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(54) Title: EMBOLIZATION DEVICE CONSTRUCTED FROM EXPANSILE POLYMER

(57) Abstract: Devices for the occlusion of body cavities, such as the embolization of vascular aneurysms and the like, and methods for making and using such devices. The devices may be comprised of novel expansile materials, novel infrastructure design, or both. The devices provided are very flexible and enable deployment with reduced or no damage to bodily tissues, conduits, cavities, etceteras.

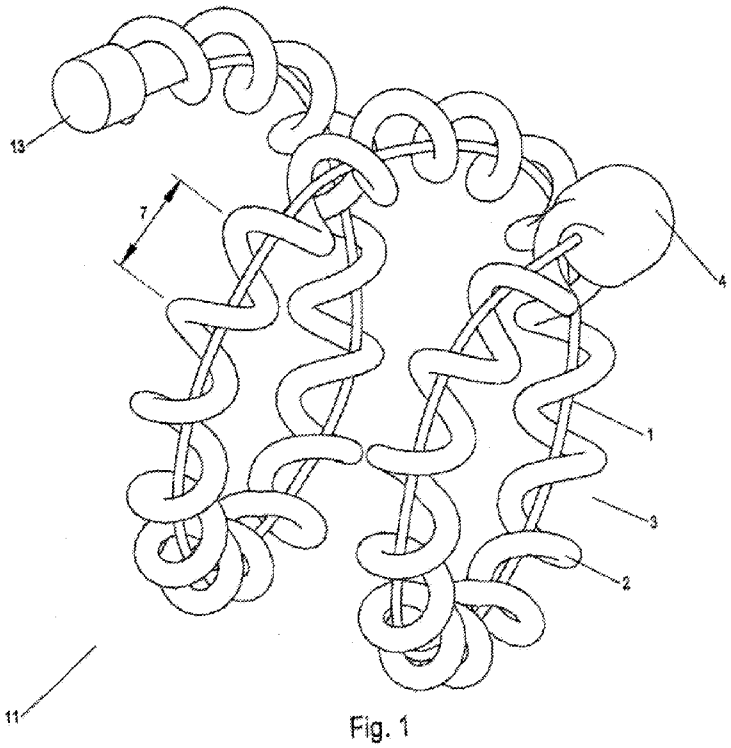

Fig. 1

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EMBOLIZATION DEVICE CONSTRUCTED FROM EXPANSILE POLYMER

RELATED APPLICATIONS

[0001] This application claims priority to U.S. Provisional Application Serial No. 61/254,962 filed October 26, 2009 entitled *Embolization Device Constructed From Expansile Polymer*, which is hereby incorporated herein by reference.

FIELD OF THE INVENTION

[0002] The present invention relates to devices for the occlusion of body cavities, such as the embolization of vascular aneurysms and the like, and methods for making and using such devices.

BACKGROUND OF THE INVENTION

[0003] The occlusion of body cavities, blood vessels, and other lumina by embolization is desired in a number of clinical situations. For example, the occlusion of fallopian tubes for the purposes of sterilization, and the occlusive repair of cardiac defects, such as a patent foramen ovale, patent ductus arteriosis, and left atrial appendage, and atrial septal defects. The function of an occlusion device in such situations is to substantially block or inhibit the flow of bodily fluids into or through the cavity, lumen, vessel, space, or defect for the therapeutic benefit of the patient.

[0004] The embolization of blood vessels is also desired in a number of clinical situations. For example, vascular embolization has been used to control vascular bleeding, to occlude the blood supply to tumors, and to occlude vascular aneurysms, particularly intracranial aneurysms. In recent years, vascular embolization for the treatment of aneurysms has received much attention. Several different treatment modalities have been shown in the prior art. One approach that has shown promise is the use of thrombogenic microcoils. These microcoils may be made of biocompatible metal alloy(s) (typically a radio-opaque material such as platinum or tungsten) or a suitable polymer. Examples of microcoils are disclosed in the following patents: U.S. Pat. No. 4,994,069--Ritchart et al.; U.S. Pat. No. 5,133,731--Butler et al.; U.S. Pat. No. 5,226,911--Chee et al.; U.S. Pat. No. 5,312,415--Palermo; U.S. Pat. No. 5,382,259--

Phelps et al.; U.S. Pat. No. 5,382,260--Dormandy, Jr. et al.; U.S. Pat. No. 5,476,472--Dormandy, Jr. et al.; U.S. Pat. No. 5,578,074--Mirigian; U.S. Pat. No. 5,582,619--Ken; U.S. Pat. No. 5,624,461--Mariant; U.S. Pat. No. 5,645,558--Horton; U.S. Pat. No. 5,658,308--Snyder; and U.S. Pat. No. 5,718,711--Berenstein et al; all of which are hereby incorporated by reference.

