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62/332,134 5 May 2016 (05.05.2016) US(71) Applicant: **480 BIOMEDICAL, INC.** [US/US]; 480 Arsenal Street, Watertown, MA 02472 (US).(72) Inventors: **CHANGCHENG, You**; 378 Moon Hill Road, Northbridge, MA 01534 (US). **PHAM, Quynh**; 8 Tuscany Drive, Methuen, MA 01844 (US). **CONCAGH, Danny**; 7 Lakewood Drive, Medfield, MA 02052 (US).(74) Agents: **BONHAM, David B.** et al.; Hacvinsky Daisak Bluni LLP, 50 Doaks Lane, Marblehead, Massachusetts 01945 (US).

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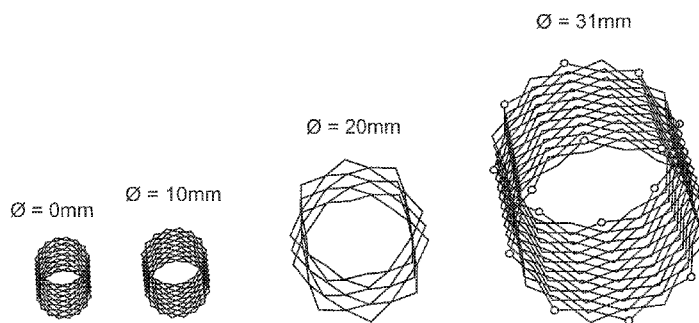


FIG. 16

(57) Abstract: This disclosure describes, *inter alia*, materials, devices, kits and methods that may be used to treat chronic sinusitis.

## IMPLANTABLE SCAFFOLDS FOR TREATMENT OF SINUSITIS

## CROSS-REFERENCE TO RELATED APPLICATIONS

[0001] This application claims the benefit of U.S. Provisional Application No. 62/186,030 entitled IMPLANTABLE SCAFFOLDS FOR TREATMENT OF SINUSITIS and filed Jun 29, 2015, U.S. Provisional Application No. 62/289,982 entitled IMPLANTABLE SCAFFOLDS FOR TREATMENT OF SINUSITIS and filed Feb 2, 2016, and U.S. Provisional Application No. 62/332,134 entitled IMPLANTABLE SCAFFOLDS FOR TREATMENT OF SINUSITIS and filed May 5, 2016, each of which is hereby incorporated by reference in its entirety.

## FIELD OF THE DISCLOSURE

[0002] This disclosure describes, *inter alia*, materials, devices, kits and methods that may be used to treat chronic rhinosinusitis.

## BACKGROUND

[0003] Chronic rhinosinusitis (CRS) is a common condition defined by symptomatic inflammation of the paranasal sinuses lasting longer than 12 weeks. Up to 16% of the population is affected by this condition. Cavities associated with CRS include the maxillary, frontal, ethmoid, ostiomeatal complex, ethmoid infundibulum and sphenoid sinuses as well as the middle meatus location, or a combination thereof. Common symptoms of CRS include impaired nasal obstruction, facial pressure or fullness, nasal discharge, and olfactory loss; these symptoms likely arise due to mucosal

inflammation, local infection, and/or impairment of mucociliary function.

[0004] While there is no approved therapy for the treatment of CRS, evidence-based medical management supports the use of a host of oral or topical corticosteroid therapies for the disease. High-volume, daily saline irrigation with adjunct application of a topical corticosteroid via nasal sprays is common as a first-line therapy. Second line agents for flare-ups and worsening disease include a short course of oral corticosteroids, although this approach can lead to unintended systemic side effects including glaucoma, osteoporosis and avascular necrosis of the hip and shoulder. It is estimated that up to 12-50% of CRS patients do not respond positively to this recommended medical regimen and are often candidates for Functional Endoscopic Sinus Surgery (FESS) and/or balloon sinuplasty dilation.

[0005] Avoidance of surgical interventions in the treatment of CRS would be ideal for patients since these procedures carry surgery-associated risks, cause post-operative pain and discomfort, and require burdensome and costly post-operative cleaning. Clinical data has demonstrated that topical corticosteroids are effective in reducing inflammation associated with CRS and thus, are a rational choice for the management of this condition.

[0006] An ideal treatment for CRS would provide local and sustained anti-inflammatory drug delivery in the sinuses of patients as an alternative treatment option to sinus surgery. Such a therapy would ideally establish safe and effective sustained drug delivery localized to the inflamed tissue and in some cases could prevent the need for surgery.

[0007] FESS involves removal of bone and tissue to enlarge sinus outflow tracts, widen sinus openings or ostia and allow for ventilation of previously obstructed sinus cavities and restoration of mucociliary clearance. Currently, there are approximately

500,000 procedures performed annually in the United States.

[0008] By removing small pieces of bone, polyps, and/or debridement of tissue within the sinus cavities, FESS has proven to be an effective way to improve the drainage pathway of the sinuses. However, a significant number of postoperative complications such as inflammation, swelling, disease recurrence, need for repeat procedures and synechiae are often observed. Postoperative care is therefore an important component of FESS. Approximately 10-20% of FESS patients become refractory, do not respond to treatment, and may require additional surgical intervention or lifelong medical therapy.

[0009] Some form of sinus packing is generally conducted postoperatively to FESS. Examples of packing materials include simple dressings moistened with saline, foam dressings based on polysaccharide gel, PEG-based materials, and middle meatal spacers. Implantable sinus stents have also been devised and these scaffolds are intended to stabilize the sinus openings and the turbinates, reduce edema, and/or prevent obstruction by tissue adhesion. They also have the capability of being integrated with therapeutic agent(s) that may be delivered topically over time. This local delivery of therapeutic agent(s) may be superior to topical application in the postoperative setting. In this regard, the USFDA-approved PROPEL™ system (Intersect ENT, Menlo Park, CA, USA) is a self-expanding, bioresorbable, steroid-eluting stent that is intended for use in the ethmoid sinus post-FESS.

## SUMMARY

[0010] As used herein, terms "sinus" and "sinus cavity" refer to both sinus cavities and nasal cavities, which include, for example, the maxillary, frontal and ethmoid sinuses, the ostiomeatal complex, the ethmoid infundibulum and the sphenoid

sinuses as well as the middle meatus (a sinus cavity).

[0011] The present disclosure describes various sinus scaffolds having fiber-based and non-fiber-based designs. These designs vary in form, dimension, and delivery location (i.e. maxillary, frontal, ethmoidal, sphenoidal sinuses, and middle meatus). In addition, therapeutic agent(s) may optionally be included within the scaffolds for local delivery over a brief or extended period of time. Therefore, these scaffolds may be used to improve sinus patency, for example, in surgically modified sinus spaces or in sinus spaces that have not previously undergone surgical modification. Moreover, these scaffolds may be used to deliver local therapeutic agent(s) to such sinus spaces, including, for instance, as part of a treatment program that is an alternative to sinus surgery (e.g., FESS) or in other instances as part of a postoperative care of FESS in some embodiments.

[0012] In various aspects, the present disclosure pertains to generally tubular scaffolds that are configured for implantation in a sinus cavity of a patient. As used herein, "generally tubular" includes hollow shapes of circular cross-section or non-circular (e.g., oval, etc.) cross-section and hollow shapes of constant diameter or variable diameter (e.g. of tapered diameter, such as in a hollow frustum). Both ends of the generally tubular scaffold may be open, one end may be open and the other end closed, or both ends may be closed. In many beneficial embodiments described herein a generally tubular scaffold is employed, which is in the shape of a hollow cylinder (i.e., having a circular cross-section and a constant diameter), in which both ends are open). The scaffolds may have a fiber-based or non-fiber-based structure and comprise a scaffold material and an optional conformal coating, which comprises a coating material that at least partially coats the scaffold material.

[0013] The scaffold material may or may not comprise a therapeutic agent, for

example, selected from the therapeutic agents described elsewhere herein, among other possibilities.

[0014] Where the scaffold comprises a therapeutic agent, the scaffold may be provided with a variety of release profiles.

[0015] In some embodiments, the scaffold may demonstrate certain cumulative release characteristic when subjected to an in vitro assay wherein the scaffold is submerged in a pH 7.4 PBS buffer solution containing 2% wt% SDS at 37 °C under gentle shaking on a rotary shaker, wherein a volume of the buffer solution in which the scaffold is submerged is at least 10 times greater than a volume of the buffer solution at which a quantity of therapeutic agent corresponding to the total amount of therapeutic agent in the scaffold is at a saturation point in the buffer solution (sometimes referred to as sink conditions), and wherein buffer is removed completely weekly for quantification and replaced with fresh buffer.

[0016] After one week in such in vitro conditions, the scaffold may demonstrate a cumulative release of therapeutic agent based on total amount of therapeutic agent in the scaffold ranging from 1% or less to 70% or more (e.g., ranging from 1% to 2% to 5% to 10% to 15% to 20% to 25% to 30% to 35% to 40% to 45% to 50% to 55% to 60% to 65% to 70%) (i.e., ranging between any two of the preceding numerical values), beneficially ranging from 2% to 50%, more beneficially ranging from 5% to 30%, in certain embodiments.

[0017] Alternatively or in addition, after two weeks in such in vitro conditions, the scaffold may demonstrate a cumulative release of therapeutic agent based on total amount of therapeutic agent in the scaffold ranging from 5% or less to 80% or more (e.g., ranging from 5% to 7% to 10% to 15% to 20% to 25% to 30% to 35% to

40% to 45% to 50% to 55% to 60% to 65% to 70% to 75% to 80%) (i.e., ranging between any two of the preceding numerical values), beneficially ranging from 7% to 50%, more beneficially ranging from 10% to 30%, in certain embodiments.

[0018] Alternatively or in addition, after four weeks in such in vitro conditions, the scaffold may demonstrate a cumulative release of therapeutic agent based on total amount of therapeutic agent in the scaffold ranging from 10% or less to 90% or more (e.g., ranging from 10% to 15% to 20% to 25% to 30% to 35% to 40% to 45% to 50% to 55% to 60% to 65% to 70% to 75% to 80% to 85% to 90%) (i.e., ranging between any two of the preceding numerical values), beneficially ranging from 20% to 75%, more beneficially ranging from 30% to 60%, in certain embodiments.

[0019] Alternatively or in addition, after eight weeks in such in vitro conditions, the scaffold may demonstrate a cumulative release of therapeutic agent based on total amount of therapeutic agent in the scaffold ranging from 25% or less to 100% (e.g., ranging from 20% to 25% to 30% to 35% to 40% to 45% to 50% to 55% to 60% to 65% to 70% to 75% to 80% to 85% to 90% to 95% to 100%) (i.e., ranging between any two of the preceding numerical values), beneficially ranging from 30% to 90%, more beneficially ranging from 40% to 80%, in certain embodiments.

[0020] In some embodiments, the scaffold may demonstrate certain cumulative in vivo release characteristic.

[0021] For example, after one week in vivo in a human sinus or a rabbit sinus, the scaffold may demonstrate a cumulative release of therapeutic agent based on total amount of therapeutic agent in the scaffold ranging from 1% or less to 45% or more (e.g., ranging from 1% to 1.5% to 2% to 3% to 5% to 10% to 15% to 20% to 25%

to 30% to 35% to 40% to 45%) (i.e., ranging between any two of the preceding numerical values), beneficially 1.5 ranging to 35%, more beneficially ranging from 3% to 20%, in certain embodiments.

[0022] Alternatively or in addition, after two weeks in vivo in a human sinus or a rabbit sinus, the scaffold may demonstrate a cumulative release of therapeutic agent based on total amount of therapeutic agent in the scaffold ranging from 3% or less to 50% or more (e.g., ranging from 3% to 5% to 7% to 10% to 15% to 20% to 25% to 30% to 35% to 40% to 45% to 50%) (i.e., ranging between any two of the preceding numerical values), beneficially ranging from 5% to 35%, more beneficially ranging from 7% to 20%, in certain embodiments.

[0023] Alternatively or in addition, after four weeks in vivo in a human sinus or a rabbit sinus, the scaffold may demonstrate a cumulative release of therapeutic agent based on total amount of therapeutic agent in the scaffold ranging from 7% or less to 60% or more (e.g., ranging from 7% to 10% to 15% to 20% to 25% to 30% to 35% to 40% to 45% to 50% to 55% to 60%) (i.e., ranging between any two of the preceding numerical values), beneficially ranging from 15% to 50%, more beneficially ranging from 20% to 30%, in certain embodiments.

[0024] Alternatively or in addition, after eight weeks in vivo in a human sinus or a rabbit sinus, the scaffold may demonstrate a cumulative release of therapeutic agent based on total amount of therapeutic agent in the scaffold ranging from 15% or less to 100% (e.g., ranging from 15% to 20% to 25% to 30% to 35% to 40% to 45% to 50% to 55% to 60% to 65% to 70% to 75% to 80% to 85% to 90% to 95% to 100%) (i.e., ranging between any two of the preceding numerical values),



beneficially ranging from 20% to 60%, more beneficially ranging from 25% to 55%, in certain embodiments.

[0025] In embodiments where the scaffolds comprise a fiber-based structure, the scaffold may comprise a braided structure containing one or more strands of the scaffold material.

[0026] In some embodiments, which may be used in conjunction with any of the above aspects and embodiments, the braided structure may comprise opposing sets of helical strands. For example, each set of helical strands may comprise between 2 and 64 members, more typically between 8 and 32 members.

[0027] In some embodiments, which may be used in conjunction with any of the above aspects and embodiments, the braided structure may comprise a first strand of material having a first stiffness and a second strand of material having a second stiffness that is greater than the first stiffness. As a specific example, the second strand of material may have a modulus of  $> 3\text{GPa}$  which may be at least 2 times the modulus of the first strand of material.

[0028] In some embodiments, which may be used in conjunction with any of the above aspects and embodiments, the braided structure may comprise cells of differing size. For example, a portion of the braided structure may be removed such that cells of differing sizes are formed or the braided structure may be braided such that cells of differing sizes are formed, among other possibilities. In some instances, the cells of differing size may include first cells having a first area and second cells having a second area, wherein first area is at least 50% greater than the second area. Variation in cell size may occur, for example, along a longitudinal length of the scaffold and/or around a circumference of the scaffold.

[0029] In some embodiments, which may be used in conjunction with any of the above aspects and embodiments, the scaffold may comprise a longitudinal elastomeric fiber that is mechanically coupled to two or more nodes of the braided structure.

[0030] In some embodiments, which may be used in conjunction with any of the above aspects and embodiments, one or more ends of the one or more strands may be woven back into the braided structure and bonded.

[0031] In some embodiments, the generally tubular scaffolds of the present disclosure may comprise a scaffold material that includes an elongate member that is wound into a spiral tubular structure. In certain of these embodiments, the elongate member is in the form of a ribbon-shaped elongate member that is wound into a spiral tubular structure. The ribbon-shaped elongate member may, for example, be in the form of a solid film or may comprise apertures (e.g., formed by forming holes in a solid film, formed by crossing fibers within a braided structure, etc.).

[0032] In some embodiments, the generally tubular scaffolds of the present disclosure comprise a scaffold material that includes a plurality of parallel open hoops. In certain of these embodiments, the open hoops are ribbon-shaped open hoops. The ribbon-shaped open hoops may, for example, be in the form of a solid film or may comprise apertures.

[0033] In some embodiments, the generally tubular scaffolds of the present disclosure comprise a scaffold material that includes a knitted structure. In certain of these embodiments, the knitted structure may comprise a single strand that can be pulled to unravel and remove the scaffold.

[0034] In some embodiments, the generally tubular scaffolds of the present disclosure may comprise a plurality of radially expandable inserts within a generally

tubular structure. In certain of these embodiments, each radially expandable insert may comprise a hub and a plurality of radially expandable arms or may comprise a braided hoop, among other possibilities.

[0035] In some embodiments, which may be used in conjunction with any of the above aspects and embodiments, a distal end of the generally tubular scaffolds may be configured to be captured by an additional device, and the generally tubular scaffolds may be configured to be inverted and removed by pulling the distal end into a lumen formed by the generally tubular scaffold.

[0036] In some embodiments, which may be used in conjunction with any of the above aspects and embodiments, the generally tubular scaffolds may comprise a conformal coating, for example, formed from an elastomeric or non-elastomeric coating material. For instance, the coating material may be an elastomeric material that comprises poly(L-lactide-co- $\epsilon$ -caprolactone) with urethane crosslinks, urea crosslinks, or both urethane and urea crosslinks; the coating material may be an elastomeric material that comprises diisocyanate-cured (e.g., hexamethylene diisocyanate-cured, etc.), hydroxyl-terminated branched poly(L-lactide-co- $\epsilon$ -caprolactone). The coating material may or may not comprise a therapeutic agent, for example, selected from the therapeutic agents described elsewhere herein, among other possibilities. The coating material may cover alternating areas along a length of the generally tubular scaffolds, and/or the coating material may cover ends of the generally tubular scaffolds while not covering an area between the ends of generally tubular scaffolds, among many other possibilities. In the case of braided structures, the coating material may cover some nodes of the braided structure while leaving other nodes uncovered. A thickness of the coating material at nodes of the braided structure may range, for example, from 1 to 100 times a thickness of the

coating material between nodes of the braided structure (e.g., ranging anywhere from 1 to 2 to 5 to 10 to 25 to 50 to 75 to 100 times a thickness of the coating material between nodes of the braided structure).

[0037] In certain embodiments, which may be used in conjunction with any of the above aspects and embodiments, the scaffold may have a conformal coating, which may be further coated with an additional conformal coating that comprises an additional coating material and a therapeutic agent, for example, selected from the therapeutic agents described elsewhere herein, among other possibilities. The additional conformal coating may range, for example, from between 1  $\mu\text{m}$  to 25  $\mu\text{m}$  in thickness (e.g., ranging from 1 to 2 to 5 to 20 to 25  $\mu\text{m}$  in thickness), among other possibilities. In certain embodiments, the additional coating material may be a biodegradable polymer such as poly(lactide-co- $\epsilon$ -caprolactone) or a mixture of poly(lactide-co- $\epsilon$ -caprolactone) and an additional polymer such as a homopolymer or copolymer of lactide, for instance, poly(lactide-co-glycolide). Where included, the additional polymer may be present, as a weight percent of the additional conformal coating, in amounts ranging, for example, from 5 to 50%. The poly(lactide-co- $\epsilon$ -caprolactone) may have, for example, a molar percentage of lactide ranging from 50 to 95% and a molar percentage of caprolactone ranging from 50 to 5%, among other possibilities. Where present, the poly(lactide-co-glycolide) may have, for example, a molar percentage of lactide ranging from 50 to 99.9% and a molar percentage of glycolide ranging from 50 to 0.1%, among other possibilities. In certain specific embodiments, the additional conformal coating may comprise from 50 to 99.9 wt% (e.g., from 50 to 60 to 70 to 80 to 90 to 95 to 99 to 99.5 to 99.9 wt%) of one or more biodegradable polymers and from 0.1 to 50 wt% (e.g., from 0.1 to 0.5 to 1 to 5 to 10 to 20 to 30 to 40 to 50 wt%) mometasone furoate, among many other possibilities. Typical amounts of mometasone furoate may range, for

example, from  $0.1 \mu\text{g}/\text{mm}^2$  or less to  $20 \mu\text{g}/\text{mm}^2$  or more (i.e., ranging from  $0.1$  or less to  $20 \mu\text{g}$  or more of mometasone furoate per square mm of scaffold surface area, where scaffold surface area,  $A$ , is calculated as  $A = nDL$ , where  $D$  is the manufactured diameter of the scaffold and  $L$  is the manufactured length of the scaffold), for example, ranging from  $0.1 \mu\text{g}/\text{mm}^2$  to  $0.2 \mu\text{g}/\text{mm}^2$  to  $0.5 \mu\text{g}/\text{mm}^2$  to  $1 \mu\text{g}/\text{mm}^2$  to  $2 \mu\text{g}/\text{mm}^2$  to  $5 \mu\text{g}/\text{mm}^2$  to  $10 \mu\text{g}/\text{mm}^2$  to  $15 \mu\text{g}/\text{mm}^2$  to  $20 \mu\text{g}/\text{mm}^2$  (i.e., ranging between any two of the preceding numerical values), more typically ranging from  $1 \mu\text{g}/\text{mm}^2$  to  $10 \mu\text{g}/\text{mm}^2$ , among other possible values.

[0038] In certain embodiments, which may be used in conjunction with any of the above aspects and embodiments, the scaffold may be further coated with a conformal topcoat layer, which is disposed over the additional conformal coating that comprises an additional coating material and a therapeutic agent. The topcoat layer may be formed, for example, from a single biodegradable polymer or a blend of biodegradable polymers selected from those described elsewhere herein. In certain embodiments, the topcoat layer may be formed from the same polymer or polymers found in the underlying additional conformal coating, but will not contain a therapeutic agent. The topcoat layer may be employed, for example, to delay and/or slow release of the therapeutic agent in the underlying additional conformal coating. The topcoat layer may range, for example, from between  $1 \mu\text{m}$  and  $30 \mu\text{m}$  in thickness, among other possibilities.

[0039] In other aspects, the present disclosure pertains to methods of treatment that comprises (a) introducing a scaffold, for example, a scaffold in accordance with any of the above aspects and embodiments, into a sinus cavity of a patient while in a radially constrained shape and (b) removing a constraint that maintains the scaffold in the constrained shape, such that the scaffold self-expands within the sinus cavity.

Examples of sinus cavities suitable for device implantation include the ethmoid sinus, the middle meatus space, the frontal sinus ostia (also referred to as the frontal recess), the maxillary sinus ostia and the sphenoid sinus ostia, among others.

[0040] In still other aspects, the present disclosure pertains to kits that comprise (a) a scaffold, for example, a scaffold in accordance with any of the above aspects and embodiments, (b) a delivery catheter and (c) an optional loading aid. In certain embodiments, a scaffold in accordance with any of the above aspects and embodiments may be loaded into a 15 French delivery catheter or smaller, into a 9 French delivery catheter or smaller, into a 6 French delivery catheter or smaller, or even into a 4 French delivery catheter or smaller. In certain embodiments, a scaffold in accordance with any of the above aspects and embodiments may be loaded into 6.5 french to 9 french catheter.

[0041] In some embodiments, the delivery catheter may be configured to maintain the scaffold in a radially constrained shape and to remove a constraint that maintains the scaffold in said radially constrained shape at a delivery location.

[0042] In some embodiments, which may be used in conjunction with any of the above aspects and embodiments, the delivery catheter may comprise an expandable device. For example, the delivery catheter may be a balloon catheter that comprises a catheter shaft having an inflation lumen and one or more inflatable balloons disposed at or near a distal end of a catheter shaft, which one or more inflatable balloons may or may not be at least partially coated with a therapeutic-agent-containing coating.

[0043] In still other aspects, the present disclosure pertains to delivery systems that comprise (a) a scaffold, for example, as scaffold in accordance with any of the above aspects and embodiments and (b) a delivery catheter, wherein the scaffold is

positioned in a radially constrained shape within the delivery catheter. Such delivery systems may be used, for example, in a method of treatment that comprises (a) introducing the scaffold into the sinus cavity of a patient while in the radially constrained shape, such that the scaffold is positioned at a delivery location in the sinus cavity and (b) removing a constraint that maintains the scaffold in the radially constrained shape, such that the scaffold self-expands within the sinus cavity.

[0044] In still other aspects, the present disclosure pertains to delivery systems that comprise (a) a scaffold, for example, as scaffold in accordance with any of the above aspects and embodiments and (b) a delivery catheter comprising an expandable device, wherein the scaffold is positioned on, in, under, proximal to, or distal to the expandable device. For example, the expandable device may be an expandable frame or an inflatable balloon. For instance, the delivery catheter may be a balloon catheter that comprises a catheter shaft having an inflation lumen and one or more inflatable balloons disposed at or near a distal end of a catheter shaft, which one or more inflatable balloons may or may not be at least partially coated with a therapeutic-agent-containing coating. Such delivery systems may be used, for example, in a method of treatment that comprises (a) introducing the scaffold into the sinus cavity of a patient such that the scaffold is positioned at a delivery location in the sinus cavity and (b) expanding the expandable device while the expandable device is positioned in the lumen of the scaffold.

[0045] In yet other aspects, the present disclosure pertains to methods of forming a coated scaffold comprising: (a) applying a first coating solution comprising a first solvent, a branched biodegradable polymer and a diisocyanate cross-linking agent to a scaffold in accordance with any of the above aspects and embodiments and (b) curing the applied first coating solution at room temperature or at elevated

temperature.

[0046] In certain embodiments, which may be used in conjunction with any of the above aspects and embodiments, the branched biodegradable polymer may be, for example, a branched poly(lactide-co- $\epsilon$ -caprolactone), for instance, a branched hydroxyl terminated poly(lactide-co- $\epsilon$ -caprolactone).

[0047] In certain embodiments, which may be used in conjunction with any of the above aspects and embodiments, the solution may further comprise a chain terminator. For example, the chain terminator may be an alcohol, for example a C8-C18 alcohol, such as 1-dodecanol and stearyl alcohol, among many other possibilities.

[0048] In certain embodiments, which may be used in conjunction with any of the above aspects and embodiments, the diisocyanate cross-linking agent may be hexamethylene diisocyanate, among many other possibilities.

[0049] In certain embodiments, which may be used in conjunction with any of the above aspects and embodiments, the first solvent may comprise dichloromethane or ethyl acetate among many other possibilities. In certain of these embodiments, the first solvent may further comprise anisole as a co-solvent.

[0050] In certain embodiments, which may be used in conjunction with any of the above aspects and embodiments, the scaffold may be a braided structure comprising one or more strands of the scaffold material and a plurality of nodes and the coating solution may be applied to at least the nodes of the scaffold.

