motifs 30 are selected to provide a spacing pattern that reduces linear alignment of holes 20 along various directions of the sheet. In so doing, the mechanical strength of the products 10 is maintained.

[0039] Of note, as shown in Fig. 2B, the distance between holes of two columns (Lr) differs from the distance (Lm) between the holes 31 at bottom corners of a motif 30. This variation in distance cause the motifs 30 of two different columns 1, 2 to fall out of alignment, so that the motif is not simply repeated, and the alignment of holes is reduced along oblique axes (81, 83—Fig. 2C).

[0040] The products 10 described herein can have a variety of shapes and sizes. For example, each of the flexible sheets of tissue matrix illustrated in Figs. 2A–2C, 3, and 4 are rectangular, which provides a simple shape for use in abdominal wall procedures. Furthermore, a rectangular shape can be trimmed or reshaped based on a specific patient's needs or surgeon's preferences. It will be appreciated, however, that other shapes can be used including circular, oval, square, triangular, bi-convex, or asymmetric shapes.

[0041] The size and shape of each of the holes 20 can also be varied. Generally, however, the holes 20 are sized and shaped to preserve the mechanical properties of the sheet of tissue matrix 10, while allowing fluid flow or passage of sutures or other anchors through the holes. For example, the holes can be sized such that they have a maximum dimension between about 1.5 mm and 2.5 mm, between about 1.6 and 2.4 mm, between 1.7 and 2.3 mm, between 1.8 and 2.2. mm, between 1.9 and 2.1 mm, about 2 mm, or any values within the aforementioned ranges.

[0042] Further, the holes 20 can be shaped to maintain sheet mechanical properties. For example, to prevent excess force due to tensile forces of sutures passed through a hole 20 or high stress points from stretching, each hole can have a rounded border (e.g., oval, circular, rounded but asymmetric). In one embodiment, all holes 20 are circular and have a diameter between about 1.5 mm and 2.5 mm, between about 1.6 and 2.4 mm, between 1.7 and 2.3 mm, between 1.8 and 2.2. mm, between 1.9 and 2.1 mm, about 2 mm, or any values within the aforementioned ranges.

[0043] In some cases, the size of the holes, position of holes, and other mechanical properties of the tissue matrix 10 are selected to maintain a uniaxial tensile strength of the tissue matrix 10. For example, the product can be configured such that a uniaxial tensile strength (as measured along an axis parallel to the length of the tissue matrix 10) is at least 50%, at least 60%, at least 70%, at least 80%, at least 85%, or at least 90%, or any values in between versus the uniaxial tensile strength of a sheet not having the holes 20.

[0044] The hole size and shape as well as other sheet properties (e.g., thickness) can be configured to provide holes that will maintain suture retention

strength if sutures or other fixation devices are passed through a hole. For example, the suture retention strength of each hole 20 can be configured such that it is at least 60%, at least 70%, at least 80%, at least 90%, at least 95%, at least 99% or approximately 100% of the suture retention strength of a region of the same tissue matrix without a hole 20.

[0045] Suture retention can be measured using a simple technique. Specifically, a suture or suture analog (e.g., a steel wire) can be passed through the tissue to form a loop, and tension can be applied until the material tears. The amount of force (Newtons) needed to tear the tissue is the suture retention strength. The suture retention strength can be measured by passing the suture through one of the holes 20 to measure the suture retention when a hole is used.

[0046] In various embodiments, the holes 20 are positioned to minimize or control the number of holes that are linearly aligned along various directions. For example, in certain embodiments, the holes 20 are positioned such that the number of holes that are linearly aligned along an oblique axis 81, 83 of the flexible sheet 10 is kept below a certain value.

[0047] As used herein "oblique axis" will be understood to refer to a direction along the flexible sheet that is parallel to the flat top or bottom surfaces of the sheet (when the flexible sheet is laid on a flat surface) but is not parallel to an axis 90 directed along the length 40 or an axis 91 directed along the width 50 of the flexible sheet 10.

[0048] In some embodiments, the number of holes that can be linearly aligned along an oblique axis is two or fewer, three or fewer, four or fewer, or five or fewer.

[0049] In addition to the holes 20 being provided in a specified pattern, one or more additional holes 22, 23 can be included. For example, as shown in Fig. 2B, one hole 22 is located at a bottom 25 of the sheet, and another hole 23 is located at a top 24 of the sheet. The holes 22, 23 are provided to identify for a surgeon where the top 24 and bottom 25 of the sheet are located (i.e., identify the orientation of the sheet so that the surgeon recognizes how the sheet should be aligned when implanted in an abdominal wall). In particular, using the pattern set forth in Figs. 2A–2C, the sheet 10 should be implanted such that the holes 22, 23 are generally aligned with an anatomic axis in an superior-inferior (rostral-caudal) direction. It will be appreciated, however, that the holes could be moved to identify a different anatomic direction for different surgical indications.

[0050] Figs. 2A–2B illustrate one embodiment for a flexible sheet of tissue matrix 10 with holes 20. The sheets 10 illustrated therein, however, may be modified in other ways. For example, Figs. 3 and 4 illustrate tissue matrix products 10', 10" including holes or perforations, but having differing sizes and differing numbers of holes. It should be understood that the size of the products and number of holes may be adjusted based on the size of the patient, the condition to be treated, or other factors determined by a surgeon.

[0051] The specific number of holes 20 in the devices 10, 10', 10" illustrated can be varied. For example, a sheet can include between 10 and 80 holes passing through the tissue matrix, between 20 and 40 holes, between 20 and 50 holes, between 10 and 30 holes, between 14 and 64 holes, or other values in between. Further the sheets can be rectangular and have a width between 10 cm and 30 cm, between 10 cm and 25 cm, between 20 cm and 25 cm, or any ranges in

between. In addition the devices 10, 10', 10" can have a length between 10 cm and 30 cm, between 15 cm and 30 cm, or between 20 cm and 25 cm.

