(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
26 May 2016 (26.05.2016)

WIPO | PCT

(10) International Publication Number
WO 2016/079649 A1

(51) International Patent Classification:
A61M 25/10 (2006.01) *A61B 17/22* (2006.01)
A61B 17/32 (2006.01)

(21) International Application Number:
PCT/IB2015/058802

(22) International Filing Date:
13 November 2015 (13.11.2015)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
62/080,831 17 November 2014 (17.11.2014) US

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

(84) Designated States *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG).

Declarations under Rule 4.17:

— *as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii))*

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

Published:

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

(54) Title: BALLOON CATHETER SYSTEM

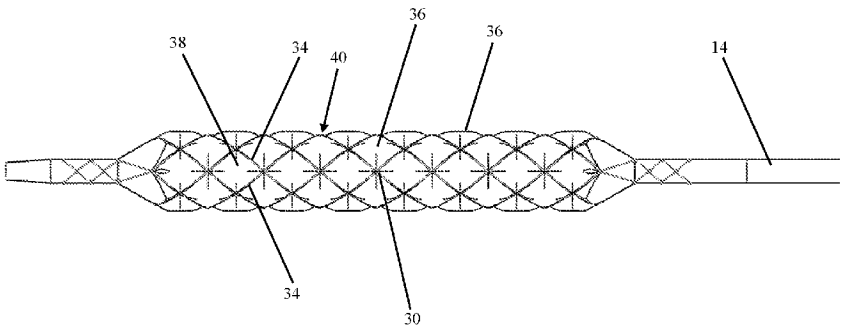

Fig 4

(57) Abstract: A system (10) for dilating a stenosed vessel is provided. The system includes a balloon (20) mounted on a catheter shaft (12), the balloon being composed of a first material and fibers (34) forming a grid (30) attached to a surface of the balloon or integrated within a wall thereof. The fibers are composed of a second material having less elasticity than the first material such that when the balloon is inflated beyond a predetermined pressure balloon regions protrude (36) from the grid formed by the fibers.

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BALLOON CATHETER SYSTEM

INCORPORATION BY REFERENCE TO ANY PRIORITY APPLICATIONS

[0001] This application claims priority benefit under 35 U.S.C. § 119(e) of U.S. Provisional Application No. 61/080,831, filed November 17, 2014, the entirety of which is incorporated by reference herein.

BACKGROUND

Field

[0002] The present disclosure relates to a balloon catheter system and method for treating biological vessels and, more particularly, to an angioplasty balloon catheter which includes a grid of fibers attached to, or integrated within a wall of the balloon. The fibers are less elastic than the balloon material and as such, when the balloon is inflated beyond a predetermined pressure a plurality of balloon regions protrude from the grid formed by the fibers.

Description of the Related Art

[0003] **[0003]** Percutaneous transluminal angioplasty (PTA) is a procedure in which a balloon catheter is inserted through an artery and guided to the region of lumen narrowing. The balloon is inflated to force the plaque material (typically fat and calcium) against the wall of the artery to open the vessel lumen and improve blood flow.

[0004] Angioplasty balloons are typically cylindrical when inflated and have different lengths and diameters to conform to different vessel sizes. The balloons are inflated at high pressure, normally between 8-20 atmospheres, in order to overcome the resistance of the plaque and achieve luminal expansion.

[0005] Standard balloons (also referred to as plain balloons) are the most commonly used technique for dilation of a lesion in a blood vessel (angioplasty); however, standard balloons suffer from several disadvantages.

[0006] Since the diameter and composition of stenotic regions of an artery are not typically uniform, inflation of a standard balloon in a vessel leads to non-uniform (axially and radially) expansion. Variability in the lesion composition (lesions can be composed of a

mixture of hard and soft plaque material) will lead to variability in resistance to dilation along the lesion and to balloon over expansion in the least resistant regions of the vessel. As a result, standard balloons can apply excessive forces to less resistant regions of the lesion thus traumatizing the vessel wall (e.g. dissections) and yet do not apply enough forces to resistant plaque regions to enable effective dilation thereof.

[0007] Trauma to the vessel wall is associated with poor long term clinical results and can accelerate or induce restenosis in the treated areas. In addition, major dissections, such as flow limiting dissections require stenting further complicating the procedure.

[0008] Attempts to solve the aforementioned limitations of standard balloon catheters by increasing forces on resistant plaque region via cutting or scoring elements (blades/wires) positioned on the balloon surface (e.g. U.S. Publication No. 20040143287 and U.S. Publication No. 20060085025) were somewhat successful but did not adequately solve problems resulting from non-uniform balloon expansion. In addition, cutting and scoring balloons are not designed to avoid traumatizing the vessel walls, but instead to control the trauma to the vessel walls by inducing controlled and predictable dissections.

[0009] Thus, there is a need for a high pressure angioplasty balloon catheter capable of effectively opening resistant plaque regions without traumatizing the vessel walls in less resistant plaque regions.

SUMMARY

[0010] According to one aspect of the present disclosure, there is provided a system for dilating a stenosed vessel comprising: (a) a balloon mounted on a catheter shaft, the balloon being composed of a first material; and (b) a plurality of fibers forming a grid attached to a surface of the balloon or integrated within a wall thereof, the plurality of fibers being composed of a second material having less elasticity than the first material such that when the balloon is inflated beyond a predetermined pressure a plurality of balloon regions protrude from the grid formed by the plurality of fibers.

[0011] According to further features of the disclosure described below, the balloon is composed of a first polymer, and the plurality of fibers are composed of a second polymer.

[0012] According to still further features in the described embodiments, a thickness of each of the plurality of fibers is selected from a range of 10-750 microns.

[0013] According to still further features in the described embodiments, a thickness of each of the plurality of fibers varies along its length.

[0014] According to still further features in the described embodiments, the grid forms a plurality of cells having an area selected from a range of 1-25 mm2.

[0015] According to still further features in the described embodiments, the grid is attached to a surface of the balloon via an adhesive.

[0016] According to still further features in the described embodiments, the grid is attached to a surface of the balloon via welding.

[0017] According to still further features in the described embodiments, a tensile modulus of each of the plurality of fibers is selected from a range of 1-150 GPa. and the tensile modulus of the balloon is selected from a range of 0.0002-0.0100 GPa.

[0018] According to still further features in the described embodiments, the cells include triangular or diamond-shaped cells or both.

[0019] According to still further features in the described embodiments, a lead angle of the cells is selected from a range of 30-180 degrees.

[0020] According to still further features in the described embodiments, a linear mass density of each of the plurality of fibers is 1-100 Denier.

[0021] According to still further features in the described embodiments, a linear mass density of each of the plurality of fibers is 50 Denier.

[0022] According to still further features in the described embodiments, the grid pattern is formed from N fibers helically wound around the balloon in a clockwise direction and N fibers helically wound around the balloon in a counterclockwise direction. The balloon can optionally include L longitudinal fibers, wherein L can be 2 or more.

[0023] According to still further features in the described embodiments, N is selected from a range of 4-16.

[0024] According to still further features in the described embodiments, N is 4.

[0025] According to still further features in the described embodiments, the predetermined pressure is at least 2 atmospheres.

[0026] According to still further features in the described embodiments, the plurality of isolated balloon regions protrude at least 0.1 mm from the surface when the balloon is inflated to its working pressure (e.g. 5-25 ATMs).

[0027] According to still further features in the described embodiments, the grid is sandwiched between the balloon and a layer of material.

[0028] According to still further features in the described embodiments, each of the plurality of fibers is a monofilament fiber.

[0029] According to still further features in the described embodiments, each of the plurality of fibers is a multifilament fiber.

[0030] According to still further features in the described embodiments, each of the plurality of fibers is composed of polypropylene, PLLA, PEEK, aramids (Kevlar®), polyester fibers (Dacron®), aromatic polyesters (Vectran®), aliphatic polyamides (nylons) and/or ultra-high molecular weight polyethylene.

[0031] According to still further features in the described embodiments, the balloon and/or the plurality of fibers are coated with a drug-containing formulation.

[0032] According to still further features in the described embodiments, the drug is an antiproliferative drug.

[0033] The present disclosure successfully addresses the shortcomings of the presently known configurations by providing a balloon catheter system, which can be used to open stenosed vessels without traumatizing the vessel wall.

[0034] Unless otherwise defined, all technical and scientific terms used herein have the same meaning as commonly understood by one of ordinary skill in the art to which this disclosure belongs. Although methods and materials similar or equivalent to those described herein can be used in the practice or testing of the present disclosure, suitable methods, and materials are described below. In case of conflict, the patent specification, including definitions, will control. In addition, the materials, methods, and examples are illustrative only and not intended to be limiting.

BRIEF DESCRIPTION OF THE DRAWINGS

[0035] The disclosure is herein described, by way of example only, with reference to the accompanying drawings. With specific reference now to the drawings in detail, it is

stressed that the particulars shown are by way of example and for purposes of illustrative discussion of the embodiments of the present disclosure only, and are presented in the cause of providing what is believed to be the most useful and readily understood description of the principles and conceptual aspects of the disclosure. In this regard, no attempt is made to show structural details of the disclosure in more detail than is necessary for a fundamental understanding of the disclosure, the description taken with the drawings making apparent to those skilled in the art how the several forms of the disclosure may be embodied in practice.

[0036] Figure 1 is a side view of a catheter including the present balloon and a magnified view of the balloon portion of the catheter.

[0037] Figure 2 is an isometric view of an inflated balloon including a grid having square-shaped openings.

[0038] Figure 3a is a side view of the balloon of Figure 2.

[0039] Figures 3b and 3c illustrate the balloon surface and braid of a deflated balloon or a balloon inflated up to a predetermined threshold (Figure 3b) and inflated beyond the threshold (Figure 3c) balloon.

[0040] Figure 4 is a side view of an inflated balloon including a grid having diamond-shaped openings.

[0041] Figure 5 is an image illustrating an angle and distances of importance between fibers of a balloon prototype constructed according to the teachings of the present disclosure.

[0042] Figures 6a-6d illustrate a 6 X 40 mm balloon braided at 6 (Figures 6b, 6d) or 10 (Figures 6a, 6c) PPI showing the balloon tapered end (Figures 6a, 6b) and center portion (Figures 6c, 6d).

[0043] Figures 7a-7d illustrate a 5 X 40 mm balloon braided at 6 (Figures 7a, 7c) or 10 (Figures 7b, 7d) PPI showing the balloon tapered end (Figures 7a, 7b) and center portion (Figures 7c, 7d).

[0044] Figure 8 is a balloon braided with a diamond pattern.

[0045] Figure 9 is a close up of the balloon of Figure 8.

DETAILED DESCRIPTION

[0046] The present disclosure relates to a balloon catheter system, which is capable of applying uniform pressure to a vessel wall even under high inflation pressures and as such can be used to dilate stenosed regions of a body vessel such as an artery while applying a uniform expansion force to all portions of the treated vessel.

[0047] The principles and operation of the present disclosure may be better understood with reference to the drawings and accompanying descriptions.

[0048] Before explaining at least one embodiment of the disclosure in detail, it is to be understood that the disclosure is not limited in its application to the details set forth in the following description or exemplified by the Examples. The disclosure is capable of other embodiments or of being practiced or carried out in various ways. Also, it is to be understood that the phraseology and terminology employed herein is for the purpose of description and should not be regarded as limiting.

[0049] In a previously filed patent application (U.S. Publication No. 20140066960, filed August 21, 2013, the entire disclosure of which is hereby incorporated by reference), the disclosure described an angioplasty balloon catheter having an expandable constraining structure positioned over a balloon. The expandable constraining structure is not attached to the balloon but is expanded thereby to constrain balloon inflation and enable isolated balloon regions to protrude from the constraining structure during inflation. This ensures that the balloon applies a uniform force on the vessel wall when inflated and reduces the likelihood of dissections and other trauma.

[0050] Although experiments have shown that the balloon catheter of U.S Publication No. 20140066960 is highly effective in dilating stenosed regions and minimizing trauma to the vessel wall, due to its metal constraining structure it has a fairly large packing diameter and limited flexibility and maneuverability through torturous vessels.

[0051] In order to traverses these limitations, the present inventors have devised a balloon catheter which is capable of providing the benefits of U.S. Publication No. 20140066960 under high inflation pressures, is easy to manufacture and can be efficiently packed for delivery while being highly maneuverable through torturous vessels. As is further described hereinbelow, such benefits are provided by a fiber grid which is attached to, or

integrated into the balloon wall and is configured for modifying the shape of the balloon surface to form pillow-like protrusions upon balloon inflation.

[0052] Balloons with integrated or attached fiber grids are known in the art (e.g. U.S. Publication No. 20060271093 or U.S. Publication No. 20050271844). However, such fiber grids are utilized to prevent balloon over-inflation and increase balloon integrity under high inflation pressures and not for modifying the shape of the inflated balloon to form pillow-like balloon protrusions through the grid.

[0053] Thus, according to one aspect of the present disclosure, there is provided a system for dilating a stenosed vessel. As used herein, the term vessel refers to any hollow conduit in the body and includes blood vessels such as arteries and veins, lymphatic vessels, GI tract vessels (e.g. intestines), ducts and any body passage, which conducts a biological fluid. As is further described hereinunder, one preferred use of the present system is in angioplasty of arteries such as peripheral (e.g. leg) arteries.

[0054] The present system includes a balloon composed of a first material (e.g. first polymer) mounted on a catheter shaft and a plurality of fibers forming a grid-like pattern attached to a surface of the balloon or integrated within a wall thereof. The fibers are composed of a second material (e.g. second polymer) which is preferably stronger and less stretchable than the first material.

[0055] As such, inflation of the balloon beyond a predetermined threshold pressure (e.g. above 3 ATMs) stretches the balloon material more than the fibers, forming channels along the balloon surface where the fibers are constrained or fixed and balloon protrusions therebetween where the balloon material is unconstrained. The grid of fibers maintains balloon uniformity (axially and radially) throughout inflation enabling the protrusions (also referred to herein as pillows) to uniformly contact the vessel wall and plaque material thus ensuring uniform force distribution along the treated vessel region and minimizing vessel trauma while effectively dilating the entire plaque region. In addition, since the channels formed by the grid fibers are recessed from the vessel wall when the balloon is inflated, they provide stress relief regions and further reduce the likelihood of trauma.

[0056] In order to enable formation of the protrusions and control protrusion height area and shape, one must carefully select the balloon and fiber material, the strength and diameter of the fibers and the shape of the grid formed thereby.

[0057] The balloon material is selected based on desired compliance (defined herein as elasticity or tensile modulus) and resistance to rupture (strength). The fiber is selected based on strength and elasticity.

[0058] The catheter shaft can be any configuration suitable for use in the desired procedure. For example, in angioplasty procedures the catheter can be configured for over-the-wire or a rapid exchange delivery and can include suitable connectors for wire insertion, inflation and the like at its proximal end. The catheter shaft can be any length and diameter suitable for angioplasty of peripheral, coronary, or cerebral blood vessels. Suitable length (L) and diameter (D) of the balloon can be in the range of about 4-40 mm L, 1.25-5 mm D for coronary applications and 20-300 mm L, 2-12 (or more) mm D for peripheral vessels applications.

[0059] The balloon can be a compliant or a semi-compliant balloon fabricated from polyamide, Pebax, polyurethane, polyethylene terephthalate, or similar material and the like at dimensions selected from a range of about 5-300 mm in length and about 2-12 (or more) mm in diameter. The balloon can be cylindrical or any other shape known in the art. For example, when utilized in angioplasty, the balloon can be roughly cylindrical in shape with tapered ends with a length of 5-300 mm and a diameter of 2-12 mm the taper is normally similar or slightly shorter than the balloon diameter. The elasticity of the balloon material can be between 0.0002 to 0.0100 GPa.

