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

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
03 February 2022 (03.02.2022)

WIPO | PCT

(10) International Publication Number
WO 2022/024117 A1

(51) International Patent Classification:
A61M 25/00 (2006.01) *A61B 17/12* (2006.01)
A61M 25/01 (2006.01)

(21) International Application Number:
PCT/IL2021/050904

(22) International Filing Date:
27 July 2021 (27.07.2021)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
276416 30 July 2020 (30.07.2020) IL

(71) Applicant: **ACCURATE MEDICAL THERAPEUTICS LTD** [IL/IL]; 19 Eli Hurvitz Street, 7608802 Rehovot (IL).

(72) Inventors: **DAGAN, Tom**; 66 Erez Street, 8496500 Omer (IL). **ZIPORY, Yuval**; 40 Nahal Meyron Street, 7175472 Modiin (IL). **HARBATER, Osnat**; 42 Bilu Street, 4358142 Raanana (IL). **MILLER, Eran**; 546 Hateenea Street, 7680300 Moshav Beit Elazari (IL).

(74) Agent: **FRIEDMAN, Nathalie** et al.; Fisher Friedman Ip Group, PO BOX 12352, 4673300 Hertzliya Pituach (IL).

(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DJ, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, IT, JO, JP, KE, KG, KH, KN, KP, KR, KW, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, WS, 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:
— *of inventorship (Rule 4.17(iv))*

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

(54) Title: EMBOLIZATION MICROCATHETER FOR DELIVERY OF LARGE BEADS

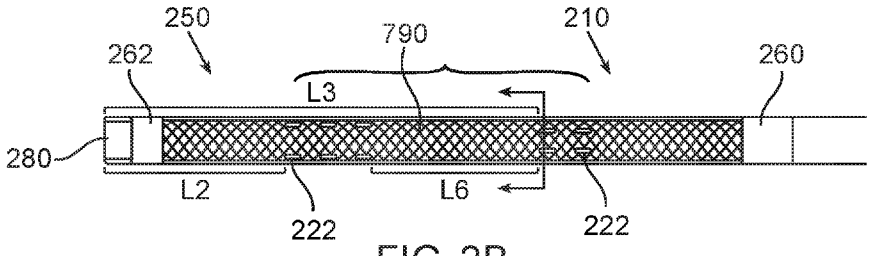

FIG. 2B

(57) Abstract: An embolization microcatheter with a wall including a braid, a polymer formed around the braid and an inner liner coating an inner surface of the wall, a radiopaque marker located in proximity to the distal end opening; wherein the part of the microcatheter extending between the proximal end of the radiopaque marker and the distal end opening is devoid of the liner and wherein the wall has a thickness of about 120 microns or less.

WO 2022/024117 A1

EMBOLIZATION MICROCATHETER FOR DELIVERY OF LARGE BEADS

TECHNICAL FIELD

The present disclosure generally relates to the field of microcatheters for embolization, specifically to large diameter embolization catheters suitable for delivery through standard delivery catheters.

BACKGROUND

Transarterial embolization therapy, tumor embolization, or transcatheter arterial embolization (TAE), involves administration of embolization material (which may include chemotherapeutics or/and radiotherapeutics) directly to a tumor (for example, liver tumors), via a microcatheter.

Embolization of tumors is typically performed utilizing microcatheters due to the requirement for selectively affecting the tumor while preventing, as much as possible, damage to healthy tissue. A major problem associated with embolization is "non-target embolization," where the embolic material travels to blood vessels, other than those directly feeding the target tumor or tumor region, thus damaging healthy tissues, resulting in unpleasant and even hazardous outcomes. Possible scenarios include gastric ulcers caused by liver embolization, as well as cases where embolic material refluxes alongside the microcatheter reaching the wall of the stomach, possibly causing ischemia and ulceration. An additional phenomenon, which is abundant especially in advanced stage liver cancer, is non-target embolization through arterioportal shunt.

A microcatheter is usually passed via a larger-lumen catheter, which is placed within the proximal part of the vessel, such as the celiac or hepatic artery, and the microcatheter is then advanced therethrough towards the tumor until reaching a target location. In some scenarios, it is advantageous to use a diagnostic catheter as the delivery medium for the microcatheter. This procedure withholds the need of replacing one catheter with another, thus saving substantial time.

Another reason that microcatheters are routinely used in embolization procedures is the size of the feeding vessels, which carry blood directly to the organ or tumor. In order to reach as close as possible to the tumor, the embolization catheter is advanced into smaller and sometimes

tortuous vessels. Accessibility to these vessels is difficult, if not precluded, with a larger and often stiffer catheter. Moreover, blood vessels in the body tend to go into spasm when manipulated, causing an ineffective embolic material delivery, so flexible micro-sized catheters are an absolute necessity.

A major drawback of trans-catheter embolization is that the embolization material, which is typically invisible, can be refluxed and reach non-target tissue and cause damage to them. In addition, reflux of embolization material may negatively affect the delivery of the embolization material to the target tissue, and thus impair treatment effectiveness and its clinical outcome.

Microcatheters with filter sections for delivery of embolization beads, while preventing backflow of the beads, have been disclosed by the inventors of the present applications. However, such catheters proved unsuitable for delivery of large embolization beads due to the beads clogging the microcatheter, while a simple enlarging of the outer diameter of the microcatheter makes them unsuitable for delivery through standard delivery catheters, such as 5.0 French delivery catheters.

SUMMARY OF THE INVENTION

The present disclosure relates to embolization microcatheters which are suitable for delivery through 5.0 French delivery catheters, while also facilitating delivery of large embolization beads, i.e. beads with a particle size of 900 microns or more.

This is advantageously achieved by the unique structure of the wall of the embolization microcatheters.

The wall is made of polymeric material(s) formed around a braid which provide structural integrity to the microcatheter (especially along the filter section thereof) as well as trackability. The wall also includes an inner liner, coating the inner surface of the wall, and configured to reduce the friction between the wall and the beads flowing therethrough. Yet, the thickness of the wall is maintained below about 120 microns (at least along the portion thereof passing through the delivery microcatheter). The main obstacle to maintaining the thinness of the wall is the radiopaque marker located in proximity to the distal end opening of the microcatheter. It was surprisingly

found by the inventors of the hereindisclosed microcatheters that the desired wall thinness may be accomplished and maintained, by having the inner liner extending only up until the radiopaque marker so as to avoid bulking, and that absence of a liner along the part of the microcatheter extending from the radiopaque marker to the distal end opening, has minimal to no influence on the delivery of the beads through the distal end opening.

The hereindisclosed embolization microcatheters may further include a filter section with a plurality of openings configured for outflow of fluids while preventing outflow of the beads, thus ensuring concentrated delivery of the embolization beads with minimal backflow.

Advantageously, the size, shape and distribution of the openings enables smooth delivery of the beads, despite their large size. This is accomplished by including two or more filter segments, each filter segment comprising a plurality of side openings having the proximal most of the circumferential sections distributed circumferentially around the microcatheter, wherein the proximal most of the circumferential sections includes fewer side openings than sections distal thereto. As a result, the outflow of fluid is relatively low at the proximal end of the filter, thus reducing the chance of clogging, and increases toward the distal end opening at which a low outflow rate is desired in order to prevent backflow. In addition, the shape and size of the openings change between the proximal end and the distal end of the filter in that the distal most part of the filter includes small, preferably square-shaped openings configured to prevent the beads to get stuck and/or sucked in as the amount of suspension fluid is reduced.

Some aspects of the present disclosure provide an embolization microcatheter comprising: an elongated tubular member forming a lumen, the elongated tubular member terminating with a distal end opening, wherein a wall of the elongated tubular member comprises a braid, a polymer formed around the braid and an inner liner coating an inner surface of the wall; wherein the wall of the part of the elongated tubular member extending between a proximal radiopaque marker and the distal end opening has a thickness of less than or equal to 130 microns; and a distal radiopaque marker located in proximity to the distal end opening; wherein the part of elongated tubular member extending between the proximal end of the radiopaque marker and the distal end opening is devoid of the liner.

According to some embodiments, the outer diameter of the elongated tubular member is less than or equal to 1.5 mm and an inner diameter of the elongated tubular member is 700 microns or more.