[0051] In certain embodiments, which may be used in conjunction with any of the above aspects and embodiments, the method may further comprise applying a second coating solution comprising an additional biodegradable polymer (e.g.,



poly(lactide-co- $\epsilon$ -caprolactone), among many other possibilities), a second solvent (e.g., comprising ethyl formate and anisole, among many other possibilities), and a therapeutic agent to the scaffold after applying the first coating solution. The therapeutic agent may be a steroidal anti-inflammatory drug such as mometasone furoate, among many other possibilities.

[0052] Other aspects of the present disclosure pertain to coated scaffolds formed by methods in accordance with any of the above aspects and embodiments.

[0053] Potential benefits of the present disclosure include one or more of the following, in association with adult and pediatric procedures, among others: (a) stabilization of sinus openings/ostia, (b) reduction of synechiae and post-operative adhesions, (c) local and extended therapeutic agent delivery for therapy as an alternative to surgery (for example, the treatment of patients that have failed medical management based on the administration of oral and/or topical steroids), preoperative and/or postoperative care, and (d) therapeutic agent delivery to refractory patients not responsive to FESS, (e) prevention of stenosis of ostia/opening of sinuses following surgical dilation.

[0054] These and other aspects, embodiments and benefits of the present disclosure will become immediately apparent to those of ordinary skill in the art upon review of the detailed description and claims to follow.

[0055] Additional enumerated aspects of the present disclosure are set forth in the following paragraphs:

[0056] Aspect 1. A scaffold configured for implantation in a sinus cavity, said scaffold comprising a generally tubular structure having a lumen and comprising a scaffold material and an optional conformal coating comprising a coating material that at least partially coats the scaffold material.

- [0057] Aspect 2. The scaffold of aspect 1, wherein the scaffold comprises a fiber-based structure.
- [0058] Aspect 3. The scaffold of aspect 1, wherein the scaffold comprises a braided structure comprising one or more strands of the scaffold material.
- [0059] Aspect 4. The scaffold of aspect 3, wherein the braided structure comprises opposing sets of helical strands.
- [0060] Aspect 5. The scaffold of aspect 4, wherein each set of helical strands comprises between 2 and 64 members.
- [0061] Aspect 6. The scaffold of aspect 3, wherein the braided structure comprises a first strand of material having a first stiffness and a second strand of material having a second stiffness that is greater than the first stiffness.
- [0062] Aspect 7. The scaffold of aspect 6, wherein the second strand of material has a modulus of  $> 5\text{GPa}$  and which is at least 2 times that of the first strand of material.
- [0063] Aspect 8. The scaffold of any of aspects 3-8, wherein the braided structure comprises cells of differing size.
- [0064] Aspect 9. The scaffold of aspect 8, wherein a portion of the braided structure is removed such that cells of differing sizes are formed or wherein the braided structure is braided such that cells of differing sizes are formed.
- [0065] Aspect 10. The scaffold of aspect 8, comprising first cells having a first area and second cells having a second area, wherein first area is at least 50% greater than the second area.
- [0066] Aspect 11. The scaffold of aspect 8, wherein a variation in cell size occurs along a longitudinal length of the scaffold.

- [0067] Aspect 12. The scaffold of aspect 8, wherein a variation in cell size occurs around a circumference of the scaffold.
- [0068] Aspect 13. The scaffold of any of aspects 3-12, further comprising a longitudinal elastomeric fiber that is mechanically coupled to two or more nodes of the braided structure.
- [0069] Aspect 14. The scaffold of any of aspects 3-13, where one or more ends of said one or more strands is woven back into the braided structure and bonded.
- [0070] Aspect 15. The scaffold of any of aspects 3-14, wherein the scaffold comprises said conformal coating comprising a coating material.
- [0071] Aspect 16. The scaffold of aspect 15, wherein the coating material comprises an elastomer.
- [0072] Aspect 17. The scaffold of aspect 16, wherein the elastomer comprises urethane crosslinks.
- [0073] Aspect 18. The scaffold of any of aspects 15-17, wherein the coating material covers some nodes of the braided structure while leaving other nodes uncovered.
- [0074] Aspect 19. The scaffold of any of aspects 15-18, wherein the coating material covers alternating areas along a length of the braided structure.
- [0075] Aspect 20. The scaffold of any of aspects 15-18, wherein the coating material covers ends of the braided structure but does not cover an area between the ends of the braided structure.
- [0076] Aspect 21. The scaffold of any of aspects 15-21, wherein a thickness of the coating material at nodes of the braided structure range from 1 to 100 times a thickness of the coating material between nodes of the braided structure.

- [0077] Aspect 22. The scaffold of any of aspects 15-21, wherein the one or more strands of the scaffold material comprise poly(lactide-co-glycolide) and wherein the coating material is an elastomeric material that comprises poly(L-lactide-co-caprolactone) with urethane crosslinks, urea crosslinks, or both urethane and urea crosslinks.
- [0078] Aspect 23. The scaffold of any of aspects 15-21, wherein the one or more strands of the scaffold material comprise poly(lactide-co-glycolide) and wherein the coating material is an elastomeric material that comprises diisocyanate-cured, hydroxyl-terminated branched poly(L-lactide-co-caprolactone).
- [0079] Aspect 24. The scaffold of aspect 24, wherein the hydroxyl-terminated branched poly(L-lactide-co-caprolactone) is cured with hexamethylene diisocyanate.
- [0080] Aspect 25. The scaffold of any of aspects 15-21, 23 and 24, wherein the scaffold is further coated with an additional coating material that comprises from 50 to 99.9 wt% poly(L-lactide-co-caprolactone) and from 0.1 to 50 wt% mometasone furoate.
- [0081] Aspect 26. The scaffold of aspect 22, wherein the scaffold is further coated with an additional coating material that comprises from 50 to 99.9 wt% poly(L-lactide-co-caprolactone) and from 0.1 to 50 wt% mometasone furoate.
- [0082] Aspect 27. The scaffold of aspect 3, wherein the braided structure is in the form of a ribbon-shaped elongate member that is wound into a spiral tubular structure.
- [0083] Aspect 28. The scaffold of aspect 1, wherein the scaffold comprises an elongate member that is wound into a spiral tubular structure.
- [0084] Aspect 29. The scaffold of aspect 1, wherein the scaffold comprises a

plurality of parallel open hoops.

[0085] Aspect 30. The scaffold of aspect 29, wherein the open hoops are ribbon-shaped open hoops.

[0086] Aspect 31. The scaffold of aspect 30, wherein the ribbon-shaped open hoops have a plurality of apertures.

[0087] Aspect 32. The scaffold of aspect 31, wherein the plurality of apertures creates a braid-like structure.

[0088] Aspect 33. The scaffold of aspect 1, wherein the generally tubular structure is a knitted structure.

[0089] Aspect 34. The scaffold of aspect 33, wherein the knitted structure comprises a single strand that can be pulled to unravel and remove the scaffold.

[0090] Aspect 35. The scaffold of aspect 1, comprising a plurality of radially expandable inserts within the generally tubular structure.

[0091] Aspect 36. The scaffold of aspect 35, wherein the radially expandable inserts comprise a hub and a plurality of radially expandable arms or wherein the radially expandable inserts comprise a braided hoop.

[0092] Aspect 37. The scaffold of aspect 1, wherein a distal end of the scaffold is configured to be captured by an additional device and wherein the scaffold is configured to be inverted and removed from the sinus cavity by pulling the distal end into the lumen.

[0093] Aspect 38. A method of treatment comprising (a) introducing a scaffold in accordance with any of aspects 1-37 into a sinus cavity of a patient while in a radially constrained shape and (b) removing a constraint that maintains the scaffold in said constrained shape, such that the scaffold self-expands within the sinus cavity.

[0094] Aspect 39. The method of aspect 38, wherein the sinus cavity is the ethmoid sinus, the middle meatus space, the frontal sinus ostia, the maxillary sinus ostia, the sphenoid sinus ostia, or the frontal sinus recess.

[0095] Aspect 40. A kit comprising (a) a scaffold in accordance with any of aspects 1-37, (b) a delivery catheter, and (c) an optional loading aid.

[0096] Aspect 41. The kit of aspect 40, wherein the delivery catheter is configured to maintain the scaffold in a radially constrained shape and to remove a constraint that maintains the scaffold in said radially constrained shape at a delivery location.

[0097] Aspect 42. The kit of aspect 40, wherein the delivery catheter comprises an expandable device.

[0098] Aspect 43. The kit of aspect 40, wherein the delivery catheter is a balloon catheter that comprises a catheter shaft having an inflation lumen and one or more inflatable balloons disposed at or near a distal end of a catheter shaft.

[0099] Aspect 44. The kit of aspect 43, wherein at least one of the one or more inflatable balloons is at least partially coated with a therapeutic-agent-containing coating.

[00100] Aspect 45. A delivery system comprising (a) a scaffold in accordance with any of aspects 1-37 and (b) a delivery catheter, wherein the scaffold is positioned in a radially constrained shape within the delivery catheter.

[00101] Aspect 46. A method of treatment using the delivery system of aspect 45, comprising: (a) introducing the scaffold into the sinus cavity of a patient while in the radially constrained shape, such that the scaffold is positioned at a delivery location in the sinus cavity and (b) removing a constraint that maintains the scaffold in the radially constrained shape, such that the scaffold self-expands within the sinus

cavity.

[00102] Aspect 47. A delivery system comprising (a) a scaffold in accordance with any of aspects 1-37 and (b) a delivery catheter comprising an expandable device, wherein the scaffold is positioned on, in, under, proximal to, or distal to the expandable device.

[00103] Aspect 48. The delivery system of aspect 47, wherein the expandable device is an inflatable balloon or an expandable frame.

[00104] Aspect 49. The delivery system of aspect 47, wherein the delivery catheter is a balloon catheter that comprises a catheter shaft having an inflation lumen and one or more inflatable balloons disposed at or near a distal end of a catheter shaft.

[00105] Aspect 50. The delivery system of aspect 49, wherein at least one of the one or more inflatable balloons is at least partially coated with a therapeutic-agent-containing coating.

[00106] Aspect 51. A method of treatment using the delivery system of aspect 47, comprising: (a) introducing the scaffold into the sinus cavity of a patient such that the scaffold is positioned at a delivery location in the sinus cavity and (b) expanding the expandable device while the expandable device is positioned in the lumen of the scaffold.

[00107] Aspect 52. The method of aspect 51, wherein the expandable device is a balloon.

[00108] Aspect 53. A method of forming a coated scaffold comprising: (a) applying a first coating solution comprising a first solvent, a branched biodegradable polymer and a diisocyanate cross-linking agent to a scaffold and (b) curing the applied first coating solution at elevated temperature, wherein the scaffold is configured for

implantation in a sinus cavity and wherein the scaffold has a generally tubular structure having a lumen and comprising a scaffold material.

[00109] Aspect 54. The method of aspect 53, wherein the branched biodegradable polymer is a branched hydroxyl terminated poly(lactide-co-caprolactone).

[00110] Aspect 55. The method of any of aspects 53-54, wherein the scaffold material comprises poly(lactide-co-glycolide).

[00111] Aspect 56. The method of any of aspects 53-54, wherein the first solution further comprises a chain terminator.

[00112] Aspect 57. The method of aspect 56, wherein the diisocyanate cross-linking agent is hexamethylene diisocyanate, wherein the chain terminator is 1-dodecanol, or a combination of both.

[00113] Aspect 58. The method of any of aspects 53-57, wherein the first solvent comprises dichloromethane.

[00114] Aspect 59. The method of aspect 58, wherein the first solvent further comprises anisole.

[00115] Aspect 60. The method of aspect 59, wherein the scaffold is a braided structure comprising one or more strands of the scaffold material and a plurality of nodes and wherein the coating solution is applied to at least the nodes of the scaffold.

[00116] Aspect 61. The method of any of aspects 53-57, wherein the method further comprises applying a second coating solution comprising a second solvent, an additional biodegradable polymer and a therapeutic agent to the scaffold after curing.

[00117] Aspect 62. The method of aspect 61, wherein the additional biodegradable



polymer is poly(lactide-co-caprolactone).

[00118] Aspect 63. The method of any of aspects 61-62, wherein the therapeutic agent is a steroidal anti-inflammatory drug.

[00119] Aspect 64. The method of any of aspects 61-62, wherein the therapeutic agent is mometasone furoate.

[00120] Aspect 65. The method of aspect 64, wherein the second solvent comprises ethyl formate and anisole.

[00121] Aspect 66. The method of any of aspects 61-65, wherein the first coating solution and the second coating solution are applied in a spray process.

[00122] Aspect 67. A scaffold formed by the method of any of aspects 53-66.

[00123] Aspect 68. The scaffold of any of aspects 1-37, wherein the scaffold material comprises a therapeutic agent.

[00124] Aspect 69. The scaffold of aspect 68, wherein the therapeutic agent is a steroidal anti-inflammatory drug.

[00125] Aspect 70. The scaffold of any of aspects 15-26, wherein the coating material comprises a therapeutic agent.

[00126] Aspect 71. The scaffold of aspect 70, wherein the therapeutic agent is a steroidal anti-inflammatory drug.

[00127] Aspect 72. The scaffold of any of aspects 15-26, further comprising an additional conformal coating that comprises an additional coating material and a therapeutic agent.

[00128] Aspect 73. The scaffold of aspect 72, wherein the therapeutic agent is a steroidal anti-inflammatory drug.

[00129] Additional aspects and embodiments of the present disclosure are discussed in the detailed description set forth below.

#### BRIEF DESCRIPTION OF THE DRAWINGS

[00130] Non-limiting embodiments of the present disclosure are described by way of example with reference to the accompanying figures, which are schematic and not intended to necessarily be drawn to scale. In the figures, each identical or nearly identical component illustrated is typically represented by a single numeral. For purposes of clarity, not every component is labeled in every figure, nor is every component of each embodiment of the disclosure shown where illustration is not necessary to allow those of ordinary skill in the art to understand the disclosure. In the figures:

[00131] FIG. 1A schematically illustrates various fiber cross-sections, in accordance with embodiments of the present disclosure.

[00132] FIG. 1B schematically illustrates multi-fiber filament cross-sections, in accordance with two embodiments of the present disclosure.

[00133] FIG. 2 is a schematic side view of a self-expanding scaffold, in accordance with an embodiment of the present disclosure;

[00134] FIG. 3A is a schematic side view of a self-expanding scaffold having uniform braid angles, in accordance with an embodiment of the present disclosure.

[00135] FIG. 3B is a schematic side view of a self-expanding scaffold having variable braid angles, in accordance with an embodiment of the present disclosure.

[00136] FIG. 4 is a schematic side view of a self-expanding scaffold having an elastomer coating, in accordance with an embodiment of the present disclosure.

[00137] FIG. 5 is a schematic side view of a self-expanding scaffold having an elastic cross-fiber, in accordance with an embodiment of the present disclosure.

[00138] FIG. 6A is a schematic side view of a self-expanding scaffold having filaments of different stiffness, in accordance with an embodiment of the present disclosure.

[00139] FIG. 6B is a schematic side view of a self-expanding scaffold having removed filament segments, in accordance with an embodiment of the present disclosure.

[00140] FIG. 6C is a schematic side view of a self-expanding scaffold having coated ends, in accordance with an embodiment of the present disclosure.

[00141] FIG. 6D is a schematic side view of a self-expanding scaffold having alternating coated and uncoated sections, in accordance with an embodiment of the present disclosure.

[00142] FIG. 7 is a photograph of a self-expanding scaffold having unequal cell sizes, in accordance with an embodiment of the present disclosure.

[00143] FIG. 8 is a schematic side view of a self-expanding scaffold having fold-back ends, in accordance with an embodiment of the present disclosure.

[00144] FIG. 9 is an illustration of a knitted scaffold, in accordance with an embodiment of the present disclosure.

[00145] FIG. 10 is a schematic perspective view of a spiral-shaped self-expanding scaffold, in accordance with an embodiment of the present disclosure.

[00146] FIG. 11A is a photograph of a spiral-shaped self-expanding scaffold formed from a braided tubular scaffold, in accordance with an embodiment of the present disclosure.

[00147] FIG. 11B is a photograph of a spiral-shaped self-expanding scaffold formed

from a two-carrier braid, in accordance with an embodiment of the present disclosure.

[00148] FIG. 12A is a schematic perspective view of a self-expanding scaffold having solid strut hoops, in accordance with an embodiment of the present disclosure.

[00149] FIG. 12B is a schematic perspective view of a self-expanding scaffold having strut hoops in the form of a two carrier braid design, in accordance with an embodiment of the present disclosure.

[00150] FIG. 13 is a schematic side view of a conformal tube, in accordance with an embodiment of the present disclosure.

[00151] FIG. 14A is a schematic perspective view of a conformal tube with an associated three-dimensional support structure in expanded form, in accordance with an embodiment of the present disclosure.

[00152] FIG. 14B is a schematic end view of a conformal tube with an associated three-dimensional support structure in crimped form, in accordance with an embodiment of the present disclosure.

[00153] FIG. 15 is a schematic side view of a scaffold in the form of a unitary polymeric structure, in accordance with an embodiment of the present disclosure.

[00154] FIG. 16 is a photograph of an 8 mm diameter scaffold, a 10 mm diameter scaffold, a 20mm diameter scaffold and a 31mm diameter scaffold, each with 16 strands, in accordance with embodiments of the present disclosure.

[00155] FIG. 17A is a graph illustrating cumulative absolute mass of mometasone furoate (MF) released in the presence of poly(lactic acid-co-caprolactone) (PLCL) as the drug carrier polymer as a function of time for three different drug loadings, in accordance with embodiments of the present disclosure.

[00156] FIG. 17B is a graph illustrating cumulative percent mass of MF released in the presence of PLCL as the drug carrier polymer as a function of time for the embodiments of FIG. 17A.

[00157] FIG. 18 is a graph illustrating cumulative percent mass of MF released in the presence of PLCL as the drug carrier polymer, with and without a topcoat comprising PLCL and PLA, as a function of time for one 400 µg MF scaffold with no topcoat and three 400 µg MF scaffolds with different topcoat thicknesses, in accordance with embodiments of the present disclosure.

[00158] FIG. 19 is a graph illustrating cumulative percent mass of MF released in the presence of D,L-PLGA as the drug carrier polymer as a function of time for 400 µg MF scaffolds containing three different types of D,L-PLGA, in accordance with embodiments of the present disclosure.

[00159] FIG. 20A is a photograph of a 31.75 mm scaffold with 16 strands, in accordance with an embodiment of the present disclosure.

[00160] FIG. 20B is a photograph of a coated node of a scaffold like that of FIG. 20A.

[00161] FIG. 21 is a graph illustrating compressive load versus compressive strain for a scaffold in accordance with an embodiment of the present disclosure.

[00162] FIGS. 22A-22E are photographs illustrating various scaffold designs, in accordance with various embodiments of the present disclosure.

[00163] FIG. 23A, FIG. 23B, FIG. 23C and FIG. 23D are photographs illustrating deployment in a swine nasal cavity of a scaffold in accordance with an embodiment of the present disclosure.

[00164] FIG. 24 is a photograph illustrating a scaffold in accordance with an embodiment of the present disclosure following deployment in a swine nasal cavity.

[00165] FIG. 25 is a photograph illustrating a 32 filament scaffold having a diameter of 13 mm diameter and a length of 10 mm, in accordance with an embodiment of the present disclosure, following deployment in the native middle meatus of a human cadaver.

[00166] FIG. 26 is a photograph illustrating a 16 filament, 10 mm scaffold in accordance with an embodiment of the present disclosure following deployment in the frontal sinus ostia of a human cadaver.

[00167] FIG 27 is a photograph illustrating a 32 filament scaffold having a diameter of 17.5 mm and a length of 10 mm, in accordance with an embodiment of the present disclosure, following deployment in the ethmoid sinus of a human cadaver following FESS.

[00168] FIGS 28A-28D are optical microscopic images of coated 8 mm scaffolds having 16 strands with and without anisole as a co-solvent during spray-coating as follows: FIG. 28A, PLGA(10:90) scaffold without anisole co-solvent; FIG. 28B, PLGA(10:90) scaffold with anisole co-solvent; FIG. 28C, PLGA(75:25) scaffold without anisole co-solvent; FIG. 28D PLGA(75:25) with anisole co-solvent.

[00169] FIGS. 29A-29C show optical images of coated scaffolds with and without anisole as a co-solvent during spray-coating as follows: FIG. 29A scaffold coated with 62 wt% elastomer relative to the weight of the base braid from solution without anisole as a co-solvent; FIG. 29B scaffold coated with 63 wt% elastomer from solution containing anisole as a co-solvent; and FIG. 29C scaffold coated with 100 wt% elastomer from solution containing anisole as a co-solvent.

[00170] FIG. 30A illustrates cumulative absolute mass of MF released from three sets of MF-coated scaffolds as a function of time.

[00171] FIG. 30B illustrates cumulative percent mass of MF released from three sets of MF-coated scaffolds as a function of time.

[00172] FIG. 31 illustrates *in vivo* drug release profiles of MF-coated PLGA(10:90) scaffolds and MF-coated PLGA(75:25) scaffolds.

[00173] FIG. 32 illustrates MF concentration in the sinus mucosa of sacrificed rabbits as a function of time post-implantation.

[00174] FIG. 33 illustrates total MF in vivo as a function of time (MF on scaffold plus MF in the sinus mucosa of scarified rabbits).

[00175] FIG. 34 illustrates cumulative percent mass of MF released from two sets of MF-coated scaffolds as a function of time.

[00176] FIG. 35 illustrates cumulative percent mass of MF released from four sets of MF-coated scaffolds as a function of time.

[00177] FIG. 36 A illustrates immediate recovery from a first amount of compression of two sets of MF-coated scaffolds with 90 and 128 braid angles, as a function of compression time.

[00178] FIG. 36 B illustrates immediate recovery from a second amount of compression of two sets of MF-coated scaffolds with 90 and 128 braid angles, as a function of compression time.

[00179] FIG. 37 A illustrates six hour recovery from a first amount of compression of two sets of MF-coated scaffolds with 90 and 128 braid angles, as a function of compression time.

[00180] FIG. 37 B illustrates six hour recovery from a second amount of compression of two sets of MF-coated scaffolds with 90 and 128 braid angles, as a function of compression time.

[00181] FIG. 38 is a schematic illustration of a testing apparatus for conducting compression testing, in accordance with an embodiment of the present disclosure.

#### DETAILED DESCRIPTION

[00182] The implantable medical devices of the present disclosure are generally tubular devices, which devices are self-expanding devices in various embodiments. As used herein, "device," "scaffold," "stent", "carrier" and "implant" may be used synonymously. Also as used herein, "self-expanding" is intended to include devices that are crimped to a reduced delivery configuration for delivery into the body, and thereafter tend to expand to a larger suitable configuration once released from the delivery configuration, either without the aid of any additional expansion devices or with the partial aid of balloon-assisted or similarly-assisted expansion. As used herein, "strength" and "stiffness" may be used synonymously to mean the resistance of the medical scaffolds of the present disclosure to deformation by radial forces or a force applied by the scaffolds against a static abutting object. Examples of strength and stiffness measurements, as used to characterize the medical scaffolds of the present disclosure, include radial resistive force and chronic outward force, as further described herein.

[00183] Scaffolds in accordance with the present disclosure are typically tubular devices which may be of various sizes, including a variety of diameters and lengths, and which may be used for a variety of sinus applications. In the case of objects of non-circular cross-section, "diameter" denotes width. In certain beneficial embodiments, the as-manufactured (or unconstrained) diameter of the scaffold may range from 5 mm or less to 60 mm or more, for example, ranging from 5 mm to 10 mm to 15 mm to 20 mm to 25 mm to 30 mm to 35 mm to 40 mm or 50 mm to 60



mm (i.e., ranging between any two of the preceding numerical values), commonly ranging from 5 to 13 mm or from 15 to 30 mm. In certain beneficial embodiments, the as-manufactured (or unconstrained) length may range from 5 mm or less to 30 mm or more, for example, ranging from 5 mm to 10 mm to 15 mm to 20 mm to 25 mm or 30 mm (i.e., ranging between any two of the preceding numerical values), commonly ranging from 10 mm to 20 mm.

[00184] In certain beneficial embodiments, scaffold mass may range from 1 to 20 mg/mm of length.

[00185] Unless indicated otherwise, scaffold diameters and scaffold lengths given herein refer to unconstrained (manufactured) diameters and lengths.

[00186] The many scaffold embodiments of the present disclosure are self-expanding in that they are manufactured at a first diameter, subsequently reduced or "crimped" to a second, reduced diameter for placement within a delivery catheter, and self-expand towards the first diameter when extruded from the delivery catheter at an implantation site. The first diameter may be at least 10% larger than the diameter of the bodily lumen into which it is implanted in some embodiments. The scaffold may be designed to recover at least about 70%, at least about 80%, at least about 90%, up to about 100% of its manufactured, first diameter, in some embodiments.

[00187] Scaffolds in accordance with the present disclosure are provided with expansion and mechanical properties suitable to render the scaffolds effective for its intended purpose in the sinus cavities. Two measures of such mechanical properties that are used herein are "radial resistive force" ("RRF") and "chronic outward force" ("COF"). RRF is the force that the scaffold applies in reaction to a crimping force, and COF is the force that the scaffold applies against a static abutting surface. In certain embodiments, the scaffolds are configured to have a relatively high RRF to be able to

hold open bodily lumens, cavities, and nasal features, and the like, yet have a relatively low COF so as to avoid applying possibly injurious forces against the walls of bodily lumens, optic nerve, brain, or the like. For example, the scaffolds of the present disclosure preferably expand to from 70 to 100% of their as-manufactured configuration after being crimped, have an RRF ranging from 50 to 300 mmHg, and/or have an acute COF (at the time of delivery into a sinus cavity) ranging from 10 to 100 mmHg.