[0060] The grid can be formed from single filament or multi-filament fibers (of the same or different filaments) that are woven or braided from any material suitable for such purposes. The fibers can be 10-750 microns in thickness, such as in the radial direction, with uniform or variable thickness throughout fiber length (over balloon). For example, the fiber can be thicker at the balloon tapers or legs and thinner at the working length.

[0061] The fibers can be made from various polymers (such as polyurethane, polyamide, polyethylene or other) or metals (such as Nitinol or Cobalt chromium alloy or other) or composites thereof, other suitable material. Specific and preferred examples include

ultra-high molecular weight polyethylene, polyvinylidene fluoride, and polyethylene terephthalate. A presently preferred material for the fibers is ultra-high molecular weight polyethylene.

[0062] Multifilament fibers are typically measured in units of Deniers, which is a unit of measure for the linear mass density of fibers. The linear mass density of the fibers can be 10-100 Deniers, preferably 50 deniers.

[0063] The elasticity of the fibers can range from 0.1-500 GPa, preferably 100 GPa.

[0064] Braid density of the fibers is also important and is determined by the picks per inch (PPI), i.e. the number of fiber crossovers per inch of balloon length; a high PPI correlates with a high burst pressure. The PPI used to fabricate the grid of the present system is preferably within a range of 2-20, more preferably 6-14.

[0065] Several approaches can be used to fabricate the present system. The present system is assembled while the balloon is an inflated or semi-inflated form under a pressure of 0.3-20 ATMs (preferably 0.3 - 8 ATMs, more preferably 0.3 – 2 ATMs). The inflation pressure used sets the extent of balloon material stretching which in turn determines the outer diameter of the constrained segment of the balloon and maximum protrusion height of the isolated balloon regions of a fully inflated balloon.

[0066] When the balloon is not inflated (or is inflated to a pressure below the threshold), the fiber braid protrudes from the surface of the balloon (Figure 3b) or is formed with the balloon surface (when sandwiched between two layers of balloon wall material) such that the balloon wall does not extend radially outwardly beyond the fiber braid. When inflated to a pressure above the threshold pressure, the isolated balloon regions protrude from the braid openings to a height that is defined as the distance between the surface of the braid fiber and outermost surface of the isolated balloon regions (arrow, Figure 3c). Such a height can be at least about 0.1 mm, and in some implementations at least about 0.1 or 0.2 or more, at the nominal inflated working pressure. In general, the height will be within the rage of from about 0.01-1 mm or 0.1-0.5 mm.

[0067] In a 3 mm balloon (which is capable of reaching diameters greater than 3 mm with over inflation), assembly of the fibers is effected over a balloon inflated to about 3

mm in diameter. When the assembled balloon is inflated inside a vessel, protrusions of the isolated balloon regions will for at this diameter, and will gradually increase in height along with inflation. At 3.5 mm in diameter, the height of the isolated balloon regions protruding from the balloon surface will begin at 3.5 mm and gradually increase in height with inflation, typically to about 0.01-0.5 mm in increased height.

[0068] The fibers are preferably attached to the balloon surface along the entire length of each fiber. Attachment is effected using an adhesive applied to the fibers or by sandwiching the fibers between two adhesive layers applied to the balloon surface, a base and cover adhesive layer. These layers can be applied via dipping, spraying, or any other approach known in the art. The base layer of the balloon wall can be any flexible adhesive layer that allows for immobilization of the fibers but retains the flexibility of the underlying balloon substrate while the cover layer further immobilizes the grid, protects it from the vessel wall and plaque and enhances vascular wall-gripping.

[0069] A smooth cover layer is particularly advantageous when the present balloon catheter is utilized for dilating in-stent restenosis. The cover layer of the present balloon prevents 'stent jailing' - a phenomenon in which struts of, for example, cutting/scoring balloons, are trapped within stent struts.

[0070] Attachment or partial-attachment of the fibers to the balloon surface may be desirable in order to maintain fiber position over the balloon throughout inflation, and thus maintain the shape and size of the isolated balloon regions. If the fibers were free to move the uniformity of balloon protrusions could not be maintained and thus uniform vessel dilation would not be possible. Fixation of the fibers in a specific grid shape is also very important over the balloon tapers where a free wire would tend to slip from its intended position more easily, again resulting in protrusion non-uniformity.

[0071] The fibers are braided over the balloon working length at a lead angle as defined by the PPI. The angle can vary from 30-180 degrees. In one embodiment, each isolated balloon region (protruding between channels) is surrounded by four crossing fibers angled at approximately 90 degrees to each other. Since the lead angle is constant and equal for all fibers, the isolated balloon regions formed between the fibers are square/rectangle. At

this configuration, the fibers are positioned to resist tension forces applied thereupon by the pressure buildup in the balloon.

[0072] In the above example, the fibers are braided lengthwise and radially, however, the present grid can also be formed by helical braiding of fibers over the working length and tapers of the balloon.

[0073] An optional top layer can be applied to the balloon following sandwiching of the fiber grid between the base and cover layers. This top layer decreases the tackiness of the balloon and improves its ability to track through a tortuous anatomy and inflate within the vessel site. The top layer can be composed of parylene or any other material commonly known in the art.

[0074] Alternatively, the balloon can be coated with a coating following sandwiching of the fiber grid between the base and cover layers. This coating can be a hydrophilic material or a hydrophobic material. The coating decreases the tackiness of the balloon and improves its ability to track through a tortuous anatomy and inflate within the vessel site. The top layer can be composed of silicone, polyurethane, polyvinylpyrrolidone, hyaluronic acid, or any other material commonly known in the art.

[0075] When assembled the balloon can be folded in regular folding techniques known in the art. The balloon can be folded to 2 - 8 pleats, with the pleats being wrapped around the balloon axis as done with plain balloon. The fibers are soft enough to allow such folding.

[0076] One specific embodiment of manufacturing process is described hereinbelow:

(i) The balloon is inflated, preferably to 0.3-2 ATMs.

(ii) A polyurethane adhesive is applied to the base layer of the balloon via spraying, dipping, or painting.

(iii) The adhesive base layer is cured and the fibers are braided over the balloon surface. A variable pitch process is used over the legs, tapers, and working length with a PPI range over the working length of 6 - 14.

(iv) A cover layer of polyurethane adhesive is applied over the braided grid to fix the fibers in place and ensure a continuous fiber coating to minimize interaction between fibers and plaque material.

(v) The adhesive cover layer is cured and an optional outer layer is applied to the balloon to minimize tackiness and enhance delivery to a vessel site.

[0077] Figures 1-4 illustrate one embodiment of the present balloon system, which is referred to herein as system 10. System 10 is configured for use in angioplasty procedures.

[0078] System 10 includes a catheter shaft 12, which is fabricated from polymer extrusions and includes longitudinal lumens running the length of shaft 12. A first lumen can accommodate a guidewire while a second lumen can serve as an inflation conduit for balloon 20 mounted on a distal portion 14 of shaft 12. Proximal portion 16 of shaft 12 includes a connector 18 having dedicated ports 22 and 24 communicating with the second and first lumens (respectively).

[0079] For coronary applications balloon 20 can be between 1.25 to 5.0 mm in diameter and 4 to 40 mm in length (when inflated as shown in Figure 2). For peripheral applications, balloon 20 can be between 2 to 12 mm in diameter and 5 to 300 mm in length. A longer balloon may taper (radially) along its length. The wall thickness of balloon 20 can vary from 1 – 250 μm (variable depending on material and specified characteristics). The balloon wall thickness can be uniform or variable.

[0080] Balloon 20 is attached to distal portion 14 of shaft 12 using approaches well known in the art (e.g. gluing or welding). A grid 30 is integrated into, or glued onto wall 32 of balloon 20 as is described above. Grid 30 is formed from two or more fibers 34 (five radial fibers 35 and four axial fibers 37 shown in Figure 2) that are braided/woven over the length of balloon 20 including working length (WL), legs (LG) and tapers (TP).

[0081] As is shown in Figure 2, when balloon 20 is inflated to nominal pressure (e.g. 6-20 ATMs), grid 30 enables isolated balloon regions 36 to protrude through openings 38 formed between fibers 34 and form channels 40 in the balloon surface. Depending on several variables in construction of balloon 20 and grid 30 including balloon and fiber material, grid shape and density and the like, isolated balloon regions 36 can protrude 0.01-0.5 mm from the balloon surface. The grid 30 can include a number of circumferential fiber portions

intersecting a number of axial fiber portions. In general, there can be about 3 to about 20 circumferential fiber portions, such as about 4 to about 10 circumferential fiber portions, and about 3 to about 10 axial fiber portions, such as about 3 to about 5 axial fiber portions. In some implementations, there can be about 10 to about 20 isolated balloon regions, such as about 12 to about 18 balloon regions or about 14 to about 16 balloon regions.

[0082] As is mentioned herein, isolated balloon regions 36 contact the plaque in the vessel and apply a uniform force thereto, while channels 40 (which are recessed from the plaque) function as stress relief regions.

[0083] Four to seventy two fibers can be positioned around balloon 20 depending on the length and diameter thereof. Fibers 34 can be laid down in any pattern as long as the grid formed thereby includes openings 38 of roughly the same area and shape. For example, fibers 34 can be laid down longitudinally (axially) and radially to form square or rectangular openings 38 (as is shown in Figures 2-3), or fibers 34 can be helically wound clockwise and counterclockwise to form diamond-shaped openings 38 as is shown in Figure 4 which illustrates a grid 30 formed from helically wound fibers 34. A combination of these two approaches can also be used by providing axial fibers to limit balloon elongation and form triangular-shaped openings 38 (Figure 5).

[0084] The number of fibers 34 correlates to the density of the braid forming the grid and the number of and area of openings 38 (forming isolated balloon regions 36).

[0085] In one embodiment of the present disclosure shown in Figures 6a-d, a balloon 20 that is 40 mm in length and 6.0 mm in diameter includes a braided grid 30 formed from 8 fibers 34, 4 longitudinal fibers 34 and 4 radially wound fibers 34. This braiding pattern forms triangular and hexagonal - shaped isolated balloon regions 3 when inflated.

[0086] In another embodiment of the present disclosure shown in Figures 8-9, balloon 20 can include helical (H) + longitudinal (L) fibers 34 (wherein the number of H fibers is greater than the number of L fibers), with L fibers longitudinally arranged around the balloon, H/2 fibers 34 helically wrapped clockwise and H/2 fibers 34 helically wrapped counterclockwise. This result in a grid 30 forming triangular and hexagonal -shaped openings 38 through which isolated balloon regions 36 protrude around the circumference of balloon 20.

[0087] The total number of isolated balloon regions 36 depends on the balloon length: In the example of Figure 3a, isolated balloon regions 36 are defined by a square with a diagonal length of $3\times\pi/4=2.35$ mm. As a result, every 2.35 mm of balloon 20 length will include $2\times4=8$ isolated balloon regions 36. A 3×20 mm balloon will therefore include $8\times20/2.35=68$ isolated balloon regions 36.

[0088] Grid 30 preferably has a variable pitch (fiber 34 angles) over the working length (WL), legs (LG), and tapers (TP) of balloon 20 (Figure 2). Such variation can accommodate for changes in balloon 20 diameters over its length (e.g. taper expands less than working length) or can alter the local compliance of a balloon region (e.g. make a taper region less compliant).

[0089] System 10 can be used in angioplasty as follows. System 10 can be guided to the stenosed region over a guide-wire (not shown) using well known angioplasty approaches. Once in position, balloon 20 can be inflated to a point where it channels 40 and isolated balloon regions 36 are formed to apply an outward radial force to the plaque at isolated balloon regions 36 and stress relief regions at channels 40. Once the region is sufficiently dilated, balloon 20 is deflated and system 10 is removed from the body.

[0090] Thus, the present disclosure provides a balloon system, which protects the vessel wall from uneven expansion, as well as enables provision of localized higher pressure forces to specific lesion regions that are resistant, such as highly calcified expansion-resistant plaque regions.

[0091] Balloon 20 of system 10 and/or grid 30 can be coated with a hydrophilic or hydrophobic coating to enhance lubricity or coated with a drug composition containing, for example, an antiproliferative drug such as sirolimus or paclitaxel using methods well known in the art.

[0092] As used herein the term "about" refers to $\pm$ 10 %.

[0093] Additional objects, advantages, and novel features of the present disclosure will become apparent to one ordinarily skilled in the art upon examination of the following examples, which are not intended to be limiting.

EXAMPLES

[0094] Reference is now made to the following examples, which together with the above descriptions, illustrate the disclosure in a non-limiting fashion.

Bench Testing of Braided Balloons

[0095] Several prototype balloons were constructed according to the teachings of the present disclosure and tested as described below.

[0096] Briefly, a nylon balloon was fabricated via blow molding and the balloon was pre-inflated to 0.3 atm. The balloon was dip-coated in a polyurethane adhesive and an ultra-high molecular weight polyethylene multifilament fiber was braided in a diamond pattern over the balloon surface. The balloon was then dip-coated in a second layer of the polyurethane adhesive followed by dip-coating in parylene. Figures 8 and 9 illustrate an inflated balloon prototype with a diamond braiding pattern. The balloons were dried and folded to determine the folded diameter.

[0097] Five types of balloons were constructed, a 6 mm (inflated diameter) X 40 mm (inflated length) balloon at two PPI densities of 6, 10 (Figures 6a-6d) and a 5 mm X 40 mm balloon at three PPI densities of 6, 10 and 14 (Figures 7-7d, PPI 14 not shown).

[0098] The following parameters were tested for each balloon type:

(i) compliance - diameter of the balloon as a function of pressure;

(ii) burst pressure - measurement of the pressure at which the balloon material fails;

(iii) fatigue - measurement of the number of repeated inflation-deflation cycles before the balloon material fails; and

(iv) profile - measurement of the diameter of the folded balloon.

[0099] Table 1 below summarizes the results with the 5 tested balloons.

Table 1

Size	PPI	Pillow Height		Burst(atm)		Dia @ 8atm (mm)		Dia @ 8atm (mm)		□□	b	c	d
		8atm (mm)	12atm (mm)	Balloon Only	Braided Balloon	Balloon Only	Braided Balloon	Balloon Only	Braided Balloon	□deg)	(mm)	(mm)	(mm)
6.0x40	6	N/A	N/A	16.40	24.25±0.07	6.70	6.40±0.00	7.10	6.65±0.07	125.5	4.3	2.6	2.3
6.0x40	10	0.18	0.26		27.60±4.10		6.30±0.10		6.47±0.06	142	4.2	1.7	1.9
5.0x40	6	0.31	0.41	17.2	24.65±0.78	5.70	5.43±0.15	6.20	5.67±0.21	125.5	3.85	2.5	2.2
5.0x40	10	0.29	0.39		29.75±2.19		5.33±0.15		5.47±0.06	141	3.65	1.4	2.4

5.0x40	14	0.16	0.26		41.20+2.83		5.10		5.20	N/A	N/A	N/A	N/A

a-d are shown in Figure 5 and denote the following:
a-(alpha) is the angle of intersection for the fibers as marked in the drawing
b- is the distance between longitudinal fibers
c- is the length of longitudinal fiber as marked in the drawing
d- is the distance as marked in the drawing

[0100] It is appreciated that certain features of the disclosure, which are, for clarity, described in the context of separate embodiments, may also be provided in combination in a single embodiment. Conversely, various features of the disclosure, which are, for brevity, described in the context of a single embodiment, may also be provided separately or in any suitable subcombination.