According to some embodiments, the thickness of the distal end of the wall is less than or equal to 120 microns.

According to some embodiments, the embolization microcatheter includes a filter formed in the wall of the elongated tubular member, the filter comprising two or more filter segments, each filter segment comprising a plurality of side openings penetrating the wall, the plurality of side openings distributed circumferentially around the elongated tubular member.

According to some embodiments, the proximal most of the filter segments comprises fewer side openings than rings distal thereto.

According to some embodiments, the distal most of the filter segment is positioned 2-4 mm proximally to the distal end opening.

According to some embodiments, the side openings of the distal most filter segment are essentially square shaped. According to some embodiments, the essentially square shaped side openings have a dimension of 50x50 microns. According to some embodiments, the essentially square shaped side openings have a cross-sectional dimension of 80x50 microns.

According to some embodiments, the side openings of the remainder of the at least two filter segments are in a form of axial slits.

According to some embodiments, the side openings of the remainder of the at least two filter segments have a width of 20 microns and wherein the length of the side openings of the remainder of the at least two filter segments varies between the side openings.

According to some embodiments, the side openings of the remainder of the at least two filter segments have a length of at least 200 microns.

According to some embodiments, at least some of the side openings of the remainder of the at least two filter segments have dimension of 2700x20 microns.

According to some embodiments, at least some of the side openings of the remainder of the at least two filter segments have a dimension of 1350x20 microns. According to some embodiments, at least some of the side openings of the remainder of the at least two filter segments have a dimension of 300x20 microns.

According to some embodiments, the braid is made of tungsten.

According to some embodiments, the inner liner comprises Polytetrafluoroethylene (PTFE).

According to some embodiments, the radiopaque marker comprises a metal marker band. According to some embodiments, the radiopaque marker is located 0.5-2 mm proximally to the distal end opening.

According to some embodiments, the embolization microcatheter is suitable for delivery of embolization beads having a particle size of about 900 microns.

According to some embodiments, the embolization microcatheter has a length of at least 1 m.

According to some embodiments, there is provided a method for delivering embolization beads, the method comprising: delivering the hereindisclosed embolization microcatheter to a target location via a delivery catheter; and injecting beads through the microcatheter.

According to some embodiments, the beads have a particle size of at least 500 microns. According to some embodiments, the beads have a particle size of at least 900 microns.

According to some embodiments, the delivery catheter is a 5.0 Fr delivery catheter.

Certain embodiments of the present disclosure may include some, all, or none of the above characteristics. One or more technical advantages may be readily apparent to those skilled in the art from the figures, descriptions and claims included herein. Moreover, while specific characteristics have been enumerated above, various embodiments may include all, some or none of the enumerated characteristics.

In addition to the exemplary aspects and embodiments described above, further aspects and embodiments will be further expanded upon in the figures and the following detailed descriptions.

BRIEF DESCRIPTION OF THE FIGURES

The features, nature and advantages of the present disclosure will become more apparent from the detailed description set forth below when taken in conjunction with the drawings in which like reference characters identify correspondingly throughout. Identical structures elements or parts that appear in more than one figure are generally labeled with the same number in all the figures in which they appear. Alternatively, elements or parts that appear in more than one figure may be labeled with different numbers in the different figures in which they appear. The dimensions of the components and features in the figures were chosen for convenience and clarity of presentation and are not necessarily shown to scale. The figures are listed below.

FIG. 1A schematically illustrates a microcatheter comprising an outer layer including a plurality of sections, the plurality of sections made of different polymeric materials, according to some embodiments;

FIG. 1B schematically illustrates a perspective, cutaway view of the distal end of the microcatheter of **FIG. 1A** illustrating the outer layer, the strike layer, the inner layer, the braided skeleton located between the inner layer and the outer layer.

FIG. 2A schematically illustrates a 3.0 Fr embolization microcatheter with a fluid barrier forming section, according to some embodiments.

FIG. 2B schematically illustrates a magnified and partially exposed view of the distal end of the microcatheter of **FIG. 2A**, according to some embodiments.

FIG. 2C schematically illustrates a magnified and partially exposed view of the distal tip of the microcatheter of **FIG. 2A**, according to some embodiments.

FIG. 2D schematically illustrates a slit formed by selective cutting through the wall of a fluid barrier forming section, such as the fluid barrier forming section of the embolization microcatheter of **FIG. 2A**, according to some embodiments.

FIG. 3 schematically illustrates an optional slit pattern of the microcatheter of **FIG. 2A**.

FIG. 4 schematically illustrates another optional slit pattern of the microcatheter of **FIG. 2A.**

DETAILED DESCRIPTION OF THE INVENTION

The detailed description set forth below, in connection with the appended drawings, is intended as a description of various configurations and is not intended to represent the only configurations in which the concepts described herein may be practiced. The detailed description includes specific details for the purpose of providing a thorough understanding of the various concepts. However, it will also be apparent to one skilled in the art that these concepts may be practiced without specific details being presented herein. In some instances, well-known features may be omitted or simplified in order to avoid obscuring the disclosure.

Reference is now made to **FIG. 1A**, which schematically illustrates an embolization microcatheter **100,** and to **FIG. 1B** which illustrates magnified/exposed views of a distal part of **FIG. 1A**.

As used herein, the terms "embolization", "transcatheter embolization", "transcatheter arterial embolization" and "TAE" may be used interchangeably and refer to the passage and lodging of an embolus within the bloodstream for therapeutic purposes, for example, as a hemostatic treatment of bleeding or as a treatment for some types of cancer by deliberately blocking blood vessels to starve the tumor cells.

Embolization microcatheter **100** is a 3.0 Fr microcatheter having an elongated tubular member **110** with an outer diameter of about 1.5 mm, or an outer diameter in the range of 1.0-1.5 mm, or 1.2-1.6 mm and an inner diameter in the range of 700-850 microns.

The proximal end **130** of microcatheter **100** includes a hub **102** which is molded on or otherwise attached to elongated tubular member **110** of microcatheter **100**.

Hub **102** is configured to allow access to the lumen of elongated tubular member **110** for a variety of functions, such as the injection of fluids or drugs, or the introduction of guidewires. Hub **102** includes a strain relief **112**, preferably mechanically coupled to hub **102**. Strain relief **112** may be made of a polymeric material and may, as illustrated, be tapered at its distal end. Strain relief **112** can be configured to provide structural support to elongated tubular member **110**, to prevent it from kinking.

According to some embodiments, the wall of elongated tubular member **110** may include a plurality of sections, each section characterized by the polymers utilized. According to some embodiments, a plurality of sections may include 3, 4, 5, 6, 7, 8, 9, 20 or more sections. Each possibility is a separate embodiment.

According to some embodiments, the different polymeric layers may contribute to different characteristics of the layer/section and thus of elongated tubular member **110**. For example, the different polymeric layers may contribute to the elasticity, flexibility, stretch-ability, strength, hardness, rigidity, ultimate tensile strength, elongation or any other characteristic of the layer and thus the microcatheter. Each possibility is a separate embodiment.

The proximal end **130** of elongated tubular member **110**, attached to strain relief **112**, includes an outer layer **132** made of a polyether block amide having a hardness of about 70D shore and/or a flexural modulus of about 74,000 psi. According to some embodiments, proximal end **132** may have a length of 600-1200mm (e.g. about 1000 mm).

Optionally, part of outer layer **132** may include a heat shrink material **134** covering the joint between strain relief **112** and elongated tubular member **110**.

Adjacent section **132**, is a second section **136** of elongated tubular member **110**, made of a polyether block amide having a hardness of about 60D-65D shore and/or a flexural modulus of about 41,000 psi. Section **136** may have a length of 20-60 mm, e.g. 40 mm.

Intermediate part **140** of elongated tubular member **110** includes section **142** having an outer layer which may be made of a polyether block amide or other suitable polymer having a hardness of about 55D shore and/or a flexural modulus of about 25,000 psi, section **144** having an outer layer made of a polymeric material having a hardness of about 40D shore such as a polycarbonate-based thermoplastic urethane having a hardness of about 40D shore, and/or a flexural modulus of about 10,000-12,000 psi; section **146** having an outer layer made of a one or more polycarbonate-based thermoplastic urethanes having a hardness of about 95A shore, and section **148** having an outer layer made of a one or more polycarbonate-based thermoplastic urethanes having a hardness of about 85A shore.