[0005] A specific type of microcoil that has achieved a measure of success is the Guglielmi Detachable Coil ("GDC"), described in U.S. Pat. No. 5,122,136--Guglielmi et al. The GDC employs a platinum wire coil fixed to a stainless steel delivery wire by a solder connection. After the coil is placed inside an aneurysm, an electrical current is applied to the delivery wire, which electrolytically disintegrates the solder junction, thereby detaching the coil from the delivery wire. The application of current also creates a positive electrical charge on the coil, which attracts negatively-charged blood cells, platelets, and fibrinogen, thereby increasing the thrombogenicity of the coil. Several coils of different diameters and lengths can be packed into an aneurysm until the aneurysm is completely filled. The coils thus create and hold a thrombus within the aneurysm, inhibiting its displacement and its fragmentation.

[0006] A more recent development in the field of microcoil vaso-occlusive devices is exemplified in U.S. Pat. No. 6,299,619 to Greene, Jr. et al., U.S. Pat. No. 6,602,261 to Greene, Jr. et al., and co-pending U.S. Pat. Appl. No. 10/631,981 to Martinez; all assigned to the assignee of the subject invention and incorporated herein by reference. These patents disclose vaso-occlusive devices comprising a microcoil with one or more expansile elements disposed on the outer surface of the coil. The expansile elements may be formed of any of a number of expansile polymeric hydrogels, or alternatively, environmentally-sensitive polymers that expand in response to a change in an environmental parameter (e.g., temperature or pH) when exposed to a physiological environment, such as the blood stream.

[0007] This invention is a novel vaso-occlusive device, a novel expansile element, and a combination thereof.

SUMMARY OF THE INVENTION

[0008] The present invention is directed to novel vaso-occlusive devices comprising a carrier member, one or more novel expansile elements, and a combination thereof. Generally, the expansile element or elements comprise an expansile polymer. The carrier member may be used to assist the delivery of the expansile element by providing a structure that, in some embodiments, allows coupling to a delivery mechanism and, in some embodiments, enhances the radiopacity of the device.

[0009] In one embodiment, the expansile polymer is an environmentally sensitive polymeric hydrogel, such as that described in U.S. Patent No. 6,878,384, issued April 12, 2005 to Cruise et al., hereby incorporated by reference. In another embodiment, the expansile polymer is a novel hydrogel comprised of sodium acrylate and a poly(ethylene glycol) derivative. In another embodiment, the expansile polymer is a hydrogel comprising a Pluronics® derivative.

[0010] In one embodiment, the expansile polymer is a novel hydrogel that has ionizable functional groups and is made from macromers. The macromers may be non-ionic and/or ethylenically unsaturated.

[0011] In one embodiment, the macromers may have a molecular weight of about 400 to about 35,000 grams/mole. In another embodiment the macromers may have a molecular weight of about 5,000 to about 15,000 grams/mole. In yet another embodiment the macromers may have a molecular weight of about 7,500 to about 12,000 grams/mole. In one embodiment the macromers have a molecular weight of 8,000 grams/mole.

[0012] In one embodiment, the hydrogel may be made of polyethers, polyurethanes, derivatives thereof, or combinations thereof. In another embodiment, the ionizable functional groups may comprise basic groups (e.g., amines, derivatives thereof, or combinations thereof) or acidic groups (e.g., carboxylic acids, derivatives thereof, or combinations thereof). If the ionizable functional groups comprise basic groups, the basic groups may be deprotonated at pHs greater than the pKa or protonated at pHs less than the pKa of the basic groups. If the ionizable functional groups comprise acidic

groups, the acidic groups may be protonated at pHs less than the pKa or de-protonated at pHs greater than the pKa of the acidic groups.

[0013] In one embodiment, the macromers may comprise vinyl, acrylate, acrylamide, or methacrylate derivatives of poly(ethylene glycol), or combinations thereof. In another embodiment, the macromer may comprise poly(ethylene glycol) di-acrylamide. In another embodiment, the hydrogel is substantially free, more preferably free of unbound acrylamide.

[0014] In one embodiment, the macromers may be cross-linked with a compound that contains at least two ethylenically unsaturated moities. Examples of ethylenically unsaturated compounds include N, N'-methylenebisacrylamide, derivatives thereof, or combinations thereof. In another embodiment, the hydrogel may be prepared using a polymerization initiator. Examples of suitable polymerization initiators comprise N,N,N',N'-tetramethylethylenediamine, ammonium persulfate, azobisisobutyronitrile, benzoyl peroxides, derivatives thereof, or combinations thereof. The polymerization initiator may be soluble in aqueous or organic solvents. For example, azobisisobutyronitrile is not water soluble; however, water soluble derivatives of azobisisobutyronitrile, such as 2,2'-azobis(2-methylproprionamidine) dihydrochloride, are available. In another embodiment, the hydrogel may be substantially non-resorbable, non-degradable or both, at physiological conditions.