[0101] Although the disclosure has been described in conjunction with specific embodiments thereof, it is evident that many alternatives, modifications, and variations will be apparent to those skilled in the art. Accordingly, it is intended to embrace all such alternatives, modifications, and variations that fall within the spirit and broad scope of the appended claims. All publications, patents, and patent applications mentioned in this specification are herein incorporated in their entirety by reference into the specification, to the same extent as if each individual publication, patent or patent application was specifically and individually indicated to be incorporated herein by reference. In addition, citation or identification of any reference in this application shall not be construed as an admission that such reference is available as prior art to the present disclosure.

WHAT IS CLAIMED IS:

1. A system for dilating a stenosed vessel comprising:

(a) a balloon mounted on a catheter shaft, said balloon being composed of a first material; and

(b) a plurality of fibers forming a grid attached to a surface of said balloon or integrated within a wall thereof, said plurality of fibers being composed of a second material having less elasticity than said first material such that when said balloon is inflated beyond a predetermined pressure a plurality of balloon regions protrude from said grid formed by said plurality of fibers.

2. The system of claim 1, wherein said balloon is composed of a first polymer and said plurality of fibers are composed of a second polymer.

3. The system of claim 1, wherein a thickness of each of said plurality of fibers is selected from a range of 10-750 microns.

4. The system of claim 1, wherein a thickness of each of said plurality of fibers varies along its length.

5. The system of claim 1, wherein said grid forms a plurality of cells having an area selected from a range of 1-25 mm^2.

6. The system of claim 1, wherein said grid is attached to a surface of said balloon via an adhesive.

7. The system of claim 1, wherein said grid is attached to a surface of said balloon via welding.

8. The system of claim 2, wherein a tensile modulus of each of said plurality of fibers is selected from a range of 1-150 GPa. and said tensile modulus of said balloon is selected from a range of 0.0002-0.0100 GPa.

9. The system of claim 2, wherein said cells include triangular and diamond-shaped cells.

10. The system of claim 2, wherein a lead angle of said cells is selected from a range of 30-180 degrees.

11. The system of claim 1, wherein a linear mass density of each of said plurality of fibers is 1-100 Denier.

12. The system of claim 1, wherein a linear mass density of each of said plurality of fibers is 50 Denier.

13. The system of claim 1, wherein said grid pattern is formed from N fibers helically wound around said balloon in a clockwise direction and N fibers helically wound around said balloon in a counterclockwise direction.

14. The system of claim 12, wherein N is selected from a range of 4-16.

15. The system of claim 12, wherein N is 4.

16. The system of claim 1, wherein said predetermined pressure is at least 2 atmospheres.

17. The system of claim 1, wherein said plurality of isolated balloon regions protrude at least 0.1 mm from said surface.

18. The system of claim 1, wherein said grid is sandwiched between said balloon and a layer of material.

19. The system of claim 1, wherein each of said plurality of fibers is a monofilament fiber.

20. The system of claim 1, wherein each of said plurality of fibers is a multifilament fiber.

21. The system of claim 1, wherein each of said plurality of fibers is composed of polypropylene, PLLA, PEEK, Kevlar, and/or ultra high molecular weight polyethylene.

22. The system of claim 1, wherein said balloon and/or said plurality of fibers are coated with a drug-containing formulation.