[00188] Scaffolds in accordance with the present disclosure may be formed from a variety of polymeric and non-polymeric materials. Scaffolds in accordance with the present disclosure may be biodegradable or non-biodegradable, or be a combination of both biodegradable and non-biodegradable materials. Where biodegradable, the scaffolds may be fully absorbed, for example, within as little as three weeks or less to as long as 52 weeks or more following placement within a sinus cavity of a patient. In some embodiments, the generally tubular structures may become fully absorbed at some time after 12 weeks of placement and before 32 weeks of placement. Biodegradable devices may also be eliminated through nasal irrigation in other embodiments, as opposed to absorption into nasal mucosa. Devices may also be designed such that discrete portion(s) resorb leading to breakup into predetermined small pieces (typically <10mm or more typically < 5mm in longest dimension) that can be eliminated from the sinuses and nasal cavity through normal mucociliary action, leading to swallowing or expulsion from the nose. In this way, the amount of acidic resorption byproducts (e.g., lactic acid, glycolic acid) which are in contact with the sinus or nasal cavity surfaces may be reduced. This can reduce irritation or inflammation of these and surrounding tissues. Additives of a basic nature may also be added to the devices in some embodiments to neutralize the acidic byproducts, which may reduce the inflammatory response associated with the

same. Moreover, multiple materials that bioresorb at different rates may also be combined in some embodiments to reduce the amount of material degrading at any one time and hence the biological response.

[00189] In various embodiments, the implantable scaffolds may comprise a generally tubular structure comprising scaffolding material. Scaffolds in accordance with the present disclosure may be fiber-based or non-fiber-based.

[00190] In various embodiments, the scaffolding material may be a biodegradable scaffolding material, typically, a biodegradable scaffolding material that comprises one or more biodegradable polymers. Non-limiting examples of biodegradable polymers for forming the biodegradable scaffolding material include biodegradable polyesters, polycarbonates, polyhydroxyalkanoates, polyanhydrides, and polyorthoesters, non-limiting examples of which include homopolymers of lactic acid (PLA), homopolymers glycolic acid (PGA), homopolymers of trimethylene carbonate (PTMC), homopolymers of caprolactone (PCL), homopolymers of polypropylene fumarate, and homopolymers of dioxanone (PDO), as well as copolymers that comprise two or more of the preceding monomers, for example, poly(lactic acid-co-glycolic acid) (PLGA), poly(lactic acid-co-caprolactone) (PLCL) and poly(glycolic acid-co-caprolactone) (PGCL). Preferred copolymers include PLGA having a molar percentage of lactic acid ranging from 10 to 90% and a molar percentage of glycolic acid ranging from 90 to 10%, more typically lactic acid ranging from 10 to 75% and a molar percentage of glycolic acid ranging from 90 to 25%; for example, PLGA 75:25 (mol/mol) or PLGA (10:90) (mol/mol) may be employed in some embodiments. The composition of PLGA polymers within these ranges may be optimized to meet the mechanical property and degradation requirements of the specific application for which the scaffold is used. In certain embodiments, the

biodegradable scaffolding material may comprise a prodrug-based polymer, for example, polyaspirin, which can be used as a single-component or a subcomponent of the generally tubular structure to make scaffolds with degradation-controlled therapeutic-agent-releasing capability.

[00191] In various embodiments, the scaffolding material may be a non-biodegradable scaffolding material, typically a non-biodegradable scaffolding material that comprises one or more non-biodegradable polymers. Non-limiting examples of non-biodegradable polymers for forming the non-biodegradable scaffolding material include polyolefins such as polyethylene (HDPE and LDPE) and polypropylene, halogenated polyolefins such as polyvinyl chloride (PVC) and fluoropolymers including polytetrafluoroethylene (PTFE) and perfluoroalkoxy alkanes (PFAs), polyaromatics such as polystyrene, polyesters such as polyethylene terephthalate (PET), polyamides such as nylon, silicones, mucoadhesive materials and biostable polyurethanes (PU).

[00192] Scaffolds in accordance with the present disclosure may optionally comprise a coating formed of a coating material that at least partially coats the scaffolding material.

[00193] Coatings may be applied for various purposes including mechanical property enhancement, degradation control, and therapeutic agent release and control. Coatings may cover all or a portion of the scaffolds or, in fiber-based techniques, all or a portion of the filaments or strands forming the scaffolds. As used herein "strands" and "filaments" may be used interchangeably and include single fiber strands and filaments (also referred to as monofilaments) and multi-fiber strands and filaments.

[00194] If a scaffold to be coated is a fiber-based structure, coatings may be applied, for example, to individual strands prior to forming the scaffold or applied to the scaffold after the formation thereof. If the scaffold is a non-fiber-based structure, coatings may be applied, for example, to a solid polymer tube or sheet either before or after the removal of material using a suitable cutting technique such as mechanical or thermal cutting. Coatings may be created using any suitable method, including spraying, electrospraying, rolling, dipping, chemical vapor deposition, electrospinning and/or coextrusion, among others. In some embodiments, coatings may include additional agents, such as therapeutic agents, as detailed further below.

[00195] In various embodiments, the coating material may be a biodegradable or non-biodegradable coating material or a combination of both, typically, a biodegradable coating material that comprises one or more biodegradable polymers or a non-biodegradable coating material that comprises one or more non-biodegradable polymers. Non-limiting examples of biodegradable polymers for forming the biodegradable coating material include the biodegradable polymers listed above. Non-limiting examples of non-biodegradable polymers for forming the non-biodegradable coating material include the non-biodegradable polymers listed above.

[00196] In various embodiments, coatings are formed that comprise an elastomer. Potential benefits of such coatings include enhancement of mechanical properties. For example, coatings may be made from an elastomeric polymer that, due to its elastic nature when compressed or elongated, applies a force to scaffold that acts in favor of radial expansion, thus enhancing recoverability and/or radial stiffness, among other properties. An additional potential benefit of the elastomer may be to encapsulate the scaffold material (which may be a braid structure, among others), maintaining integrity and providing smooth, soft surfaces that minimize irritation of

tissue at contact points while providing good conformability. In this regard, certain aspects of the designs described herein, including those resulting from composite structures and combinations of bioresorbable filaments and elastomeric coatings, provide properties that may not be achieved from other bioresorbable stent designs. Potential benefits include higher radial resistive force and/or chronic outward force with lower amounts of polymer, lower profile (thickness of stent wall) and/or better conformability due to spring-like structures at each fiber crossover point, thereby enabling delivery to the target location through smaller delivery systems or guide catheters and/or providing good apposition and conformability to the target location with smaller as-fabricated stent diameter. Better conformability may lead to more efficient drug delivery to the tissue based as a result of improved tissue contact. Furthermore, better conformability may facilitate manipulation of the implant post-deployment by the surgeon to a desired position. For example, when readjusting one side of the implant, the opposite side of the implant has a tendency to readjust its position unless it is well-contoured and adherent to the tissue.

[00197] Coating thickness for the elastomer coating may vary widely, with typical coating thicknesses ranging, for example, from 5 to 50  $\mu\text{m}$ , among other thicknesses. Where a braided scaffold is coated, the elastomer coating may range, for example, between 30 and 150 % by weight of the braided scaffold substrate.

[00198] Elastomers include thermoset and thermoplastic elastomers. The thermoset or thermoplastic elastomer beneficially has a glass transition temperature ( $T_g$ ) that is lower than room temperature ( $25^\circ\text{C}$ ) and is more beneficial when lower than  $10^\circ\text{C}$ . The thermoset elastomers may provide a high elongation to break with low permanent deformation under cyclic mechanical testing. Examples of elastomers include, for example, poly(glycolide-co- $\epsilon$ -caprolactone) (PGCL) or poly(lactide-co- $\epsilon$ -

caprolactone) (PLCL), including poly(L-lactide-co- $\epsilon$ -caprolactone) and poly(D,L-lactide-co- $\epsilon$ -caprolactone). In certain embodiments, the PLCL may have a molar percentage of lactide ranging from 20 to 80% and a molar percentage of caprolactone ranging from 80 to 20%, more typically, a molar percentage of lactide ranging from 30 to 50% and a molar percentage of caprolactone ranging from 50 to 70%.

[00199] In certain embodiments, the biodegradable coating material is a thermoset elastomer formed from polymeric polyols including diols, triols, tetraols and/or higher alcohols. Such polymers may be crosslinked with a crosslinker that is a bi- or multi-functional small molecule or polymer. For example, crosslinks may be formed by reacting such polymers with bi- or multi-functional isocyanates, which may be in form of a small molecule or polymer.

[00200] In the event that the coating comprises a thermoset elastomer polymer, the crosslink density may be varied to yield desired mechanical properties. For example, optional chain terminators may be used in thermoset elastomeric materials such as polyester urethanes to control crosslink density. The chemical crosslink density is adjusted by using such chain terminators to control the degree of crosslinking taking place during the polyester-urethane curing. The crosslink density of the resultant elastomers depends on the concentration of chain terminators incorporated into the elastomeric network. Examples of suitable chain terminators include any suitable monofunctional compound such as monofunctional isocyanates, alcohols, amines, acyl chlorides, and sulfonyl chlorides.

[00201] In certain embodiments, the thermoset elastomer comprises a polyester polyol, diisocyanate crosslinker and an optional chain terminator. Such a thermoset elastomer may be prepared by a process that comprises the steps of: at least

partially dissolving a polyester polyol in a solvent to form a solution; adding a diisocyanate crosslinker to said solution; optionally adding a chain terminator to said solution; coating said solution onto the scaffolding material; and curing said solution. Where solvent-based processing is employed, a less volatile co-solvent may be used to improve the node accumulation of thermoplastic elastomers during the coating process.

[00202] Non-limiting examples of suitable polyols for forming urethane-crosslinked elastomers include, for example, branched (3 arms or more) poly(lactic acid-co-caprolactone) (PLCL) and poly(glycolide-co-caprolactone) (PGCL) polyols. Besides branched polymers, linear polymer diols may also be used to create an elastic coating upon curing with isocyanates (e.g., hexamethylene diisocyanate) and other appropriate reagents. To reduce inflammation caused by material degradation, poly(trimethylene carbonate) (PTMC) based polyols may also be used to create an elastic coating. Various catalysts, including but not limited to,  $\text{Sn}(\text{Oct})_2$ ,  $\text{Zn}(\text{Oct})_2$ , dibutyl tin dilaurate (DBTL), 1,4-diazabicyclo[2.2.2]octane (DABCO), and 1,8-diazabicycloundec-7-ene (DBU), may be used to facilitate the curing process.

[00203] In some embodiments, scaffolds and/or coatings may be fabricated using a shape-memory polymer that can change in size, shape, and/or conformability to mold to sinus anatomy. Non-limiting examples of shape-memory polymers include segmented polyurethanes made of oligolactide, oligocaprolactone, oligolactide-co-glycolide, oligo(trimethylene carbonate), or oligodioxanone coupled isocyanates and various chain extenders, (multi)block copolymers of lactide (glycolide) and caprolactone, dioxanone, or trimethylene carbonate, polymer blends of polylactide and polyamide elastomers.



[00204] As previously indicated, scaffolds in accordance with the present disclosure may be fiber-based or non-fiber-based. In fiber-based embodiments, polymeric materials may be first manufactured into fibers with cross-sectional dimension ranging, for example, from 10  $\mu\text{m}$  to 1000  $\mu\text{m}$ , more typically, 100  $\mu\text{m}$  to 300  $\mu\text{m}$ . Such fibers may be formed using a number of technologies including, for example, extrusion or spinning technologies.

[00205] The shape of the cross-section of the fibers may vary widely. Referring to Fig. 1A, such cross-sections include fibers having round cross-section 10, oval cross-section 12, and polygonal cross-section (e.g., triangular cross-section 14, quadrilateral cross-section 16, for instance, in the shape of a rectangle, parallelogram, trapezoid, etc., pentagonal cross-section, hexagonal cross-section 18, and so forth). Fiber cross-section may be varied by selecting a die of suitable cross-section for use during fiber manufacture.

[00206] Polymeric materials may also be formed into sheets, for example, through a suitable casting or extrusion process (e.g., solvent casting, melt casting, solvent-based extrusion, melt extrusion, etc.) The sheets may thereafter be cut into fibers (e.g., fibers having a polygonal cross-section, for instance, in the shape of a triangle or a quadrilateral such as rectangle, parallelogram, trapezoid, etc.).

[00207] The strength of the fibers may be optimized in certain embodiments, for example, by drawing at appropriate draw ratios or annealing at appropriate temperatures.

[00208] Strength and/or flexibility of the fibers may also be optimized by braiding fibers of homogeneous or heterogeneous cross-section into multi-fiber strands (e.g., fish-wire-type structures). The fibers that are braided may be of the same composition or of different composition. Moreover, the fibers that are braided may

be of the same diameter or different diameter. Two embodiments are shown in FIG. 1B, which illustrates (a) a cross-section of a multi-fiber strand 11 formed from strands of the same material and having the same diameter and (b) a cross-section of a multi-fiber strand 13 formed from strands of different composition and having different diameter.

[00209] Once the polymeric strands are prepared, fiber-based scaffolds may be made thereof. For example, single-fiber strands and/or multi-fiber strands of various shapes (e.g., as illustrated in FIGS. 1A-1B, among others) may be braided into a generally tubular structure. The strands that form the braids may vary widely in diameter, ranging, for example, from 10 to 1000  $\mu\text{m}$ , among other possibilities. In certain embodiments, the materials forming the strands may have an elastic modulus within the range of about 1 GPa to about 10 GPa, and more preferably within the range of about 4-9 GPa.

[00210] To facilitate low-profile aspects of the present disclosure (e.g., the delivery of the scaffolds into small diameter sinus cavities), in certain beneficial embodiments, the strands used in forming scaffolds may have a diameter ranging from 100 to 500  $\mu\text{m}$ , more beneficially ranging from 125 to 250  $\mu\text{m}$ . The use of small diameter strands results in a scaffold with minimal wall thickness and the ability to collapse (i.e., to be crimped) within low diameter catheter delivery systems. In certain embodiments, the diameters of strands may be chosen so as to render the scaffold deliverable from a 15 French delivery catheter or smaller, from a 9 French delivery catheter or smaller, from a 6 French delivery catheter or smaller, or even from a 4 French delivery catheter or smaller.

[00211] FIG. 2 illustrates an embodiment of a braided scaffold 100, which comprises at least one strand (e.g., a single-fiber or multi-fiber strand) woven to form a

substantially tubular configuration having a length 130, a width 131, and first and second ends 132, 133 along the longitudinal dimension. For example, the tubular structure may comprise two sets of strands 110 and 120, with each set extending in an opposed helical configuration along the longitudinal dimension of the scaffold. In certain embodiments, the number of helical strands forming the scaffold may range, for example, from 8 to 48 strands, among other possibilities. The sets of strands 110 and 120 cross each other at a braid angle 140. The braid angle 140 may range, for example, from about 30 degrees or less to about 150 degrees or more, among other values, for example, ranging anywhere from 30 degrees to 40 degrees to 50 degrees to 60 degrees to 70 degrees to 80 degrees to 90 degrees to 100 degrees to 110 degrees to 120 degrees to 130 degrees to 140 degrees to 150 degrees (i.e., ranging between any two of the preceding numerical values). Strands may be woven together using a variety of methods known in the art including, for example, various 1x1, 1x2 and 2x2 designs and may be woven using particular known weave patterns such as Regular pattern "1 wire, 2-over/2-under", Diamond half load pattern "1 wire, 1-over/1-under", or Diamond pattern "2 wire, 1-over/1-under".

[00212] Various factors contribute to the radial strength of scaffold 100, including the diameter(s) of the strands, the braid angle 140, the strand material(s), and the number of strands used, among others.

[00213] Strands may cross each other at a braid angle which is constant or which may change around the circumference of the scaffold and/or along the longitudinal dimension of the scaffold. FIG. 3A shows an embodiment in which a scaffold 100 has strands of constant braid angle, whereas FIG. 3B shows an embodiment in which a scaffold 100 has strands of variable braid angle. In the particular embodiment of FIG. 3B, a first region 100a having strands of a first braid angle transitions into a

second region 100b having strands of a second braid angle that is less than the first braid angle. Various filament braiding patterns may be used to manufacture such constructs.

[00214] Potential attributes of a design with variable braid angles include one or more of the following, among others: (1) it allows for the orientation of segments with specific density for preferential therapeutic agent delivery; (2) it allows for tailored radial force depending on scaffold location; and (3) it may be used to provide a tapered tubular design that is useful for non-cylindrical anatomy.

[00215] In general, the shape and diameter of a scaffold in accordance with the present disclosure may change along the length of the device. In certain embodiments, in a cylindrical design the diameter at the ends of the device may be larger than the diameter at the midpoint (e.g. a dumbbell or hourglass shape). For instance, the diameter at the ends of the device may be 1.5 times or more, even 2 times or more, than the diameter at the midpoint. As another example, the shape of the device may be triangular at one end and hexagonal at the other end.

[00216] Radial stiffness for braided scaffolds may be tailored by partially or completely locking various strand cross-over points (also referred to as "nodes"). Nodes may be partially or completely locked, for example, by welding the strands at cross-over points, for instance, using heat (e.g., using a suitable laser such as a pico or femto laser), by using a suitable adhesive, by wrapping crossover points with a suitable filament, or by coating cross-over points with a suitable material that holds the filaments together, among other possible techniques. In some embodiments, elastomers may be coated onto the braids, for example, using procedures such as those described in U.S. Patent Nos. 8,137,396, 8,540,765, and 8,992,601, the disclosures of which are hereby incorporated by reference.

[00217] Underlying braids, either with or without previously locked nodes, may be subject to elastomer coating. One embodiment is illustrated in FIG. 4, which shows a braided scaffold 100 that is completely coated with an elastomer 100e. Varying the node accumulation of the coated elastomer may optimize both radial resistive force (RRF) and chronic outward force (COF) for this sinus cavity.

[00218] In alternative embodiments, scaffolds may be provided in which the nodes of the braided structure are connected using an elastic member such as an elastic filament or strand. One such embodiment is illustrated in FIG. 5, which shows a scaffold 100 in which an elastic strand 111 is attached to the braid 110 at various points along the length of the braid 110. In these embodiments, the braid itself provides the framework to support the sinus cavity, while the elastic filament or strand 111 is provided to enhance scaffold recovery during deployment. The elastic filament or strand 111 may be, for example, woven into the scaffold 100 during braiding process or introduced to the scaffold 100 after it is formed. In the latter case, the braid 110 forming the scaffold 100 may be made from softer, non-elastic materials that conform to sinus walls and have desired degradation profiles. The number of elastic filaments or strands 111 used in a given scaffold 100 may be tailored to afford appropriate recovery and radial stiffness.

[00219] A conformable scaffold is desirable in various embodiments, as it may be used to improve apposition to contacted tissues, reduce damage to the contacted tissue and, where a therapeutic agent is delivered, also increase the therapeutic agent delivery efficacy due to increased tissue contact.

[00220] Various strategies may be employed to increase conformability of the braided scaffolds. For example, in some embodiments, some or all of the nodes of the braids may be partially locked or not locked at all to allow at least some filaments at least

some freedom to slide over one another. In a constrained space, scaffolds with freely movable filaments will have a tendency to better adapt to the geometry of the surrounding environment.

[00221] Alternatively or in addition, scaffolds may be braided from filaments of different stiffness (e.g., having a combination of higher and lower stiffness). The stiffness of a given strand is determined, for example, by its inherent material properties, by its processing conditions, and by its dimension. One embodiment of this type of scaffold is schematically illustrated in FIG. 6A in which a scaffold 100 is shown that is formed from strands of higher stiffness 112 and strands of lower stiffness 113. In one specific embodiment, the strands of higher stiffness 112 may have an elastic modulus higher than 3 GPa and filament diameter greater than 100  $\mu\text{m}$ , while the strands of lower stiffness 113 may have an elastic modulus lower than 3 GPa and filament diameter less than 200  $\mu\text{m}$ . Filaments with lower stiffness may provide a weaker point in the scaffold to allow for deformation to comply with the sinus cavities, whereas filaments with higher stiffness may maintain mechanical integrity.

[00222] Conformability may also be improved by removing some of the strands from within the braided structure. One embodiment of this type of scaffold is schematically illustrated in FIG. 6B in which a scaffold 100 is shown in which cells of varying size are formed. In particular, a scaffold containing larger diamond shaped cells 114 and smaller diamond shaped cells 115 are shown. In some embodiments, a severed strand may be partially or completely locked at a cross-over point nearest to the severed tip of the strand.

[00223] In related embodiments, different sized cells are created during the course of the braiding process, for example, through selection of a suitable braiding pattern.

One embodiment of a scaffold 100 having larger braided cells 114 and smaller braided cells 115 is shown in FIG. 7.

[00224] Where cells of differing sizes are formed, the larger cells may have an area ranging from 1.1 times to 10 or more times an area of the smaller cells.

[00225] Potential advantages of scaffolds having a combination of larger and smaller cells is that the larger cells may provide flexibility (e.g. for ease of crimping and better conformability), whereas the smaller cells may maintain mechanical integrity.

[00226] Another route to create conformable scaffolds is to braid the scaffolds using a rigid rubber material such as carbon fiber reinforced silicone, poly(acrylonitrile butadiene), and poly(styrene butadiene) rubbers, among others. This results in completely elastic braids.

[00227] In some embodiments, a coating layer may be formed over all or a part of the scaffold structure. By employing a relatively non-elastic material for the coating layer (e.g., one formed using a relatively stiff polymer such as D,L-PLGA), the stiffness of the scaffold may be improved. Moreover, where the implant is formed using braids that are inherently elastic and where the coating layer is a degradable layer, upon degradation of the degradable layer, the scaffold strands will have increased conformability.

[00228] Furthermore, the coating layer may be applied in a pattern in order to tailor the conformability of the braided scaffolds. As one specific example, FIG. 6C shows an embodiment of a scaffold 100 where coated regions 116 are provided at each end of the scaffold 100 while an uncoated region 117 is provided at the center of the scaffold 100. Such a design may be used to provide ends having enhanced stiffness, which may allow the device to be better anchored into the sinus cavities. Moreover, leaving the middle region of the scaffold 100 uncoated may enhance the ability of

the stent to comply with the shape of the sinus cavities at the time of implantation. As another specific example, FIG. 6D shows an embodiment of a scaffold 100 where coated regions 116 and uncoated regions 117 are provided in an alternating pattern. The presence of uncoated regions 117 provides regions of increased flexibility along the length of the scaffold, which may provide enhanced conformability to irregular surfaces such as those associated with the sinus cavities.

[00229] Regions of coated and uncoated material may be provided using various techniques. For instance, in some embodiments, a mask may be used in a spray coating process to create specific patterns of coated and uncoated regions.

[00230] By masking a part of the tubular braids longitudinally during spray coating, a U-shaped coating region (when viewed longitudinally) may be created. In these scaffolds, the coated region is relatively stiff while the uncoated region is relatively soft. The coated region would provide scaffold recoverability after deployment into sinus cavities. On the other hand, the soft uncoated region may readily deform to adapt the irregular surface of sinus cavities, affording optimized conformability. In one particular embodiment, such a scaffold may be useful to maintain patency in select cases where an opening is made between the left and right paranasal sinuses.

[00231] In some embodiments, the scaffold may be cut longitudinally, allowing the circumference of the scaffold to be readily resized to match the geometry of sinus cavities upon deployment, which may provide better compliance and conformability.

[00232] To reduce potential tissue irritation or patient discomfort caused by sharp scaffold edges, the scaffold edges may be coated and/or braided scaffolds may be made in which the end filaments are turned back toward the center of the scaffold. For instance, the filament ends may be woven back into the scaffold structure and bonded, for example, at the nodes. Bonding may be conducted using the techniques



described hereinabove for bonding filaments at the nodes (e.g., by welding, application of a suitable adhesive, application of an elastomeric coating, etc.). A scaffold 100 of this type is schematically illustrated in FIG. 8 in which the end filaments 118 are turned back toward the center of the scaffold 100.

[00233] To the extent that difficulty may be encountered when short scaffolds are braided on large diameter mandrels (i.e., when forming scaffolds with large diameter to length ratios), zig-zag strands, including single- and multi-fiber strands, may be fabricated prior to braiding. The zig-zag strands may then be wound or looped around the mandrels, preferably in braided pattern. The ends of the filaments may then be attached, for example, using the techniques described hereinabove for bonding filaments at the nodes (e.g., by welding, application of a suitable adhesive, application of an elastomeric coating, etc.) to complete the braided structure. The size and shape of the final scaffold may be controlled by the turn angle, orientation and strut length of the zig-zag filaments. Such a braid may also have fold-back ends as depicted above.

[00234] In certain embodiments, it is beneficial to provide sinus scaffolds with a capability of being readily removed if it is desired to do so. In the case of a relatively soft braided scaffold, a tool with one or more hooks at the end may be used to capture a distal end of the implanted scaffold. Alternatively, the device could be removed by standard surgical instruments available to ENT surgeons. Then, the braid may be inverted by pulling the end, and thus the exterior surface, into the lumen. In this way, the scaffold may be removed by peeling off the sinus wall, reducing additional abrasion, irritation, and damage to sinus tissue.

[00235] Other scaffolds are based on non-braided structures or hybrid braided/non-braided structures.

[00236] For instance, in various embodiments, scaffolds are provided which are formed from woven or knitted strands. A scaffold 100 in the form of a knitted tube is illustrated in Fig. 9. Such a woven or knitted scaffold may provide the mechanical properties necessary to provide a stenting function, while also having enhanced compliance and conformability (as well as facilitating therapeutic agent delivery in some embodiments). In addition, in the case of a knitted structure, one end of a single strand used to form the tube may be pulled to unravel the stent, enabling removal of the scaffold, in some embodiments.