[0052] The products described herein are generally described with reference to acellular tissue matrices, but it will be appreciated that the tissue matrices can be pre-treated with exogenous cells or other therapeutic components prior to or after implantation. Accordingly, the devices can include tissue matrix products from which substantially all native cellular material has been removed, but which include exogenous cellular sources such as stem cells, fibroblasts, platelets, blood cells, or other cell sources.

[0053] The devices described herein can be used in a variety of different surgical operations, including in operations for treatment of abdominal wall issues. For example, Fig. 1 illustrates implantation of devices 10 at a variety of different positions within an abdominal wall. Although one of skill in the art will recognize that a certain procedure may require only one of the devices 10 of Fig. 1, each of the illustrated implantation locations (as well as others) may be desirable, depending upon the specific procedure being performed. The illustrated implantation locations would be recognized by surgeons and can include onlay 170, inlay 171, retromuscular 172, preperitoneal 173, or intraperitoneal 174, but additional sites can be used.

[0054] In some embodiments, the device 10 may also be implanted next to a drainage device 200, such as a drainage bulb, which may include a tube that passes to a surgical location 220 near an implanted device.

[0055] Furthermore, the devices 10 can be implanted during open, laparoscopic, or using any suitable surgical approach. The holes 20 can be used to

receive sutures, clips, staples, or other fixation devices that facilitate positioning and securing the device and/or surrounding tissues in place.

[0056] The holes 20 can be formed in a variety of ways. For example, in one embodiment, the holes are produced using a machine press with a cutting die selected to include elongated sharpened extensions. The sharpened extensions can be placed in a desired pattern to cut or puncture holes 20 while also including a knife or cutting die to cut the perimeter of the device 10. Alternatively the holes can be cut individually, by hand or using suitable cutting tools.

WHAT IS CLAIMED IS:

1. A tissue matrix product, comprising:

   a flexible sheet comprising a tissue matrix, wherein the flexible sheet includes a group of holes passing through the tissue matrix, wherein the holes are formed in a pattern comprised of a repeating motif of five holes.

2. The product of claim 1, wherein the repeating motif includes a rectangular shape with a hole positioned at each corner of the rectangle and one hole positioned at the center of the rectangle.

3. The product of claim 1 or 2, wherein the flexible sheet has a rectangular shape.

4. The product of any one of claims 1–3, wherein the motif is repeated in at least two columns.

5. The product of claim 4, wherein the motif is repeated in at least three columns.

6. The product of either of claims 4 and 5, wherein the motif is repeated in at least two rows.

7. The product of either of claims 4 and 5, wherein the motif is repeated in at least three rows.

8. The product of either of claims 6 and 7, wherein a distance between each column is greater than a distance between each row.

9. The product of any one of claims 1–8, wherein each hole has a maximum dimension between about 1.5 mm and 2.5 mm.

10. The product of any one of claims 1–9, wherein each hole has a rounded border.

11. The product of any one of claims 1–10, wherein each hole is circular.

12. The product of any one of claims 1–11, wherein the tissue matrix comprises an acellular tissue matrix.

13. The product of any one of claims 1–12, wherein the tissue matrix comprises a dermal tissue matrix.

14. The product of any one of claims 1–13, wherein the tissue matrix is a human tissue matrix.

15. The product of any one of claims 1–13, wherein the tissue matrix is a porcine tissue matrix.

16. The product of any one of claims 1–15, wherein substantially all native cellular material has been removed from the tissue matrix.

17. The product of any one of claims 1–16, wherein the flexible sheet of tissue matrix with the group of holes has a uniaxial tensile strength measured in any direction along the sheet that is at least 60% of the uniaxial tensile strength of a sheet without the group of holes.

18. The product of any one of claims 1–16, wherein the flexible sheet of tissue matrix with the group of holes has a uniaxial tensile strength measured in any direction along the sheet that is at least 70% of the uniaxial tensile strength of a sheet without the group of holes.

19. The product of any one of claims 1–16, wherein the flexible sheet of tissue matrix with the group of holes has a uniaxial tensile strength measured in any direction along the sheet that is at least 80% of the uniaxial tensile strength of a sheet without the group of holes.

20. The product of any one of claims 1–19, wherein the suture retention strength of any one of the holes is at least 80% of the suture retention strength of a region of the tissue matrix without the hole.

21. The product of any one of claims 1–19, wherein the suture retention strength of any one of the holes is at least 90% of the suture retention strength of a region of the tissue matrix without the hole.

22. The product of any one of claims 1–19, wherein the suture retention strength of any one of the holes is at least 95% of the suture retention strength of a region of the tissue matrix without the hole.

23. A tissue matrix product, comprising:

a flexible sheet comprising a tissue matrix, wherein the flexible sheet includes a group of between 10 and 80 holes passing through the tissue matrix, wherein the flexible sheet comprises a rectangular shape having a width

between 10 cm and 30 cm and a length between 10 cm and 30 cm, and the holes have a maximum dimension between about 1.5 mm and 2.5 mm, and wherein the holes are arranged in a pattern such that a uniaxial tensile strength measured in any direction along the sheet is at least 60% of the uniaxial tensile strength of a sheet without the group of holes.

24. The product of claim 23, wherein the flexible sheet of tissue matrix with the group of holes has a uniaxial tensile strength measured in any direction along the sheet that is at least 70% of the uniaxial tensile strength of a sheet without the group of holes.

25. The product of claim 23, wherein the flexible sheet of tissue matrix with the group of holes has a uniaxial tensile strength measured in any direction along the sheet that is at least 80% of the uniaxial tensile strength of a sheet without the group of holes.