23. The system of claim 21, wherein said drug is an antiproliferative drug.

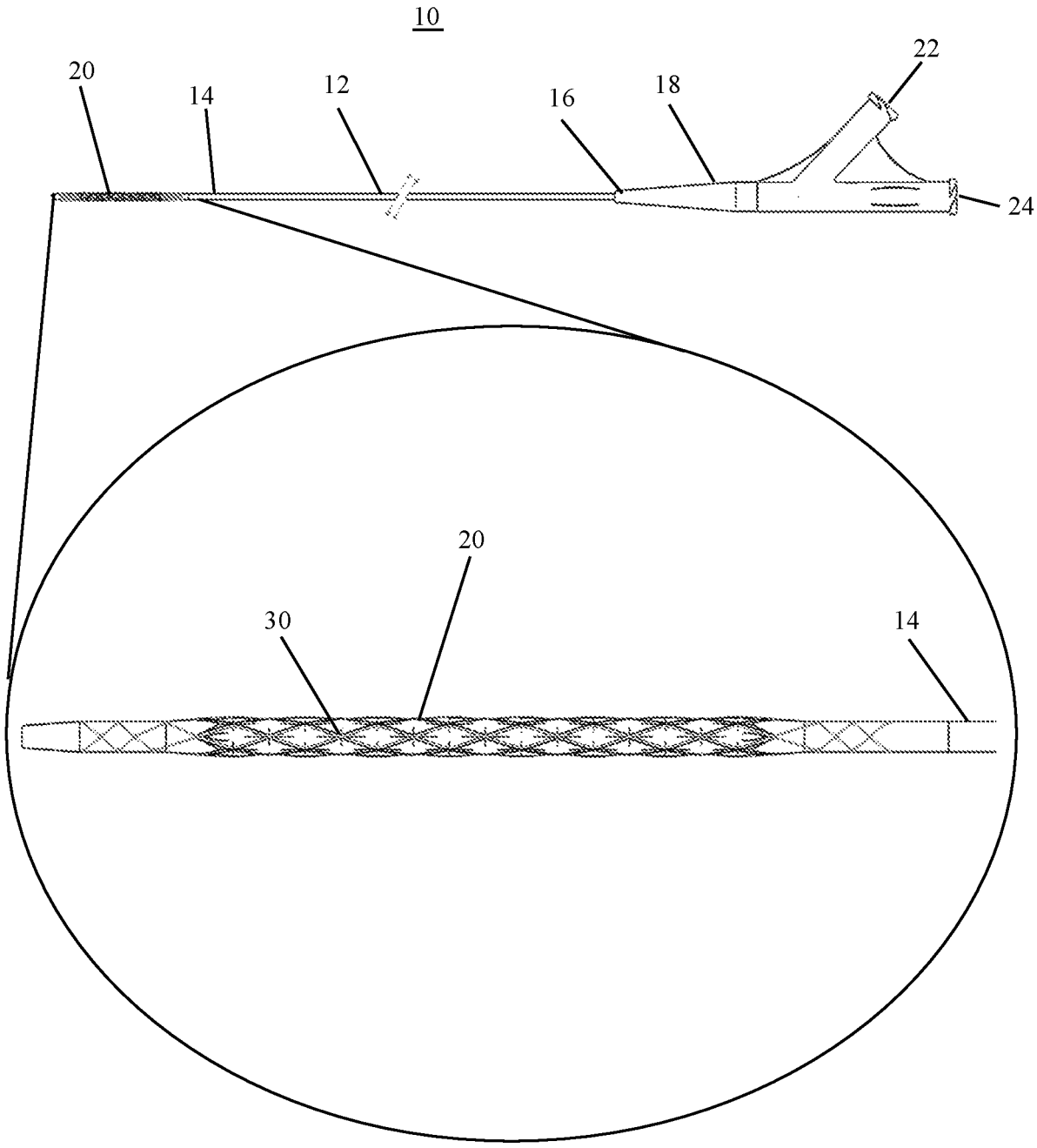


Fig 1

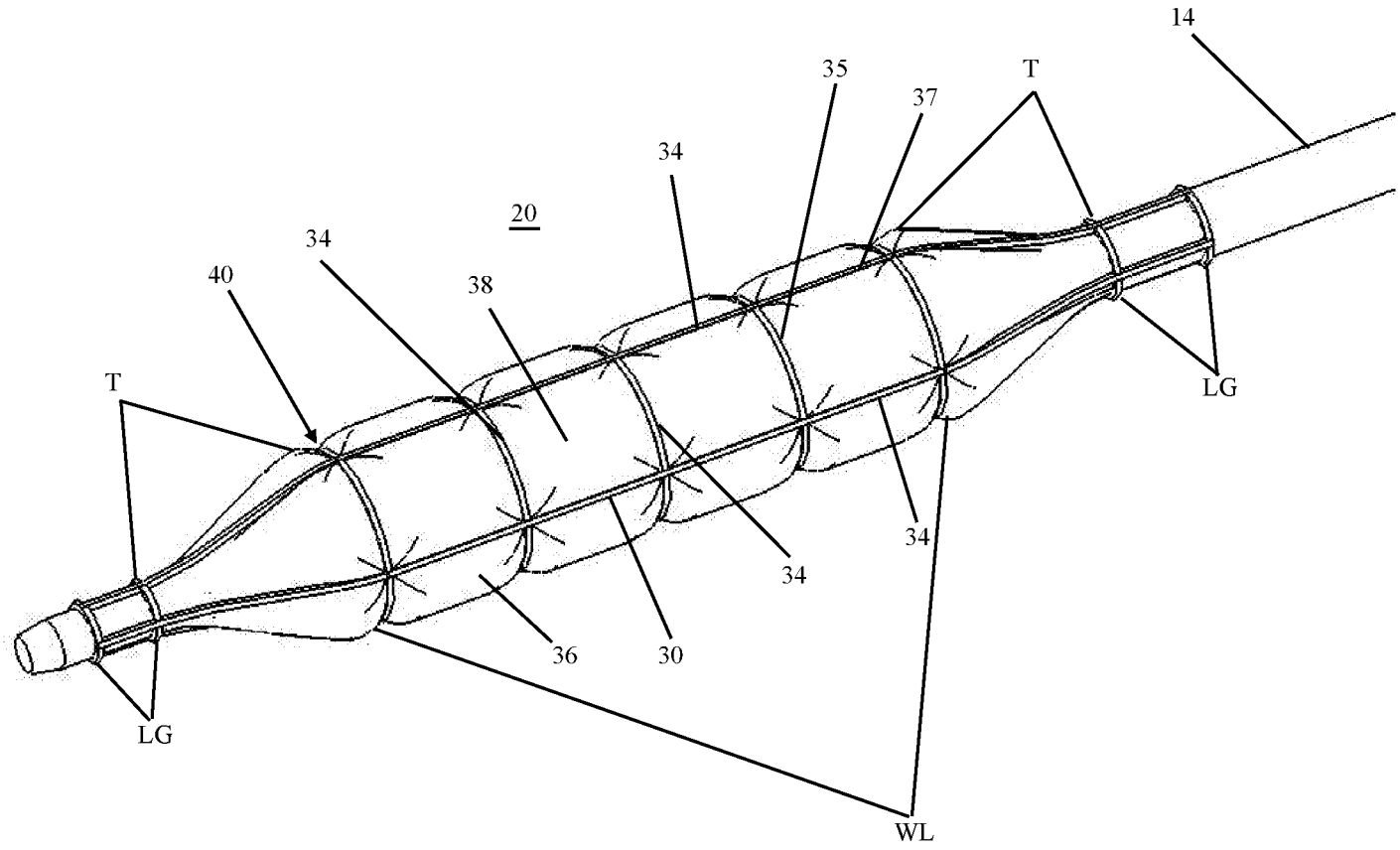


Fig 2

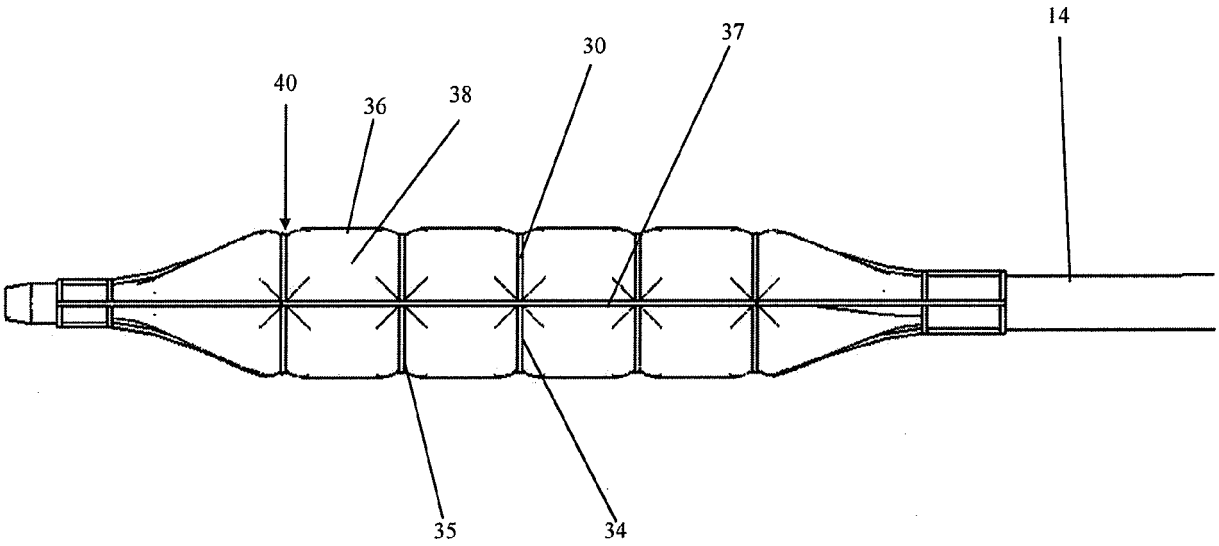


Fig 3a

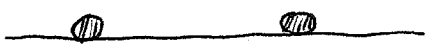


Fig 3b

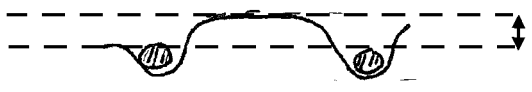


Fig 3c

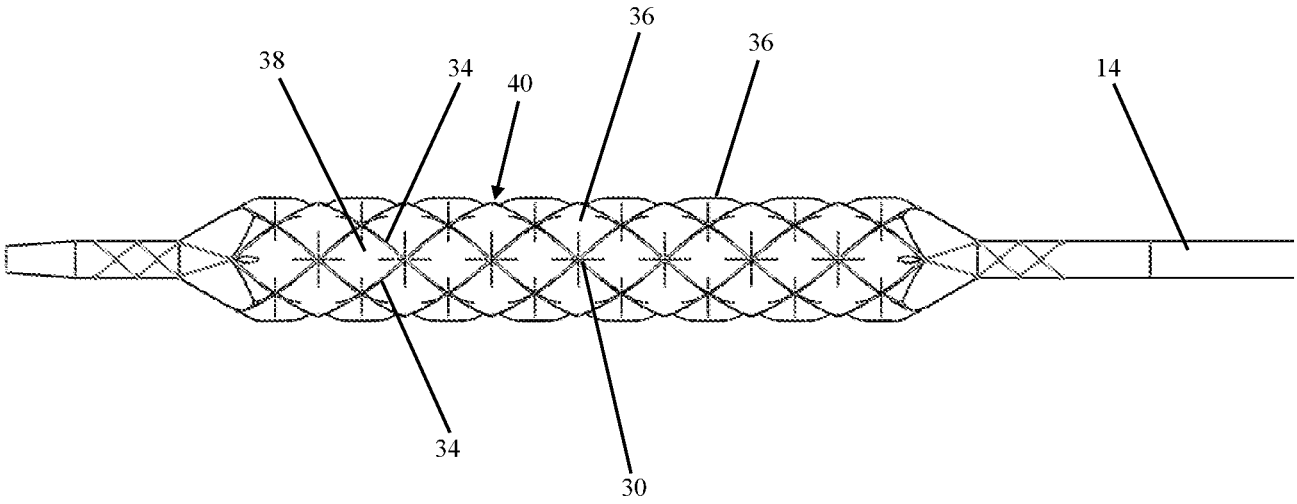


Fig 4

5/9

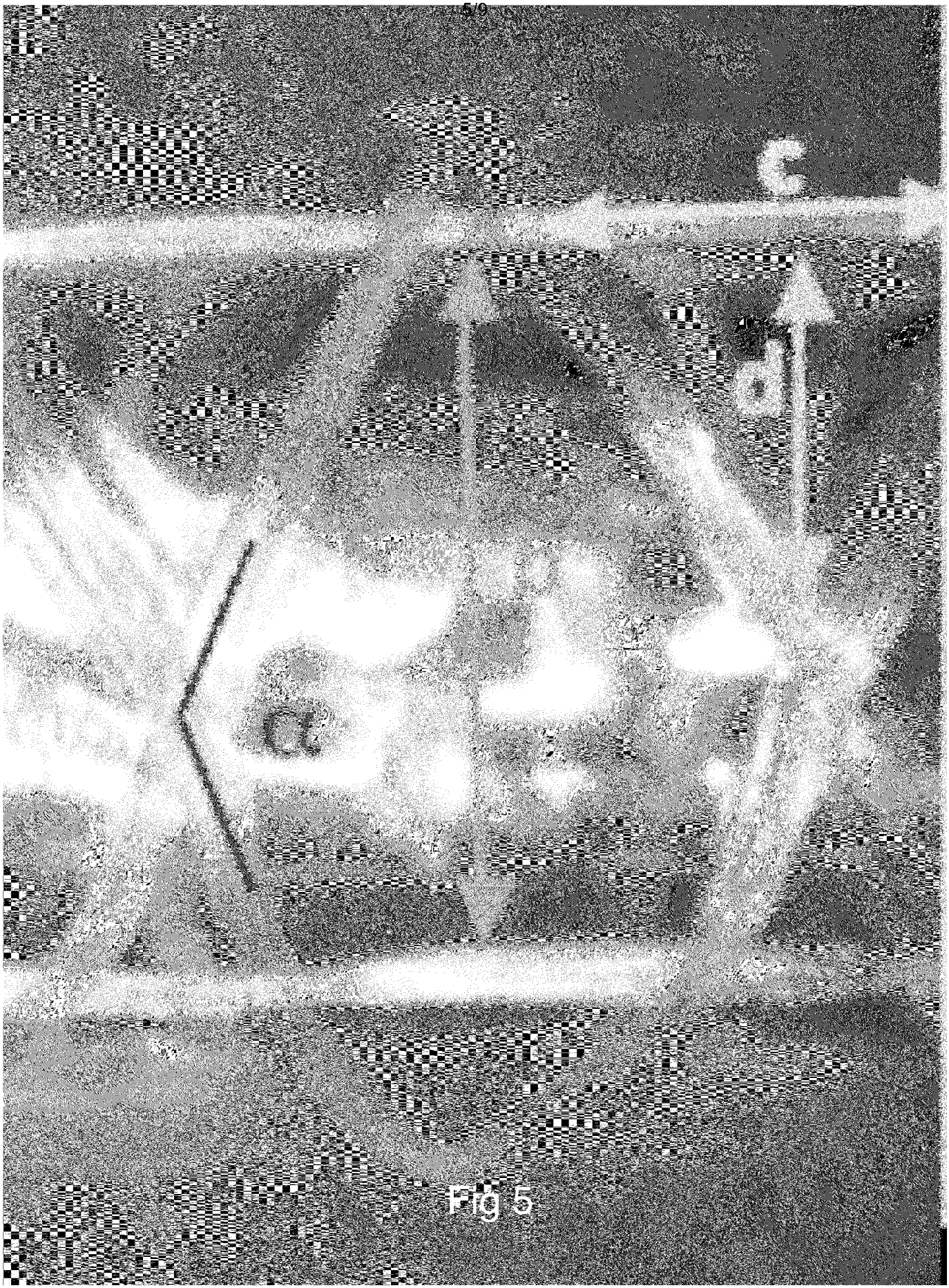
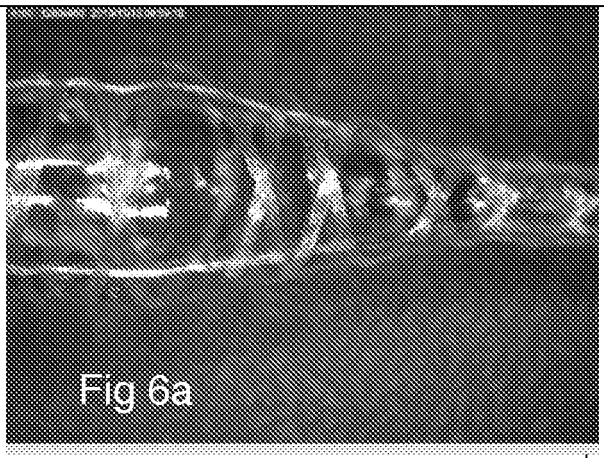


Fig 5



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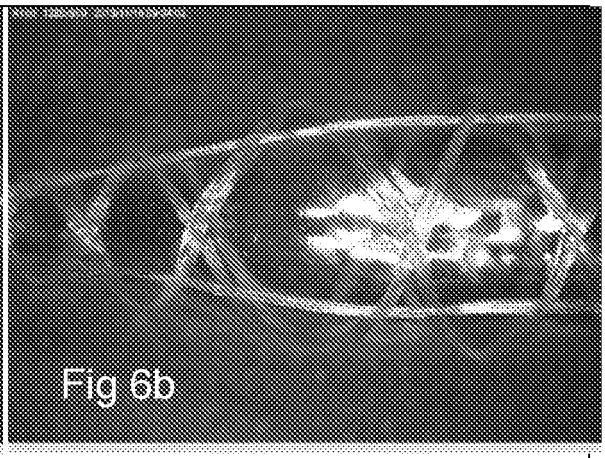

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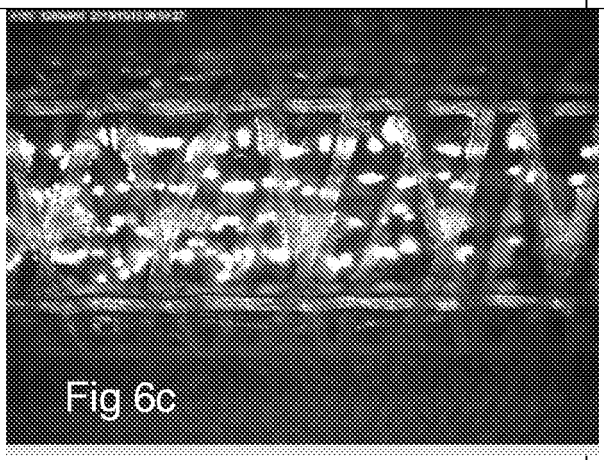

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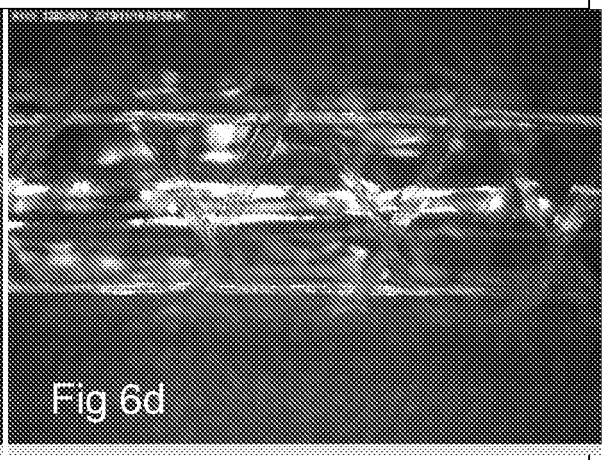
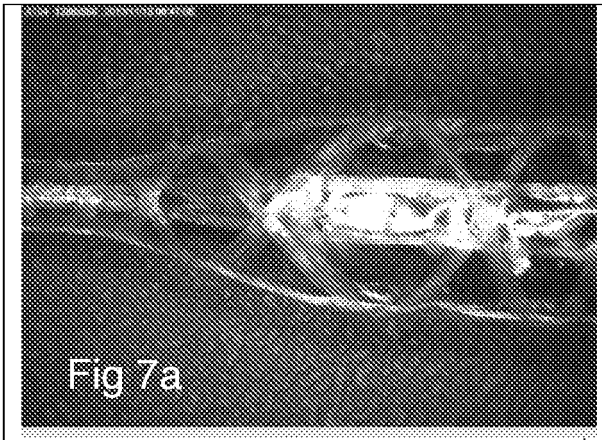
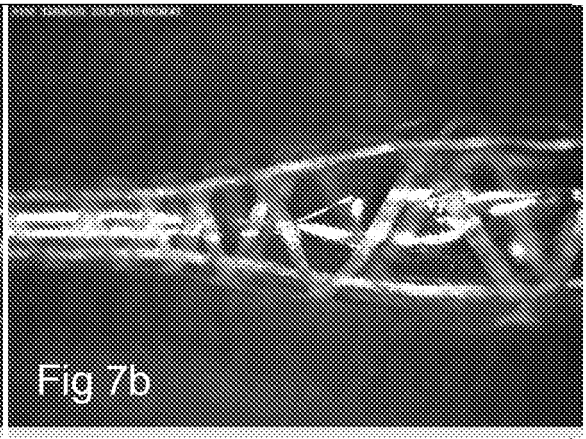
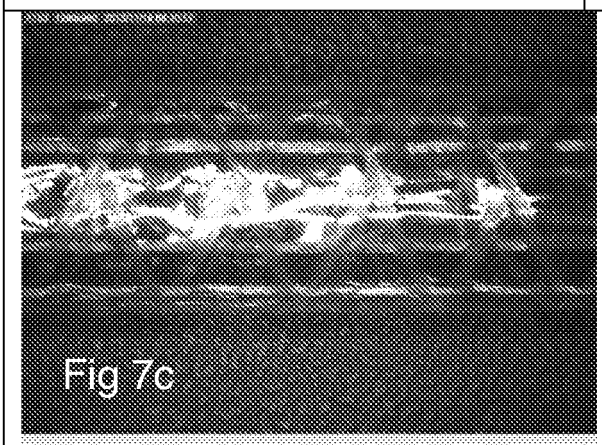


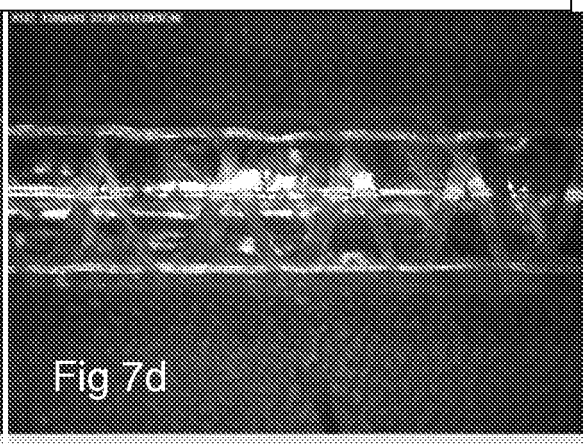
6.0x40mm, 6PPI





5.0x40mm Balloon, 6PPI	5.0x40mm Balloon, 10PPI





5.0x40mm Balloon, 6PPI	5.0x40mm Balloon, 10PPI

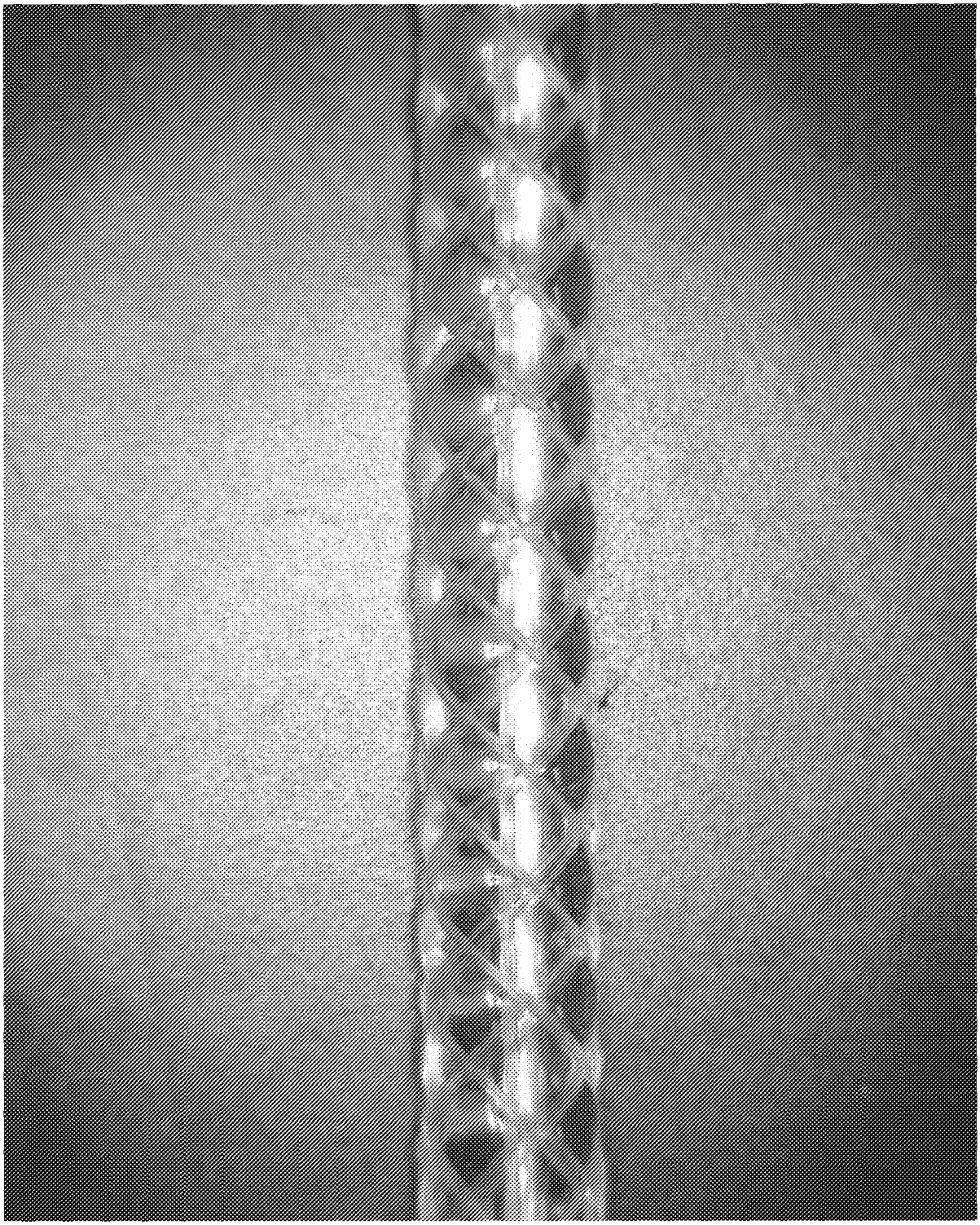


Fig 8

Fig 9

INTERNATIONAL SEARCH REPORT

International application No
PCT/IB2015/058802

A. CLASSIFICATION OF SUBJECT MATTER
INV. A61M25/10 A61B17/32 A61B17/22
ADD.

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
A61M A61B

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
EPO-Internal, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 2011/172698 A1 (DAVIES JR WILLIAM F [US] ET AL) 14 July 2011 (2011-07-14) figures 3a, 9a paragraph [0012] paragraph [0043] paragraph [0051] paragraph [0059] - paragraph [0060] paragraph [0061] paragraph [0062] paragraph [0068] paragraph [0070] ----- -/--	1-23

[X] Further documents are listed in the continuation of Box C.