[00237] In various other embodiments, scaffolds may be in a spiral (e.g., helical) form. In some of these embodiments, a spiral form may be formed from a single strand (e.g., a single- or multi-fiber strand). An example of such a scaffold 100 is schematically illustrated in FIG. 10.

[00238] In other of these embodiments, a spiral form may be formed from multi-stranded constructs. Examples of multi-stranded constructs include, for example, substantially two-dimensional structures (e.g., ribbon-shaped structures) which can be shaped into a spiral form. Two embodiments of spiral-shaped scaffolds of this type are shown in FIG. 11A and FIG. 11B. In the embodiment shown in FIG. 11A, a spiral shaped scaffold 100 is formed from a pre-existing tubular structure such as, for example, braided tubular structure (e.g., one of those previously described), which is subsequently cut into a spiral. In the embodiment shown in FIG. 11B, a scaffold 100 is formed by fashioning a previously formed substantially two-dimensional braid pattern 119 into a spiral structure, for example, by placing the substantially two-dimensional braid pattern on a mandrel and annealing it for a time and at a temperature suitable to form the two-dimensional braid pattern into a spiral shape.

Examples of such braid patterns include multi-carrier braid patterns, such as a 2-carrier (shown in Fig. 11B), 3-carrier, 4-carrier, etc. braid pattern.

[00239] It is noted that scaffolds analogous to the various braided structures described herein may be in the form of a unitary polymeric structure. The use of a unitary polymeric structure may provide a reduced profile when compared to the use of fiber-based techniques, which yield a minimum profile that is the sum of the widths of overlapping strands. One embodiment of such a structure is shown in FIG. 15, in which a scaffold 100 is illustrated and is characterized by a regular, repeating pattern such as a lattice structure. When the scaffold 100 is a unitary polymeric structure, it may be fabricated using a variety of suitable techniques, such as by mechanical cutting or laser cutting a pattern into a solid polymer tube or a solid polymer ribbon

[00240] In various other embodiments, the scaffold may be in the form of an open cylinder. For example, as shown in FIGS. 12A and 12B, the scaffold 100 may be formed from a series of individual hoops 121 which are axially aligned with one another and connected at one end. In the embodiment shown in FIG. 12A, individual hoops 121 are solid hoops (e.g., in the form of a ribbon). In the embodiment shown in FIG. 12B, individual hoops 121 comprise cells, in particular, diamond-shaped cells analogous to those formed with a 2-carrier braid. Benefits of these designs may include one or more of the following, among others: the hoops are straightforward to crimp to size; and upon delivery, the scaffold unfurls to an expanded diameter. Because each hoop is allowed to expand to different widths, the scaffold may be more conformal in variable sized spaces.

[00241] In still other embodiments, a scaffold 100 may be in the form of a polymeric tube such as that shown in FIG. 13. Such a device is beneficial, for example, in that

it may conform to the sinus wall 200 and, optionally release one or more therapeutic agents. The tube may utilize materials such as the scaffold materials described above, among others, and include thermally-forged PCL, or PLCL with high caprolactone content, among many other possible materials.

[00242] In a related device design, a tubular conformal scaffold like that shown in FIG. 13 may be attached to a crimpable three-dimensional support structure which may assist the tubular scaffold in expansion and support of the sinus. A specific example of such a device is shown in FIG. 14, which shows the tubular scaffold 110 attached to a crimpable three-dimensional structure 122. The structure 122 is crimpable to allow for minimally invasive delivery. Structures 122 may be provided at the ends of the tubular scaffold 110, and if desired, at one or more points along a length of the tubular scaffold 110. Examples of materials suitable for forming the crimpable three-dimensional structure include degradable or non-degradable elastomeric materials that can be compressed and recover from that deformation. In other embodiments, braided stent structures like those discussed hereinabove may be used as crimpable three-dimensional structures.

[00243] Supplemental agents such as therapeutic agents and inactive release-controlling agents may be integrated into the various devices described herein.

[00244] Examples of therapeutic agents are any suitable agents having desired biological effects, including small molecule agents, biologics, cells including stem cells, gene therapies and RNAi, among others. Specific examples of therapeutic agents include: analgesic agents including simple analgesics such as aspirin and paracetamol, non-steroidal anti-inflammatory drugs such as ibuprofen, diclofenac, naproxen, celecoxib, ketoprofen, piroxicam and sulindac, and opioids such as codeine tramadol, dextropropoxyphene, paracetamol, morphine, oxycodone and

pethidine hydrochloride; anesthetic agents such as lidocaine, bupivacaine, and ropivacaine; statins such as atorvastatin, cerivastatin, fluvastatin, lovastatin, mevastatin, pitavastatin, pravastatin, rosuvastatin, and simvastatin; steroidal anti-inflammatory drugs such as glucocorticoids, mometasone furoate, beclomethasone dipropionate, budesonide, ciclesonide, flunisolide, fluticasone furoate, fluticasone propionate, dexamethasone, cortisone, prednisone, methylprednisolone, triamcinolone acetonide, betamethasone, dexamethasone, prednisolone, corticosterone, estrogen, sulfasalazine, rosiglitazone, mycophenolic acid, and mesalamine; antihistamines including H<sub>1</sub>-receptor antagonists such as diphenhydramine, loratadine, fexofenadine, cyproheptadine, promethazine, desloratadine, chlorpheniramine, hydroxyzine and pyrilamine and H<sub>2</sub>-receptor antagonists such as cimetidine, famotidine, lafutidine, nizatidine, ranitidine, roxatidine and tiotidine; antimicrobial agents such as mupirocin, gentamycin and tobramycin; antibiotic agents such as penicillin, cefoxitin, oxacillin and tobramycin; endostatin, angiostatin and thymidine kinase inhibitors, and its analogs or derivatives; antileukotriene agents (e.g. monteleukast, zafirlukast, zileuton, etc.); antifungal agents; and probiotics, among many others.

[00245] Further examples of therapeutic agents may be selected from anti-thrombogenic agents such as heparin, heparin derivatives, urokinase, and PPACK (dextrophenylalanine proline arginine chloromethylketone), enoxaparin, hirudin; anti-proliferative agents such as angiopeptin, or monoclonal antibodies capable of blocking smooth muscle cell proliferation, acetylsalicylic acid, paclitaxel, sirolimus, tacrolimus, everolimus, zotarolimus, vincristine, sprycel, amlodipine and doxazosin; immunosuppressants such as sirolimus, tacrolimus, everolimus, zotarolimus, and dexamethasone; antineoplastic/antiproliferative/anti-mitotic agents such as paclitaxel, 5-fluorouracil, cisplatin, vinblastine, cladribine, vincristine, epothilones,

methotrexate, azathioprine, halofuginone, adriamycin, actinomycin and mutamycin; anti-coagulants such as D-Phe-Pro-Arg chloromethyl ketone, an RGD peptide-containing compound, heparin, antithrombin compounds, platelet receptor antagonists, anti-thrombin antibodies, anti-platelet receptor antibodies, aspirin (aspirin is also classified as an analgesic, antipyretic and anti-inflammatory drug), dipyridamole, hirudin, prostaglandin inhibitors, platelet inhibitors and antiplatelet agents such as trapidil or liprostin, tick antiplatelet peptides; DNA demethylating drugs such as 5-azacytidine, which is also categorized as a RNA or DNA metabolite that inhibit cell growth and induce apoptosis in certain cancer cells; vascular cell growth promoters such as growth factors, Vascular Endothelial Growth Factors (VEGF, all types including VEGF-2), growth factor receptors, transcriptional activators, and translational promoters; vascular cell growth inhibitors such as antiproliferative agents, growth factor inhibitors, growth factor receptor antagonists, transcriptional repressors, translational repressors, replication inhibitors, inhibitory antibodies, antibodies directed against growth factors, bifunctional molecules consisting of a growth factor and a cytotoxin, bifunctional molecules consisting of an antibody and a cytotoxin; cholesterol-lowering agents; vasodilating agents; and agents which interfere with endogenous vasoactive mechanisms; anti-oxidants, such as probucol; angiogenic substances, such as acidic and basic fibroblast growth factors, estrogen including estradiol (E2), estriol (E3) and 17-Beta Estradiol; drugs for heart failure, such as digoxin, beta-blockers, angiotensin-converting enzyme (ACE) inhibitors including captopril and enalapril, statins and related compounds; macrolides such as sirolimus and everolimus; and agents that have a primary mechanism of action of inhibiting extracellular matrix remodeling, and a secondary mechanism of action of inhibiting cell proliferation such as 5-fluorouracil, doxycyclin, carvedilol, curcumin, and tranilast.

[00246] Other therapeutic agents include bacteria or other microflora that may be beneficial to re-establishing a healthy microbiome in the nasal cavity and sinuses as well as agents or nutrients that may promote a healthy microbiome.

[00247] Inactive release-controlling agents may also be included to enhance control over the therapeutic agent release kinetics. Examples of inactive release-controlling agents include soluble polymers such as polyethylene glycol (PEG) (also known as polyethylene oxide, PEO), PEG-vinyl alcohol copolymers, polyacrylate and polymethacrylate esters containing cationic and anionic functionality, polyvinyl pyrrolidone, and dextran, as well as small molecule additives such as cyclodextrin or citrate esters such as acetyltributyl citrate (ATBC) or acetyltriethyl citrate (ATEC).

[00248] In embodiments where the scaffold delivers one or more therapeutic agents at the site of implantation, the therapeutic agent(s) may be provided in the device for delivery therefrom in a number of ways.

[00249] For example, the therapeutic agent may be directly embedded within a polymeric construct (e.g., filaments, sheets, solid tubes, etc.) that is subsequently used to form a generally tubular scaffold as described herein. In one embodiment, therapeutic agent and polymer(s) are dissolved in an appropriate solvent to make a homogenous solution or a suspension, or therapeutic agent and polymer(s) are heated to form a polymer melt containing the therapeutic agent. The solution, suspension or melt is then subjected to suitable solvent-based or melt-based processing such as extrusion, wet spinning, dry spinning, melt spinning, electrospinning or other process to afford therapeutic-agent-loaded polymeric constructs (e.g., filaments, sheets, tubes, etc.) with embedded therapeutic agents. In some embodiments, a polymeric region that does not contain a therapeutic agent (e.g., a polymer core) is coextruded with a therapeutic-agent-loaded polymeric

coating to form therapeutic-agent-loaded polymeric constructs.

[00250] In some embodiments, therapeutic-agent-loaded polymeric constructs may then be subsequently processed into additional forms that are subsequently used to form generally tubular scaffolds as described herein. As a specific example, a solvent-cast therapeutic-agent-loaded polymeric construct in the form of a sheet may be made by controlled evaporation of a solution of a therapeutic agent and one or more carrier polymers. After removal of the solvent(s), the therapeutic-agent-loaded polymer sheet may be laser cut into therapeutic-agent-loaded polymeric constructs in the form of flat filaments for braid manufacture.

[00251] In some embodiments, the therapeutic agent may be applied onto a pre-formed construct (e.g., a filament, a sheet, or a tube, including a pre-formed device scaffold) in the presence or absence of a carrier material (e.g., a polymeric coating material such as those described above) using a suitable application technique such as spray-coating, dip-coating, rolling or vapor deposition, among others. The therapeutic agent releasing profile may be tailored, for example, by the thickness of the coating layer, by the addition of inactive ingredients and, where a polymer is provided as a carrier, changing the carrier polymer (e.g. changing the composition and/or molecular weight of the polymer) and/or the therapeutic-agent-to-polymer ratio.

[00252] A topcoat of a therapeutic-agent-free polymer layer may also be employed to regulate the delivery of the therapeutic agent from the device into bodily tissue. In embodiments pertaining non-biodegradable topcoats, the topcoat may act as a diffusion barrier such that the rate of delivery of the therapeutic agent(s) is limited by the rate of its diffusion through the topcoat. In some embodiments pertaining to biodegradable topcoats, the topcoat may also act as a diffusion barrier such that the



rate of delivery of the therapeutic agent(s) is limited by the rate of its diffusion through the topcoat. In other embodiments pertaining to biodegradable topcoats, the therapeutic agent(s) cannot diffuse through the topcoat, such that delivery thereof is simply delayed until the degradation of the topcoat is complete.

[00253] Electrospinning provides another potential method to introduce therapeutic agent onto a pre-formed construct. In one embodiment, a fiber-based or non-fiber-based scaffold may be covered by an electrospun fiber mesh, such as a core-sheath fiber mesh. During electrospinning, the therapeutic agent may be either dissolved or suspended in a core polymer solution. The therapeutic agent release profiles may be tuned by adjusting the therapeutic agent loading, the particulate size of the therapeutic agent (where a suspension is employed), the types of polymers used to form the core and sheath, respectively, as well as the thickness of the sheath.

[00254] In other embodiments, core-sheath fibers are first fabricated through coaxial electrospinning of a core polymer solution or suspension with therapeutic agent and a sheath polymer solution. The therapeutic-agent-loaded fibers may be further braided onto a multi-fiber strand that will be used to manufacture devices. For example, a fish-wire-shaped composite strand may be formed and thereafter fabricated into a braided scaffold as described previously. In these designs, the therapeutic agent release may be dictated by the electrospun fibers.

[00255] In some embodiments, biologically active agents such as proteins and/or polysaccharides may be incorporated into electrospun fibers.

[00256] In some embodiments, the devices described herein can be used in conjunction with sinuplasty. For example, scaffolds such as those described herein can be deployed into the sinus cavities with the assistance of an expandable device such as an expandable frame (e.g., an expandable wire frame) or a balloon, among

other possibilities. In such embodiments, a scaffold in accordance with the present disclosure may be positioned on, in, under, proximal to, or distal to the expandable device, either at a manufacturing site or by a healthcare professional at the time of delivery. The expandable device may be a drug-eluting device (e.g., via a drug-containing coating disposed on the expandable device) or a non-drug-eluting device. Examples of therapeutic agents which may be released by a drug-eluting device are described above.

[00257] Thus, in the case of a balloon, the balloon may be coated or uncoated, and a scaffold in accordance with the present disclosure may be positioned on, in, under, proximal to, or distal to a balloon catheter suitable for sinuplasty, either at a manufacturing site or by a healthcare professional at the time of delivery. The catheter may include an inflatable balloon assembly disposed at or near a distal end of a catheter shaft that comprises an inflation lumen for the balloon. In an uninflated state, the balloon assembly does not significantly increase the overall width of the distal end of the catheter. This allows the distal portion of the catheter to be inserted into a patient and guided to a desired treatment site in the patient's sinuses. Once at the treatment site, the balloon assembly is inflated to position the scaffold against the sinus wall proximate to the treatment site. The balloon assembly can include any number of individual balloons in a number of configurations, depending upon the treatment site. Additionally, the sinuplasty may be completed before delivery of the scaffold, after delivery of the scaffold, simultaneously with delivery of the scaffold, or any combination of perioperative procedural sequences.

[00258] In some embodiments, the devices described herein can be used as an adjunctive therapy. For instance, scaffolds such as those described herein can be

deployed into the sinus cavities using a therapeutic-agent-eluting delivery device such as, for example, a therapeutic-agent-eluting balloon. Alternatively, scaffolds can be deployed into the sinus cavities, after the cavities have been treated with a therapeutic-agent-releasing spray such as a hydrogel spray, or irrigation liquid that contains one of the therapeutic agents previously described in this disclosure.

[00259] The scaffolds of the present disclosure may be radiopaque such that they are visible using conventional fluoroscopic techniques. In one embodiment, radiopaque additives are included within the polymer material of the scaffold and/or its coating, where present. Examples of suitable radiopaque additives include particles comprising iodine, bromine, barium sulfate, platinum, iridium, tantalum, and/or palladium. In another embodiment, the radiopaque groups, such as iodine, are introduced onto the polymer backbone. In yet another embodiment, one or more biostable or biodegradable radiopaque markers, for example, comprising platinum, iridium, tantalum, and/or palladium may be produced in the form of a tube, coil, wire, sphere, or disk, which is then placed at the ends of the scaffold or at other predetermined locations thereon.

[00260] To facilitate delivery, the scaffold may be loaded into a delivery catheter just prior to being implanted into a patient. Loading the scaffold in close temporal proximity to implantation avoids the possibility that the polymer of the scaffold will relax during shipping, storage, and the like within the delivery catheter. One aspect of the disclosure thus includes a method of delivering a scaffold of the disclosure that comprises a step of loading the scaffold into a delivery catheter within a short period of time, for example, within one hour, before implantation into a body lumen. It should be noted, however, that it is not required that the scaffolds of the present disclosure are loaded into delivery catheters just prior to being implanted.

[00261] In certain embodiments, scaffolds may be provided which are suitable for implantation into the vacated space that is formed during an ethmoidectomy, among other uses (e.g., using a 6 mm catheter, among other devices). Such scaffolds may range, for instance, from 10 to 30 mm in diameter, more particularly, from 15 to 20 mm in diameter, among other possible values. Such scaffolds may range, for instance, from 5 to 20 mm in length, more particularly, from 8 to 12 mm in length, among other possible values. In certain beneficial embodiments, the scaffolds comprises a braided scaffold material, which may comprise, for example, from 8 to 64 braiding strands, more particularly, from 16 to 32 braiding strands, among other possible values. In certain beneficial embodiments, braid angle may vary, for instance, from 30 to 150 degrees, more particularly, from 60 to 130 degrees, among other possible values. In certain beneficial embodiments, diameter of the strands that form the braids may vary from 50 to 500  $\mu\text{m}$ , more particularly, from 150 to 300  $\mu\text{m}$ , among other possible values. In certain beneficial embodiments, scaffold mass may range, for instance, from 1 to 20 mg/mm of length, more particularly, from 2 to 10 mg/mm, among other possible values. In certain beneficial embodiments, scaffolds have a % diameter recovery of at least 85% after being compressed to a diameter of that is 30% of the unconstrained diameter for 10 minutes. Where drug is released, in non-refractory patients the drug may be released over a period of 3 to 6 weeks, among other values, whereas in refractory patients the drug may be released over a period of 8 to 26 weeks, among other values

[00262] In certain embodiments, scaffolds may be provided which are suitable for implantation into the middle meatus space, among other uses (e.g., using a 3-4 mm delivery catheter, among other possible devices). Such scaffolds may range, for instance, from 5 to 20 mm in diameter, more particularly, from 10 to 15 mm in diameter, among other possible values. Such scaffolds may range, for instance,

from 5 to 20 mm in length, more particularly, from 8 to 12 mm in length, among other possible values. In certain beneficial embodiments, the scaffolds comprises a braided scaffold material, which may comprise, for example, from 8 to 64 braiding strands, more particularly, from 16 to 32 braiding strands, among other possible values. In certain beneficial embodiments, braid angle may vary, for instance, from 30 to 150 degrees, more particularly, from 60 to 130 degrees, among other possible values. In certain beneficial embodiments, diameter of the strands that form the braids may vary from 100 to 500  $\mu\text{m}$ , more particularly, from 150 to 300  $\mu\text{m}$ , among other possible values. In certain beneficial embodiments, scaffold mass may range, for instance, from 1 to 20 mg/mm of length, more particularly, from 2 to 10mg/mm of length, among other possible values. In certain beneficial embodiments, scaffolds have a % diameter recovery of at least 85% after being compressed to a diameter of that is 30% of the unconstrained diameter for 10 minutes. In certain beneficial embodiments, scaffolds have a RRF ranging from 30 to 500mmHg upon being measured in an MSI radial force tester at a diameter less than the manufactured diameter, among other possible values. In certain beneficial embodiments, scaffolds have an acute COF ranging from 5 to 100mmHg upon being measured in an MSI radial force tester at a diameter less than the manufactured diameter, among other possible values. Where drug is released, it may be released over a period of 8 to 26 weeks, among other values.

[00263] In certain embodiments, scaffolds may be provided which are suitable for implantation into the sinus ostia, among other uses (frontal, maxillary, or sphenoid) or the frontal sinus recess (e.g., using a 3-4 mm delivery catheter, among other possible devices). Such scaffolds may range, for instance, from 4 to 20 mm in diameter, more particularly, from 6 to 10 mm in diameter, among other possible values. Such scaffolds may range, for instance, from 5 to 20 mm in length, more

particularly, from 6 to 12 mm in length, among other possible values. In certain beneficial embodiments, the scaffolds comprise a braided scaffold material, which may comprise, for example, from 8 to 64 braiding strands, more particularly, from 16 to 32 braiding strands, among other possible values. In certain beneficial embodiments, braid angle may vary, for instance, from 30 to 150 degrees, more particularly, from 60 to 130 degrees, among other possible values. In certain beneficial embodiments, diameter of the strands that form the braids may vary from 100 to 500  $\mu\text{m}$ , more particularly, from 150 to 300  $\mu\text{m}$ , among other possible values. In certain beneficial embodiments, scaffold mass may range, for instance, from 1 to 20 mg/mm of length, more particularly, from 2 to 10mg/mm, among other possible values. In certain beneficial embodiments, scaffolds have a % diameter recovery of at least 85% after being compressed to a diameter of that is 30 % of the unconstrained diameter for 10 minutes. In certain beneficial embodiments, scaffolds have a RRF ranging from 30 to 500mmHg upon being measured in an MSI radial force tester at a diameter less than the manufactured diameter, among other possible values. In certain beneficial embodiments, scaffolds have an acute COF ranging from 5 to 100mmHg upon being measured in an MSI radial force tester at a diameter less than the manufactured diameter, among other possible values. Where drug is released, it may be released over a period of 6 to 26 weeks, among other values.

[00264] In some aspects, the scaffolds described herein may be provided in a kit that includes (a) one or more scaffolds, (b) delivery catheters, and (c) optional loading aids (e.g., crimping mechanisms), among other components.

**Example 1**

[00265] Uniformly braided scaffolds (see, e.g. Fig. 3A) were first manufactured using a PLGA(85:15) copolymer by spooling fiber spun monofilaments onto individual bobbins. Each bobbin was placed on a braiding machine, strung through rollers and eyelets and wrapped around a mandrel of desired OD (e.g. 7, 8, or 10 mm). The braiding tension of the machine was set as appropriate for the size of the monofilament. The pix/inch was set to obtain a braid angle with optimal properties including radial strength. The braid pattern was selected and the monofilaments were braided off the spool onto the mandrel by the braiding machine. Tie wraps were used on the end of each mandrel to keep the tension on the filaments, which can be useful for heat annealing and obtaining high modulus properties. The braided polymer was heat annealed on the mandrel, and then cut into desired lengths with a blade and removed from the mandrel.

[00266] The braided PLGA scaffolds were coated with a support coating made from poly(L-lactide-co- $\epsilon$ -caprolactone) (PLCL) cured with hexamethylene diisocyanate (HDI) in the presence of 1-dodecanol (DD) as a chain terminator with the optional use of a catalyst. In particular, a four-arm hydroxyl terminated PLCL (40:60) (mol/mol), HDI, and DD were dissolved in dichloromethane to make a stock solution for spray-coating. The solution was spray-coated onto the braided scaffolds. After thoroughly curing at elevated temperatures, the scaffolds were cut into various lengths for radial force and recovery testing. FIG. 16 shows the macroscopic images of 8 mm, 10 mm, 20mm and 31mm scaffolds, each with 16 strands and a braid angle of approximately 100-135 degrees. Some properties of these and analogous scaffolds with different manufactured diameters, numbers of strands, and braid angles are compiled in Table 1 (wherein @ [D0 -1] mm refers to measurement 1 mm

below the manufactured diameter, i.e. 6 mm for the 7 mm scaffolds, 7 mm for the 8 mm scaffolds, and 9 mm for the 10 mm scaffolds). All scaffolds have shown excellent diameter recovery (Rec. %) after simulated use. They have variable radial stiffness (RRF and COF) depending on the design.

TABLE 1

Entry	Diameter (mm)	Filaments	Filament diameter (in)	Braid angle (deg)	Mass (mg/mm)	RRF/COF@[D <sub>0</sub> - 1] mm (mmHg)	Rec.%
1	7	32	0.006"	127	2.6	492/166	97.9
2	7	24	0.006"	127	2.1	436/133	98.1
3	7	16	0.006"	127	1.6	363/66	97.9
4	8	32	0.006"	127	2.6	431/66	98.8
5	8	16	0.006"	127	1.6	251/18	99.3
6	10	32	0.006"	127	2.6	175/30	98.4
7	10	32	0.006"	110	2.0	54/10	98.6
8	10	16	0.0065"	127	1.8	99/4	97.4
9	10	16	0.0065"	110	1.4	31/4	98.6

## Example 2

[00267] The scaffolds prepared in Example 1 were further coated with an additional conformal coating comprising a mixture of PLCL and mometasone furoate (MF) as active agent. The PLCL in the MF-containing coating comprised about 70% (mol%) lactic acid, with the balance being caprolactone (PLCL 70:30). A homogenous solution of MF and PLCL was prepared in dichloromethane (DCM). Then, the DCM solution was spray-coated onto a 7 mm scaffold with 24 strands.

[00268] The amount of MF carried by each scaffold was controlled by the thickness and loading rate of the MF-containing coating. By controlling thickness to between <1  $\mu\text{m}$  to 10  $\mu\text{m}$  and loading rate from about 1 wt % to about 40 wt % MF relative to total dry coating weight, the inventors have found a drug loading for a 7 mm diameter scaffold to beneficially be about 10 to 2400  $\mu\text{g}$  per 10 mm of scaffold



length, more beneficially 100 to 1600  $\mu\text{g}$  per 10 mm of scaffold length. Fig.17A shows the cumulative MF released in mass for scaffolds with different drug loading rates (5, 10 and 20 weight% corresponding to 100, 200 and 400  $\mu\text{g}$  MF per 10 mm of scaffold length. Significantly, the inventors found that the percentage drug release profiles are marginally affected by the drug-loading rates within a certain range (see Fig. 17B).