[0015] In one embodiment, the invention comprises a method for preparing an environmentally-responsive hydrogel for implantation in an animal. The method includes combining at least one, preferably non-ionic, macromer with at least one ethylenically unsaturated moiety, at least one macromer or monomer having at least one ionizable functional group and at least one ethylenically unsaturated moiety, at least one polymerization initiator, and at least one solvent to form a hydrogel. The solvent may include aqueous or organic solvents, or combinations thereof. In another embodiment, the solvent is water. Next, the hydrogel may be treated to prepare an environmentally-responsive hydrogel, preferably one that is responsive at physiological conditions. The ionizable functional group(s) may be an acidic group (e.g., a carboxylic acid, a derivative thereof, or combinations thereof) or a basic group (e.g., an amine, derivatives thereof, or

combinations thereof). If the ionizable functional group comprises an acidic group, the treating step may comprise incubating the hydrogel in an acidic environment to protonate the acidic groups. If the ionizable functional group comprises a basic group, the treating step may comprise incubating the hydrogel in a basic environment to de-protonate the basic groups. In certain embodiments, it is preferable that the acidic groups are capable of being de-protonated or, conversely, the basic groups are capable of being protonated, after implantation in an animal.

[0016] In one embodiment, the ethylenically unsaturated macromer may have a vinyl, acrylate, methacrylate, or acrylamide group; including derivatives thereof or combinations thereof. In another embodiment, the ethylenically unsaturated macromer is based upon poly(ethylene glycol), derivatives thereof, or combinations thereof. In another embodiment, the ethylenically unsaturated macromer is poly(ethylene glycol) di-acrylamide, poly(ethylene glycol) di-acrylate, poly(ethylene glycol) di-methacrylate, derivatives thereof, or combinations thereof. In another embodiment, the ethylenically unsaturated macromer is poly(ethylene glycol) di-acrylamide. The ethylenically unsaturated macromer may be used at a concentration of about 5% to about 40% by weight, more preferably about 20% to about 30% by weight. The solvent may be used at a concentration of about 20% to about 80% by weight.

[0017] In one embodiment, the combining step also includes adding at least one cross-linking agent comprising an ethylenically unsaturated compound. In certain embodiments of the present invention, a cross-linker may not be necessary. In other words, the hydrogel may be prepared using a macromer with a plurality of ethylenically unsaturated moieties. In another embodiment, the polymerization initiator may be a reduction-oxidation polymerization initiator. In another embodiment, the polymerization initiator may be N,N,N',N'-tetramethylethylenediamine, ammonium persulfate, azobisisobutyronitrile, benzoyl peroxides, 2,2'-azobis(2-methylproprionamidine) dihydrochloride, derivatives thereof, or combinations thereof. In another embodiment, the combining step further includes adding a porosigen.

[0018] In one embodiment, the ethylenically unsaturated macromer includes poly(ethylene glycol) di-acrylamide, the macromer or monomer or polymer with at least

one ionizable group and at least one ethylenically unsaturated group includes sodium acrylate, the polymerization initiator includes ammonium persulfate and N,N,N,',N' tetramethylethylenediamine, and the solvent includes water.

[0019] In one embodiment, the ethylenically unsaturated macromer has a molecular weight of about 400 to about 35,000 grams/mole. In another embodiment, the ethylenically unsaturated macromer has a molecular weight of about 5,000 to about 15,000 grams/mole. In one embodiment, the ethylenically unsaturated macromer has a molecular weight of about 7,500 to about 12,000 grams/mole. In another embodiment, the environmentally-responsive hydrogel is substantially non-resorbable, or non-degradable or both at physiological conditions. In certain embodiments, the environmentally-responsive hydrogel may be substantially free or completely free of unbound acrylamide.

[0020] In one embodiment, the carrier member comprises a coil or microcoil made from metal, plastic, or similar materials. In another embodiment, the carrier member comprises a braid or knit made from metal, plastic, or similar materials. In another embodiment, the carrier member comprises a plastic or metal tube with multiple cuts or grooves cut into the tube.

[0021] In one embodiment, the expansile element is arranged generally co-axially within the carrier member. In another embodiment, a stretch resistant member is arranged parallel to the expansile element. In another embodiment, the stretch resistant member is wrapped, tied, or twisted around the expansile element. In another embodiment, the stretch resistant member is positioned within the expansile element. In another embodiment, the stretch resistant member is located within or partially surrounded by the expansile element.

[0022] In one embodiment, the device comprising the expansile element and carrier member are detachably coupled to a delivery system. In another embodiment, the device is configured for delivery by pushing or injecting through a conduit into a body.