[X] See patent family annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
29 January 2016	05/02/2016

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

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Form PCT/ISA/210 (second sheet) (April 2005)

INTERNATIONAL SEARCH REPORT

International application No
PCT/IB2015/058802

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 2011/112863 A1 (QUATRO VASCULAR PE LTD [SG]; KONSTANTINO EITAN [US]; FELD TANHUM [IL]) 15 September 2011 (2011-09-15) figures 2A, 2B1, 2B2, 3A-5B paragraph [0013] paragraph [0025] - paragraph [0026] paragraph [0027] - paragraph [0029] paragraph [0035] - paragraph [0036] -----	1-23
X	WO 2013/119735 A1 (FELD TANHUM [IL]; KONSTANTINO EITAN [US]) 15 August 2013 (2013-08-15)	1,6,7, 13,17
A	figures 1, 2 paragraph [0014] paragraph [0015] paragraph [0018] -----	2-5, 8-12, 14-16, 18-23
A	US 2006/271093 A1 (HOLMAN THOMAS J [US] ET AL) 30 November 2006 (2006-11-30) cited in the application paragraph [0080] -----	1-23

1

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/IB2015/058802

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(19)中华人民共和国国家知识产权局

(12)发明专利申请

(10)申请公布号 CN 107106822 A
(43)申请公布日 2017.08.29

(21)申请号 201580062444.0

(22)申请日 2015.11.13

(30)优先权数据
62/080,831 2014.11.17 US

(85)PCT国际申请进入国家阶段日
2017.05.17

(86)PCT国际申请的申请数据
PCT/IB2015/058802 2015.11.13

(87)PCT国际申请的公布数据
WO2016/079649 EN 2016.05.26

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代理人 程纾孟

(51)Int.Cl.
A61M 25/10(2013.01)

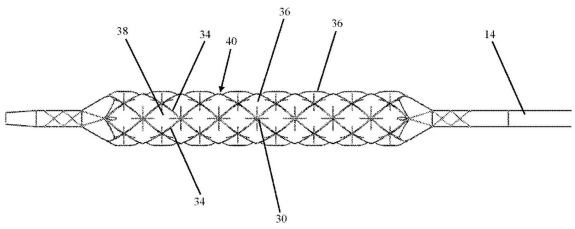
权利要求书1页 说明书9页 附图8页

(54)发明名称

气囊导管系统

(57)摘要

提供了一种用于使狭窄管扩张的系统(10)。所述系统包括安装在导管轴(12)上的气囊(20),所述气囊由第一材料组成,以及形成附接至气囊的表面或集成在其壁内的网格(30)的纤维(34)。所述纤维由具有比第一材料低的弹性的第二材料组成,使得当将气囊充气超过预定压力时,气囊区域从由纤维形成的网格中突出(36)。



CN 107106822 A

1.一种用于将狭窄管扩张的系统,所述系统包括:

(a)安装在导管轴上的气囊,所述气囊由第一材料组成;和

(b)形成附接至所述气囊的表面或集成在其壁内的网格的多条纤维,所述多条纤维由具有比所述第一材料低的弹性的第二材料组成,使得当将所述气囊充气超过预定压力时,多个气囊区域从由所述多条纤维形成的所述网格中突出。

2.权利要求1所述的系统,其中所述气囊由第一聚合物组成并且所述多条纤维由第二聚合物组成。

3.权利要求1所述的系统,其中所述多条纤维中的每一条的粗细选自10-750微米的范围。

4.权利要求1所述的系统,其中所述多条纤维中的每一条的粗细沿着它的长度变化。

5.权利要求1所述的系统,其中所述网格形成具有选自1-25mm^{2}的范围的面积的多个单元。

6.权利要求1所述的系统,其中所述网格通过粘合剂附接至所述气囊的表面。

7.权利要求1所述的系统,其中所述网格通过焊接附接至所述气囊的表面。

8.权利要求2所述的系统,其中所述多条纤维中的每一条的拉伸模量选自1-150GPa的范围,并且所述气囊的所述拉伸模量选自0.0002-0.0100GPa的范围。

9.权利要求2所述的系统,其中所述单元包括三角形和菱形单元。

10.权利要求2所述的系统,其中所述单元的导前角选自30-180度的范围。

11.权利要求1所述的系统,其中所述多条纤维中的每一条的线质量密度是1-100旦尼尔。

12.权利要求1所述的系统,其中所述多条纤维中的每一条的线质量密度是50旦尼尔。

13.权利要求1所述的系统,其中所述网格图案由在所述气囊周围以顺时针方向螺旋卷绕的N条纤维和在所述气囊周围以逆时针方向螺旋卷绕的N条纤维形成。

14.权利要求12所述的系统,其中N选自4-16的范围。

15.权利要求12所述的系统,其中N是4。

16.权利要求1所述的系统,其中所述预定压力是至少2大气压。

17.权利要求1所述的系统,其中所述多个孤立的气囊区域从所述表面突出至少0.1mm。

18.权利要求1所述的系统,其中所述网格夹在所述气囊和材料层之间。

19.权利要求1所述的系统,其中所述多条纤维中的每一条是单丝纤维。

20.权利要求1所述的系统,其中所述多条纤维中的每一条是复丝纤维。

21.权利要求1所述的系统,其中所述多条纤维中的每一条由聚丙烯、PLLA、PEEK、凯夫拉尔、和/或超高分子量聚乙烯组成。

22.权利要求1所述的系统,其中所述气囊和/或所述多条纤维涂布有含药物的配制物。

23.权利要求21所述的系统,其中所述药物是抗增殖药物。

气囊导管系统

[0001] 对任何优先权申请的援引加入

[0002] 本申请根据35U.S.C.§119(e)要求2014年11月17日提交的美国临时申请号61/080,831的优先权权益,其全部内容通过引用结合在本文中。

[0003] 背景

[0004] 领域

[0005] 本公开涉及用于处理生物管的气囊导管系统和方法,并且更具体地,涉及血管成形术气囊导管,其包括附接至气囊壁或集成在气囊壁内的纤维的网格。纤维比气囊材料弹性低,以使得当将气囊充气超过预定压力时,多个气囊区域从由纤维形成的网格中突出。

[0006] 相关领域描述

[0007] 经皮腔内血管成形术(percutaneous transluminal angioplasty,PTA)是其中将气囊导管通过动脉插入并且引导至腔狭窄化(lumen narrowing)的区域的手术。将气囊充气以迫使斑块物质(通常是脂肪和钙)紧靠动脉壁以打开管腔并且改善血液流动。

[0008] 血管成形术气囊当被充气时通常为圆柱形并且具有不同的长度和直径以适应不同的管尺寸。气囊在通常8-20大气压之间的高压下被充气,从而克服斑块的阻力并且实现腔膨胀。

[0009] 标准气囊(也被称为普通气囊)是用于血管中病变的扩张(血管成形术)的最常用的技术;然而,标准气囊遭遇若干缺点。

[0010] 因为动脉的狭窄区域的直径和组成通常是不均匀的,管中标准气囊的膨胀导致非均匀(轴向和径向)膨胀。病变组成的变化性(病变可以由硬和软的斑块物质的混合物组成)将会导致对沿着病变的扩张的阻力的变化性,并且导致在管的最小阻力区域中气囊过度膨胀。作为结果,标准气囊可以向病变的较低阻力的区域施加过度的力,因此对管壁造成创伤(例如,夹层(dissection)),并且不能向有阻力的斑块区域施加足够的力以实现其有效的扩张。

[0011] 对管壁的创伤伴随着不良的长期临床结果,并且可以加速或引发被处理的区域中的再狭窄症(restenosis)。此外,大多数夹层,如限流夹层,需要支架植入(stenting),使程序进一步复杂化。

[0012] 通过经由位于气囊表面上的切割或划擦元件(刀片/线)增加在有阻力的斑块区域上的力来解决标准气囊导管的前述限制的尝试(例如,美国公布号20040143287和美国公布号20060085025)或多或少是成功的,但是未充分解决由非均匀气囊膨胀引起的问题。此外,切割和划刻气囊不是被设计为避免对管壁造成创伤,而是被设计为通过引发受控制的和可预测的夹层来控制对管壁的创伤。

[0013] 因此,需要能够在不对较低阻力的斑块区域中的管壁造成创伤的情况下有效打开有阻力的斑块区域的高压血管成形术气囊导管。

[0014] 概述

[0015] 根据本公开的一个方面,提供一种使狭窄管扩张的系统,所述系统包括:(a)安装在导管轴上的气囊,所述气囊由第一材料组成;和(b)形成附接至气囊的表面或集成在其壁

内的网格的多条纤维，所述多条纤维由具有比第一材料低的弹性的第二材料组成，使得当将所述气囊充气超过预定压力时，多个气囊区域从由多条纤维形成的网格中突出。

[0016] 根据以下所述的本公开的另外的特征，气囊由第一聚合物组成并且多条纤维由第二聚合物组成。

[0017] 根据在所描述的实施方案中的又一些特征，多条纤维中的每一条的粗细选自10-750微米的范围。

[0018] 根据在所描述的实施方案中的又一些特征，多条纤维中的每一条的粗细沿着它的长度变化。

[0019] 根据在所描述的实施方案中的又一些特征，网格形成具有选自1-25mm^{2}的范围的面积的多个单元。

[0020] 根据在所描述的实施方案中的又一些特征，网格通过粘合剂附接至气囊的表面。

[0021] 根据在所描述的实施方案中的又一些特征，网格通过焊接附接至气囊的表面。

[0022] 根据在所描述的实施方案中的又一些特征，多条纤维中的每一条的拉伸模量选自1-150GPa的范围，并且气囊的拉伸模量选自0.0002-0.0100GPa的范围。

[0023] 根据在所描述的实施方案中的又一些特征，单元包括三角形或菱形单元或二者。

[0024] 根据在所描述的实施方案中的又一些特征，单元的导前角选自30-180度的范围。

[0025] 根据在所描述的实施方案中的又一些特征，多条纤维中的每一条的线质量密度是1-100旦尼尔。

[0026] 根据在所描述的实施方案中的又一些特征，多条纤维中的每一条的线质量密度是50旦尼尔。

[0027] 根据在所描述的实施方案中的又一些特征，网格图案由在气囊周围以顺时针方向螺旋卷绕的N条纤维和在气囊周围以逆时针方向螺旋卷绕的N条纤维形成。气囊可以任选包括L条纵向纤维，其中L可以是2以上。

[0028] 根据在所描述的实施方案中的又一些特征，N选自4-16的范围。

[0029] 根据在所描述的实施方案中的又一些特征，N是4。

[0030] 根据在所描述的实施方案中的又一些特征，预定压力是至少2大气压。

[0031] 根据在所描述的实施方案中的又一些特征，当将气囊充气至它的工作压力(例如，5-25ATM)时，多个孤立的气囊区域从表面中突出至少0.1mm。

[0032] 根据在所描述的实施方案中的又一些特征，网格夹在气囊和材料层之间。

[0033] 根据在所描述的实施方案中的又一些特征，多条纤维中的每一条是单丝纤维。

[0034] 根据在所描述的实施方案中的又一些特征，多条纤维中的每一条是复丝纤维。

[0035] 根据在所描述的实施方案中的又一些特征，多条纤维中的每一条由聚丙烯、PLLA、PEEK、芳纶(凯夫拉尔(Kevlar)®)、聚酯纤维(达可纶(Dacron)®)、芳族聚酯(高强度聚芳酯纤维(Vectran)®)、脂族聚酰胺(尼龙)和/或超高分子量聚乙烯组成。

[0036] 根据在所描述的实施方案中的又一些特征，气囊和/或多条纤维涂布有含药物的配制物。

[0037] 根据在所描述的实施方案中的又一些特征，药物是抗增殖药物。

[0038] 通过提供可以用于在不对管壁造成创伤的情况下打开狭窄管的气囊导管系统，本公开成功地解决了目前已知构造的缺点。

[0039] 除非另外定义，在本文中所使用的所有技术与科学术语具有与本公开所属领域的普通技术人员通常理解的相同的含义。尽管与在本文中所描述的那些类似或等同的方法和材料可以用于实施或测试本公开，下面描述适合的方法和材料。在相抵触的情况下，将会以专利说明书(包括定义)为准。此外，材料、方法、和实例仅是说明性的而且并非意图是限制性的。

[0040] 附图简述

[0041] 在本文中参照附图仅通过举例的方式描述本公开。现在详细地具体参照附图，要强调的是，所示出的细节是通过举例的方式并且仅用于本公开的实施方案的说明性讨论的目的，并且是为了提供据信是本公开的原理和概念方面的最有用和容易理解的说明而给出。就此而言，未尝试比基本理解本公开所需更详细地示出本公开的结构细节，随着附图进行说明，使得本领域技术人员理解如何能够在实践中实施本公开的若干形式。

[0042] 图1是包括本发明的气囊的导管的侧视图和导管的气囊部分的放大视图。

[0043] 图2是包括具有正方形开口的网格的充气气囊的等距视图。

[0044] 图3a是图2的气囊的侧视图。

[0045] 图3b和3c说明了泄气的气囊或充气至预定阈值(图3b)和充气超过阈值(图3c)的气囊的气囊表面和编织物。

[0046] 图4是包括具有菱形开口的网格的充气气囊的侧视图。

[0047] 图5是图示根据本公开的教导构建的气囊原型的纤维之间的重要的角度和距离的图像。

[0048] 图6a-6d说明了以6(图6b、6d)或10(图6a、6c)PPI编织的6X 40mm气囊，示出了气囊锥形末端(图6a、6b)和中心部(图6c、6d)。

[0049] 图7a-7d说明了以6(图7a、7c)或10(图7b、7d)PPI编织的5X 40mm气囊，示出了气囊锥形末端(图7a、7b)和中心部(图7c、7d)。

[0050] 图8是以菱形图案编织的气囊。

[0051] 图9是图8的气囊的靠近图。

[0052] 详细描述

[0053] 本公开涉及气囊导管系统，其即使在高充气压力下也能够向管壁施加均匀的压力，并且因此可以用于使身体管如动脉的狭窄区域扩张，而向所处理的管的所有部分施加均匀的膨胀力。

[0054] 可以参照附图和所附说明书更好地理解本公开的原理和操作。

[0055] 在详细解释本公开的至少一个实施方案之前，应该理解的是，本公开在其应用中不限于在以下描述中给出的或通过实施例例示出的细节。本公开能够具有其他实施方案或者能够以多种方式实施或进行。此外，应该理解的是，在本文中采用的措辞和术语是出于说明的目的并且不应被认为是限制。

[0056] 在之前提交的专利申请(2013年8月21日提交的美国公布号20140066960，其全部公开内容通过引用结合于此)中，公开内容描述了血管成形术气囊导管，其具有位于气囊之上的可膨胀约束结构。可膨胀约束结构不附接至气囊，但是由此膨胀，以约束气囊充气并且使得孤立的气囊区域能够在充气期间从约束结构中突出。这确保了气囊当充气时在管壁上施加均匀的力并且降低夹层和其他创伤的可能性。

[0057] 尽管实验已经显示美国公布号20140066960的气囊导管在使狭窄区域扩张和使对管壁的创伤最小化中非常有效，但由于其金属约束结构，其具有相当大的包装直径以及有限的柔韧性和通过曲折管的可操作性。

[0058] 为了跨越这些限制，本发明的发明人设计了一种气囊导管，其能够提供美国公布号20140066960的在高充气压力下的益处，容易制造并且可以高效率地包装以用于运输，同时具有通过曲折管的高度可操作性。如在下文中进一步描述的，通过附接至气囊壁或集成至气囊壁中并且被配置用于改变气囊表面的形状以在气囊充气时形成枕状突起的纤维网格提供了这样的益处。

[0059] 具有集成或附接的纤维网格的气囊是本领域中已知的(例如，美国公布号20060271093或美国公布号20050271844)。然而，这样的纤维网格用于在高充气压力下防止气囊过度充气并且增加气囊完整性，而不是用于改变充气气囊的形状以形成通过网格的枕状气囊突起。