### Example 3

[00269] To provide more linear release profiles, a topcoat comprising PLCL (70:30) and PLA was further coated onto the drug coated scaffolds. A homogenous solution of 0.75 wt% PLCL and 0.25 wt% PLA was prepared in DCM. Then, the DCM solution was spray-coated onto a 7 mm scaffold with 24 strands in a single coating layer with variable coating passes resulting in different top coat thickness. As shown in Fig. 18, the MF release can be tuned by changing the thickness of topcoat. The thicker is the topcoat, the slower is the drug release. In combination of this approach with different drug loading rate, it is readily to provide different daily dosage with programmable release duration.

### Example 4

[00270] Biodegradable polymers such as D,L-PLGA have also be used as the drug carrier. Conformal coatings comprising a mixture of D,L-PLGA and mometasone furoate (MF) as active agent were formed. The coatings contained 20 wt% MF. The D,L-PLGA in the mometasone-containing coating comprised D,L-PLGA having about 50% lactide and 50%  $\epsilon$ -caprolactone (50:50) (mol%), D,L-PLGA having about 75% lactide and 25%  $\epsilon$ -caprolactone (75:25) or D,L-PLGA having about 85% lactide and

15%  $\epsilon$ -caprolactone (85:15). In each case a homogenous solution of MF and D,L-PLGA was prepared in anisole/ethyl formate (50:50 v/v). Then, the solution was spray-coated onto a 7 mm scaffold with 24 strands.

[00271] As exemplified in FIG. 19, the drug released from the scaffolds with these polymers as the coating layer is drastically slower than that coated with PLCL(70:30). In the case of D,L-PLGA, and without wishing to be bound by theory, the drug release is most likely controlled by the degradation of the carrier polymer, with drug molecules to be released in a later stage after the polymer starts to degrade.

[00272] In this context, a scaffold with dual layers of drug coating can be manufactured to achieve sustainable release of MF over a long period of time. For example, a top layer comprising PLCL(70:30) and MF may be formed over a bottom layer comprising DL-PLGA and MF. Without wishing to be bound by theory, in the early stage, it is believed that drug released would be dominated by the diffusion-controlled release of MF from the top layer, whereas in the later stage, the drug in the bottom layer would be released in association with the degradation of DL-PLGA.

### Example 5

[00273] A scaffold consisting of 16 monofilament strands (0.0065" filament diameter, PLGA 85:15) was braided onto a large diameter mandrel (3.175 cm) in a 1 x 1 braid pattern at 25 picks per inch. The scaffolds were then annealed at 130°C for 24 hours, cut to a working length and then placed onto fixtures in preparation for spray coating.

[00274] An elastomer solution was prepared using 5 wt% PLCL(40:60) dissolved in DCM. A crosslinker, hexamethylene diisocyanate (45:1 NCO:OH) and zinc octoate

catalyst (0.1 wt%) were added to the final solution. The elastomer solution was spray coated onto the scaffold and cured at 100°C for 24 hrs in an open vial. A photograph of one stent produced in this matter is shown in Fig. 20A and a photograph of a coating node of such as stent is shown in Fig. 20B.

[00275] A flat plate compression test was conducted to assess the mechanical performance of the scaffold post curing. The scaffold was compressed longitudinally up to 50% of the initial diameter. The results are shown in Fig. 21, wherein compressive load is per unit length of the scaffold.

#### **Example 6**

[00276] A multifilament strand was prepared by twisting two 0.007" PLGA 85:15 monofilament strands together. The multifilament strand was then hand woven using a fixture into a variety of braid patterns. An example of the fixture used to prepare multifilament scaffold is shown in Fig. 22. The fixture was also used to prepare scaffolds using monofilament strands. After weaving, filament ends were secured to the fixture using tape and subsequently annealed at 100°C overnight to set the filaments and maintain filament cross-over points. Scaffolds were then spray coated using an elastomer solution containing 5 wt% PLCL 40:60, HDI (45:1 NCO:OH) and zinc catalyst (0.1 wt%) in methylene chloride. All scaffolds were cured at 100°C for 24 hrs in an open vial.

[00277] Table 2 contains data generated from five different braid patterns (shown in FIGS. 22A-22E) after spray coating. All scaffolds were measured for diameter, weight, braid angle, acute recovery and recovery post deployment.

TABLE 2

	<b>Monofilament</b>	<b>Twisted multifilament</b>			
<b>Device</b>	<b>4 filament braid</b>	<b>4 filament braid</b>	<b>4 filament low braid angle</b>	<b>2 filament braid</b>	<b>2 filament low braid angle</b>
	<b>See Fig. 22A</b>	<b>See Fig. 22B</b>	<b>See Fig. 22C</b>	<b>See Fig. 22D</b>	<b>See Fig. 22E</b>
<b>Mass / length device (mg/mm)</b>	3.8	5.5	10	2.9	3.8
<b>Mass (mg)</b>	77.0	~ 110	203	57.4	76.6
<b>Braid angle</b>	~75	~70	~45	~80	~ 50
<b>Device diameter (mm)</b>	~ 38	~ 38	~ 38	~ 38	~ 38
<b>Acute recovery</b>	83%	60%	Buckled (non-circular recovery)	78%	85%
<b>Recovery (&gt; 10 mins post-deploy)</b>	85%	68%		90%	85%

[00278] Recovery testing was performed by crimping and transferring the scaffolds through a series of large to small tubes using an outer braided mesh sheath until a crimp diameter of 4-5 mm was reached. The acute recovery and post deployment recovery is reported as a percentage of the initial diameter.

**Example 7**

[00279] *In vivo* performance of a scaffold in accordance with the present disclosure was examined within a swine cadaver. This study utilized a scaffold in accordance with the present disclosure, approximately 7mm in diameter and having a 32 filament braid (ref. Table 1, entry 1), and delivered through a 7.5F catheter.

[00280] The device was implanted into folds of the nasal turbinate of a swine cadaver. The scaffold deployed in the swine nasal cavity in a smooth, controlled fashion by withdrawing the device outer sheath while holding a middle pusher in place. FIG. 23A, FIG. 23B, FIG. 23C and FIG. 23D are photographs illustrating the deployment process. The delivery catheter was approximately 2.8 mm in diameter. The scaffold expanded to fill the space between the nasal septum and a nasal turbinate as seen in FIG. 24.

[00281] These deployments identified some potential benefits of the scaffolds of the present disclosure, including: (a) controlled, accurate delivery, (b) improved apposition/conformability to nasal cavity walls and (c) reduced device profile.

**Example 8**

[00282] A human cadaver study was conducted to assess the clinical performance of scaffolds in accordance with the present disclosure in the human anatomy. Device prototypes and delivery system prototypes were integrated to test multiple scenarios within the representative anatomy, both before and after functional endoscopic sinus surgery. Endpoints included visual appearance via endoscopy and clinical feedback.

[00283] Several small diameter scaffold prototypes in accordance with the present disclosure are described in Table 1, while two large diameter scaffold prototypes are described in Table 3.

TABLE 3

Design	Mass (mg)	Diameter (cm)	Length (mm)	Filaments	Filament diameter (in)	Braid angle (deg)	Number of scaffolds	Load at 50% compression (N)	% Recovery
2 filament braid offset	60	~ 3.8	20	2	0.0075" twisted	50	1	0.034	85
4 filament braid (monofilament)	77	~ 3.8	20	4	0.0075"	70	1	0.032	85

[00284] Scaffolds formed using procedures along the lines described in Example 1 were placed in the middle meatus, providing mechanical force to displace the middle turbinate medially and demonstrating the potential to deliver drug to the ethmoid sinuses. Five deployments were conducted: (a) a 16 filament, 8 mm scaffold, (b) a 32 filament, 8 mm scaffold, (c) a 16 filament, 10 mm scaffold, (d) a 32 filament, 10 mm scaffold and (d) a 32 filament, 13 mm scaffold. Although all devices conformed relatively well to the tissues, displacing the middle turbinate medially (MT) and providing outward force on the uncinate process (UP) laterally, the 32 filament, 13 mm scaffold appeared to provide the best fit for the particular space into which it had been implanted. FIG. 25, is a photograph illustrating the 32 filament, 13 mm scaffold (length of 10 mm) following deployment in the middle meatus of a human cadaver. The implant conformed well to the tissues with appropriate medialization of middle turbinate.

[00285] Devices in accordance with the present disclosure were also placed in the frontal recesses of human cadavers. In a first cadaveric specimen, the frontal recess could not be accessed prior to surgical intervention. The ostia to the frontal sinus was approximately 1 mm in diameter and could not accommodate the delivery device. Functional endoscopic sinus surgery (FESS) was conducted to remove

ethmoid cells and expand the passage to the frontal sinus. Following this procedure, 32 filament (Table 1, entry 6) and 16 filament (Table 1, group 8) implants were deployed into the frontal sinus ostia. Although both devices conformed well to the tissue, 16 filament device appeared to exhibit enhanced conformance for the particular space into which it had been implanted. FIG. 26 is a photograph illustrating the 16 filament, 10 mm scaffold following deployment in the frontal sinus ostia.

[00286] In a second cadaver, the frontal sinus ostia was accessible prior to surgical intervention. 10mm, 16 filament implants (n=1 from Table 1, entry 8 and n=1 from Table 1, entry 9) were deployed into the frontal sinus before and after FESS, respectively. These implants conformed well to the sinus ostia.

[00287] A 16 filament, 10 mm diameter scaffold, a 4 filament, 38 mm scaffold, a 2 filament, 38 mm scaffold, and a 32 filament, 17.5 mm scaffold were placed the ethmoid sinus of human cadavers following functional endoscopic sinus surgery, with the 10 mm diameter scaffold appearing to be undersize for the particular space into which it had been implanted, the 38 mm scaffolds appearing to be oversize for the particular space into which it had been implanted, and with the 17.5 mm scaffold appearing to provide the best fit for the particular space into which it had been implanted. FIG. 27, which is a photograph illustrating a 32 filament scaffold having a diameter of 17.5 mm and a length of 10 mm after deployment in the ethmoid sinus following FESS.

[00288] This study utilized 7.5 French and 9 French catheter systems. The 7.5F system was used to access all frontal sinuses, while the 9F system was used for device deployments into the ethmoid sinus. Both catheter diameters were acceptable, and devices functioned appropriately during use. A 90-degree bend was

appropriate for reaching the frontal sinus. Catheters of this type are described, for example, in "SINUS SCAFFOLD DELIVERY SYSTEMS," Attorney Docket No. 81354800002, Serial No. 62/186,311, filed on June 29, 2015, which is hereby incorporated by reference.

[00289] All devices were easily repositioned using standard tools following deployment. All devices were easily removed from the body.

### Example 9

[00290] Uniformly braided PLGA(10:90) or PLGA(75:25) scaffolds (diameter = 8 mm, 16 strands, having a braid angle of 120°) were coated with a support coating made from poly(L-lactide-co- $\epsilon$ -caprolactone) (PLCL) cured with hexamethylene diisocyanate (HDI) in the presence of 1-dodecanol (DD) as a chain terminator and zinc octoate ( $\text{Zn}(\text{Oct})_2$ ) as a catalyst. More particularly, four-arm PLCL (40:60), HDI, DD, and  $\text{Zn}(\text{Oct})_2$  were dissolved in dichloromethane (DCM) to make a stock solution for spray-coating. The solution was spray-coated onto the braided scaffolds using standard procedures. After drying at room temperature under a nitrogen environment overnight, the scaffolds were thoroughly cured at 60 °C and then cut into 10 mm length for radial force and recovery testing. To improve the node accumulation of elastomer on the scaffolds, anisole (AN) was used as a co-solvent in the spray-coating solution. After drying and curing treatment as described above, these scaffolds were also subject to mechanical performance evaluation. FIGS. 28A-28D are optical microscopic images of coated 8 mm scaffolds having 16 strands with and without anisole as a co-solvent during spray-coating as follows: FIG. 28A, PLGA(10:90) scaffold without anisole co-solvent; FIG. 28B, PLGA(10:90) scaffold with anisole co-solvent; FIG. 28C, PLGA(75:25) scaffold without anisole co-solvent; and



FIG. 28D PLGA(75:25) with anisole co-solvent. Some properties of these scaffolds are compiled in Table 4.

TABLE 4

Base braid material	Solvent for coating	Wt% of elastomer	RRF / mmHg (5.5 mm)	COF / mmHg (5.5 mm)	Rec.% of initial diameter
PLGA(10:90)	DCM	93	70	21	98.4
PLGA(10:90)	DCM/AN	95	151	65	98.5
PLGA(75:25)	DCM	98	70	24	98.8
PLGA(75:25)	DCM/AN	96	139	77	99.6

[00291] All scaffolds showed excellent diameter recovery after simulated deployment.

However, the scaffolds have drastically different radial stiffness depending on the node accumulation of elastomer. The base braid material does not significantly impact the radial stiffness of the coated scaffolds as these two materials have comparable modulus. Similarly, 22 mm diameter PLGA(10:90) scaffolds were coated with the same elastomer in the absence and presence of anisole as a co-solvent during spray-coating as described above. The scaffolds have 32 strands and a braid angle of 128 or 140. FIGS. 29A-29C show optical images of coated scaffolds with and without anisole as a co-solvent during spray-coating as follows: FIG. 29A scaffold coated with 62 wt% elastomer relative to the weight of the base braid (i.e., the ratio between the mass of the elastomer and the mass of the base braid) from solution that does not contain anisole as a co-solvent; FIG. 29B scaffold coated with 63 wt% elastomer relative to the weight of the base braid from solution containing anisole as a co-solvent; and FIG. 29C scaffold coated with 100 wt% elastomer relative to the weight of the base braid from solution containing anisole as a co-solvent. As above, the presence of anisole during scaffold coating improves the node accumulation of the resultant elastomer on the scaffolds. In addition, more

coating material would lead to further node accumulation. To evaluate their mechanical performance, these 22 mm diameter scaffolds (Length = 10 mm) were subject to compression test in between two parallel flat aluminum plates assembled onto an INSTRON equipment. The scaffolds were compressed to 75% of their initial diameter and the forces at the compression and the rebound stages were recorded as a function of the compressive distance. Table 2 summarizes the compression force (Fc) and the rebound force (Fr) at 50% compression. These forces are normalized to the scaffold length.

TABLE 5

Braid angle	Solvent for coating	Wt% of elastomer	Fc / mN mm <sup>-1</sup> (50% compression)	Fr / mN mm <sup>-1</sup> (50% compression)	Rec.% of initial Diameter
128	DCM	62	7.6	5.2	94.8
	DCM/AN	63	14.7	10.3	96.5
	DCM/AN	100	14.7	10.3	96.8
140	DCM	87	15.5	10.8	98.1
	DCM/AN	82	18.9	12.6	98.5
	DCM/AN	118	20.8	13.4	—

[00292] It is noted that higher braid angle provides higher compression and rebound force of the scaffold. On the other hand, the node accumulation of the elastomer helps to enhance the stiffness of the scaffolds. However, it has been found that further increasing the quantity of the coating material only marginally improves the compression strength of the scaffolds once a certain level of materials has been introduced onto the nodes.

### Example 10

[00293] In this Example, scaffolds were further coated with an additional conformal coating comprising a mixture of PLCL and mometasone furoate (MF) as active agent.

The PLCL in the MF-containing coating comprised about 70% (mol%) lactic acid, with the balance being caprolactone (PLCL 70:30). A homogenous solution of MF and PLCL was prepared in ethyl formate and anisole (50:50 v/v). Then, the solution was spray-coated onto a scaffold of  $d = 10$  mm with 16 strands or a scaffold of  $d = 22$  mm with 32 strands. The amount of MF carried by each scaffold was controlled by the thickness and loading rate of the MF-containing coating. In the case of 10 mm scaffolds, drug layers containing 20 wt% MF (80 wt% PLCL) and 40 wt% MF (60 wt% PLCL), respectively, have been coated onto the scaffolds to afford 240  $\mu\text{g}$  and 590  $\mu\text{g}$  MF per scaffold, respectively. In another case, 800  $\mu\text{g}$  MF has been coated onto a 22 mm scaffold with 20 wt% MF (80 wt% PLCL) in the drug layer. The drug layer of these 22 mm and 10 mm scaffolds has comparable thickness.

[00294] The *in vitro* release of MF from these MF-coated scaffolds was determined. Each scaffold was incubated in a pre-defined amount of pH 7.4 PBS buffer with 2% SDS at 37 °C under gentle shaking. At each indicated time point (see FIGS. 30A and 30B), the buffer was removed completely for quantification of MF by HPLC and new buffer was added. FIGS. 30A and 30B illustrate respectively cumulative absolute and percent mass of MF released from these three sets of scaffolds. As expected, the amount of MF released daily depends on the total MF loading in the scaffolds. On the other hand, the 10 mm scaffolds with 40 wt% MF loading rate exhibit significantly slower percent release than their analogs with 20 wt% MF loading rate. This result is different from what the present inventors have observed for scaffolds with relatively low MF loading rates (e.g. from 5 wt% to 20 wt%). It is hypothesized that the high loading rate of MF in the drug coating layer may result in crystallization of MF, consequently leading to slower drug release. In this regard, tailoring drug crystal size is a method of choice to get control over the drug release profile. Interestingly, the 22 mm and 10 mm scaffolds with 20 wt% MF loading rate show

essentially identical percent releasing profiles, suggesting that the releasing profile is barely affected by the dimension of the scaffolds when the drug layer has similar thickness.

#### **Example 11**

[00295] Scaffolds of PLGA (10:90) carrying 590  $\mu\text{g}$  MF and scaffolds of PLGA (75:25) carrying 530  $\mu\text{g}$  MF were manufactured at a diameter of 10 mm and length of 6.5 mm. These scaffolds were sterilized using ethylene oxide and implanted into the left and right maxillary sinus cavities of healthy young, 4-6 month old New Zealand white rabbits. Scaffolds were explanted at 3, 7, 14, and 28 days and analyzed for residual drug content using HPLC-UV. Kinetic drug release (KDR) profiles were generated by subtracting the residual drug from the initially loaded drug determined gravimetrically. The tissue that surrounded the scaffold while deployed was collected and analyzed to obtain the tissue drug concentration. FIG. 31 illustrates the in vivo KDR profiles for MF-coated PLGA(10:90) and PLGA(75:25) scaffolds. FIG. 32 shows the MF concentration in the sinus mucosa of sacrificed rabbits at given time points. FIG. 33 shows the total amount of MF on the scaffold plus the amount of drug in the sinus mucosa of scarified rabbits at given time points.

#### **Example 12**

[00296] Braided PLGA 17.5 mm diameter scaffolds (PLGA 10:90, 32 strands) were coated with a support coating made from poly(L-lactide-co- $\epsilon$ -caprolactone), specifically, L-PLCL (40:60), cured with hexamethylene diisocyanate (HDI) in the presence of 1-dodecanol (DD) as a chain terminator with the optional use of a  $\text{Zn}(\text{Oct})_2$  catalyst as described above. Then, an additional therapeutic-agent-

containing layer comprising 30wt% MF and 70wt% PLCL was further coated onto the scaffold from a homogenous solution of MF and PLCL prepared in ethyl formate and anisole (70:30 v/v) as described above, except that D,L-PLCL(80:20) or D,L-PLCL(90:10) was used as the carrier polymer, rather than L-PLCL(70:30) as described above in Example 10.

[00297] The *in vitro* release of MF from these MF-coated scaffolds was further determined as described above in Example 10. As shown in FIG. 34, the MF release rate associated with of D,L-PLCL(80:20) ( $T_g = 20\text{ }^{\circ}\text{C}$ ) is much faster than that of D,L-PLCL(90:10) ( $T_g = 35\text{ }^{\circ}\text{C}$ ). Without wishing to be bound by theory, it is believed that the glass transition temperature ( $T_g$ ) of the carrier polymer plays an important role in determining the drug release profile. In this regard, in the absence of  $T_g$  effects, it would have normally been expected for the copolymer having the least amount of the more hydrophobic monomer (caprolactone), i.e., D,L-PLCL(90:10), to demonstrate the faster release.

### Example 13

[00298] Braided PLGA 17.5 mm diameter scaffolds (PLGA 10:90, 32 strands) were coated with a support coating made from poly(L-lactide-co- $\epsilon$ -caprolactone), specifically, L-PLCL (40:60), cured with hexamethylene diisocyanate (HDI) in the presence of 1-dodecanol (DD) as a chain terminator with the optional use of a catalyst as described above. Then, an additional therapeutic-agent-containing layer comprising 30wt% MF and 70wt% polymer material was further coated onto the scaffold from a homogenous solution of MF and polymer material prepared in ethyl formate and anisole (70:30 v/v) as described above, except that in addition to L-PLCL(70:30) as described above in Example 10, the polymeric materials tested

further included a blend of PLCL(70:30) and PLGA(75:25) in a 75:25 wt/wt ratio, a blend of PLCL(70:30) and PLGA(85:15) in a 75:25 wt/wt ratio, and a blend of PLCL(70:30) and PLA in a 75:25 wt/wt ratio.

[00299] The *in vitro* release of MF from these MF-coated scaffolds was further determined as described above in Example 10. As shown in FIG. 35, the MF release rate is reduced when copolymers of higher lactide content are blended into PLCL(70:30). Without wishing to be bound by theory, it is believed that MF release rate decreases with increasing T<sub>g</sub> of the polymer that is blended with the PLCL(70:30). In this regard, PLA has the highest glass transition temperature among the three polymers used (PLGA(75:25) T<sub>g</sub> ~ 50 °C, PLGA(85:15) T<sub>g</sub> ~ 55 °C, and PLA T<sub>g</sub> ~ 60 °C).

#### Example 14

[00300] Uniformly braided PLGA(10:90) scaffolds (diameter = 17.5 mm, length = 10 mm, 32 strands, having a braid angle of 90° or 128°) were coated with a support coating made from poly(L-lactide-co-ε-caprolactone) (PLCL) cured with hexamethylene diisocyanate (HDI) in the presence of 1-dodecanol (DD) as a chain terminator with the optional use of a catalyst as described above and further coated with a conformal coating comprising a mixture of PLCL and mometasone furoate as described in prior Example 10.

[00301] To evaluate their mechanical performance, as shown schematically in FIG. 38, these scaffolds 100 were laid on their sides and compressed in between two parallel flat plates 210a, 210b of a compression apparatus 200 in a chamber maintained at 34 °C and 80 % relative humidity. Stated differently, scaffolds 100 were placed in a compressed state between two parallel flat plates 210a, 210b such

that the axis **A** of the tubular scaffold is parallel to the parallel flat plates and such that the tubular scaffold 100 is compressed between the parallel flat plates to a point where a distance **d** between the parallel flat plates is a percentage of the initial unconstrained diameter such that the tubular scaffold has a first minimum width **D** measured perpendicular to the axis **A** that is equal to the distance **d**, when the scaffold 100 is compressed in the compression apparatus 200. The scaffolds were compressed to either 1.5 mm (8.6% of their initial diameter) or 3 mm (17.1% of their initial diameter). On a weekly basis the scaffolds were removed from the compression apparatus and the recovered minimum width **D** (also referred to as the second minimum width **D**) of each scaffold was measured both immediately after removal from the compression apparatus and six hours after removal from the compression apparatus. % recovery is calculated by dividing the second minimum width **D** immediately after removal or 6 hours after removal from the compression plates by the first minimum width **D** (which is equal to the distance **d** across the gap between the parallel plates, i.e.  $\mathbf{D} \text{ (in mm)}/1.5 \text{ mm} \times 100$  or  $\mathbf{D} \text{ (in mm)}/3 \text{ mm} \times 100$ ).

[00302] In some embodiments, after being maintained in a compressed state for 10 weeks at a distance **d** that is 8.5% of the manufactured diameter of the scaffold (e.g., a 17.5 mm scaffold compressed to 1.5 mm), and after removal the tubular scaffold 100 from the compressed state for a period of six hours, the first minimum width **D** of the tubular scaffold (distance **d**) may recover to a second minimum width **D** measured perpendicular to the axis that is at least 450% (e.g., 450% to 1000%) of the first minimum width **D** (theoretical maximum 1166%). In some embodiments, after being maintained in a compressed state for 10 weeks at a distance **d** that is 17% of the manufactured diameter of the scaffold (e.g., a 17.5 mm scaffold compressed to 3.0 mm), and after removal the tubular scaffold 100 from the compressed state for a period of six hours, the first minimum width **D** of

the tubular scaffold may recover to a second minimum width **D** measured perpendicular to the axis that is at least 250% (e.g., 250% to 500%) of the first minimum width **D** (theoretical maximum 583%).

[00303] Results for the 90° and 128° braid angle scaffolds compressed to 1.5 mm immediately after removal is presented in FIG. 36A and results for the 90° and 128° braid angle scaffolds compressed to 3.0 mm immediately after removal is presented in FIG. 36B. As can be seen from FIG. 36A, the immediate recovery of 90° braid angle scaffolds from 1.5 mm compression is approximately 230% after 1 week and approximately 250% after 10 weeks. The immediate recovery of 128° braid angle scaffolds from 1.5 mm compression is approximately 175% after 1 week and approximately 190% after 10 weeks. As can be seen from FIG. 36B, immediate recovery of 90° braid angle scaffolds from 3.0 mm compression is approximately 165% after 1 week and approximately 170% after 10 weeks. The immediate recovery of 128° braid angle scaffolds from 3.0 mm compression is approximately 140% after 1 week and approximately 175% after 10 weeks.