Section **142** may have a length of about 30 to about 80 mm, e.g. 40 mm. Section **144**, may have a length of about 30 mm to about 70 mm (e.g. about 50 mm). Section **146** may have a length of about 80 mm to about 150 mm (e.g. about 130 mm). Section **148** may have a length of about 20 mm to about 60 mm (e.g. about 45 mm).

According to some embodiments, the distal end may refer to the distal 100mm, 50mm, 30mm, 20mm, 15mm, 10mm, 5mm or 2mm of microcatheter **100**. Each possibility is a separate embodiment. According to some embodiments, the distal end may refer to the part of the microcatheter extending between the proximal marker and distal end opening **180**.

According to some embodiments, the polymeric material of all sections in the intermediate part **140** is softer than that of the polymeric material of the wall section in proximal end **130** of tubular member **110**.

According to some embodiments, the polymeric material of section **148** is softer than that of section **146**. According to some embodiments, the polymeric material of section **146** is softer than that of section **144**. According to some embodiments, the polymeric material of section **144** is softer than that of section **142**.

Distal end **150** of elongated tubular member **110** includes sections **152** having an outer layer made of a polymeric material having a hardness of about 85A shore such as a polycarbonate-based thermoplastic urethane having a hardness of about 85A shore and section. The polymer of section **152** may further include a polymeric radiopaque marker, such as but not limited to tantalum

powder; section **154** having an outer layer made of a polymeric material having a hardness of about 95A shore such as a polycarbonate-based thermoplastic urethane having a hardness of about 95A shore. According to some embodiments, the distal tip **170** of elongated tubular member **110** terminates with a distal end opening. According to some embodiments, the distal tip refers to the distal marker **162** and distal end opening **180**.

As used herein, the term "distal end opening" refers to the end opening of the microcatheter leading into the lumen thereof. According to some embodiments, distal end opening **180** defines the termination of the microcatheter at the distal end thereof. According to some embodiments, distal end opening **180** may have an inner diameter essentially equal to the inner diameter of the microcatheter lumen. According to some embodiments, the distal end opening **180** may have an inner diameter which is smaller than the inner diameter of the microcatheter lumen leading to a narrowing of the lumen toward the end thereof.

Section **152** includes a proximal marker **160** (seen in **FIG. 1B**), section **154** terminates with a distal marker **162** (also seen in **FIG. 1B**). According to some embodiments, distal end **150** may have a length of 10-20 mm. According to some embodiments, section **152** may have a length of 2-10 mm (e.g. about 6 mm). According to some embodiments, section **154** may have a length of 5-20 mm (e.g. about 10 mm). According to some embodiments, proximal marker **160** may be a radiopaque powder embedded in part of outer layer of section **152**, as essentially described herein. According to some embodiments, proximal marker **160** may be positioned approximately 5-20 mm, or 10-15 mm from the distal end opening **180**. According to some embodiments, distal marker **162** may be a radiopaque alloy submerged in outer layer **154**. According to some embodiments, distal marker **162** may be positioned approximately 1 mm proximally from distal end opening **180**.

Reference is now made to **FIG. 1B** which schematically illustrates a perspective, cutaway view of the distal part of distal end **150** of microcatheter **100** shown in **FIG. 1A** extending from proximal marker **160** to a tip **170** and encompassing section **154** of elongated tubular member **110**. As stated above, the wall of section **154**. As seen from the exploded view, underneath the outer layers is a braid **190**.

According to some embodiments, braid **190** extends along the entire length of tubular member **110**. Alternatively, braid **190** extends along only a portion of elongated tubular member

110, such as only along section **154**, along sections **152** and **154**, along sections **152**, **154** and **148**, along sections **152**, **154**, **148** and **146**, along sections **152**, **154**, **148**, **146** and **144**, or along sections **152**, **154**, **148**, **146**, **144** and **142**. Each possibility is a separate embodiment.

According to some embodiments, braid **190** has a picks-per-inch (PPI) value ensuring that, in combination with a low durometer polymer, a flexible distal end is obtained, and in combination with a polymer having a higher durometer a relatively stiff proximal end is provided. According to some embodiments, the braided skeleton may have a wire arrangement of 75-150 Picks Per Inch (PPI), 100-150 PPI or 100-150 PPI. Each possibility is a separate embodiment. As a non-limiting example, the braided skeleton may have a wire arrangement of about 140 PPI or about 145 PPI. Those skilled in the art will appreciate the term picks-per-inch (PPI) is a measurement of braid wire density and represents the number of picks (e.g. weft wires) per inch of braid.

As used herein the terms "braid" and "braided skeleton" may refer to a structural element, such as a tubal element formed of a plurality of interlaced wires. According to some embodiments, the braid may be formed of at least three interlaced wires forming a tube. According to some embodiments, the braid may include 8-48 wires or 12-32 wires. As a non-limiting example, the braid may include 16 wires. Each possibility is a separate element. According to some embodiments, the wires forming the braid may have a diameter in the range of 10-60 microns such as 15-40 microns or 20-30 microns or any other suitable diameter within the range of 10-60 microns. Each possibility is a separate embodiment. As a non-limiting example, the wires forming the braid may have a diameter of 25 microns. According to some embodiments, the skeleton may extend along essentially the entire length of the catheter. According to some embodiments, the braid may be made from tungsten, stainless steel, Nickel titanium (also referred to as Nitinol), nitinol, cobalt chrome, platinum iridium, nylon or any combination thereof. Each possibility is a separate embodiment.

According to some embodiments, at least some of the wires forming the braided skeleton may be braided in a same or opposite direction, i.e. left/right handed. Advantageously, the braiding structure allows good torque-ability (better than a coiled skeleton), low flexural rigidity (i.e. good flexibility), good push-ability (better than a coiled skeleton), and superior kink-resistance.

According to some embodiments, at least some of the wires forming the braided skeleton may be non-circular/round.

Underneath braid **190** is an inner liner **192**, which may be made of Polytetrafluoroethylene (PTFE). According to some embodiments, inner liner **192** may have a thickness of 10-30 micron or 10-25 micron. Each possibility is a separate embodiment. According to some embodiments, the liner is a film cast liner.

Advantageously, in order to compensate for the bulkiness distal marker **162**, the part of elongated tubular member **110** extending from the distal end of the distal marker **162**, to distal end opening **180** is devoid of inner liner **192**, thereby essentially maintaining the inner and outer diameters of elongated tubular member **110**, despite the bulkiness of distal marker **162**, which enables smooth delivery through a 5.0 Fr delivery catheter (not shown).

According to some embodiments, the total thickness of the wall of the distal end of the elongated tubular member does not exceed about 130 microns, at least along the part of the elongated tubular member to be inserted through the 5.0 Fr delivery catheter. According to some embodiments, the total thickness of the wall of the distal end of the elongated tubular member does not exceed about120 microns, at least along the part of the elongated tubular member to be inserted through the 5.0 Fr delivery catheter.

Reference is now made to **FIG. 2A-FIG. 2C**, which schematically illustrate an embolization microcatheter **200** and magnified/exposed views of parts thereof. Embolization microcatheter **200** may be similar to embolization microcatheter **100** apart from embolization microcatheter **200** also including a filter **220**. Reference is also made to **FIG. 2D**, which schematically illustrates the structure of filter **220**. Embolization microcatheter **200** is a 3.0 Fr microcatheter having an elongated tubular member **210** with an outer diameter in the range of about 1.0-1.5 mm, or in the range of about 1.2 mm - 1.6 mm and an inner diameter in the range of 700-850 microns. Embolization microcatheter **200** is particularly suitable for delivery of large embolization beads, such as but not limited to embolization beads having an average particle size of 500 microns or more, 600 microns or more, 700 microns or more, 800 microns or more, 900 microns or more and 1000 microns or more. Each possibility is a separate embodiment.

Filter **220** including a plurality of penetrating side openings formed in the wall of elongated tubular member **210**, is schematically illustrated in **FIG. 2B**.

As used herein, the term "plurality" with reference to the side openings refers to 2 or more, 3 or more, 5 or more, 10 or more, 15 or more, 20 or more or 25 or more axial slits. Each possibility is a separate embodiment.