26. The product of any one of claims 23–25, wherein the flexible sheet includes a group of between 14 and 64 holes.

27. The product of any one of claims 23–25, wherein the flexible sheet includes a group of between 20 and 40 holes.

28. The product of any one of claims 23–25, wherein the flexible sheet includes a group of between 20 and 50 holes.

29. The product of any one of claims 23–25, wherein the flexible sheet includes a group of between 10 and 30 holes.

30. The product of any one of claims 23–25, wherein the flexible sheet includes a group of between 14 and 64 holes.

31. The product of any one of claims 23–30, wherein the flexible sheet has a width between 10 cm and 25 cm and a length between 15 cm and 30 cm.

32. The product of any one of claims 23–30, wherein the flexible sheet has a width between 15 cm and 25 cm and a length between 15 cm and 30 cm.

33. The product of any one of claims 23–30, wherein the flexible sheet has a width between 10 cm and 20 cm and a length between 10 cm and 20 cm.

34. The product of any one of claims 23–30, wherein the flexible sheet has a width between 20 cm and 25 cm and a length between 25 cm and 30 cm.

35. The product of any one of claims 23–34, wherein the holes have a maximum dimension between about 1.8 mm and 2.5 mm.

36. The product of any one of claims 23–34, wherein the holes have a maximum dimension between about 1.8 mm and 2.2 mm.

37. The product of any one of claims 23–36, wherein each hole has a rounded border.

38. The product of any one of claims 23–37, wherein each hole is circular.

39. The product of any one of claims 23–38, wherein the tissue matrix comprises an acellular tissue matrix.

40. The product of any one of claims 23–39, wherein the tissue matrix comprises a dermal tissue matrix.

41. The product of any one of claims 23–40, wherein the tissue matrix is a human tissue matrix.

42. The product of any one of claims 23–40, wherein the tissue matrix is a porcine tissue matrix.

43. The product of any one of claims 23–42, wherein substantially all native cellular material has been removed from the tissue matrix.

44. The product of any one of claims 23–43, wherein the suture retention strength of any one of the holes is at least 80% of the suture retention strength of a region of the tissue matrix without the hole.

45. The product of any one of claims 23–43, wherein the suture retention strength of any one of the holes is at least 90% of the suture retention strength of a region of the tissue matrix without the hole.

46. The product of any one of claims 23–43, wherein the suture retention strength of any one of the holes is at least 95% of the suture retention strength of a region of the tissue matrix without the hole.

47. The product of any one of claims 23–46, wherein the holes are formed in a pattern comprised of a repeating motif of five holes.

48. The product of claim 47, wherein the repeating motif includes a rectangular shape with a hole positioned at each corner of the rectangle and one hole positioned at the center of the rectangle.

49. The product of any one of claims 47–48, wherein the motif is repeated in at least two columns.

50. The product of claim 49, wherein the motif is repeated in at least three columns.

51. The product of either of claims 49 and 50, wherein the motif is repeated in at least two rows.

52. The product of either of claims 49 and 50, wherein the motif is repeated in at least three rows.

53. The product of either of claims 51 and 52, wherein a distance between each column is greater than a distance between each row.

54. A tissue matrix product, comprising:

a flexible sheet comprising a tissue matrix, wherein the flexible sheet includes a group of between 10 and 80 holes passing through the tissue matrix, wherein the flexible sheet comprises a rectangular shape having a width between 10 cm and 30 cm and a length between 10 cm and 30 cm, and the holes have a maximum dimension between about 1.5 mm and 2.5 mm, and wherein the holes are arranged in a pattern such that a straight line drawn obliquely across a top or bottom surface of the tissue matrix can pass through no more than three of the holes.

55. The product of claim 54, wherein the flexible sheet of tissue matrix with the group of holes has a uniaxial tensile strength measured in any direction along the sheet that is at least 70% of the uniaxial tensile strength of a sheet without the group of holes.

56. The product of claim 54, wherein the flexible sheet of tissue matrix with the group of holes has a uniaxial tensile strength measured in any direction along the sheet that is at least 80% of the uniaxial tensile strength of a sheet without the group of holes.

57. The product of any one of claims 54–56, wherein the flexible sheet includes a group of between 14 and 64 holes.

58. The product of any one of claims 54–56, wherein the flexible sheet includes a group of between 20 and 40 holes.

59. The product of any one of claims 54–56, wherein the flexible sheet includes a group of between 20 and 50 holes.

60. The product of any one of claims 54–56, wherein the flexible sheet includes a group of between 10 and 30 holes.

61. The product of any one of claims 54–56, wherein the flexible sheet includes a group of between 14 and 64 holes.

62. The product of any one of claims 54–61, wherein the flexible sheet has a width between 10 cm and 56 cm and a length between 15 cm and 56 cm.

63. The product of any one of claims 54–61, wherein the flexible sheet has a width between 15 cm and 56 cm and a length between 15 cm and 56 cm.

64. The product of any one of claims 54–61, wherein the flexible sheet has a width between 10 cm and 20 cm and a length between 10 cm and 20 cm.

65. The product of any one of claims 54–61, wherein the flexible sheet has a width between 20 cm and 56 cm and a length between 25 cm and 30 cm.

66. The product of any one of claims 54–65, wherein the holes have a maximum dimension between about 1.8 mm and 2.5 mm.

67. The product of any one of claims 54–65, wherein the holes have a maximum dimension between about 1.8 mm and 2.2 mm.

68. The product of any one of claims 54–67, wherein each hole has a rounded border.

69. The product of any one of claims 54–68, wherein each hole is circular.

70. The product of any one of claims 54–69, wherein the tissue matrix comprises an acellular tissue matrix.

71. The product of any one of claims 54–70, wherein the tissue matrix comprises a dermal tissue matrix.

72. The product of any one of claims 54–71, wherein the tissue matrix is a human tissue matrix.

73. The product of any one of claims 54–71, wherein the tissue matrix is a porcine tissue matrix.

74. The product of any one of claims 54–73, wherein substantially all native cellular material has been removed from the tissue matrix.