[00304] Results for the 90° and 128° braid angle scaffolds compressed to 1.5 mm, 6 hours after removal, is presented in FIG. 37A and Table 6, and results for the 90° and 128° braid angle scaffolds compressed to 3.0 mm, 6 hours after removal, is presented in FIG. 37B and Table 7. The 6 hour recovery of 90° braid angle scaffolds from 1.5 mm compression was approximately 540% after 1 week and approximately 510% after 10 weeks. The 6 hour recovery of 128° braid angle scaffolds from 1.5 mm compression was approximately 550% after 1 week and approximately 480% after 10 weeks. The 6 hour recovery of 90° braid angle scaffolds from 3.0 mm compression was approximately 280% after 1 week and approximately 270% after 10 weeks. The 6 hour recovery of 128° braid angle



scaffolds from 3.0 mm compression was approximately 300% after 1 week and approximately 190% after 10 weeks.

**Table 6**

	1.5mm Gap - 90 Braid Angle		1.5mm Gap - 128 Braid Angle	
	6hr Recovery (mm)	6hr Recovery (%)	6hr Recovery (mm)	6hr Recovery (%)
1wk	8.09	539%	8.23	549%
2wk	5.36	357%	4.43	295%
3wk	5.74	383%	5.16	344%
4wk	5.7	380%	5.36	357%
5wk	6.26	417%	6.5	433%
6wk	6.08	405%	6.01	401%
7wk	5.17	345%	4.7	313%
8wk	6.1	407%	5.89	392%
9wk	7.2	480%	7.33	488%
10wk	7.62	508%	7.2	480%

**Table 7**

	3mm Gap - 90 Braid Angle		3mm Gap - 128 Braid Angle	
	6hr Recovery (mm)	6hr Recovery (%)	6hr Recovery (mm)	6hr Recovery (%)
1wk	8.49	283%	8.88	296%
2wk	6.24	208%	5.24	175%
3wk	6.67	222%	6.15	205%
4wk	6.65	222%	6.04	201%
5wk	7.14	238%	6.52	217%
6wk	6.81	227%	6.47	216%
7wk	6.23	208%	6.26	209%
8wk	7.12	237%	8.09	270%
9wk	7.65	255%	6.64	221%
10wk	8.2	273%	5.61	187%

[00305] As can be seen from FIG. 37A, recovery of 90° braid angle scaffolds from 1.5 mm compression appears to be similar to recovery of 128° braid angle scaffolds from 1.5 mm compression at all time points, with each showing a substantial drop in

recovery between 1 week and 2 weeks. Representative recovery data is provided in Table 6.

[00306] Likewise, as can be seen from FIG. 37B, recovery of 90° braid angle scaffolds from 3.0 mm compression appears to be similar to recovery of 128° braid angle scaffolds from 3.0 mm compression out to 7 weeks, with each showing a substantial drop in recovery between 1 week and 2 weeks. Representative recovery data is provided in Table 7.

[00307] Although various embodiments are specifically illustrated and described herein, it will be appreciated that modifications and variations of the present disclosure are covered by the above teachings and are within the purview of the appended claims without departing from the spirit and intended scope of the disclosure. For example, while the scaffolds are described herein for sinus applications, such scaffolds may also be useful for other applications such as Eustachian tube stenting.

## CLAIMS:

1. A scaffold adapted for delivery to a human sinus comprising:
  - (a) a tubular scaffold comprising a plurality of braided polymeric strands that comprise a first biodegradable polymer material and
  - (b) a conformal coating over the tubular scaffold that comprises a crosslinked biodegradable elastomer.
2. The scaffold of claim 1, wherein the first biodegradable polymer material comprises poly(lactide-co-glycolide).
3. The scaffold of any of claims 1-2, wherein the scaffold comprises between 8 and 64 polymeric strands.
4. The scaffold of any of claims 1-3, wherein the braided polymeric strands cross each other at a braid angle ranging from 80° to 140°.
5. The scaffold of any of claims 1-4, wherein the biodegradable elastomer material comprises poly(lactide-co-caprolactone).
6. The scaffold of claim 5, wherein the biodegradable elastomer material comprises poly(lactide-co-caprolactone) having molar percentage of lactide ranging from 30 to 50% and a molar percentage of caprolactone ranging from 50 to 70%.
7. The scaffold of any of claims 5-6, wherein the biodegradable elastomer material comprises urethane and/or urea crosslinks.
8. The scaffold of any of claims 1-7, wherein the biodegradable elastomer material is formed by reacting a branched poly(lactide-co-caprolactone) polyol with a diisocyanate crosslinking agent.

9. The scaffold of claim 8, wherein the branched poly(lactide-co-caprolactone) polyol is reacted with the diisocyanate crosslinking agent in the presence of a 1-substituted C8-C18 alcohol.
10. The scaffold of any of claims 1-9, further comprising a therapeutic-agent-containing layer comprising a therapeutic agent and a second biodegradable polymer material which may be the same as or different from the first biodegradable polymer material.
11. The scaffold of claim 10, wherein the second biodegradable polymer material comprises poly(lactide-co-caprolactone).
12. The scaffold of claim 11, wherein the second biodegradable polymer material comprises poly(lactide-co-caprolactone) having molar percentage of lactide ranging from 70 to 95 % and a molar percentage of caprolactone ranging from 5 to 30%.
13. The scaffold of any of claims 11 to 13, wherein the therapeutic agent is a steroid.
14. The scaffold of claim 14, wherein the steroid is mometasone furoate.
15. The scaffold of any of claims 1-14, further comprising a topcoat layer comprising a third biodegradable polymer material disposed over the therapeutic-agent-containing layer, wherein the third biodegradable polymer material may be the same as or different from the first biodegradable polymer material and wherein the third biodegradable polymer material may be the same as or different from the second biodegradable polymer material.
16. The scaffold of any of claims 1-15, wherein the scaffold has an unconstrained diameter selected from (a) an unconstrained diameter ranging from 6 to 10 mm, (b) an unconstrained diameter ranging from 10 to 15 mm, (c) an unconstrained diameter

ranging from 15 to 20 mm, and (d) an unconstrained diameter ranging from 20 to 60 mm.

17. The scaffold of any of claims 1-16, wherein after holding the tubular scaffold in a 34 °C, 80 % relative humidity environment for 10 weeks in a compressed state between two parallel flat plates such that the axis of the tubular scaffold is parallel to the parallel flat plates and such that the tubular scaffold is compressed between the parallel flat plates to a point where a first distance between the parallel flat plates is 17% of the initial unconstrained diameter such that the tubular scaffold has a first minimum width measured perpendicular to the axis that is equal to the first distance, and wherein after removal the tubular scaffold from the compressed state for six hours, the minimum width of the tubular scaffold recovers to a second minimum width measured perpendicular to the axis that is at least 250% of the first minimum width.
18. The scaffold of any of claims 1-16, wherein after holding the tubular scaffold in a 34 °C, 80 % relative humidity environment for 10 weeks in a compressed state between two parallel flat plates such that the axis of the tubular scaffold is parallel to the parallel flat plates and such that the tubular scaffold is compressed between the parallel flat plates to a point where a first distance between the parallel flat plates is 8.5% of the initial unconstrained diameter such that the tubular scaffold has a first minimum width measured perpendicular to the axis that is equal to the first distance, and wherein after removal the tubular scaffold from the compressed state for six hours, the minimum width of the tubular scaffold recovers to a second minimum width measured perpendicular to the axis that is at least 450% of the first minimum width.
19. A scaffold of any of claims 1-16, loaded into a delivery catheter.

20. A method of treatment, wherein a scaffold in accordance with any of claims 1-15 is delivered to a human sinus.
21. The method of claim 20, wherein the scaffold is delivered to an ethmoid sinus of a human patient and wherein the scaffold has an unconstrained diameter ranging from 15 mm to 20 mm.
22. The method of claim 21, wherein the scaffold is delivered to the ethmoid sinus after functional endoscopic sinus surgery (FESS).
23. The method of claim 20, wherein the scaffold is delivered to a frontal sinus ostium, a maxillary sinus ostium or a sphenoid sinus ostium of a human patient and wherein the scaffold has an unconstrained diameter ranging from 6 mm to 10 mm.
24. The method of claim 23, wherein the scaffold is delivered after functional endoscopic sinus surgery (FESS).
25. The method of claim 20, wherein the scaffold is delivered to a middle meatus sinus space of a human patient and wherein the scaffold has an unconstrained diameter ranging from 10 mm to 15 mm.
26. A scaffold adapted for delivery to human sinus comprising:
- (a) a tubular scaffold comprising a first biodegradable polymer material and
  - (b) a therapeutic-agent-containing layer comprising a therapeutic agent and a second biodegradable polymer material which may be the same as or different from the first biodegradable polymer material.
27. The scaffold of claim 26, wherein the first biodegradable polymer material comprises poly(lactide-co-glycolide).

28. The scaffold of any of claims 26-27, wherein the scaffold comprises a plurality of braided polymeric strands.
29. The scaffold of any of claims 26-28, further comprising a conformal coating disposed between the tubular scaffold and the therapeutic-agent-containing layer, the conformal coating comprising a crosslinked biodegradable elastomer.
30. The scaffold of claim 29, wherein the biodegradable elastomer material comprises poly(lactide-co-caprolactone).
31. The scaffold of any of claims 26-30, wherein the second biodegradable polymer material comprises poly(lactide-co-caprolactone).
32. The scaffold of claim 31, wherein the poly(lactide-co-caprolactone) has a molar percentage of lactide ranging from 60 to 95 % and a molar percentage of caprolactone ranging from 5 to 40%.
33. The scaffold of any of claims 31-32, wherein the second biodegradable polymer material further comprises an additional polymer selected from a homopolymer of lactide and a copolymer comprising lactide and an additional monomer.
34. The scaffold of any of claim 31-32, wherein the second biodegradable polymer material further comprises an additional polymer selected from copolymer of lactide and glycolide having molar percentage of lactide ranging from 45 to 99% and a molar percentage of glycolide ranging from 1 to 55%
35. The scaffold of any of claims 26-34, wherein the therapeutic agent is a steroid.
36. The scaffold of claim 35, wherein the steroid is mometasone furoate.



37. The scaffold of any of claims 26-36, wherein the therapeutic agent is present in an amount ranging from ranging from 0.1 to 20  $\mu\text{g}$  of therapeutic agent per square mm of scaffold area,  $A$ , where scaffold area is calculated as  $A = \pi DL$ , where  $D$  is the manufactured diameter of the scaffold and  $L$  is the manufactured length of the scaffold.
38. The scaffold of any of claims 26-36, wherein the therapeutic agent is present in an amount ranging from ranging from 1 to 10  $\mu\text{g}$  of therapeutic agent per square mm of scaffold area,  $A$ , where scaffold area is calculated as  $A = \pi DL$ , where  $D$  is the manufactured diameter of the scaffold and  $L$  is the manufactured length of the scaffold.
39. The scaffold of any of claims 26-38, wherein the thickness of the therapeutic-agent-containing layer ranges from 1  $\mu\text{m}$  to 25  $\mu\text{m}$ .
40. The scaffold of any of claims 26-39, wherein cumulative release of therapeutic agent, based on total amount of therapeutic agent in the scaffold, ranges from 1% to 70% after one week, when the scaffold is submerged in a pH 7.4 PBS buffer solution containing 2% wt% SDS at 37 °C under gentle shaking on a rotary shaker, wherein a volume of the buffer solution in which the scaffold is submerged is at least 10 times greater than a volume of the buffer solution at which a quantity of therapeutic agent corresponding to the total amount of therapeutic agent in the scaffold is at a saturation point in the buffer solution, and wherein buffer is removed completely weekly for quantification and replaced with fresh buffer.
41. The scaffold of claim 40, wherein cumulative release of therapeutic agent based on total amount of therapeutic agent in the scaffold ranges from 5% to 80% after two weeks.

42. The scaffold of any of claims 40-41, wherein cumulative release of therapeutic agent based on total amount of therapeutic agent in the scaffold ranges from 10% to 90% after four weeks.
43. The scaffold of any of claims 40-42, wherein cumulative release of therapeutic agent based on total amount of therapeutic agent in the scaffold ranges from 25% to 100% after eight weeks.
44. The scaffold of any of claims 26-39, wherein after being implanted one week in a human sinus or a rabbit sinus, in vivo release of therapeutic agent based on total amount of therapeutic agent in the scaffold, ranges from 1% to 45%.
45. The scaffold claim 44, wherein after being implanted two weeks in a human sinus or a rabbit sinus, in vivo release of therapeutic agent based on total amount of therapeutic agent in the scaffold, ranges from 3% to 50%.
46. The scaffold of any of claims 44-45, wherein after being implanted four weeks in a human sinus or a rabbit sinus, in vivo release of therapeutic agent based on total amount of therapeutic agent in the scaffold, ranges from 7% to 60%.
47. The scaffold of any of claims 44-46, wherein after being implanted eight weeks in a human sinus or a rabbit sinus, in vivo release of therapeutic agent based on total amount of therapeutic agent in the scaffold, ranges from 15% to 70%.
48. The scaffold of any of claims 26-47, further comprising a topcoat layer comprising a third biodegradable polymer material disposed over the therapeutic-agent-containing layer, wherein the third biodegradable polymer material may be the same as or different from the first biodegradable polymer material and wherein the third biodegradable polymer

material may be the same as or different from the second biodegradable polymer material.

49. A method of treatment, wherein a scaffold in accordance with any of claims 26-48 is delivered to a sinus of a human patient.

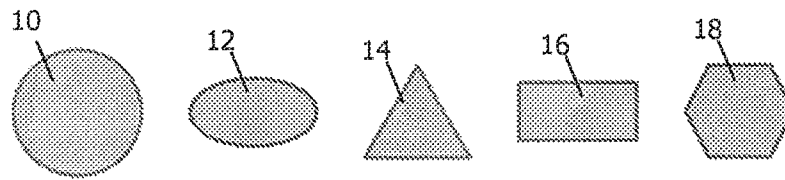


FIG. 1A

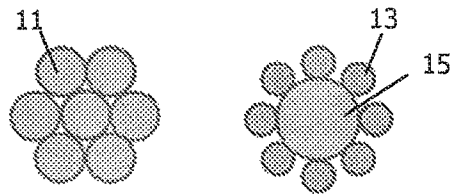


FIG. 1B

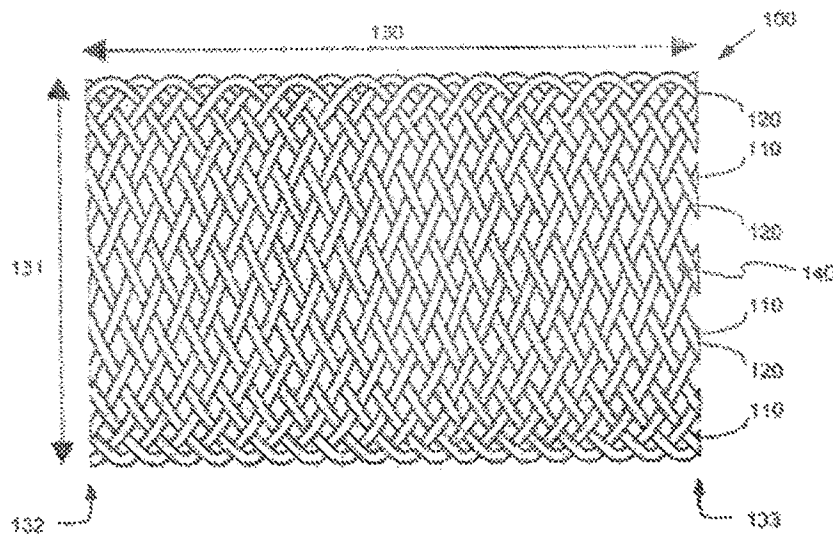


FIG. 2

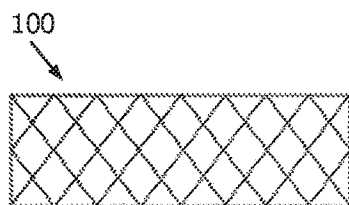


FIG. 3A

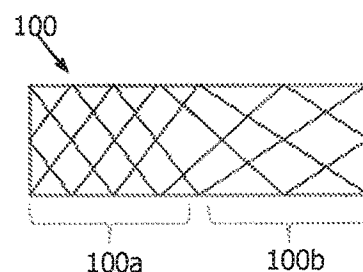


Fig. 3B

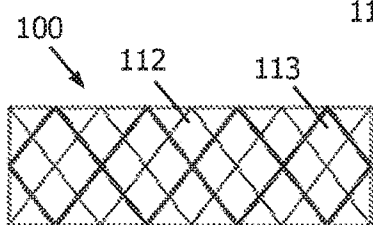
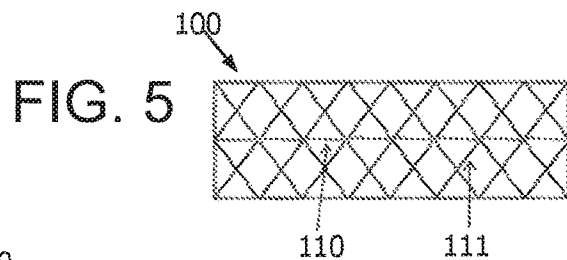
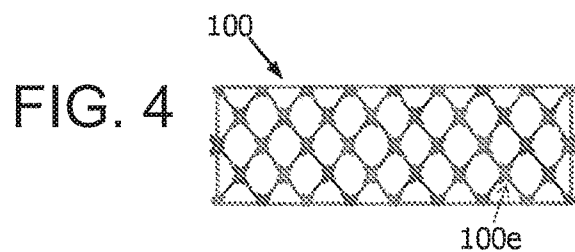