According to some embodiments, the filter **220** may be an integral part of elongated tubular member **110** and may extend along a length of 0.3mm-20mm, such as 1mm-10mm, 1mm-5mm, 1.5mm-5 mm, 2mm-5mm or any other in-between suitable length. Each possibility is a separate embodiment.

According to some embodiments, filter **220** may have a total open area, formed by the side openings, in the range of 0.2-1mm^2, 0.2-0.6mm^2, 0.3-1mm2, 0.3-0.5mm^2, 0.4-0.6mm^2, 0.5-1.5mm^2, 1.0-3.5mm^2, 1.5-4mm^2, 2.0-3.5mm^2 or any other suitable area within the range of 0.1-4mm^2. Each possibility is a separate embodiment. According to some embodiments, at least 5%, at least 10%, or at least 15% of filter **220** is open area formed by the side openings. According to some embodiments, 5%-30%, at least 7%-25%, 7%-20%, 5%-15% of filter **220** is open area formed by the side openings. Each possibility is a separate embodiment.

According to some embodiments, the side openings may be formed by selective cutting (e.g. selective laser cutting), that is, without cutting the wires forming braid **290** as illustrated in **FIG. 2D**. According to some embodiments, the part of the liner positioned below the wires remains intact. According to some embodiments, both the polymeric layer and the inner liner positioned between the wires of braid **290** are penetrated when forming the slits. Advantageously, the selective cutting of the polymeric layer (leaving braid **290** essentially intact may provide subdivision of at least some of the side-openings into two or more sub-side-openings (here sub-side-opening **225a-225d**) separated by the braid but not by the polymeric outer layer.

One optional structure of filter **220** is provided in **FIG. 3**. As seen in **FIG. 3**, filter **320** may include four filter sections **321**, **322**, **323** and **324** each filter section comprising a plurality of side openings **325**, **326**, **327** and **328**, distributed in circumferential rings around filter member **320**.

According to some embodiments, the proximal most filter section, filter section **321** has fewer side openings than filter sections distal thereto. According to some embodiments, filter section **321** may include 1-4 or 1-3 rings of side openings, such as, but not limited to 2 rings of side opening. According to some embodiments, each of the rings may include 1-5 side openings or 1-3 side openings, such as, but not limited to 2 side openings per ring. According to some embodiments, filter section **321** may include a total of 1-5, 2-4 side openings, such as but not limited to 2 side openings.

According to some embodiments, side openings of the proximal most circumferential sections, are circumferentially shifted relative to side openings in its neighboring circumferential section.

According to some embodiments, side openings **325** in a first ring of filter section **321** may be circumferentially shifted relative to side openings in its neighboring ring and/or circumferentially shifted relative to side openings **326** of filter section **322**.

According to some embodiments, filter section **322** may include 1-5 or 2-4 rings of side openings, such as, but not limited to 3 rings of side opening. According to some embodiments, each of the rings may include 1-5 side openings or 2-4 side openings, such as, but not limited to 3 side openings per ring. According to some embodiments, filter section **322** may include a total of 5-15, 6-10 side openings, such as but not limited to 9 side openings.

According to some embodiments, side openings **326** in a first ring of filter section **322** may be circumferentially shifted relative to side openings in its neighboring ring.

According to some embodiments, filter section **323** may include 2-10 or 3-7 rings of side openings, such as, but not limited to 5 rings of side opening. According to some embodiments, each of the rings may include 2-15 side openings or 4-8 side openings, such as, but not limited to 6 side openings per ring. According to some embodiments, filter section **323** may include a total of 10-50, 20-40 side openings, such as but not limited to 30 side openings.

According to some embodiments, side openings **325**, **326** and **327** of filter sections **321**, **322** and **323** respectively may be essentially rectangularly shaped axial slits. Due to the shape of

the filter **220**, side openings **325**, **326** and **327** may be conical, i.e. have a larger cross-section at the outer surface than at the inner surface of filter **220**.

The sizes provided below relate to measures made at the inner surface.

According to some embodiments, side openings **325**, **326** and **327** may have a dimension of about 150x20 microns.

According to some embodiments, each ring of side openings **325**, **326** and **327** of filter sections **321**, **322** and **323** may be spaced apart from its neighboring ring by 100-200 microns or by 120-180 microns, such as but not limited to 150 microns.

According to some embodiments, the distal most of filter section, filter section **324** is positioned about 2-5 mm proximally to the distal end opening. According to some embodiments, the distal most of filter section, filter section **324** is positioned about 3 mm proximally to the distal end opening.

According to some embodiments, the side openings **328** of filter section **324** are essentially square shaped. Advantageously, the square-shaped size of the side openings **328** enables outflow of fluid, while ensuring minimal interference to the flow of beads towards distal end opening, despite the beads already being concentrated due to the outflow of fluid through side openings **325**, **326** and **327**. According to some embodiments, filter section **324** may include 3-10 or 4-6 rings of side openings, such as, but not limited to 5 rings of side opening. According to some embodiments, each of the rings may include 3-10 side openings or 4-8 side openings, such as, but not limited to 6 side openings per ring.

According to some embodiments, side openings **328** of filter section **324** may have a dimension of about 50x50 microns.

According to some embodiments, the distal most ring of side openings **328** may be spaced apart by 1-10 mm or 2-7 mm, such as but not limited to 2 mm from a distal most of the rings of side openings **327** in filter section **323**.

According to some embodiments, the distal most ring of side openings **328** may be spaced apart by 1-10 mm or 2-5 mm, such as but not limited to 3 mm from the distal end opening.

According to some embodiments, each ring of side openings **328** of filter section **324** may be spaced apart from its neighboring ring by 20-100 microns or by 30-60 microns, such as but not limited to 50 microns.

According to some embodiments, the slits may be positioned at a same or a different longitudinal position. Each possibility is a separate embodiment. According to some embodiments the distribution of the slits may be staggered, zig-zagged or any other suitable even or uneven distribution.

Advantageously, the filter **320** may be configured for kink-free bending despite the plurality of slits formed in the wall thereof. According to some embodiments, the flexibility of the filter **220** is determined by the number of side openings, their minimal cross-sectional dimension, their width, length spacing, geometry, distance from distal outlet etc., as essentially described herein, may enable kink-free bending thereof.

As used herein the term "kink-free bending" may refer to a bending of filter **320**, which does impede flow therethrough. According to some embodiments, filter **320** may be configured for kink-free bending at an angle of about 180 degrees. According to some embodiments, filter **320** may be configured for kink-free bending at a minimum bending radius in the range of about 0.5 to 1.5 mm, for example 0.5 to 1.2, 0.5 to 1 mm, or any radius in-between.

Advantageously, microcatheter **300** including filter **320** provides effective reflux prevention, which requires a relatively high density of side openings, while a small kink-free radius (e.g. in the range of 0.5 to 1.5 mm) and tensile strength of at least 5N is still ensured.

According to some embodiments, the microcatheter **300** may have a length of at least 50 cm, at least 60 cm, at least 75 cm, or at least 1m. Each possibility is a separate embodiment.

According to some embodiments, the outer wall of the microcatheter **300** may be non-tapered essentially along its/their entire length.

One optional structure of filter **220** is provided in **FIG. 4**. As seen in **FIG. 4**, filter **420** may include two filter sections **421** and **422** each filter section comprising a plurality of side openings **425** and **427**, distributed in circumferential rings around elongated tubular filter **420**.

Due to the shape of the filter **220**, side openings side openings **425** and **427** may be conical, i.e. have a larger cross-section at the outer surface than at the inner surface of filter **220**.

The sizes provided below relate to measures made at the inner surface.

According to some embodiments, filter section **421** may include 2-10 or 2-6 annular rings of side openings, such as, but not limited to 5 rings of side opening. According to some embodiments, each of the rings may include 1-10 side openings or 2-8 side openings, such as, but not limited to 6 side openings per ring. According to some embodiments, filter section **421** may include a total of 10-60 side openings or 20-40 side openings, such as but not limited to 30 side openings. According to some embodiments, side openings **425** may be essentially square or rectangularly shaped. According to some embodiments, side openings **425** may have a width of 50-150 microns or 50-100 microns such as e.g. about 80 microns. According to some embodiments, side openings **425** may have a length of 20-100 microns or such as e.g. about 50 microns. According to some embodiments, each of the rings of side opening may be spaced apart longitudinal from its neighboring ring by 20-100 microns, e.g. by approximately 50 microns. According to some embodiments, the distal most of side openings **425** may be positioned about 2-5 mm e.g. about 3 mm, from the distal end opening of the microcatheter.