[0060] 因此，根据本公开的一个方面，提供一种使狭窄管扩张的系统。如在本文中所使用的，术语管是指体内的任何中空导管并且包括引导生物液体的血管如动脉和静脉、淋巴管、胃肠道管(例如，肠)、导管和任何身体通道。如在下文中进一步描述的，本发明的系统的一个优选用途是在动脉如周围(例如，腿)动脉的血管成形术中。

[0061] 本发明的系统包括由第一材料(例如，第一聚合物)组成的安装在导管轴上的气囊，以及形成附接至气囊的表面或集成在其壁内的网格状图案的多条纤维。纤维由与第一材料相比优选更坚固并且较不可伸展的第二材料(例如，第二聚合物)组成。

[0062] 因此，气囊充气超过预定阈值压力(例如，高于3ATM)使得气囊材料拉伸得比纤维多，形成沿着气囊表面的在纤维被约束或固定处的通道以及在其之间的在气囊材料不受约束处的气囊突起。纤维的网格在整个充气期间维持气囊均匀性(轴向和径向)，使得突起(在本文中也被称为枕)能够均匀接触管壁和斑块物质，因此确保沿着被处理的管区域的均匀的力分布并且在使整个斑块区域有效扩张的同时使管创伤最小化。此外，因为由网格纤维形成的通道当将气囊充气时从管壁凹入，它们提供了应力消除区域并且进一步减少了创伤的可能性。

[0063] 为了使得能够形成突起并且控制突起高度、面积和形状，人们必须仔细选择气囊和纤维材料、纤维的强度和直径以及由此形成的网格的形状。

[0064] 基于所需柔度(在本文中被定义为弹性或拉伸模量)和耐断裂性(强度)选择气囊材料。基于强度和弹性选择纤维。

[0065] 导管轴可以是任何适合在所需手术中使用的构造。例如，在血管成形术手术中，导管可以被配置用于在线上方(over-the-wire)或快速交换运输(rapid exchange delivery)，并且可以在其近端包括适用于线插入、充气等的连接器。导管轴可以是适用于周围、冠状、或脑血管的血管成形术的任何长度和直径。气囊的适合的长度(L)和直径(D)可以在约4-40mm L、1.25-5mm D(对于冠状血管应用来说)和20-300mm L、2-12(以上)mm D(对于周围血管来说)的范围内。

[0066] 气囊可以是以选自约5-300mm的长度和约2-12(以上)mm的直径的范围的尺寸由聚酰胺、派伯克斯(Pebax)、聚氨酯、聚对苯二甲酸乙二醇酯、或相似材料等制造的柔性或半柔性气囊。气囊可以是圆柱形或本领域中已知的任何其他形状。例如，当在血管成形术中使用

时，气囊的形状可以是具有长度为5-300mm并且直径为2-12mm的锥形末端的大致圆柱形，锥部通常与气囊直径相比相似或略短。气囊材料的弹性可以在0.0002至0.0100GPa之间。

[0067] 网格可以通过由适用于这样的目的的任何材料纺织或编织的单丝或复丝纤维(具有相同或不同的丝)形成。纤维粗细可以是10-750微米，如在径向方向上，具有在整个纤维长度内(在整个气囊内)均匀的或可变化的粗细。例如，纤维可以在气囊锥部或腿部较粗并且在工作长度处较细。

[0068] 纤维可以由各种聚合物(如聚氨酯、聚酰胺、聚乙烯或其他)或金属(如镍钛诺(Nitinol)或钴铬合金或其他)或其复合材料、其他适合的材料制成。具体和优选的实例包括超高分子量聚乙烯、聚偏二氟乙烯、和聚对苯二甲酸乙二醇酯。用于纤维的目前优选的材料是超高分子量聚乙烯。

[0069] 复丝纤维通常以旦尼尔的单位测量，其为纤维的线质量密度的度量单位。纤维的线质量密度可以是10-100旦尼尔，优选50旦尼尔。

[0070] 纤维的弹性可以在0.1-500GPa的范围内，优选100GPa。

[0071] 纤维的编织物密度(braid density)也是重要的并且由每英寸纬数(picks per inch，PPI)、即每英寸气囊长度的纤维交叉的数量确定，高PPI与高破裂压力有关。用于制造本发明的系统的网格的PPI优选在2-20、更优选6-14的范围内。

[0072] 多种方法可以用于制造本发明的系统。在气囊在0.3-20ATM(优选0.3-8ATM，更优选0.3-2ATM)的压力下是充气或半充气形式时，组装本发明的系统。所使用的充气压力设定气囊材料拉伸的程度，其进而确定气囊的被约束区段的外径和完全充气气囊的孤立的气囊区域的最大突起高度。

[0073] 当未将气囊充气(或充气至低于阈值的压力)时，纤维编织物从气囊的表面突出(图3b)或者随气囊表面形成(当夹在气囊壁材料的两层之间时)，以使得气囊壁不超出纤维编织物向外径向延伸。当充气至高于阈值压力的压力时，孤立的气囊区域从编织物开口中突出至被定义为编织物纤维的表面和孤立的气囊区域的最外表面之间的距离的高度(箭头，图3c)。在标称充气工作压力下，这样的高度可以是至少约0.1mm，并且在一些实施中至少约0.1或0.2以上。通常，高度将会在约0.01-1mm或0.1-0.5mm的范围内。

[0074] 在3mm气囊(其能够利用过度充气达到大于3mm的直径)中，纤维的组装在充气至直径约3mm的气囊上进行。当将组装的气囊在管内部充气时，孤立的气囊区域的突起将会在该直径形成，并且将会随着充气而高度逐渐增加。在直径为3.5mm时，从气囊表面中突出的孤立的气囊区域的高度将会开始为3.5mm并且随着充气而高度逐渐增加，通常增加的高度增加至约0.01-0.5mm。

[0075] 纤维优选沿着每条纤维的整个长度附接至气囊表面。使用施加至纤维的粘合剂或者通过将纤维夹在施加至气囊表面的两个粘合层(基底层和覆盖层)之间来进行附接。可以通过浸渍、喷雾、或本领域中已知的任何其他方法施加这些层。气囊壁的基底层可以是允许纤维的固定但是保持下面的气囊基底的柔韧性的任何柔性粘合层，而覆盖层进一步固定网格，保护其免受管壁和斑块影响并且增强血管壁抓持(gripping)。

[0076] 当本发明的气囊导管用于对支架内再狭窄症(in-stent restenosis)扩张时，光滑的覆盖层是尤其有利的。本发明的气囊的覆盖层防止“支架拘禁(stent jailing)”——一种例如切割/划擦气囊的支柱被捕获在支架支柱内的现象。

[0077] 为了在整个充气期间维持在气囊上的纤维位置，并且因此维持孤立的气囊区域的形状和尺寸，纤维至气囊表面的附接或部分附接可以是理想的。如果纤维自由移动，则不能维持气囊突起的均匀性，并且因此均匀的管扩张将是不可能的。在气囊锥部上，特定网格形状的纤维的固定也是非常重要的，在那里游离的线将会倾向于更容易从其预期位置滑动，再一次导致突起不均匀。

[0078] 根据由PPI所定义的，在整个气囊工作长度内以导前角(lead angle)编织纤维。角度可以从30-180度变化。在一个实施方案中，每个孤立的气囊区域(在通道之间突出)被彼此成大约90度角的四条交叉纤维包围。因为导前角对于所有纤维来说是恒定并且相等的，纤维之间所形成的孤立的气囊区域是正方形/矩形。在这种构造下，放置纤维以抵抗由气囊中累积的压力施加在其上的张力。

[0079] 在以上实例中，纵向和径向编织纤维，然而，本发明的网格还可以通过在气囊的整个工作长度和锥部内螺旋编织纤维而形成。

[0080] 在将纤维网格夹在基底层和覆盖层之间后，可以将任选的顶层施加至气囊。该顶层降低了气囊的粘性并且提高其通过曲折解剖结构前进和在管位置内充气的能力。顶层可以由聚对二甲苯或本领域中通常已知的任何其他材料组成。

[0081] 备选地，在将纤维网格夹在基底层和覆盖层之间后，可以用涂层涂布气囊。这种涂层可以是亲水材料或疏水材料。涂层降低了气囊的粘性并且提高其通过曲折解剖结构前进和在管位置内充气的能力。顶层可以由有机硅、聚氨酯、聚乙烯吡咯烷酮、透明质酸、或本领域中通常已知的任何其他材料组成。

[0082] 当组装时，可以以本领域中已知的常规折叠技术折叠气囊。可以将气囊折叠为2-8个褶，并且像对普通气囊所做的那样，褶包裹在气囊轴周围。纤维足够软以允许这样的折叠。

[0083] 在下文中描述了制造过程的一个具体实施方案：

[0084] (i)将气囊充气，优选充气至0.3-2ATM。

[0085] (ii)通过喷雾、浸渍、或涂抹将聚氨酯粘合剂施加至气囊的基底层。

[0086] (iii)将粘合剂基底层固化并且在气囊表面上编织纤维。以6-14的在工作长度内的PPI范围在腿部、锥部、和工作长度上使用可变节距工艺。

[0087] (iv)在编织的网格上施加聚氨酯粘合剂的覆盖层以将纤维固定在适当位置并且确保连续纤维涂层以使纤维和斑块物质之间的相互作用最小化。

[0088] (v)将粘合剂覆盖层固化并且将任选的外层施加至气囊以使粘性最小化并且改善向管位置的运输。

[0089] 图1-4说明了本发明的气囊系统的一个实施方案，其在本文中被称为系统10。系统10被配置用于在血管成形术手术中使用。

[0090] 系统10包括导管轴12，其由聚合物挤出制造并且包括在轴12的长度延伸的纵向腔。第一腔可以容纳引导线，而第二腔可以充当安装在轴12的远端部14的用于气囊20的充气导管。轴12的近端部16包括具有(分别)与第二和第一腔通讯的专用端口22和24的连接器18。

[0091] 对于冠状血管应用来说，气囊20直径可以在1.25至5.0mm之间并且长度可以在4至40mm之间(当如在图2中所示充气时)。对于周围血管应用来说，气囊20直径可以在2至12mm

之间并且长度可以在5至300mm之间。较长的气囊可以沿着其长度逐渐变细(径向)。气囊20的壁厚度可以从1-250μm变化(取决于材料和特定特征可变)。气囊壁厚度可以是均匀的或可变的。

[0092] 气囊20使用在本领域内公知的方法(例如,胶粘或焊接)与轴12的远端部14连接。网格30集成或胶粘至如上所述的气囊20的壁32中或上。网格30由两条以上纤维34(在图2中所示的五条径向纤维35和四条轴向纤维37)形成,其在包括工作长度(WL)、腿部(LG)和锥部(TP)在内的气囊20的整个长度内编织/纺织。

[0093] 如在图2中所示,当将气囊20充气至标称压力(例如,6-20ATM)时,网格30使得孤立的气囊区域36能够通过在纤维34之间形成的开口38突出并且在气囊表面中形成通道40。取决于包括气囊和纤维材料、网格形状和密度等在内的在气囊20和网格30的构建中的多种变量,孤立的气囊区域36可以从气囊表面中突出0.01-0.5mm。网格30可以包括横穿许多轴向纤维部分的许多圆周纤维部分。通常,可以存在约3至约20个圆周纤维部分,如约4至约10个圆周纤维部分,以及约3至约10个轴向纤维部分,如约3至约5个轴向纤维部分。在一些实施中,可以存在约10至约20个孤立的气囊区域,如约12至约18个气囊区域或约14至约16个气囊区域。

[0094] 如在本文中提及的,孤立的气囊区域36接触管中的斑块并且向其施加均匀的力,同时通道40(其从斑块凹入)起应力消除区域的作用。

[0095] 可以根据其长度和直径在气囊20周围放置四至七十二个纤维。纤维34可以以任何形式放下,只要由此形成的网格包括大致相同面积和形状的开口38即可。例如,纤维34可以纵向(轴向)和径向放下以形成正方形或矩形开口38(如在图2-3中所示),或者纤维34可以顺时针和逆时针螺旋卷绕以形成如在图4(其图示了由螺旋卷绕的纤维34形成的网格30)中所示的菱形开口38。还可以通过提供轴向纤维以限制气囊伸长并且形成三角形开口38(图5)来使用这两种方法的组合。

[0096] 纤维34的数量与形成网格的编织物的密度和开口38(形成孤立的气囊区域36)的区域的数量相关。

[0097] 在图6a-d中所示的本公开的一个实施方案中,长度为40mm并且直径为6.0mm的气囊20包括由8条纤维34(4条纵向纤维34和4条径向卷绕的纤维34)形成的编织网格30。当充气时,这种编织图案形成三角形和六边形的孤立的气囊区域3。

[0098] 在图8-9中所示的另一个实施方案中,气囊20可以包括螺旋(H)+纵向(L)纤维34(其中H纤维的数量大于L纤维的数量),并且L纤维纵向设置在气囊周围,H/2纤维34顺时针螺旋包裹并且H/2纤维34逆时针螺旋包裹。这得到了形成在气囊20圆周周围孤立的气囊区域36通过其突出的三角形和六边形开口38的网格30。

[0099] 孤立的气囊区域36的总数量取决于气囊长度:在图3a的实例中,孤立的气囊区域36由具有3×π/4=2.35mm的对角线长度的正方形限定。作为结果,气囊20长度的每2.35mm将会包括2×4=8个孤立的气囊区域36。3×20mm的气囊因此将会包括8×20/2.35=68个孤立的气囊区域36。

[0100] 网格30在气囊20的工作长度(WL)、腿部(LG)、和锥部(TP)内优选具有可变节距(纤维34角度)(图2)。这样的变化可以适应气囊20直径在其长度内的变化(例如,锥部膨胀得比在工作长度内小)或者可以改变气囊区域的局部柔度(例如,使锥部区域变得较不柔性)。

[0101] 系统10可以在如下血管成形术中使用。可以使用公知的血管成形术方法将系统10引导至在引导线(未示出)上的狭窄区域。一旦在适当位置,就可以将气囊20充气至形成其通道40和孤立的气囊区域36的程度,以向在孤立的气囊区域36的斑块和在通道40的应力消除区域施加向外的径向力。一旦将区域充分扩张,即将气囊20泄气并且从身体中移除系统10。

[0102] 因此,本公开提供了气囊系统,其保护管壁免受不均匀膨胀的影响,并且实现了向有阻力的特定病变区域如高度钙化的阻碍膨胀的斑块区域提供局部较高压力。

[0103] 系统10的气囊20和/或网格30可以使用在本领域内公知的方法涂布有亲水或疏水涂层以提高润滑性或者涂布有含有例如抗增殖药物如西罗莫司(sirolimus)或紫杉醇(paclitaxel)的药物组合物。

[0104] 如在本文中所使用的术语“约”是指±10%。

[0105] 在检查并非意欲限制的以下实施例时,对于在本领域中普通技术人员来说,本公开的另外的目的、优点、和新的特征将会变得显而易见。

实施例

[0106] 现在参照以下实施例,连同以上描述,以非限制性方式对本公开进行说明。

[0107] 编织气囊的工作台测试

[0108] 根据本公开的教导构建多种原型气囊并且根据以下所述进行测试。

[0109] 简而言之,通过吹塑成型制造尼龙气囊并且将气囊预充气至0.3atm。在聚氨酯粘合剂中浸涂气囊并且在气囊表面上以菱形图案编织超高分子量聚乙烯复丝纤维。之后在第二层聚氨酯粘合剂中浸涂气囊,接着在聚对二甲苯中浸涂。图8和9图示了具有菱形编织图案的充气气囊原型。将气囊干燥并且折叠以确定折叠直径。