FIG. 6A

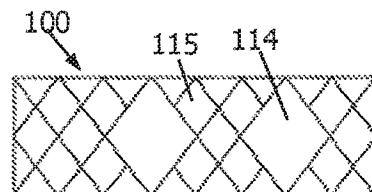


FIG. 6B

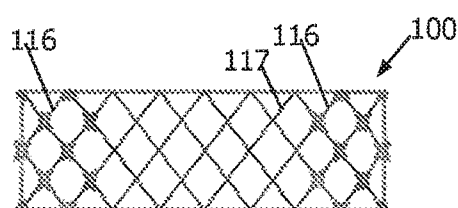


FIG. 6C

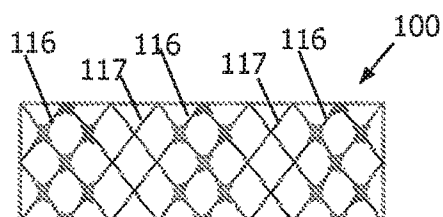


FIG. 6D

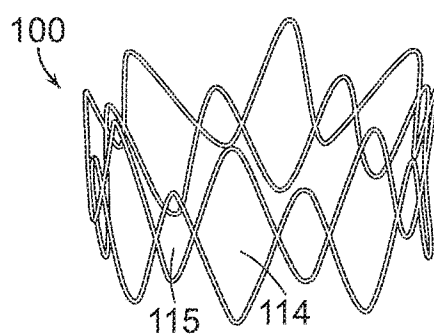


FIG. 7

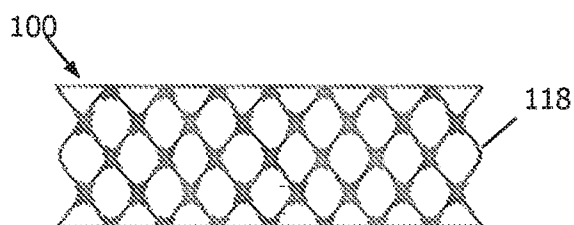


FIG. 8

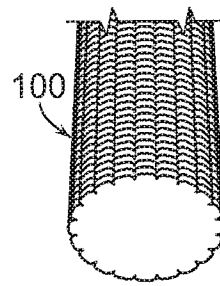


FIG. 9

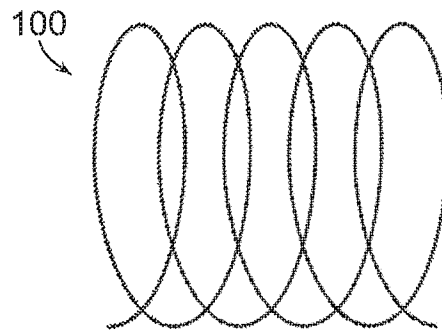


FIG. 10

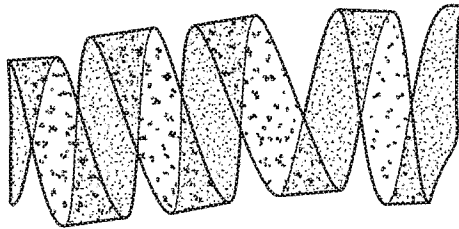


FIG. 11A

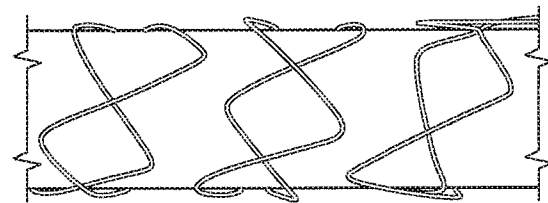


FIG. 11B

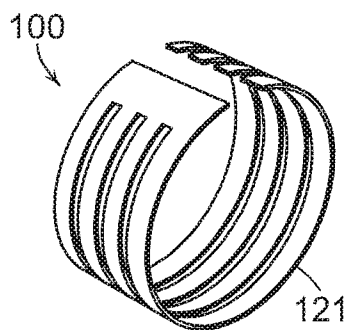


FIG. 12A

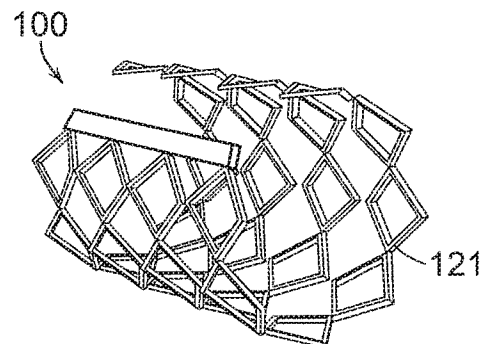


FIG. 12B



FIG. 13

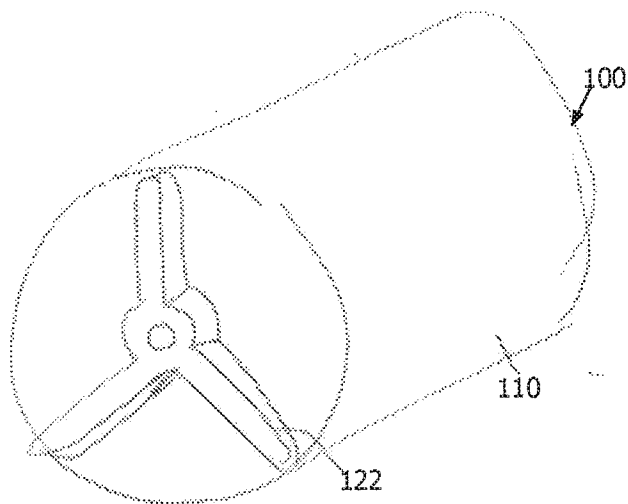


FIG. 14A

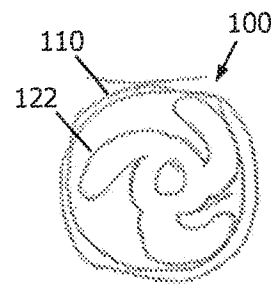


FIG. 14B

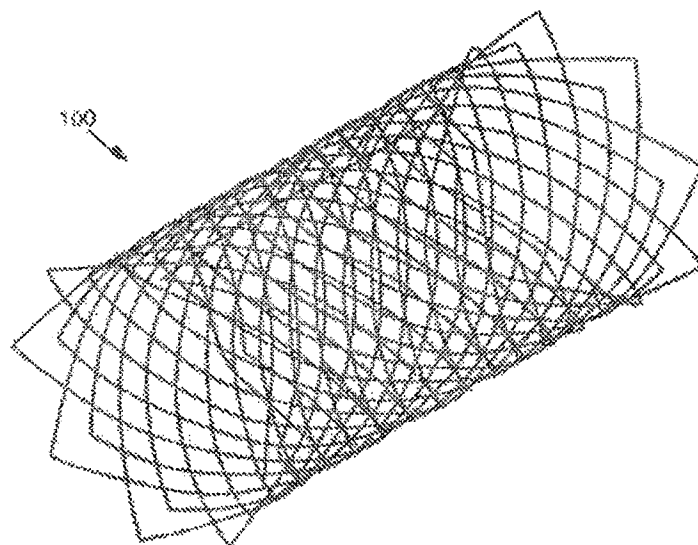


FIG. 15

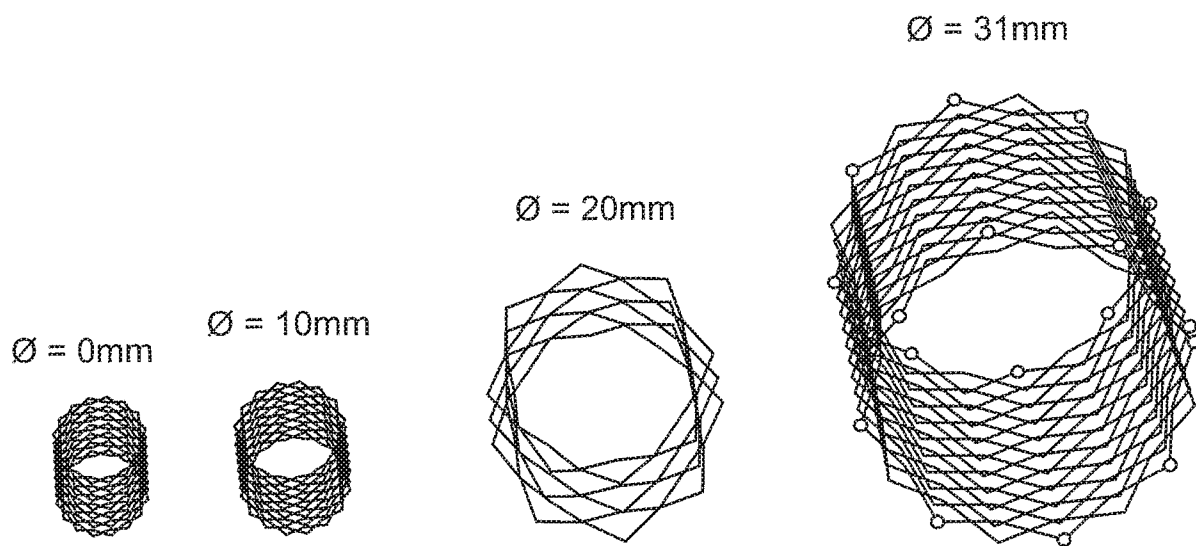


FIG. 16

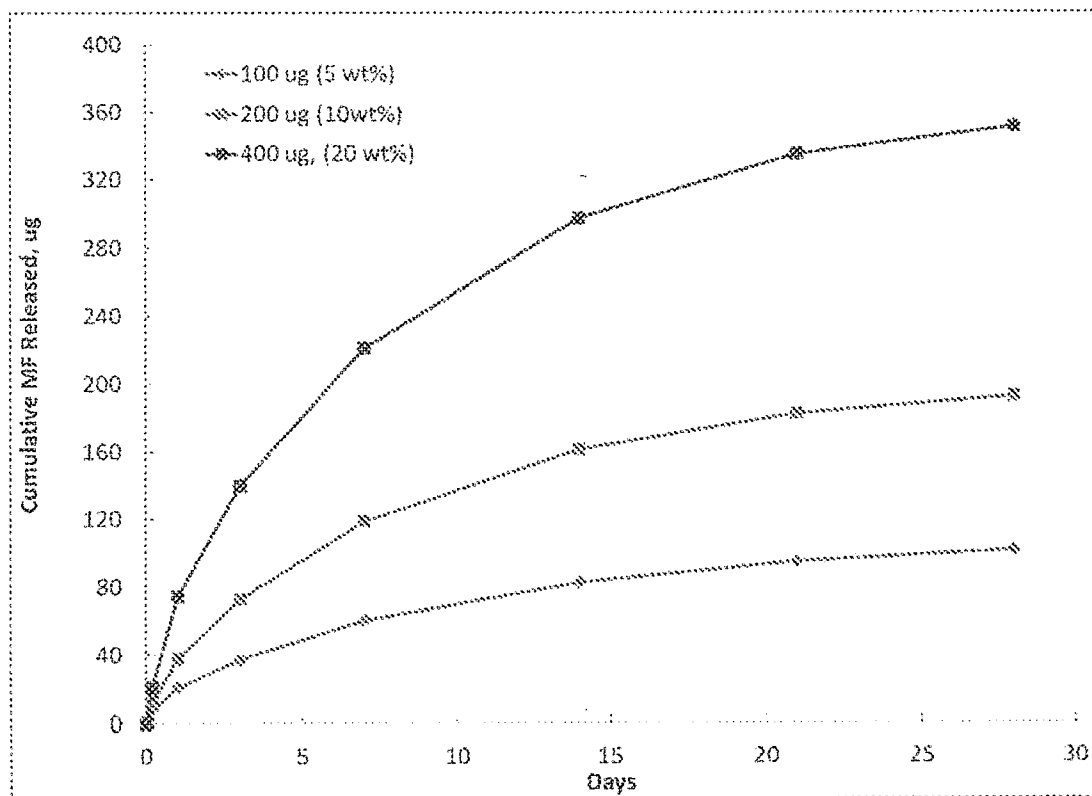


FIG. 17A



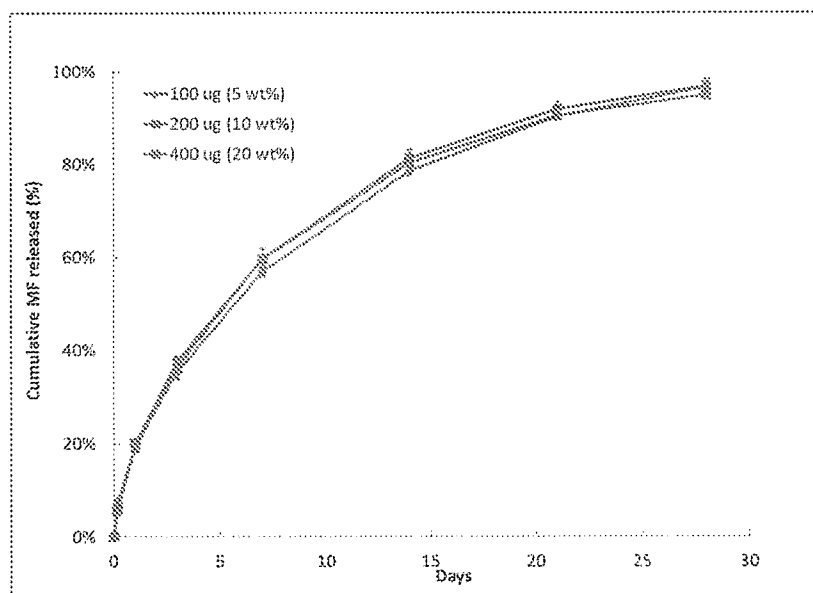


FIG. 17B

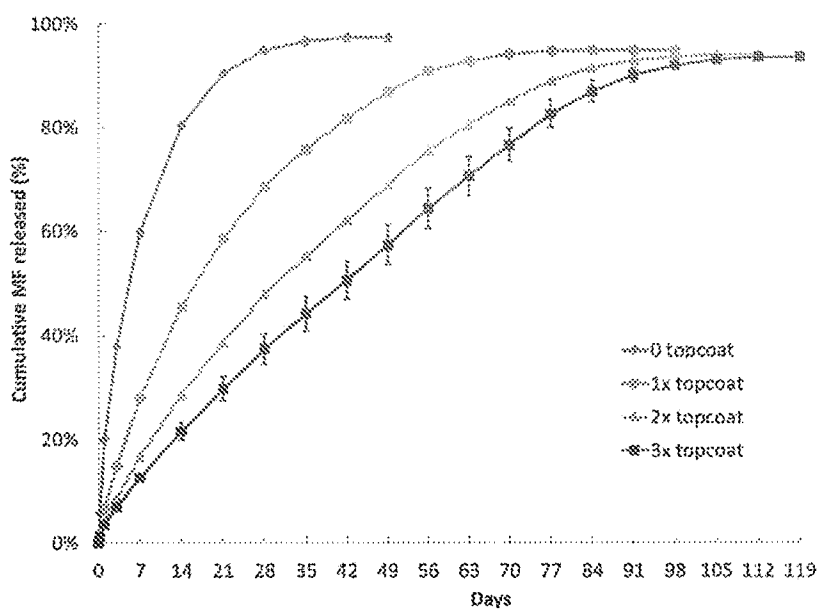


FIG. 18

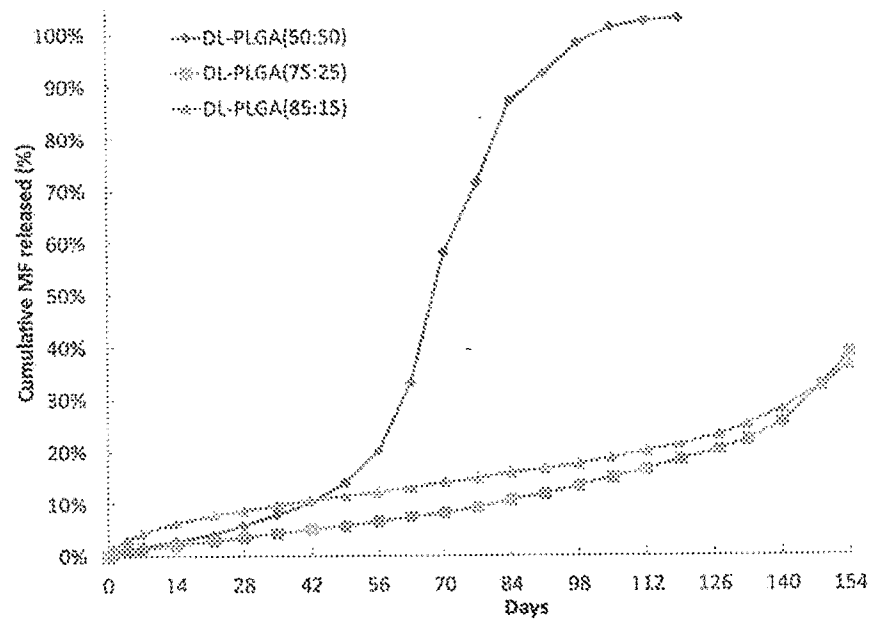


FIG. 19

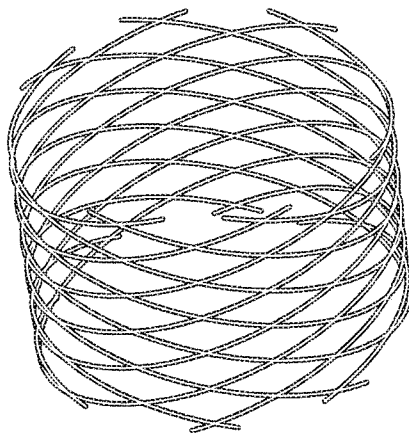


FIG. 20A

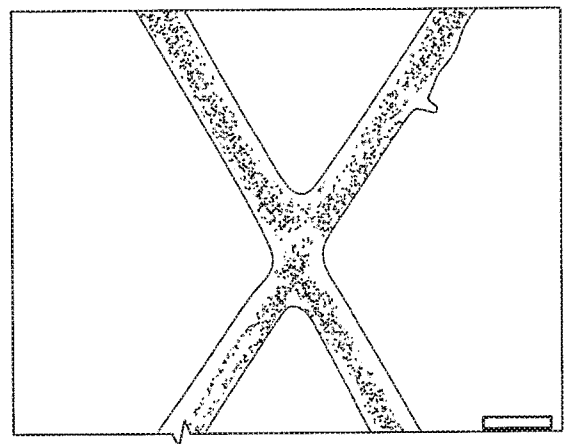


FIG. 20B

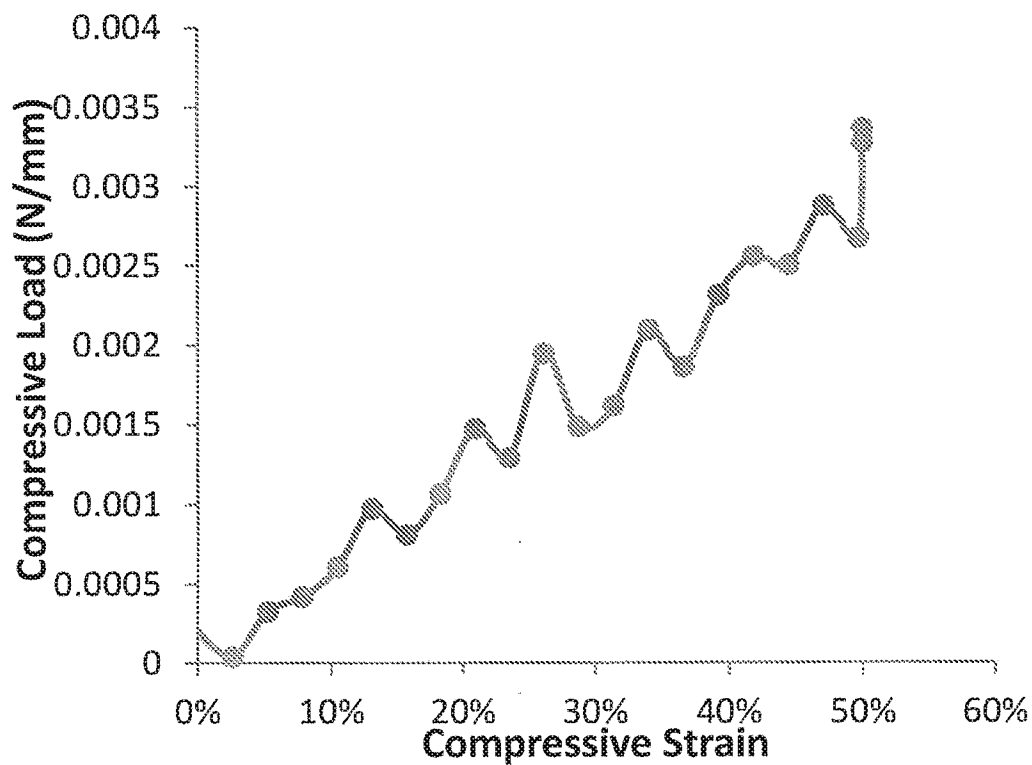


FIG. 21

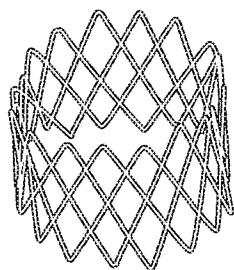


FIG. 22A

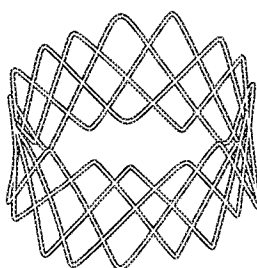


FIG. 22B

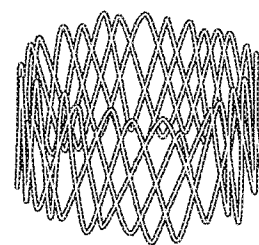


FIG. 22C

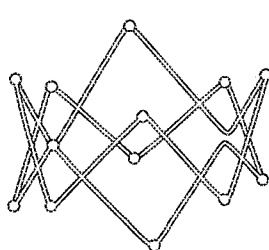


FIG. 22D

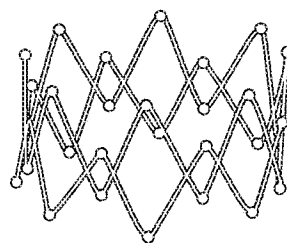


FIG. 22E

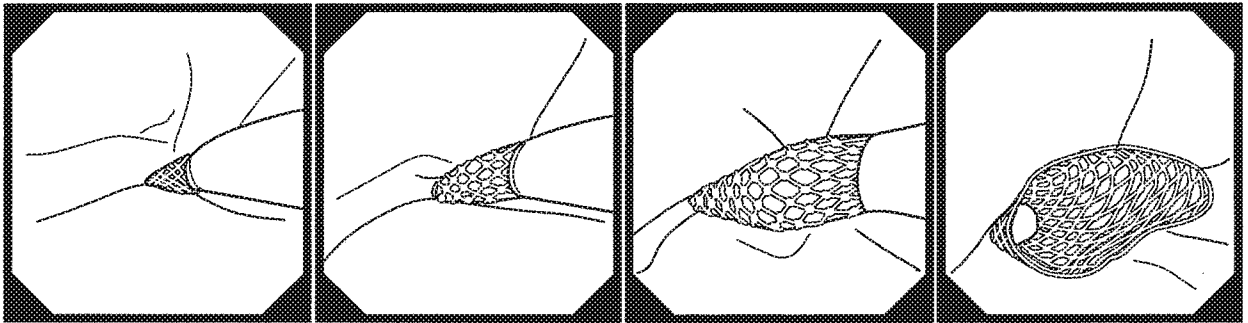


FIG. 23A

FIG. 23B

FIG. 23C

FIG. 23D

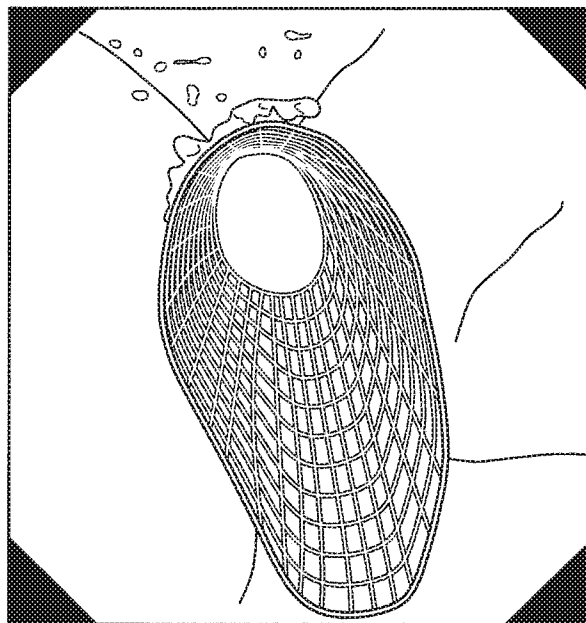


FIG. 24

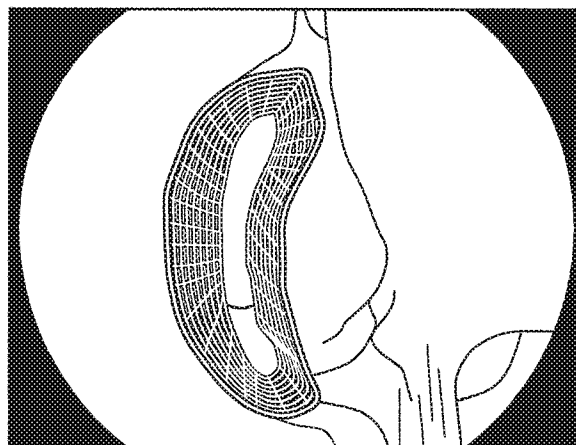


FIG. 25

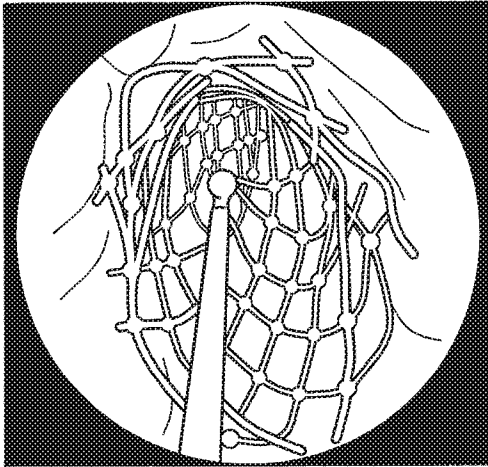


FIG. 26

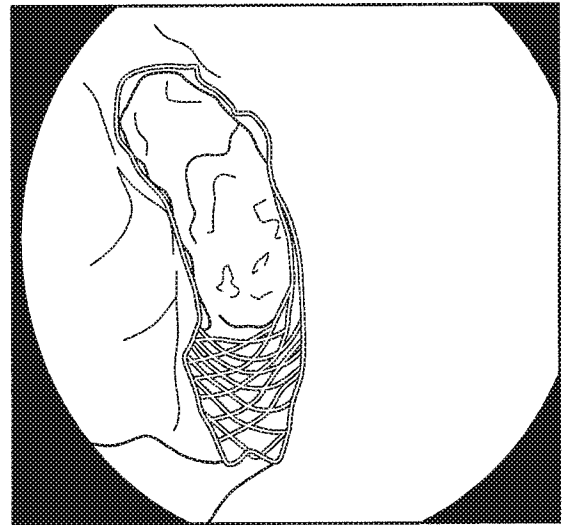


FIG. 27

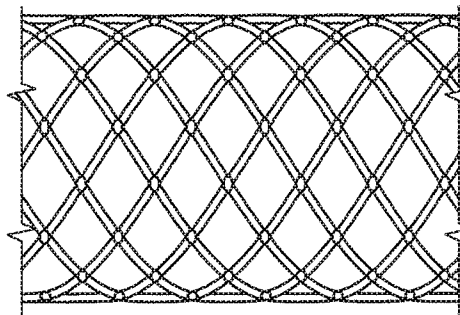


FIG. 28A

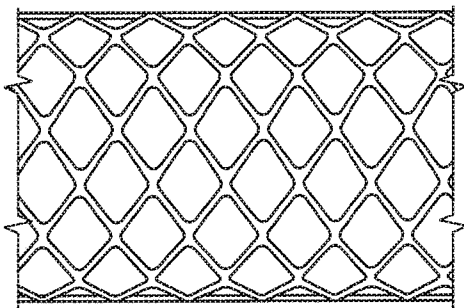


FIG. 28B

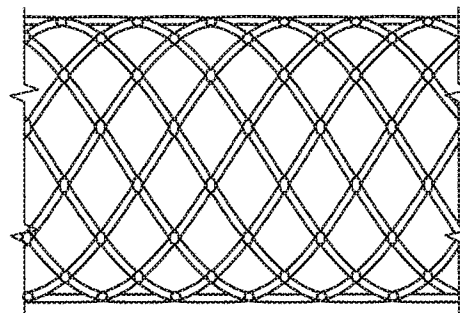


FIG. 28C

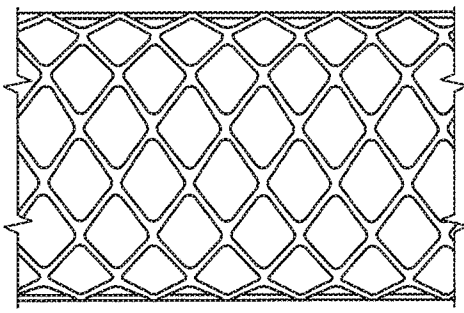


FIG. 28D

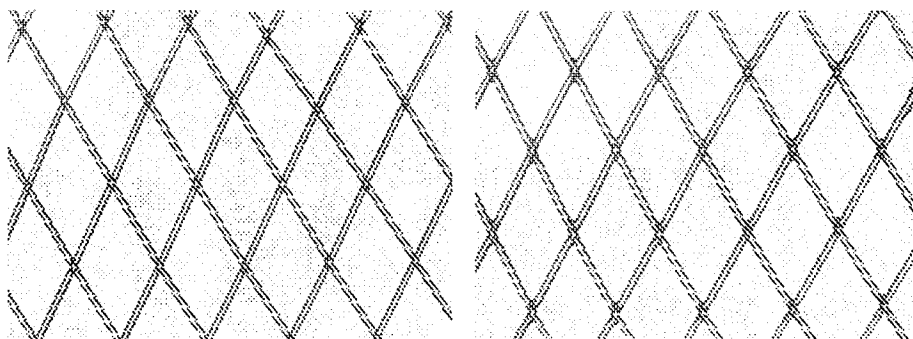


FIG. 29A

FIG. 29B

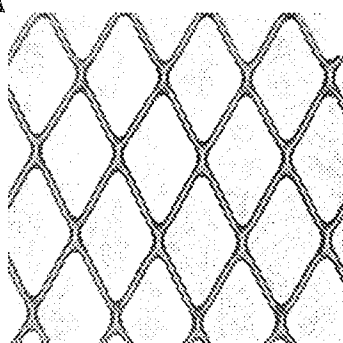


FIG. 29C

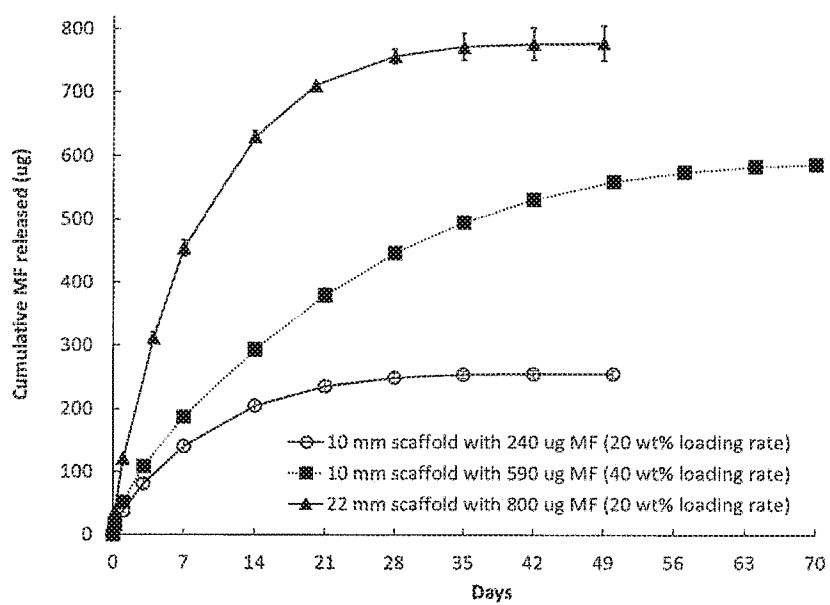


FIG. 30A

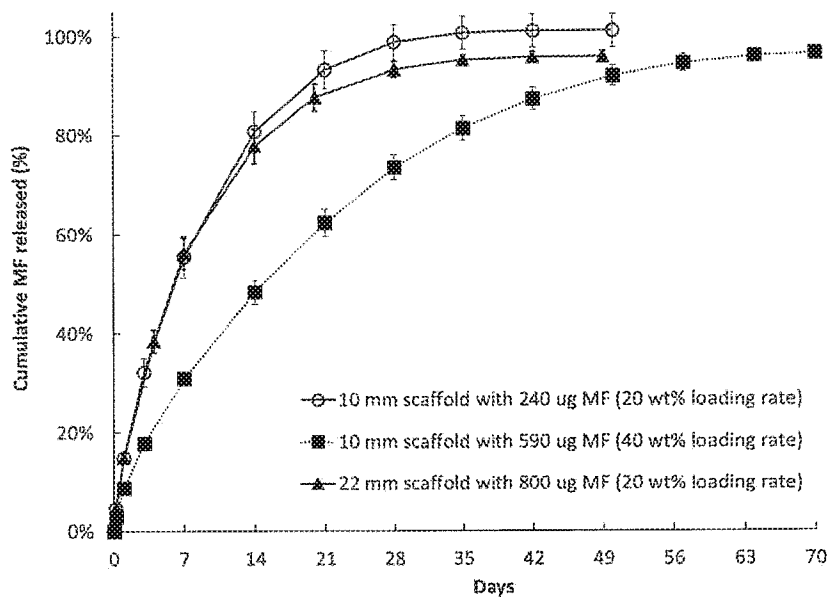


FIG. 30B

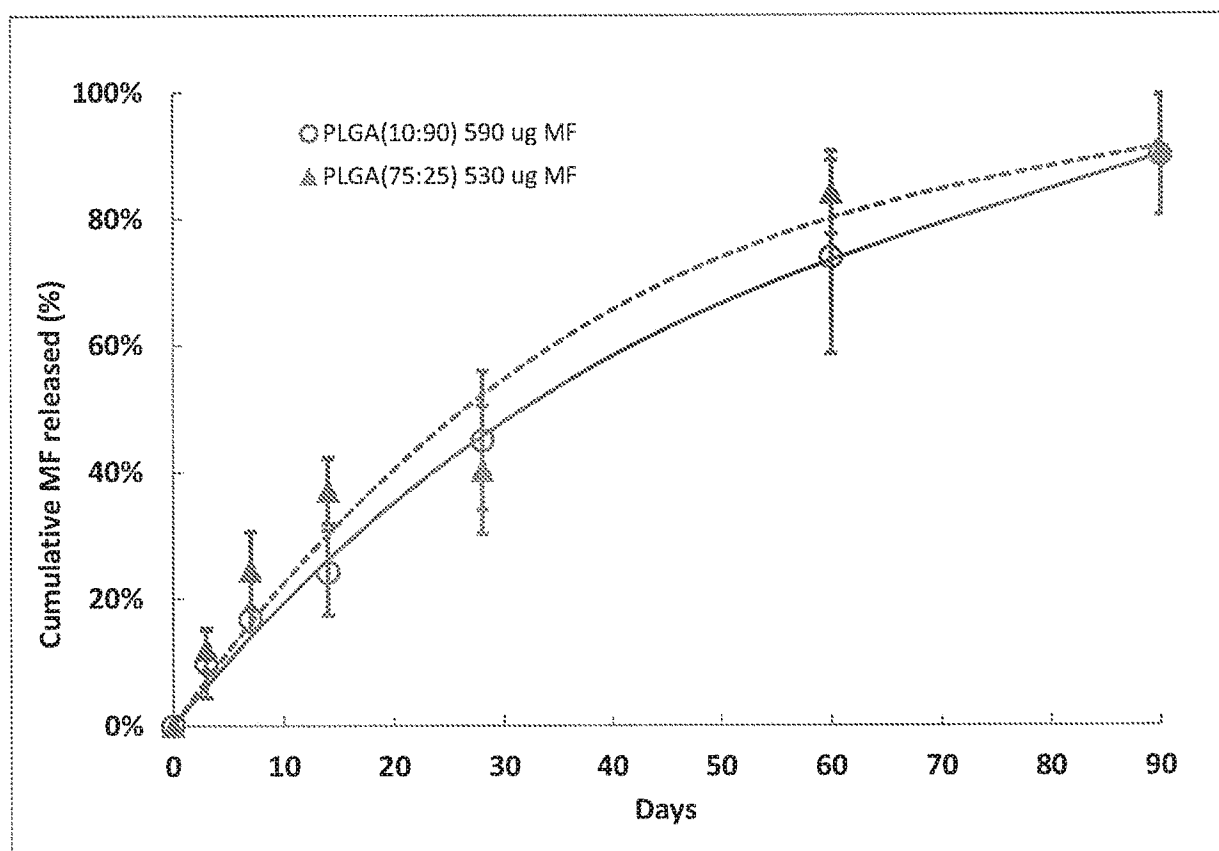


FIG. 31

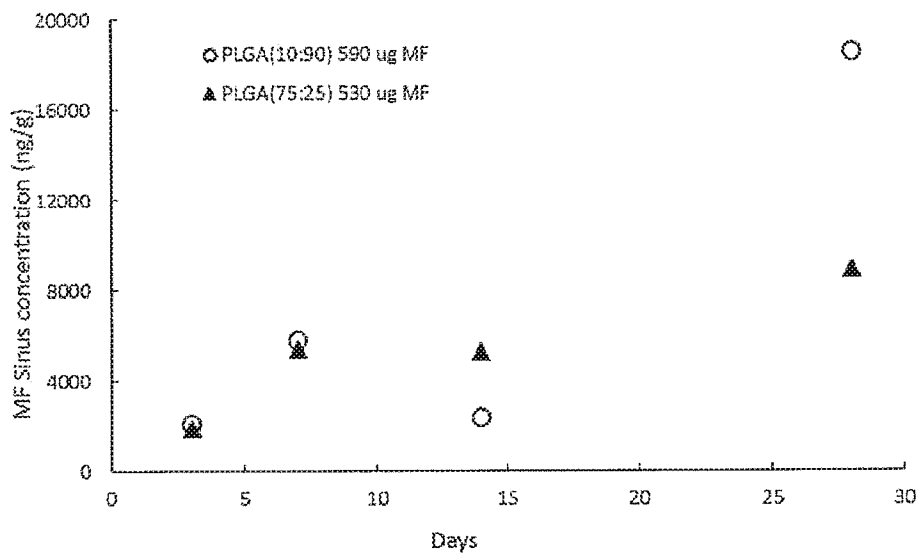


FIG. 32

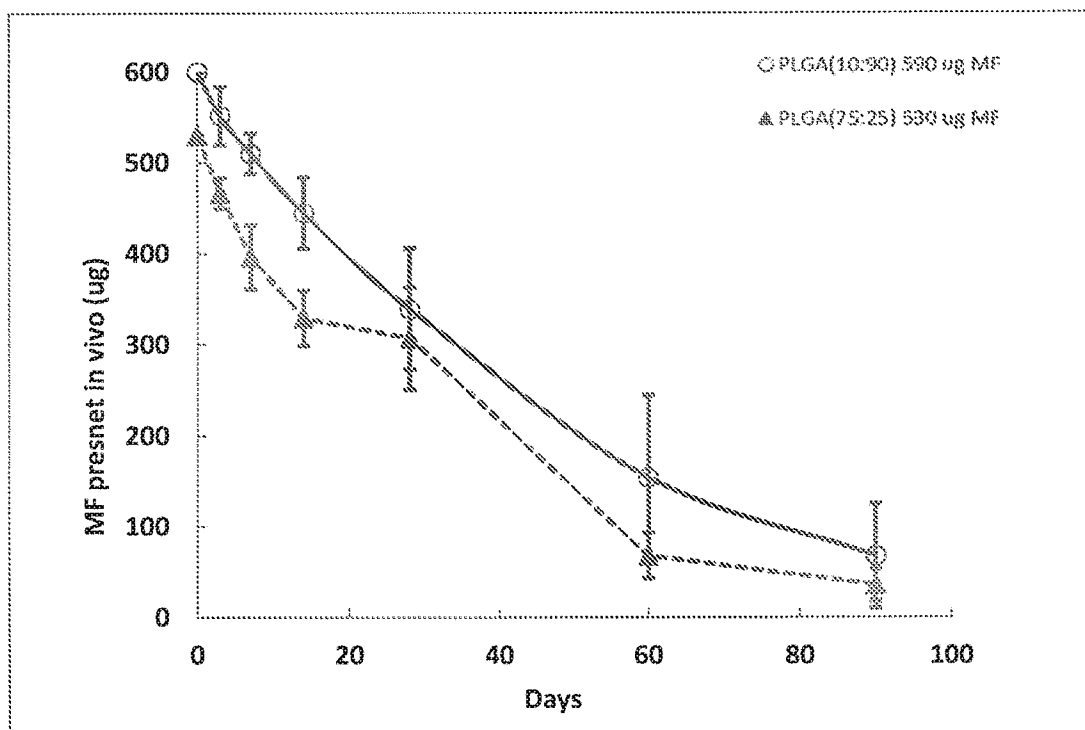


FIG. 33



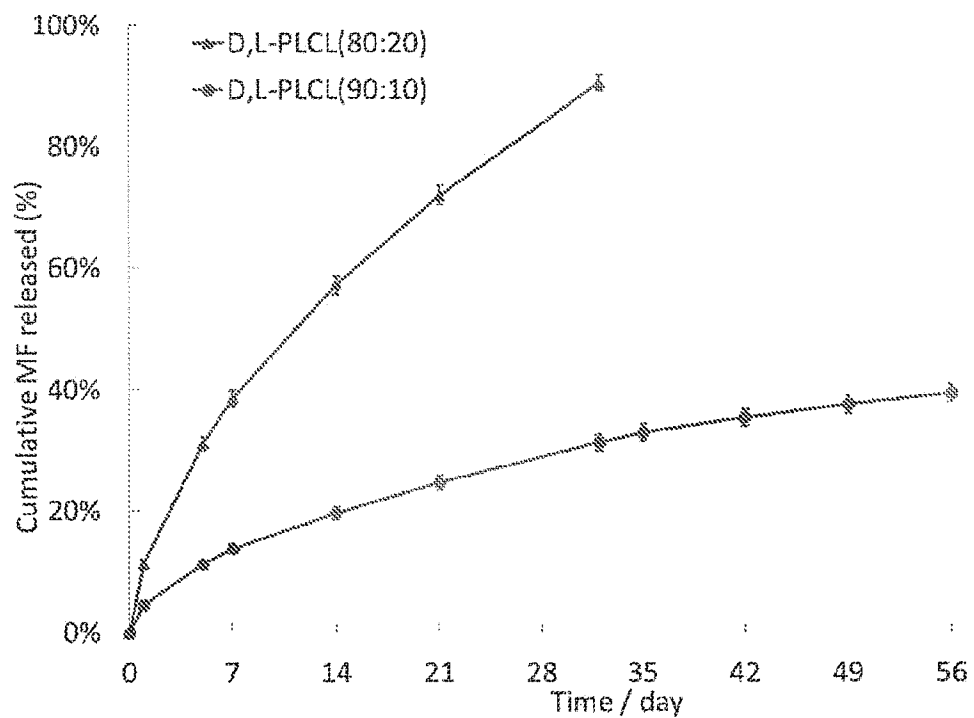


Fig. 34

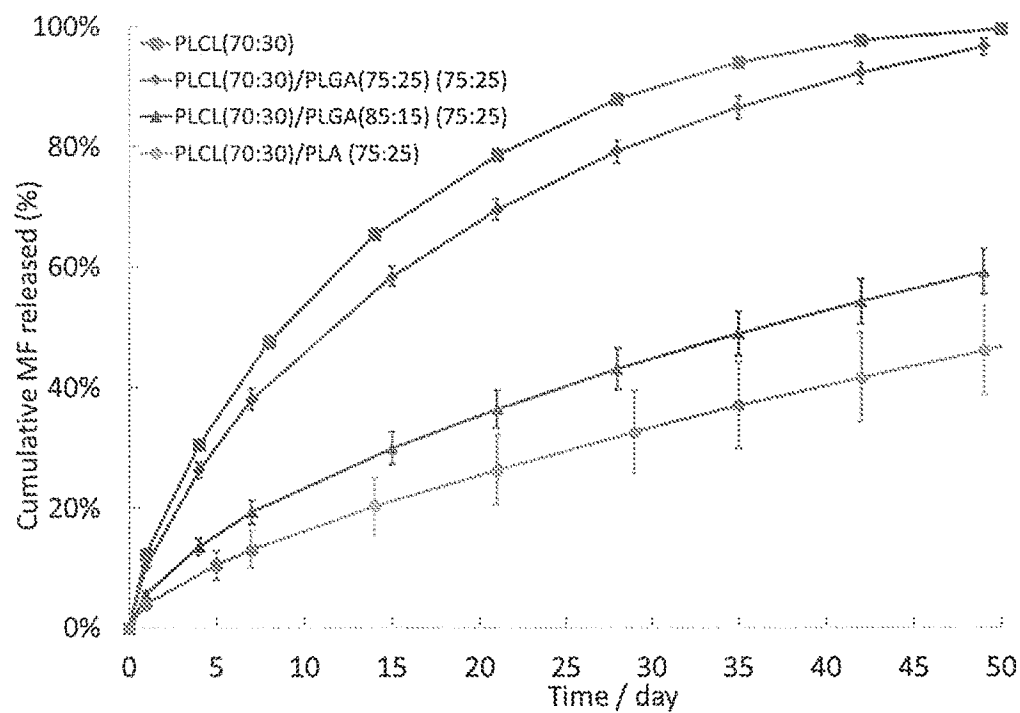


Fig. 35

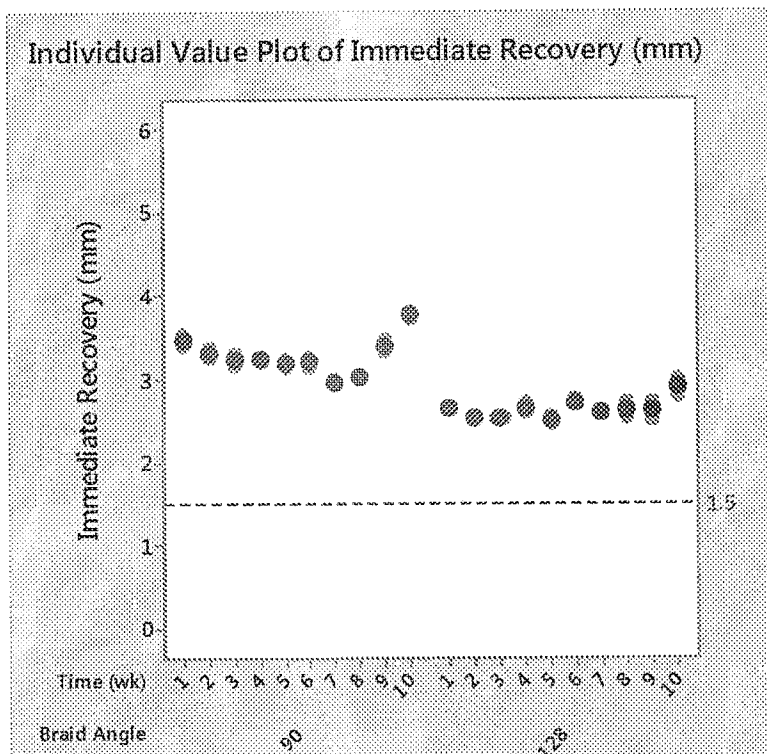


Fig. 36A

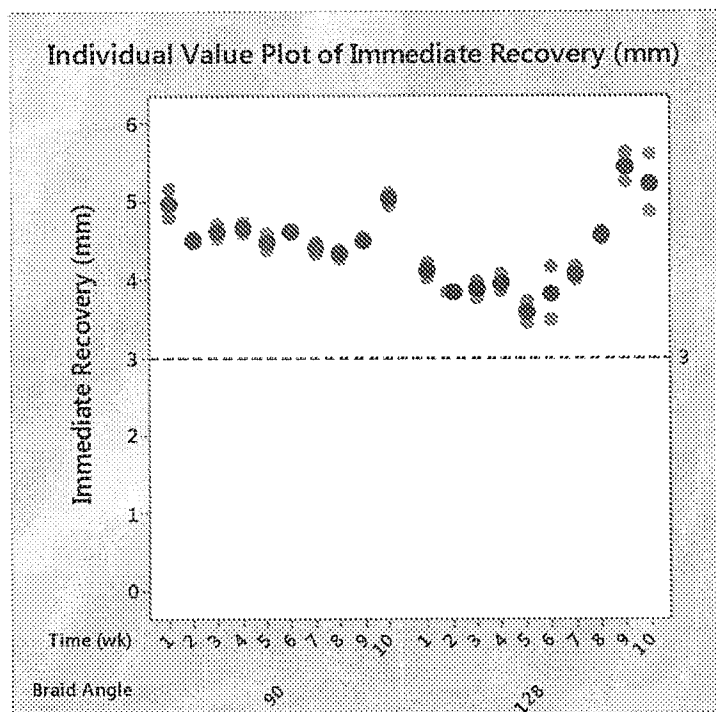


Fig. 36B

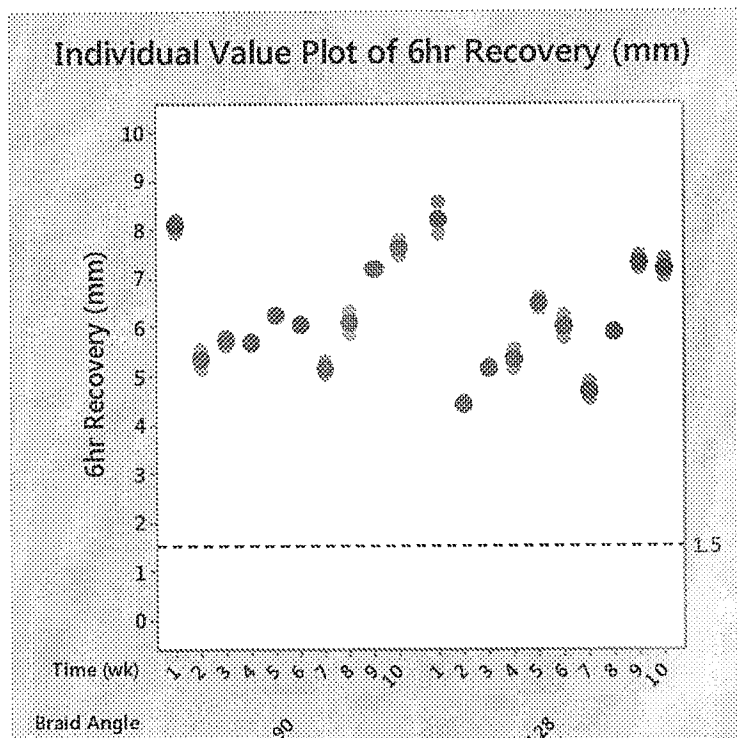