Advantageously, the square-shaped size of the side openings **425** enables outflow of fluid while ensuring minimal interference to the flow of beads towards distal end opening, despite the beads already being concentrated due to the outflow of fluid through side openings **325**, **326** and **327**.

According to some embodiments, filter section **422** may include 5-50 or 10-30 or 10-20 side opening **427**. According to some embodiments, the width of side openings **427** may by in the range of 10-50 or 10-30 microns, e.g. about 20 microns. According to some embodiments, at least some of side opening **427** may have a different length. According to some embodiments, at least some of side opening **427**, such as side opening **427a** may have a length in a range of about 1 mm – 4mm or about 2 mm – 3.5 mm, e.g. about 2.7 mm. According to some embodiments, at least some of side opening **427**, such as side opening **427b** may have a length in a range of about 0.8 mm – 2 mm or about 1 mm – 1.5 mm, e.g. about 1.35 mm. According to some embodiments, at least some of side opening **427**, such as side opening **427c** may have a length in a range of about

0.2 mm – 1 mm or about 0.2 mm – 0.5 mm, e.g. about 0.3 mm. Advantageously, filter **220** may be formed by selective cutting of the polymeric layer (leaving braid **290** essentially intact). According to some embodiments, at least some of side openings **427** may include sub-side-openings (illustrated as with numbers **225a-225d** in **FIG. 2D**) separated by braid **290**, but not by the polymeric outer layer.

According to some embodiments, each of side openings **427** is spaced apart longitudinally from a neighboring side opening of side opening may be spaced apart from its neighboring side opening by 20-200 microns. According to some embodiments, the longitudinal spacing between side openings **427** may vary. According to some embodiments, at least some of side openings **427** are axially shifted vis-à-vis a neighboring side opening. According to some embodiments, the distal most of side openings **427** may be positioned about 3-10 mm e.g. about 5 mm, from the distal end opening of the microcatheter.

According to some embodiments, filter **420** may have a length of 5-15 mm or about 5-10 mm.

According to some embodiments, the slits may be positioned at a same or at a different longitudinal position. Each possibility is a separate embodiment. According to some embodiments the distribution of the slits may be staggered, zig-zagged or any other suitable even or uneven distribution.

Advantageously, the filter **420** may be configured for kink-free bending despite the plurality of slits formed in the wall thereof. According to some embodiments, the flexibility of the filter **220** is determined by the number of side openings, their minimal cross-sectional dimension, their width, length spacing, geometry, distance from distal outlet etc., as essentially described herein, may enable kink-free bending thereof.

As used herein the term "kink-free bending" may refer to a bending of filter **420**, which does impede flow therethrough. According to some embodiments, filter **420** may be configured for kink-free bending at an angle of about 180 degrees. According to some embodiments, filter **420** may be configured for kink-free bending at a minimum bending radius in the range of about 0.5 to 1.5 mm, for example 0.5 to 1.2, 0.5 to 1 mm, or any radius in-between.

Advantageously, microcatheter **400** including filter **420** provides effective reflux prevention, which requires a relatively high density of side openings, while a small kink-free radius (e.g. in the range of 0.5 to 1.5 mm) and tensile strength of at least 5N is still ensured.

According to some embodiments, the microcatheter **400** may have a length of at least 50 cm, at least 60 cm, at least 75 cm, or at least 1m. Each possibility is a separate embodiment. Each possibility is a separate embodiment.

According to some embodiments, the outer wall of the microcatheter **400** may be non-tapered essentially along its/their entire length.

As used herein, the terms "approximately" and "about" refer to +/-10%, or +/-5%, or +-2% vis-à-vis the range to which it refers. Each possibility is a separate embodiment.

While a number of exemplifying aspects and embodiments have been discussed above, those of skill in the art will envisage certain modifications, additions and sub-combinations thereof. It is therefore intended that the following appended claims and claims hereafter introduced be interpreted to include all such modifications, additions and sub-combinations as are within their true spirit and scope.

CLAIMS

1. An embolization microcatheter comprising:

   an elongated tubular member forming a lumen, the elongated tubular member terminating with a distal end opening, wherein a wall of the elongated tubular member comprises a braid, a polymer formed around the braid and an inner liner coating an inner surface of the wall; wherein the wall of the part of the elongated tubular member extending between a proximal radiopaque marker and the distal end opening has a thickness of less than or equal to 130 microns; and

   a distal radiopaque marker located in proximity to the distal end opening;

   wherein the part of elongated tubular member extending between the proximal end of the distal radiopaque marker and the distal end opening is devoid of the liner.

2. The embolization microcatheter according to claim 1, wherein an outer diameter of the elongated tubular member is less than or equal to 1.5 mm and an inner diameter of the elongated tubular member is 700 microns or more.

3. The embolization microcatheter according to any one of claims 1-2, wherein the thickness of the distal end of the wall is less than or equal to 120 microns.

4. The embolization microcatheter according to any one of claims 1-3, further comprising a filter formed in the wall of the elongated tubular member, the filter comprising two or more filter segments, each filter segment comprising a plurality of side openings penetrating the wall, the plurality of side openings distributed circumferentially around the elongated tubular member.

5. The embolization microcatheter according to claim 4, wherein a proximal most of the filter segments comprises fewer side openings than rings distal thereto.

6. The embolization microcatheter according to any one of claim 4-5, wherein a distal most of the filter segment is positioned 2-4 mm proximally to the distal end opening.

7. The embolization microcatheter according to any one of claims 4-6, wherein side openings of the distal most filter segment are essentially square shaped.

8. The embolization microcatheter according to claim 7, wherein the essentially square shaped side openings have a dimension of 50x50 microns.

9. The embolization microcatheter according to claim 7, wherein the essentially square shaped side openings have a dimension of 80x50 microns.

10. The embolization microcatheter according to claim 7, wherein the side openings of the remainder of the at least two filter segments are in a form of axial slits.

11. The embolization microcatheter according to claim 10, wherein the side openings of the remainder of the at least two filter segments have a width of 20 microns and wherein the length of the side openings of the remainder of the at least two filter segments varies between the side openings.

12. The embolization microcatheter according to claim 11, wherein the side openings of the remainder of the at least two filter segments have a length of at least 200 microns.

13. The embolization microcatheter according to any one of claims 10-12, wherein at least some of the side openings of the remainder of the at least two filter segments have dimension of 2700x20 microns.

14. The embolization microcatheter according to any one of claims 10-12, wherein at least some of the side openings of the remainder of the at least two filter segments have a dimension of 1350x20 microns.

15. The embolization microcatheter according to any one of claims 10-12, wherein at least some of the side openings of the remainder of the at least two filter segments have a dimension of 300x20 microns.

16. The embolization microcatheter according to any one of claims 1-15, wherein the braid is made of tungsten.

17. The embolization microcatheter according to any one of claim 1-16, wherein the inner liner comprises Polytetrafluoroethylene (PTFE).

18. The embolization microcatheter according to any one of claim 1-17, wherein the radiopaque marker comprises a metal marker band.

19. The embolization microcatheter according to any one of claims 1-18, wherein the radiopaque marker is located 0.5-2 mm proximally to the distal end opening.

20. The embolization microcatheter according to any one of claims 1-19, being suitable for delivery of embolization beads having a particle size of about 900 microns.

21. The embolization microcatheter according to any one of claims 1-20, having a length of at least 1 m.

22. A method for delivering embolization beads, the method comprising:

delivering the embolization microcatheter of any one of claims 1-21 to a target location via a delivery catheter; and

injecting beads through the microcatheter.