[0110] 构建了五种类型的气囊,在6、10两种PPI密度(图6a-6d)下的6mm(充气直径)X40mm(充气长度)气囊以及在6、10和14三种PPI密度(图7-7d,PPI 14未示出)下的5mm X 40mm气囊。

[0111] 针对每种气囊类型测试以下参数:

[0112] (i)柔度——作为压力的函数的气囊直径;

[0113] (ii)破裂压力——气囊材料失效的压力的测量;

[0114] (iii)疲劳——在气囊材料失效之前的重复充气-泄气循环的次数的测量;和

[0115] (iv)外形——折叠气囊的直径的测量。

[0116] 以下表1总结了关于5种测试的气囊的结果。

[0117] 表1

[0118]

尺寸	PPI	枕高度	破裂(atm)	Dia @ 8atm (mm)	Dia @ 8atm (mm)	α	b	c	d

[0119]

		8atm (mm)	12atm (mm)	仅气囊	编织气囊	仅气囊	编织气囊	仅气囊	编织气囊	(度)	(mm)	(mm)	(mm)
6.0x40	6	N/A	N/A	16.40	24.25±0.07	6.70	6.40±0.00	7.10	6.65±0.07	125.5	4.3	2.6	2.3
6.0x40	10	0.18	0.26		27.60±4.10		6.30±0.10		6.47±0.06	142	4.2	1.7	1.9
5.0x40	6	0.31	0.41	17.2	24.65±0.78	5.70	5.43±0.15	6.20	5.67±0.21	125.5	3.85	2.5	2.2
5.0x40	10	0.29	0.39		29.75±2.19		5.33±0.15		5.47±0.06	141	3.65	1.4	2.4
5.0x40	14	0.16	0.26		41.20±2.83		5.10		5.20	N/A	N/A	N/A	N/A

[0120] a-d在图5中示出并且表示以下：

[0121] a-(α)是如在图中标记的纤维的交叉角

[0122] b-是纵向纤维之间的距离

[0123] c-是如在图中标记的纵向纤维的长度

[0124] d-是如在图中标记的距离

[0125] 应理解的是，在单独的实施方案的上下文中为了清楚而描述的本公开的某些特征也可以在单个实施方案中以组合形式提供。反之，在单个实施方案的上下文中为了简洁而描述的本公开的多个特征也可以单独或以任何适合的子组合形式提供。

[0126] 尽管本公开已经结合其具体实施方案进行描述，明显的是，许多备选方案、修改、和变化对本领域技术人员来说将会是显而易见的。因此，意在包括落在所附权利要求的精神和广义范围内的所有这样的备选方案、修改、和变化。在本说明书中提及的所有出版物、专利、和专利申请在本文中通过引用整体结合在说明书中，其程度如同各个单独的出版物、专利或专利申请被具体地且单独地指示为通过引用结合在本文中一样。此外，在本申请中的任何参考文献的引用或确定不应被解释为认可这样的参考文献可作为本公开的现有技术获得。