75. The product of any one of claims 54–74, wherein the suture retention strength of any one of the holes is at least 80% of the suture retention strength of a region of the tissue matrix without the hole.

76. The product of any one of claims 54–74, wherein the suture retention strength of any one of the holes is at least 90% of the suture retention strength of a region of the tissue matrix without the hole.

77. The product of any one of claims 54–74, wherein the suture retention strength of any one of the holes is at least 95% of the suture retention strength of a region of the tissue matrix without the hole.

78. The product of any one of claims 54–77, wherein the holes are formed in a pattern comprised of a repeating motif of five holes.

79. The product of claim 78, wherein the repeating motif includes a rectangular shape with a hole positioned at each corner of the rectangle and one hole positioned at the center of the rectangle.

80. The product of any one of claims 78–79, wherein the motif is repeated in at least two columns.

81. The product of claim 80, wherein the motif is repeated in at least three columns.

82. The product of either of claims 80 and 81, wherein the motif is repeated in at least two rows.

83. The product of either of claims 80 and 81, wherein the motif is repeated in at least three rows.

84. The product of either of claims 82 and 83, wherein a distance between each column is greater than a distance between each row.

85. A method of treatment comprising:

selecting an anatomic site for treatment;

implanting the tissue product of any one of claims 1–84 in or on the anatomic site.