23. The method of claim 22, wherein the beads have a particle size of at least 500 microns.

24. The method of claim 23, wherein the beads have a particle size of at least 900 microns.

25. The method according to any one of claims 22-24, wherein the delivery catheter is a 5.0 Fr delivery catheter.

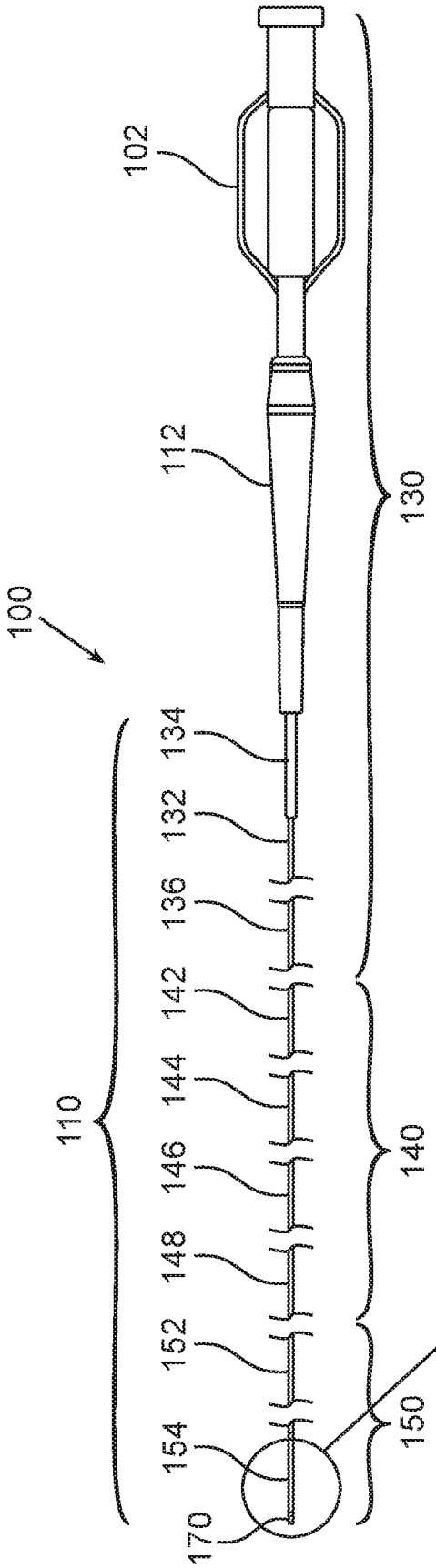
100
102
112
130
110
134
132
136
142
144
146
148
152
154
140
150
170