Fig. 37A

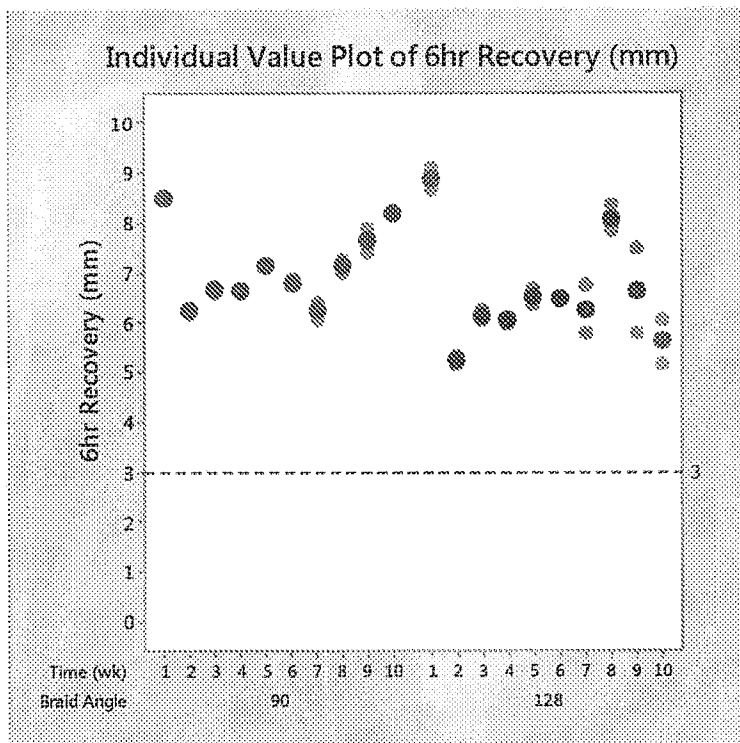


Fig. 37B

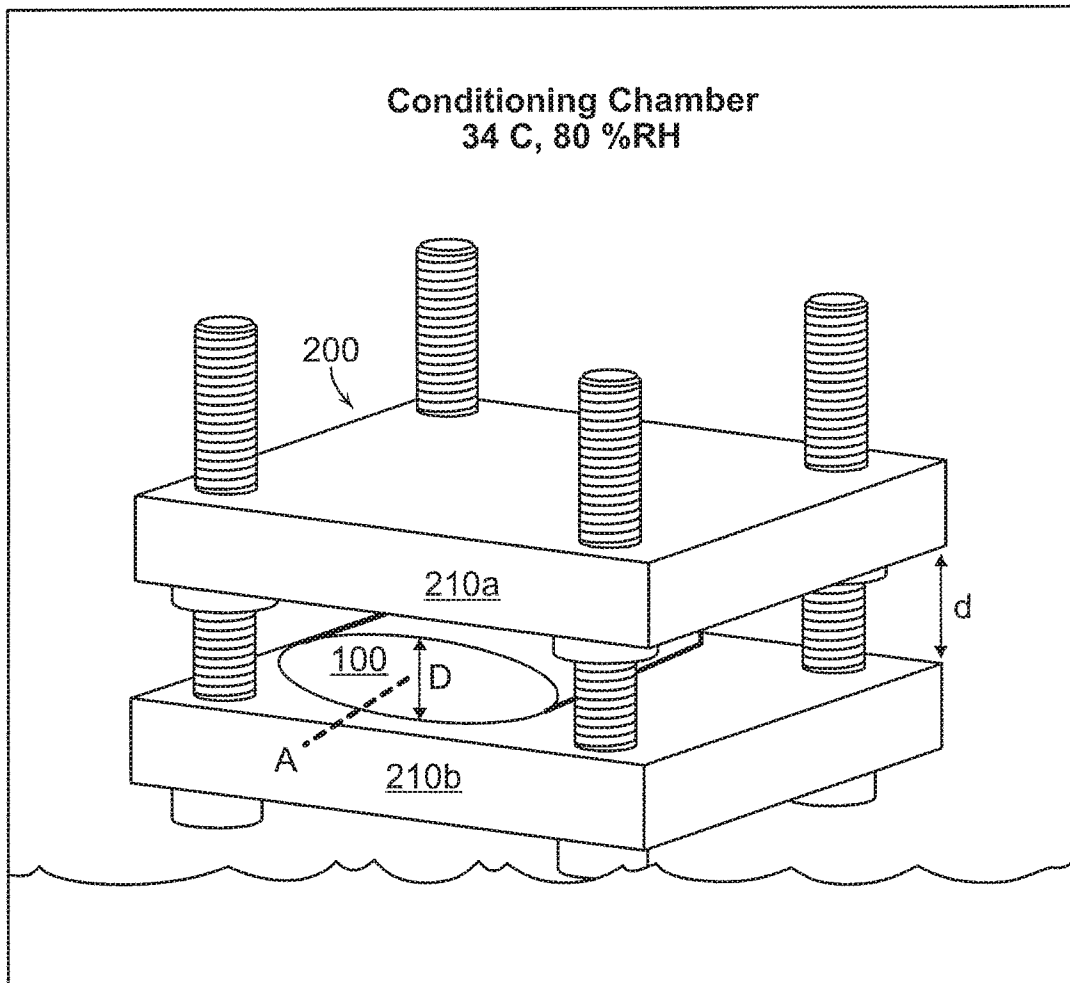


FIG. 38

# INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 16/40204

## A. CLASSIFICATION OF SUBJECT MATTER

IPC(8) - A61F 2/04 (2016.01)

CPC - A61F 2/04, A61F 2/186, A61K 9/0092, A61K 9/0043, A61K 9/70

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)

IPC(8) - A61F 2/04 (2016.01)

CPC - A61F 2/04, A61F 2/186, A61K 9/0092, A61K 9/0043, A61K 9/70

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched (UPC) 424/434; 606/199; 604/514 (CPC) A61F 2/86, 2/88, 2/90; A61F 2/07, 2002/07\* (Search term limited; see below)

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

PubWest (PGPB, USPT, EPAB, JPAB); Google; PatBase (All);

Search Terms: implant, scaffold, sinus, sinusitis, nose, nasal\*, tube, tubular, stent\*, degradable\*, biodegradable\*, absorber\*, bioabsorber\*, resorbable\*, bioresorbable\*, PLGA, poly lactic acid\*, polylactic acid\*, glycolic acid\*, coglycolic acid\*, coat\*, layer, elastomer\*, PLC, urethane, urea, cross-link\*, crosslink\*

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 2014/0100644 A1 (PALASIS et al.) 10 April 2014 (10.04.2014) Entire document, especially Abstract, para[0002]- para[0003], para[0005]- para[0006], para[0015]- para[0016], para[0021], para[0024], para[0031]- para[0034] and FIGS. 1-5.	1-3, 26-28
A	US 2010/0222881 A1 (PREWETT et al.) 02 September 2010 (02.09.2010) Entire document.	1-3, 26-28
A	US 2005/0186243 A1 (HUNTER et al.) 25 August 2005 (25.08.2005) Entire document.	1-3, 26-28
A	US 8,137,396 B2 (BUSOLD et al.) 20 March 2012 (20.03.2012) Entire document.	1-3, 26-28

☐ Further documents are listed in the continuation of Box C.

\* 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

18 August 2016

Date of mailing of the international search report

15 SEP 2016

Name and mailing address of the ISA/US

Mail Stop PCT, Attn: ISA/US, Commissioner for Patents

P.O. Box 1450, Alexandria, Virginia 22313-1450

Facsimile No. 571-273-8300

Authorized officer:

Lee W. Young

PCT Helpdesk: 571-272-4300

PCT OSP: 571-272-7774

# INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 16/40204

## 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.:  
because they relate to subject matter not required to be searched by this Authority, namely:
  
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.: 4-25, 29-49  
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 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.