86. The method of claim 85, wherein the anatomic site is an abdominal wall.

87. The method of claim 85, wherein the implant is positioned between a rectus abdominis muscle and fascia.

88. The method of claim 85, wherein the implant is positioned within a peritoneal cavity.

89. The method of claim 85, wherein the implant is positioned adjacent a linea alba.

90. The method of claim 85, wherein the anatomic site is within or proximate a breast.

91. The method of any one of claims 85–90, further comprising implanting a drainage tube near the tissue product.

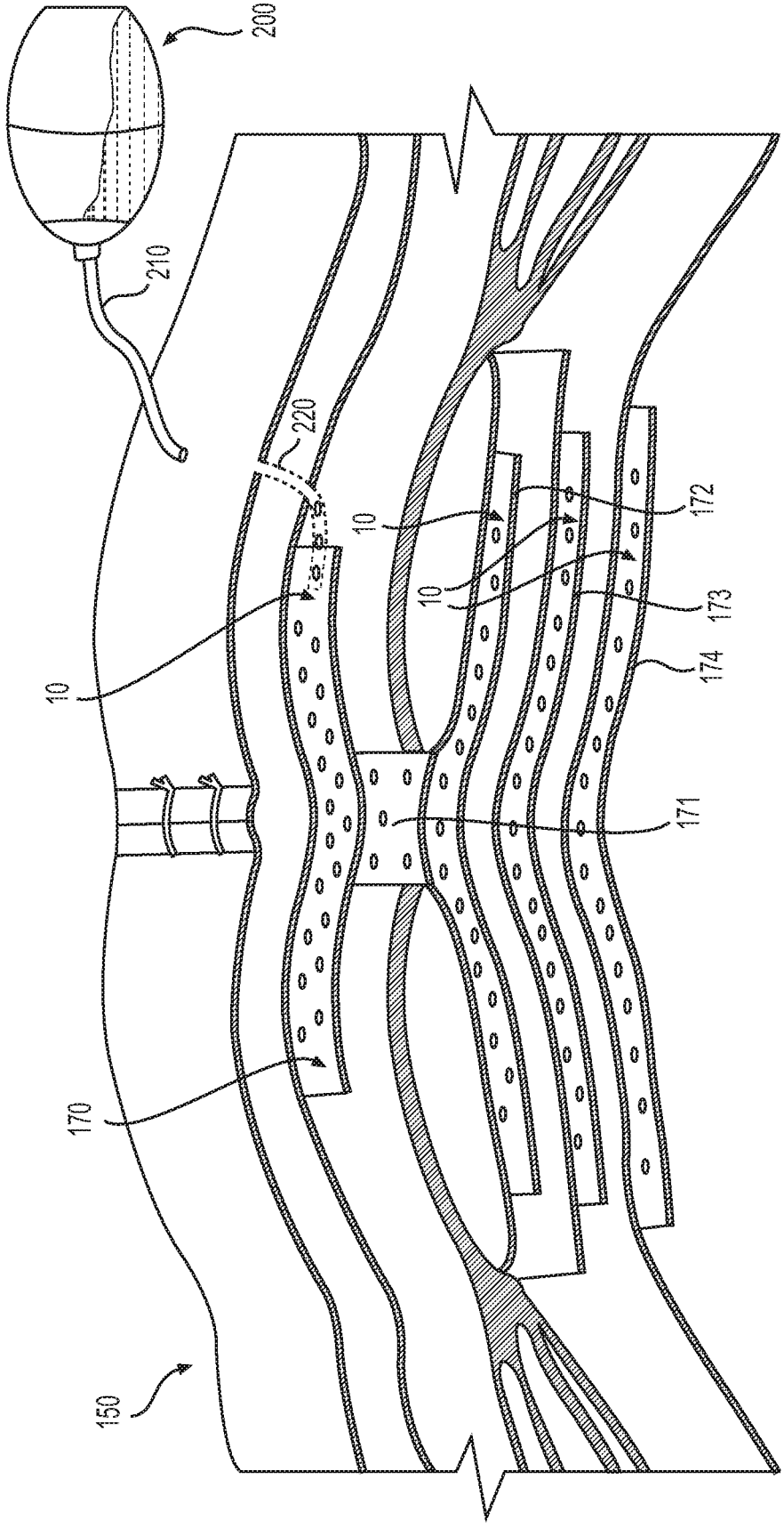

FIG. 1

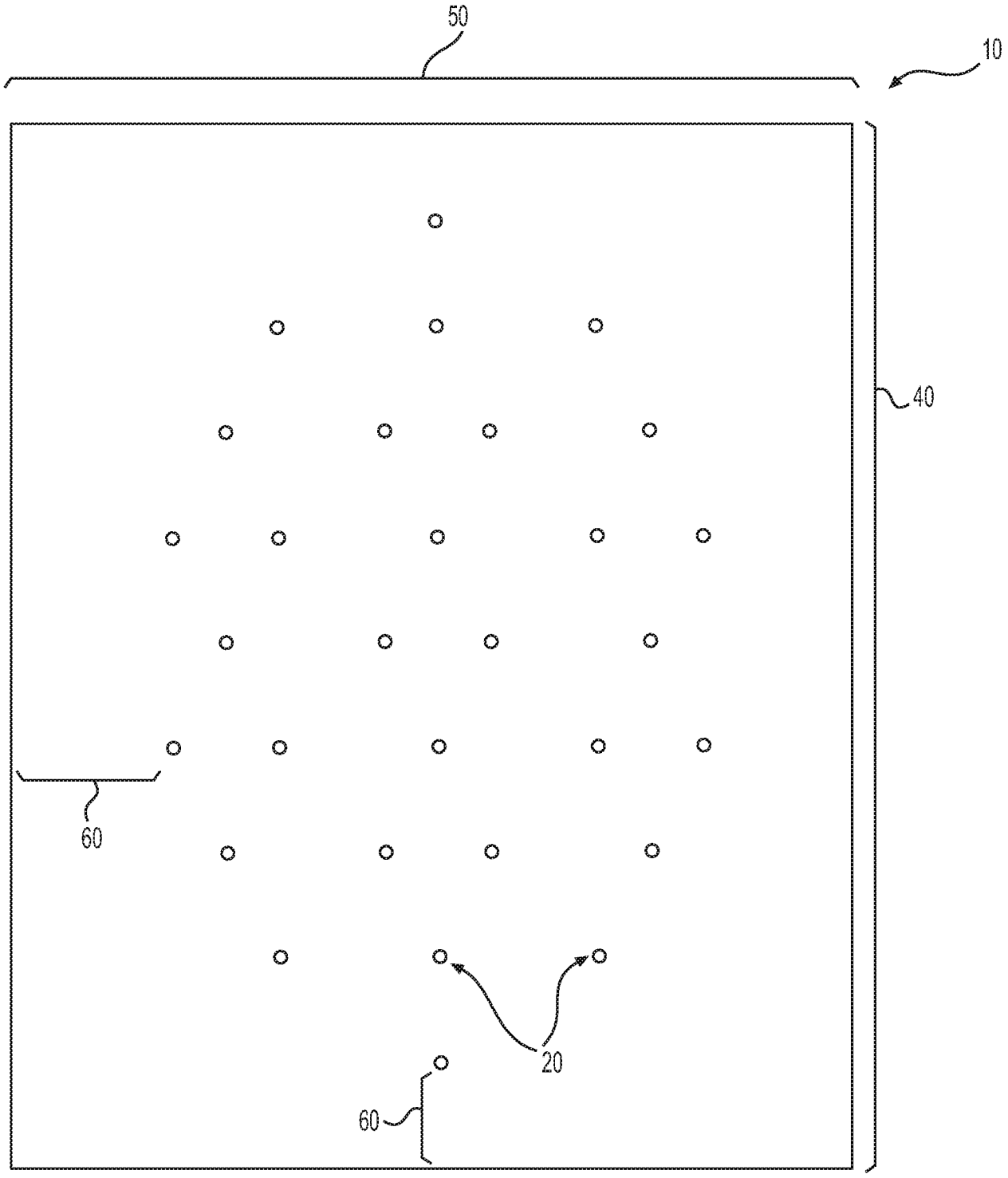

FIG. 2A

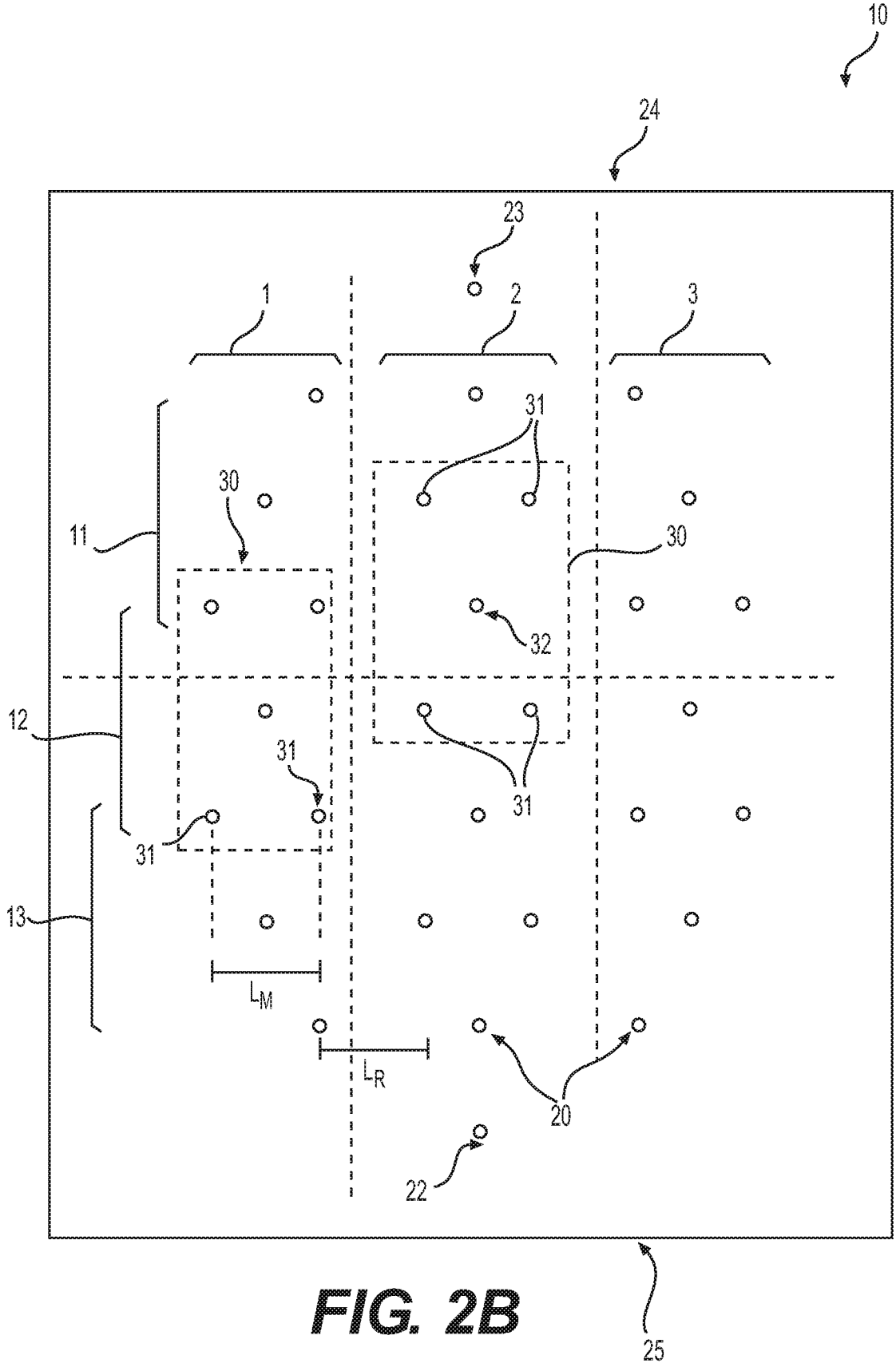

FIG. 2B

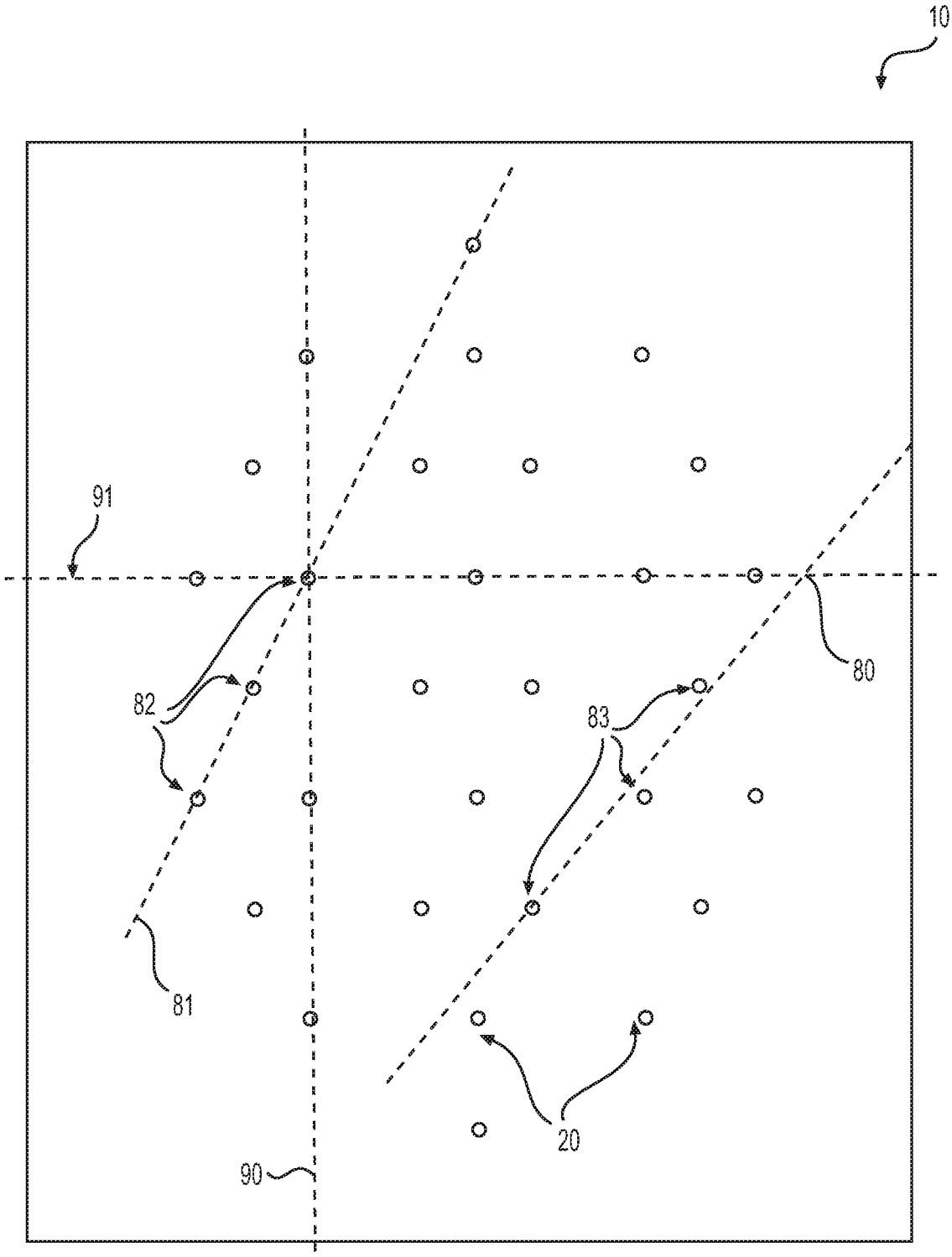

FIG. 2C

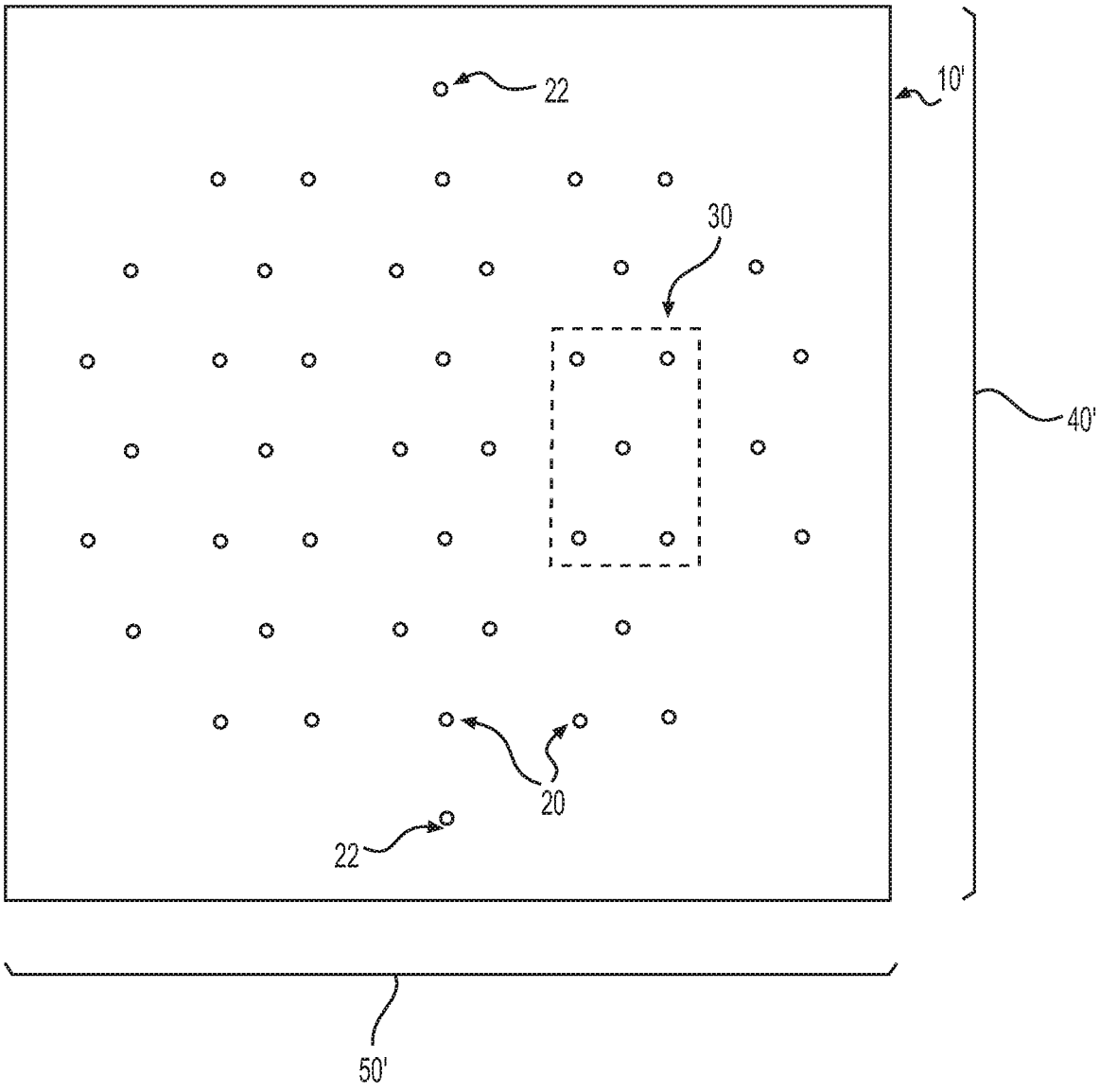

FIG. 3

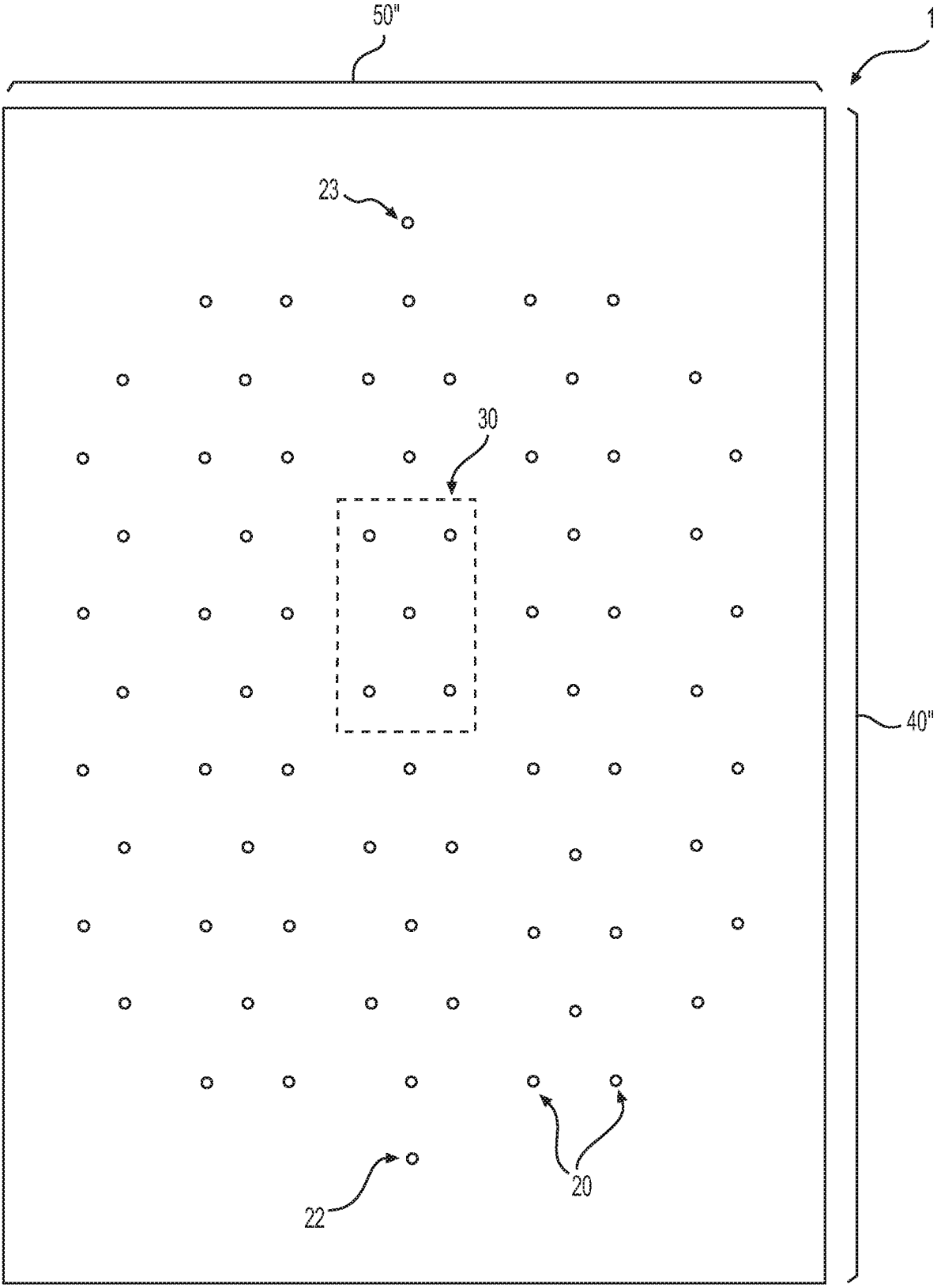