FIG. 1A

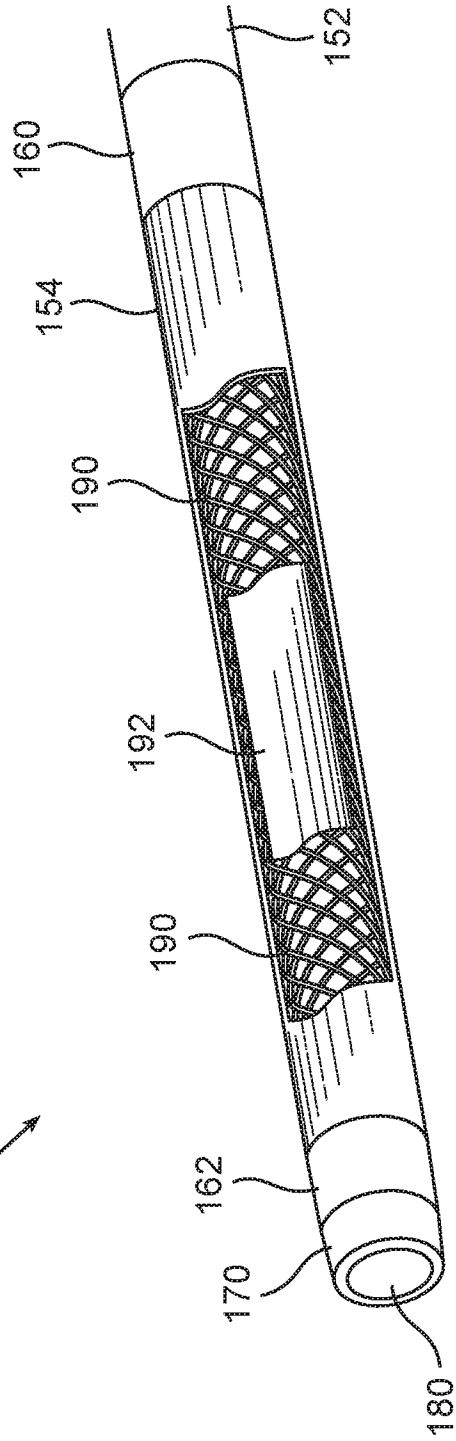
160
152
154
190
192
190
162
170
180

FIG. 1B

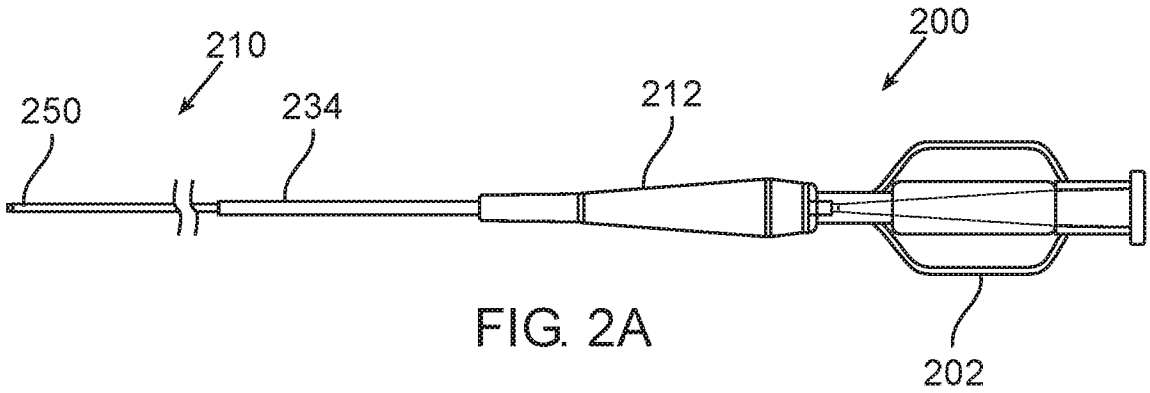

FIG. 2A

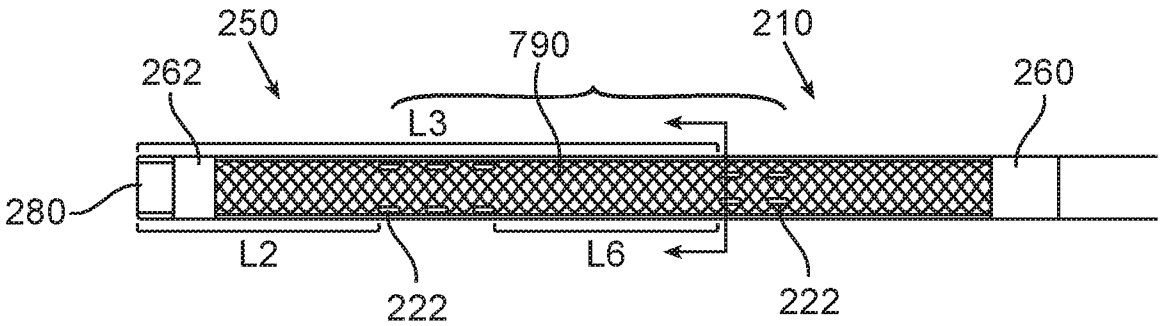

FIG. 2B

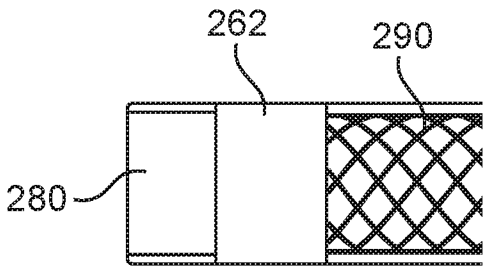

FIG. 2C

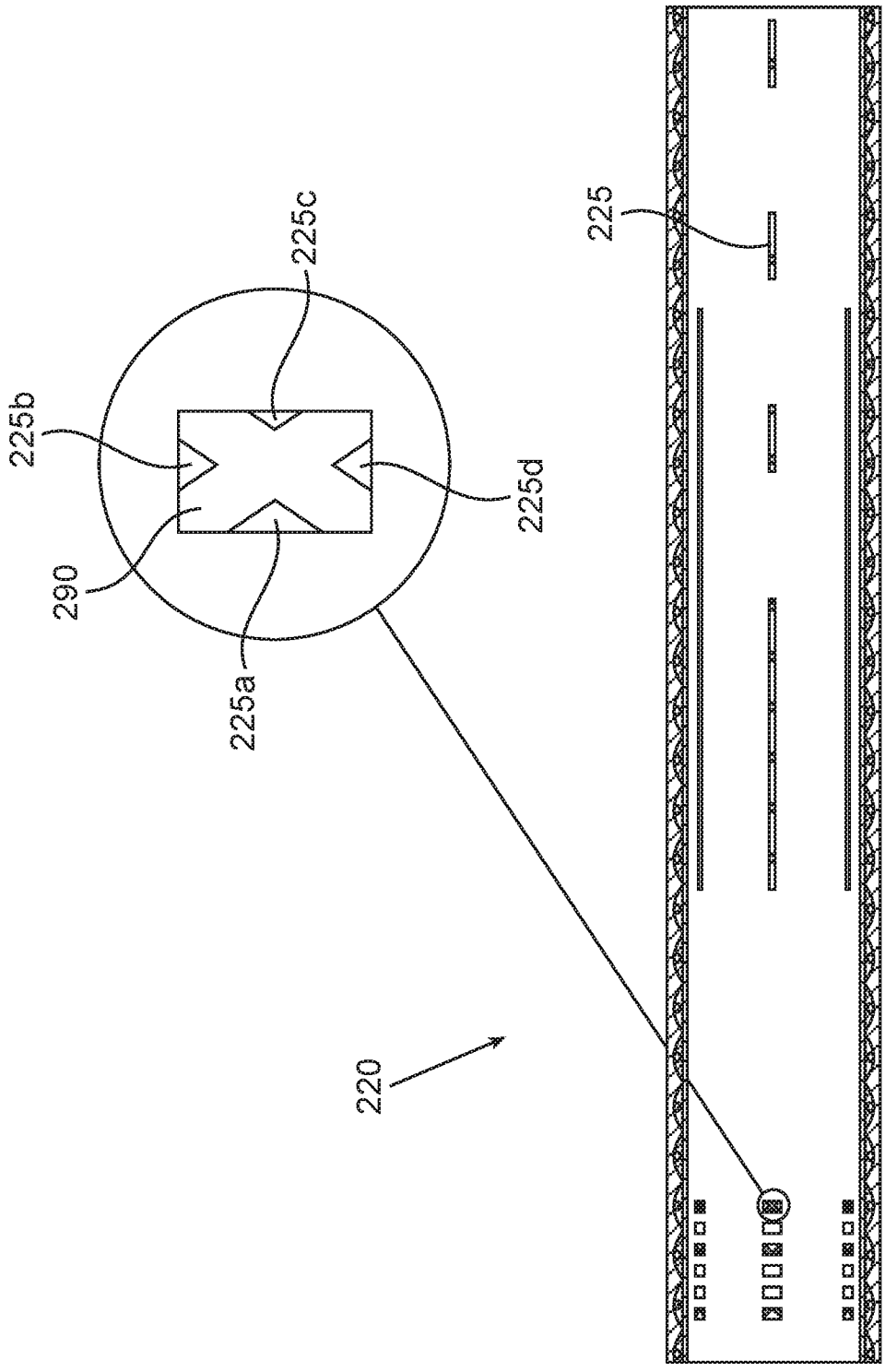

FIG. 2D

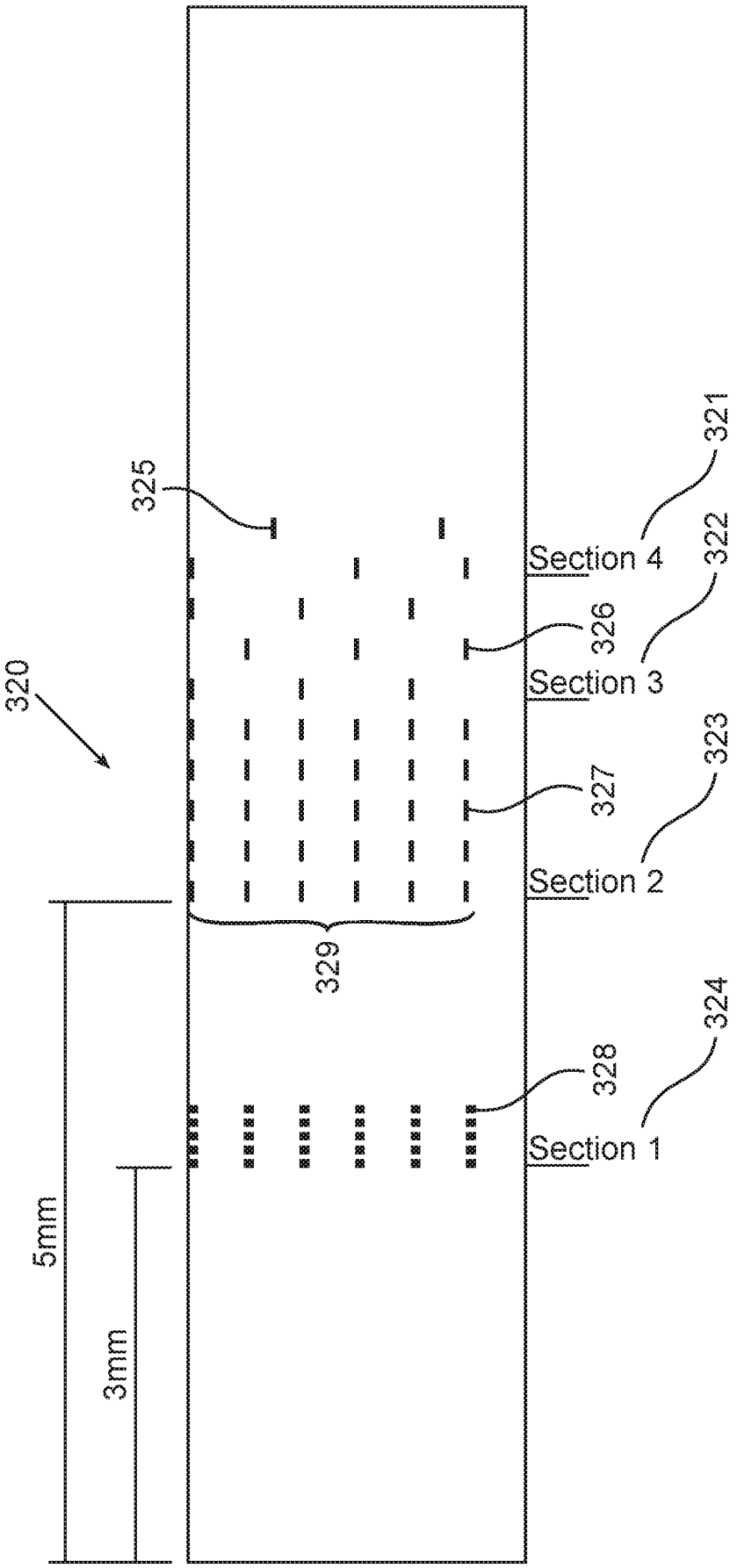
320
325
321
Section 4
322
326
Section 3
327
323
Section 2
329
328
324
Section 1
5mm
3mm