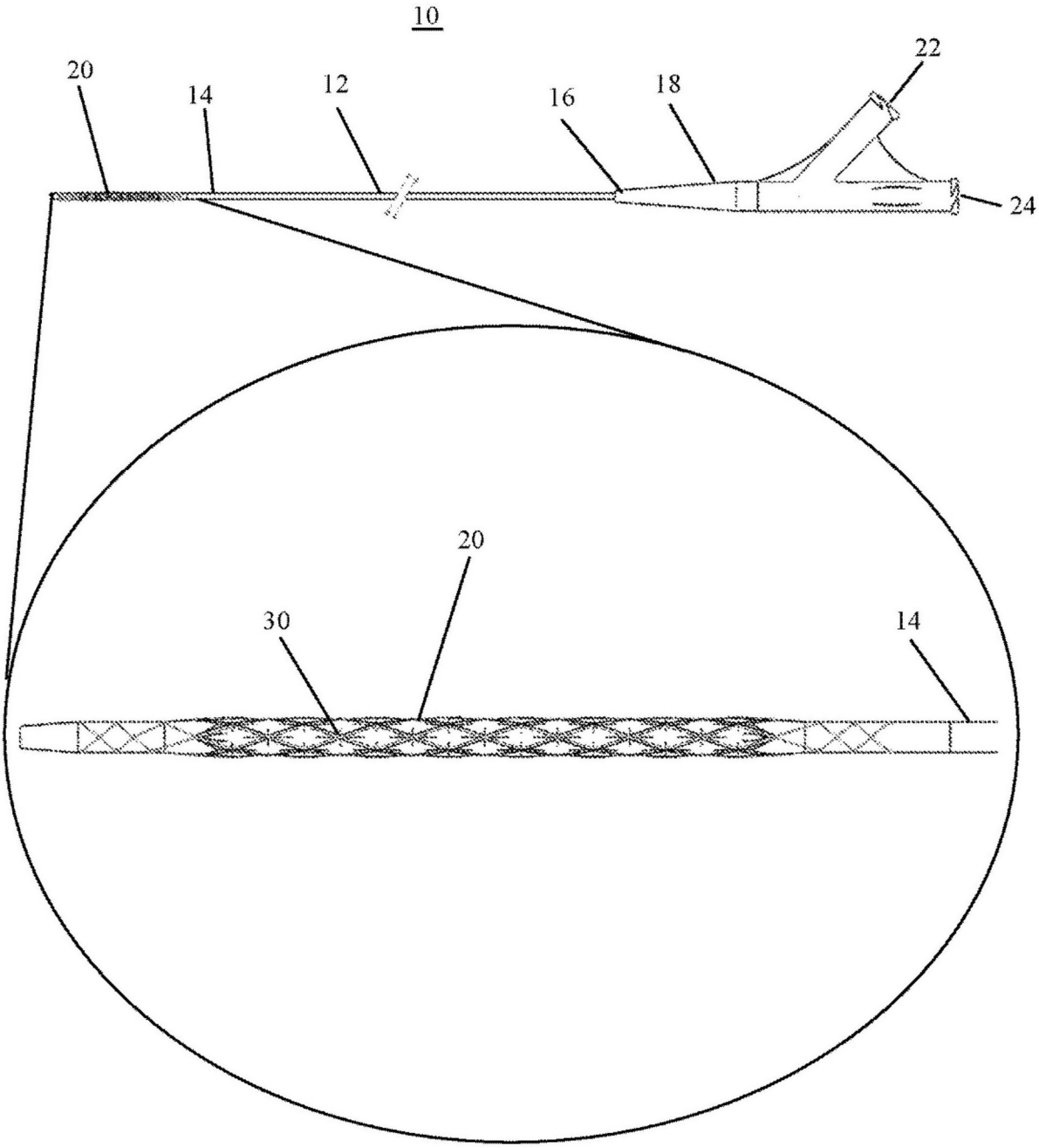


图1

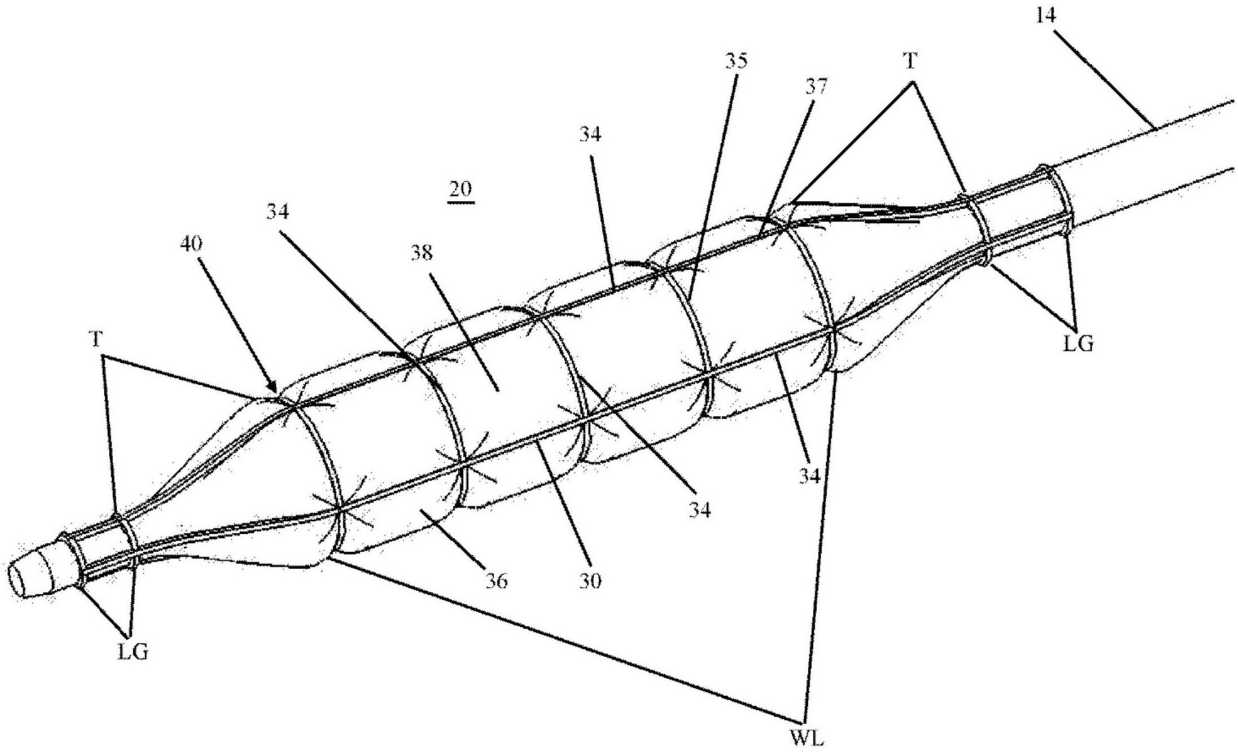


图2

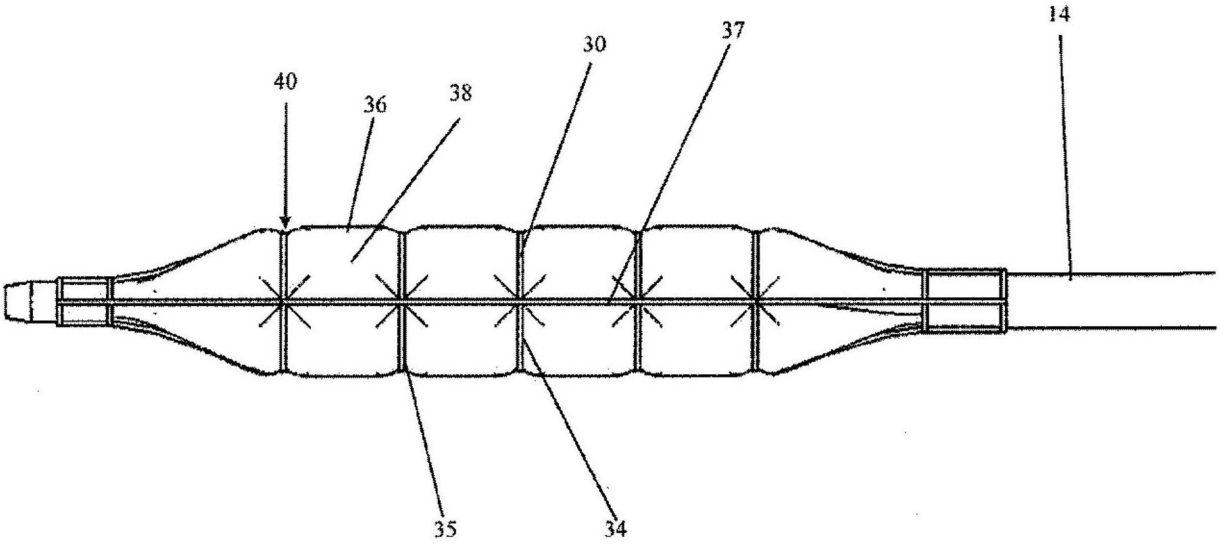


图3a

图3b

图3c

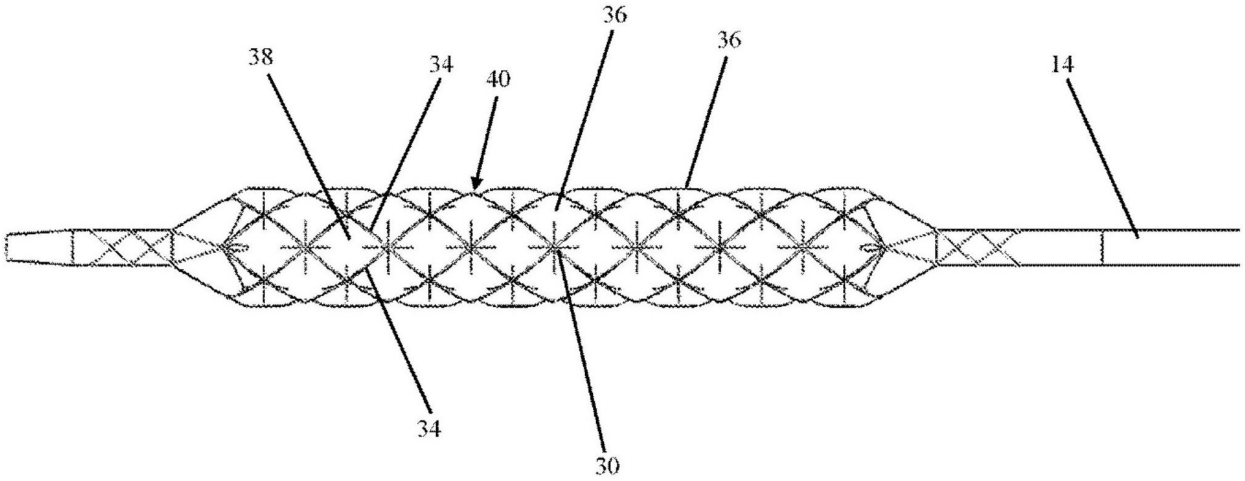


图4

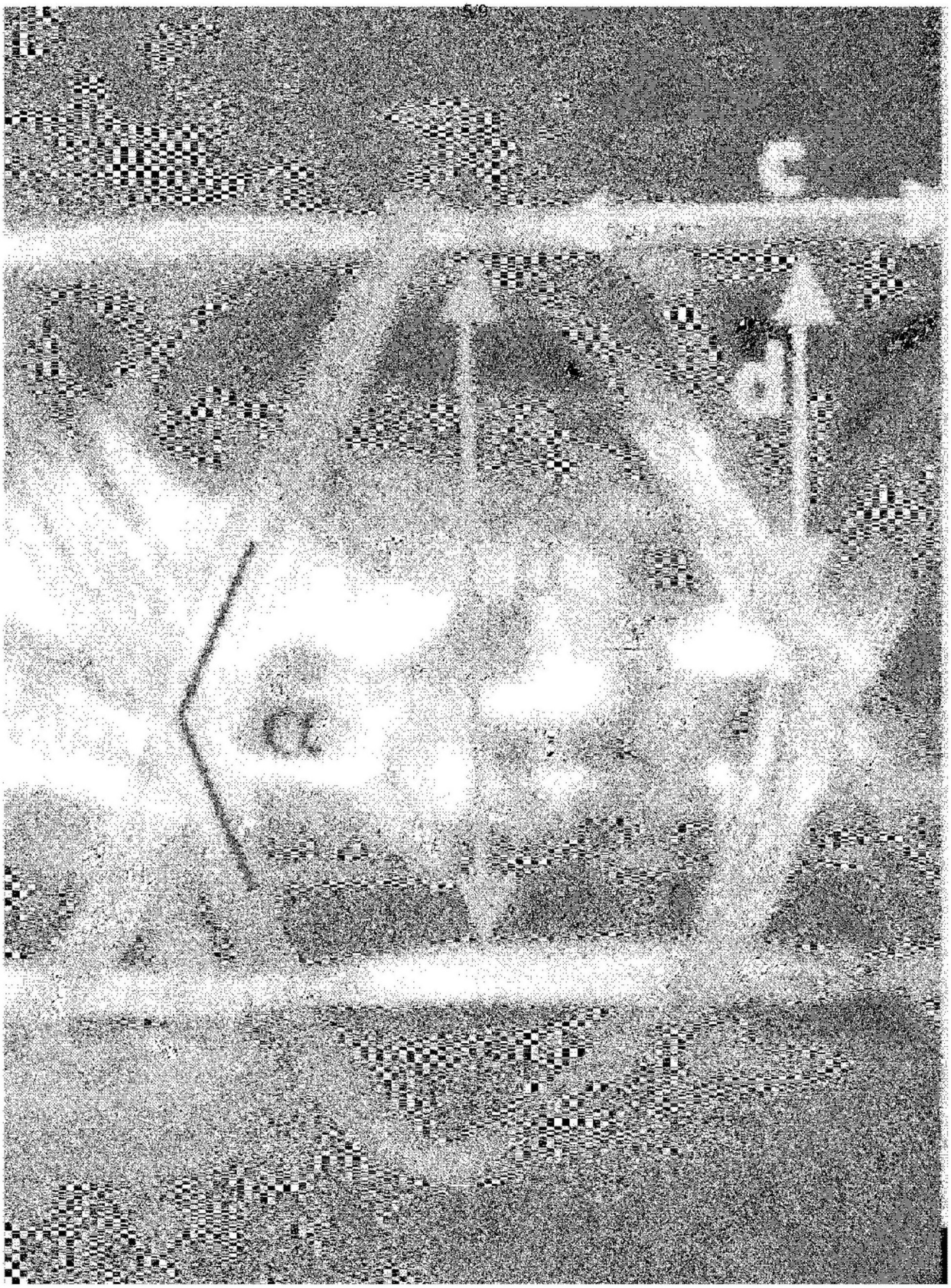


图5

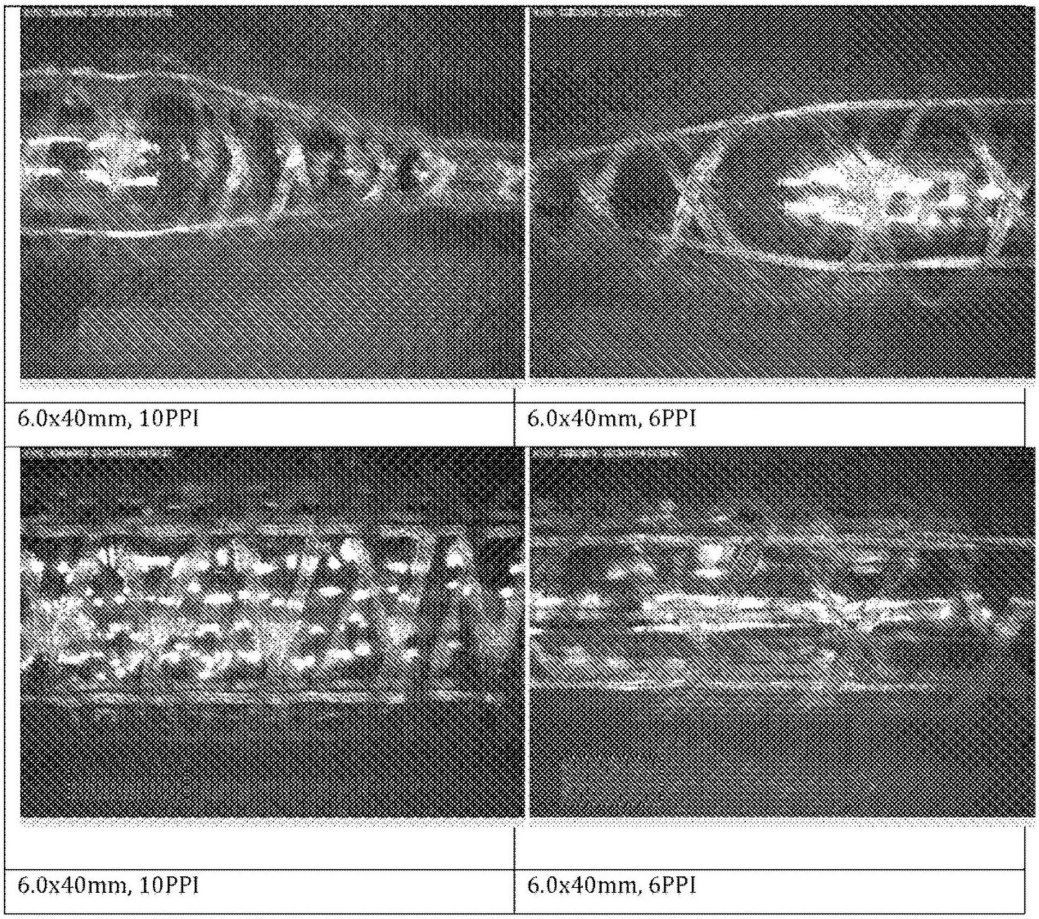


图 6a 图 6b

图 6c 图 6d

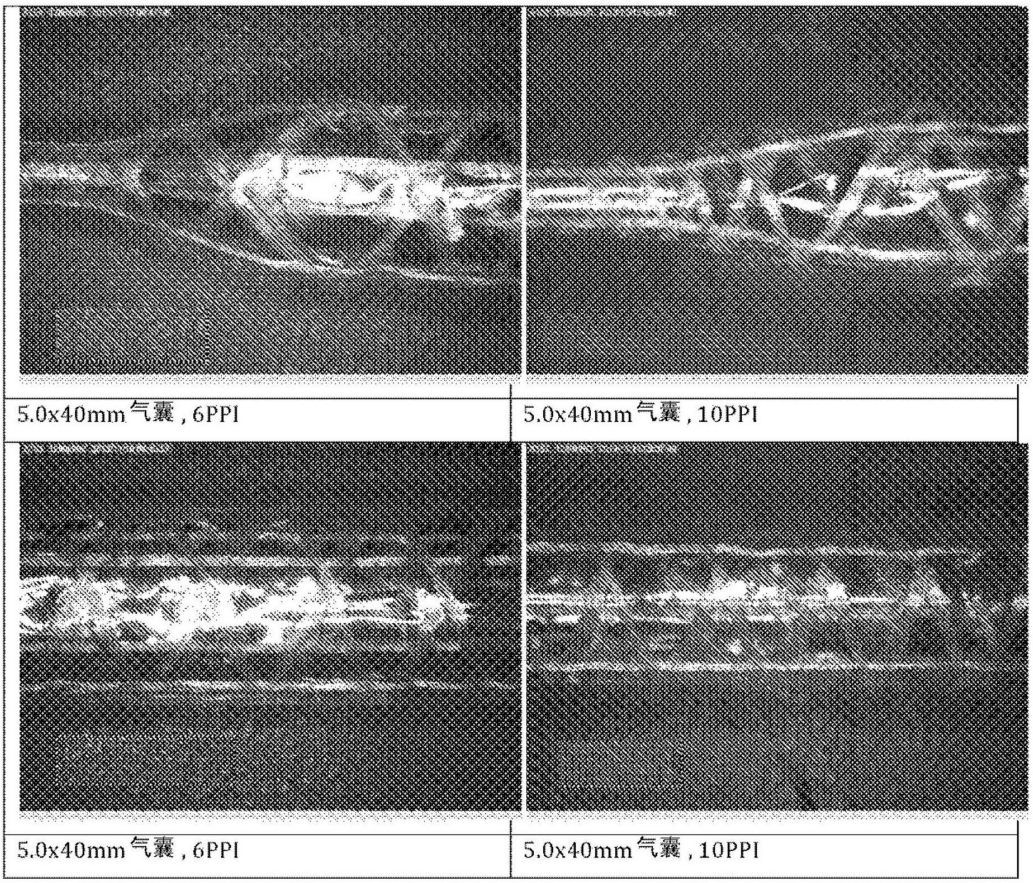


图 7a 图 7b

图 7c 图 7d

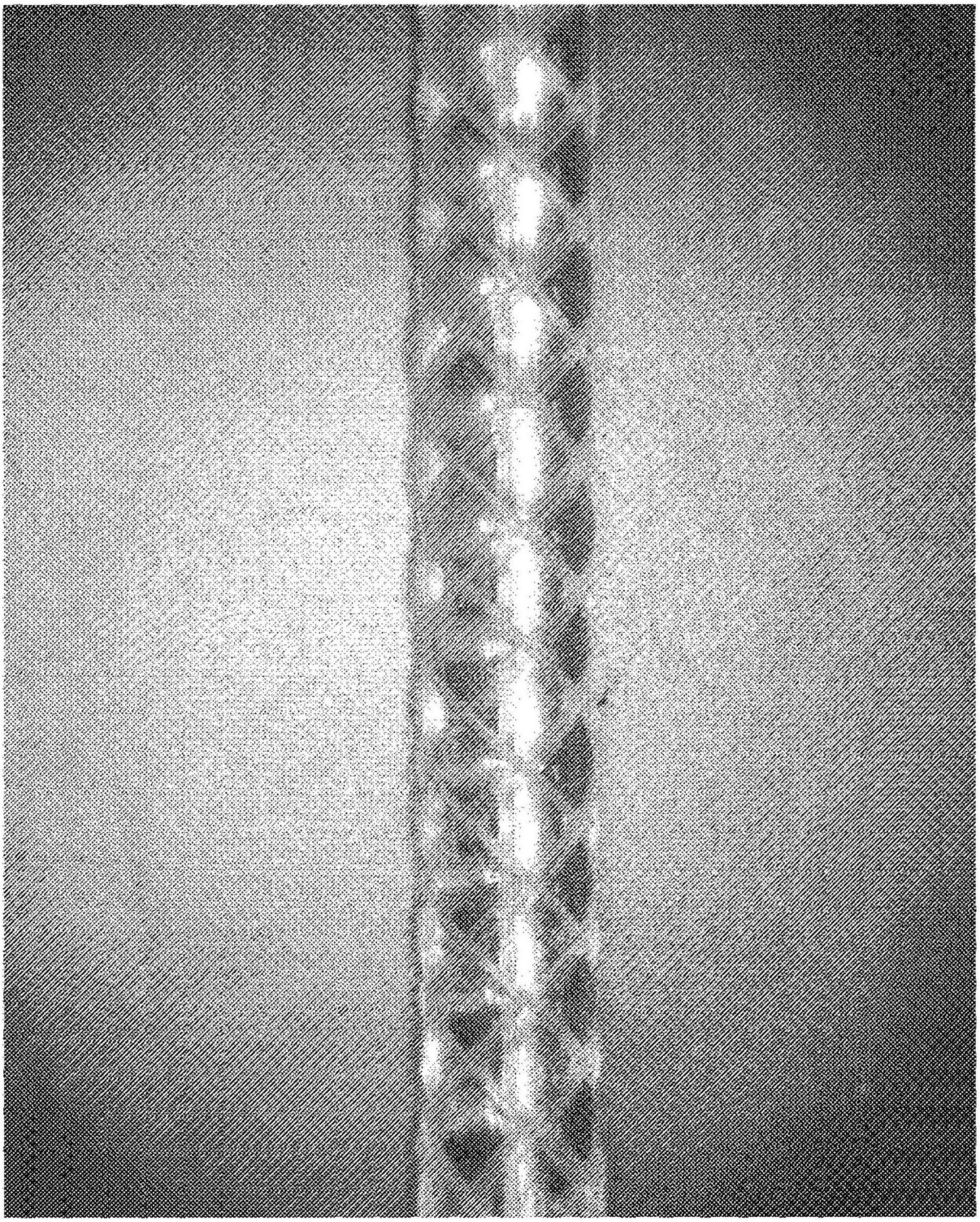


图8

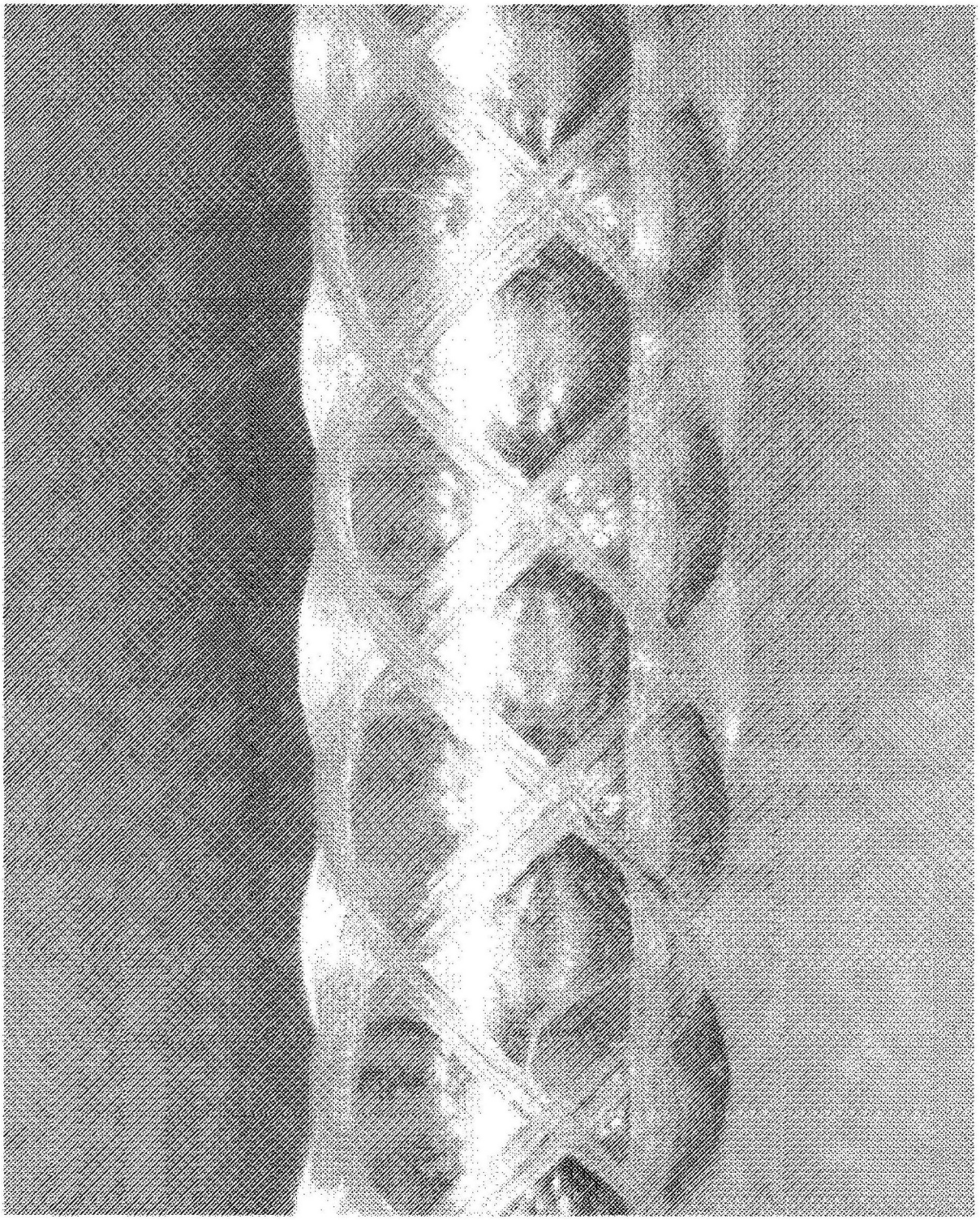


图9