FIG. 4

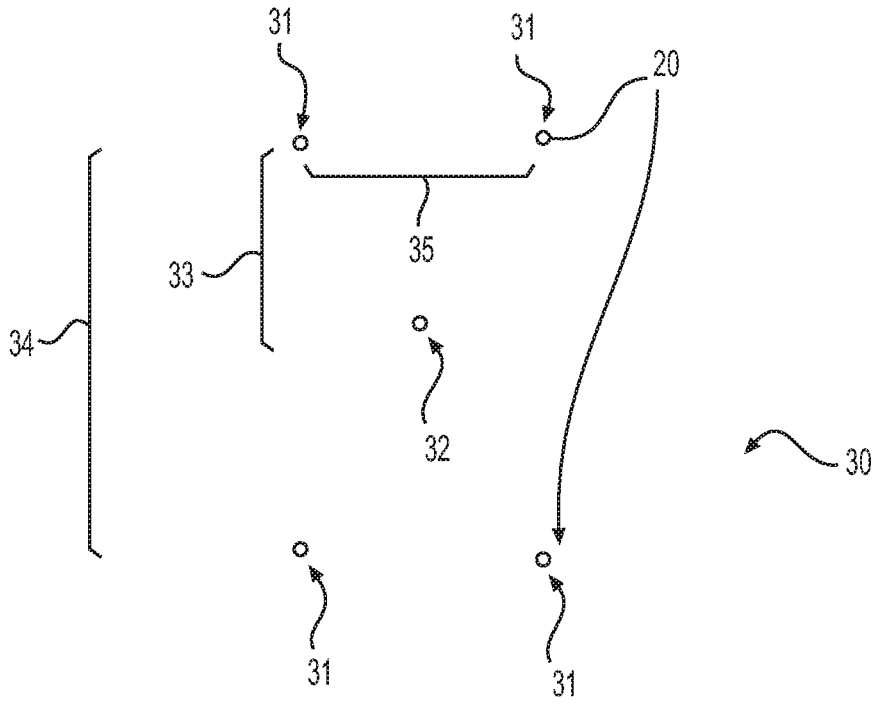

FIG. 5

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2016/050865

A. CLASSIFICATION OF SUBJECT MATTER
INV. A61F2/00 A61L27/50
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 A61L

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

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 2004/034374 A1 (ZATZSCH STEFFEN [DE] ET AL) 19 February 2004 (2004-02-19) paragraphs [0009], [0010], [0023]; figure 1	1-84
X	WO 97/06837 A1 (INTEGRA LIFESCIENCES CORP [US]) 27 February 1997 (1997-02-27) page 4, line 11 - page 7, line 18; figure 4	1-84
X	US 2011/166673 A1 (PATEL UMESH H [US] ET AL) 7 July 2011 (2011-07-07) paragraph [0059] - paragraph [0064]; figure 11	1-84

☐ 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	Date of mailing of the international search report
8 November 2016	21/11/2016

Name and mailing address of the ISA/	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016	Skorovs, Peteris

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INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2016/050865

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. [X] Claims Nos.: 85-91
because they relate to subject matter not required to be searched by this Authority, namely:

Rule 39.1(iv) PCT - Method for treatment of the human or animal body by surgery

2. [ ] Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. [ ] Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

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

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

1. [ ] As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.

2. [ ] As all searchable claims could be searched without effort justifying an additional fees, this Authority did not invite payment of additional fees.

3. [ ] As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. [ ] No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

[ ] The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.

[ ] The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.

[ ] No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/US2016/050865

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 2004034374 A1	19-02-2004	AT 502598 T	15-04-2011
		DE 10237531 A1	26-02-2004
		DK 1389450 T3	09-05-2011
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		WO 9706837 A1	27-02-1997
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		US 2011166673 A1	07-07-2011
		US 2016206785 A1	21-07-2016
		WO 2012078669 A1	14-06-2012

擇要

本發明涉及組織基質產品。所述產品可以包括具有孔或穿孔（20）的組織基質（10），在某些位置處定位以改善某些體內功能，而沒有顯著的損失力量或其它重要的性質。