FIG. 3

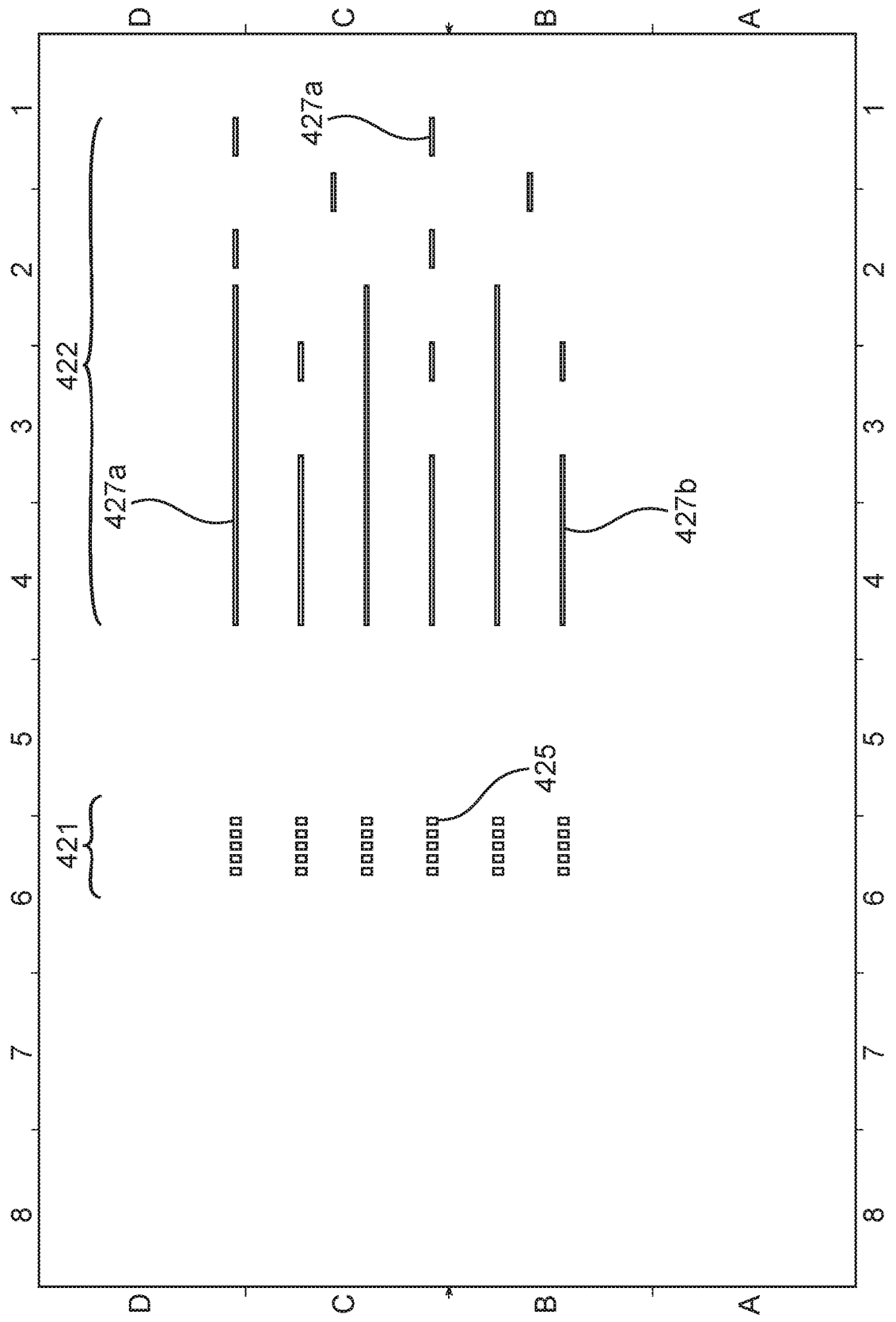

FIG. 4

INTERNATIONAL SEARCH REPORT

International application No.
PCT/IL2021/050904

A. CLASSIFICATION OF SUBJECT MATTER
See extra sheet.

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)
See extra sheet.

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)
Databases consulted: Google Patents, Orbit, Similari (AI-based)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 2015005801 A1 COVIDIEN LP 01 Dec 2015 (2015/12/01) Abstract; Fig. 1; [0007] - lines 9-10, [0051] – lines 5-17, [0052]	1-25
A	US 2020230355 A1 ACCURATE MEDICAL THERAPEUTICS LTD 23 Jul 2020 (2020/07/23) Fig. 1A-B – 155, 190, 192; [0093] – lines 20-22	1,22
A	US 2019217052 A1 ACCURATE MEDICAL THERAPEUTICS LTD 18 Jul 2019 (2019/07/18) Fig. 3A-B; [0038]	1,22
A	WO 2019087191 A1 ACCURATE MEDICAL THERAPEUTICS LTD 09 May 2019 (2019/05/09) Figs. 1, 7B-C; page 25 – lines 3-4, 17	1,22

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

☒ See patent family annex.

* Special categories of cited documents:
"A" document defining the general state of the art which is not considered to be of particular relevance
"D" document cited by the applicant in the international application
"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
20 Oct 2021	25 Oct 2021

Name and mailing address of the ISA:	Authorized officer
Israel Patent Office Technology Park, Bldg.5, Malcha, Jerusalem, 9695101, Israel Email address: pctoffice@justice.gov.il	RINGEL Avigail Telephone No. 972-73-3927190

INTERNATIONAL SEARCH REPORT

International application No.

PCT/IL2021/050904

A. CLASSIFICATION OF SUBJECT MATTER:

IPC (20210101) A61M 25/00, A61M 25/01, A61B 17/12

CPC (20130101) A61M 25/0067, A61M 2025/0042, A61M 25/0053, A61M 25/0045, A61M 25/0054, A61M 25/0023, A61M 25/005, A61M 25/007, A61M 25/0108, A61M 2025/0081, A61B 17/12131, A61B 17/12109, A61M 25/0068, A61B 17/12186

B. FIELDS SEARCHED:

* Minimum documentation searched (classification system followed by classification symbols)

IPC (20210101) A61M 25/00, A61M 25/01, A61B 17/12

CPC (20130101) A61M 25/0067, A61M 2025/0042, A61M 25/0053, A61M 25/0045, A61M 25/0054, A61M 25/0023, A61M 25/005, A61M 25/007, A61M 25/0108, A61M 2025/0081, A61B 17/12131, A61B 17/12109, A61M 25/0068, A61B 17/12186

INTERNATIONAL SEARCH REPORT
Information on patent family members

International application No.
PCT/IL2021/050904

Patent document cited search report	Publication date	Patent family member(s)	Publication Date
US 2015005801 A1	01 Dec 2015	US 2015005801 A1	01 Jan 2015
US 2020230355 A1	23 Jul 2020	US 2020230355 A1	23 Jul 2020
		BR 112020002723 A2	28 Jul 2020
		CN 111132715 A	08 May 2020
		EP 3664881 A1	17 Jun 2020
		EP 3664881 A4	26 May 2021
		IL 272295 D0	31 Mar 2020
		JP 2020530323 A	22 Oct 2020
		KR 20200039681 A	16 Apr 2020
		WO 2019030761 A1	14 Feb 2019
US 2019217052 A1	18 Jul 2019	US 2019217052 A1	18 Jul 2019
		US 11129960 B2	28 Sep 2021
		AU 2017260879 A1	15 Nov 2018
		BR 112018072050 A2	12 Feb 2019
		CA 3021780 A1	09 Nov 2017
		CA 3021780 C	08 Sep 2020
		CN 109414266 A	01 Mar 2019
		CN 109414266 B	23 Jul 2021
		EP 3451942 A1	13 Mar 2019
		EP 3451942 A4	21 Aug 2019
		EP 3451942 B1	20 Jan 2021
		IL 262767 D0	31 Dec 2018
		IL 262767 A	29 Apr 2021
		JP 2019520102 A	18 Jul 2019
		JP 6921116 B2	18 Aug 2021
		KR 20190017764 A	20 Feb 2019
		PL 3451942 T3	26 Jul 2021
		RU 2018137377 A	04 Jun 2020

INTERNATIONAL SEARCH REPORT
Information on patent family members

International application No.
PCT/IL2021/050904

Patent document cited search report	Publication date	Patent family member(s)	Publication Date
		RU 2018137377 A3	04 Jun 2020
		RU 2728692 C2	30 Jul 2020
		WO 2017191636 A1	09 Nov 2017
WO 2019087191 A1	09 May 2019	WO 2019087191 A1	09 May 2019
		BR 112020008852 A2	20 Oct 2020
		CN 111447882 A	24 Jul 2020
		EP 3703583 A1	09 Sep 2020
		EP 3703583 A4	30 Dec 2020
		IL 274383 D0	30 Jun 2020
		JP 2021501647 A	21 Jan 2021
		KR 20200085285 A	14 Jul 2020
		US 2021177430 A1	17 Jun 2021