[0023] In one embodiment, the expansile element is environmentally sensitive and exhibits delayed expansion when exposed to bodily fluids. In another embodiment, the

expansile element expands quickly upon contact with a bodily fluid. In another embodiment, the expansile element comprises a porous or reticulated structure that may form a surface or scaffold for cellular growth.

[0024] In one embodiment, the expansile element expands to a dimension that is larger than the diameter of the carrier member in order to provide enhanced filling of the lesion. In another embodiment, the expansile element expands to a dimension equal to or smaller than the diameter of the carrier member to provide a scaffold for cellular growth, release of therapeutic agents such as pharmaceuticals, proteins, genes, biologic compounds such as fibrin, or the like.

BRIEF DESCRIPTION OF THE DRAWINGS

[0025] **Fig. 1** is a perspective view showing one embodiment of the present invention prior to expansion of the expansile element;

[0026] **Fig. 2** is a perspective view showing a device similar to **Fig. 1** in an expanded state;

[0027] **Fig. 3** is a perspective view of an alternative embodiment of the present invention;

[0028] **Fig. 4** is a perspective view of an alternative embodiment wherein the carrier member comprises a fenestrated tube, braid or knit;

[0029] **Fig. 5** is a perspective view of an alternative embodiment incorporating a stretch resistant member running approximately parallel to the expansile element;

[0030] **Fig. 6** is a perspective view of an alternative embodiment incorporating a stretch resistant member approximately intertwined with the expansile element;

[0031] **Fig. 7** is a perspective view of an alternative embodiment wherein the expansile element has formed a loop or fold outside the carrier member.

[0032] **Fig. 8** is a perspective view of an alternative embodiment showing a device similar to those shown in **Fig.1** and **Fig. 2** wherein the expansile element is not expanded to a diameter larger than the carrier member.

[0033] **Fig. 9** is a side view of an embodiment showing a device similar to those shown in **Fig.1** and **Fig. 2.**

[0034] **Fig. 10** is an exploded perspective view of the device of **Fig. 9**.

[0035] **Fig. 11** is a side view of the device of **Fig. 9** connected to a delivery device.

[0036] **Fig. 12** is a side view of a preferred embodiment of an implant according to the present invention.

[0037] **Fig. 13** is a said view of a preferred embodiment of an implant according to the present invention.

DESCRIPTION OF THE INVENTION

[0038] As used herein, the term "macromer" refers to a large molecule containing at least one active polymerization site or binding site. Macromers have a larger molecular weight than monomers. For example, an acrylamide monomer has a molecular weight of about 71.08 grams/mole whereas a poly(ethylene glycol) di-acrylamide macromer may have a molecular weight of about 400 grams/mole or greater. Preferred macromers are non-ionic, i.e. they are uncharged at all pHs.

[0039] As used herein, the term "environmentally responsive" refers to a material (e.g., a hydrogel) that is sensitive to changes in environment including but not limited to pH, temperature, and pressure. Many of the expansile materials suitable for use in the present invention are environmentally responsive at physiological conditions.

[0040] As used herein, the term "non-resorbable" refers to a material (e.g., a hydrogel) that cannot be readily and/or substantially degraded and/or absorbed by bodily tissues.

[0041] As used herein, the term "unexpanded" refers to the state at which a hydrogel is substantially not hydrated and, therefore, not expanded.

[0042] As used herein, the term "ethylenically unsaturated" refers to a chemical entity (e.g., a macromer, monomer or polymer) containing at least one carbon-carbon double bond.

[0043] Referring to **Fig. 1-8**, the device comprises an expansile element 1 and a carrier member 2. The expansile element 1 may be made from a variety of suitable biocompatible polymers. In one embodiment, the expansile element 1 is made of a bioabsorbable or biodegradable polymer, such as those described in U.S. Patent Nos. 7,070,607 and 6,684,884, the disclosures of which are incorporated herein by reference. In another embodiment, the expansile element 1 is made of a soft conformal material, and more preferably of an expansile material such as a hydrogel.

[0044] In one embodiment, the material forming the expansile element 1 is an environmentally responsive hydrogel, such as that described in U.S. Patent No. 6,878,384, the disclosure of which is incorporated herein by reference. Specifically, the hydrogels described in U.S. Patent No. 6,878,384 are of a type that undergoes controlled volumetric expansion in response to changes in such environmental parameters as pH or temperature. These hydrogels are prepared by forming a liquid mixture that contains (a) at least one monomer and/or polymer, at least a portion of which is sensitive to changes in an environmental parameter; (b) a cross-linking agent; and (c) a polymerization initiator. If desired, a porosigen (e.g., NaCl, ice crystals, or sucrose) may be added to the mixture, and then removed from the resultant solid hydrogel to provide a hydrogel with sufficient porosity to permit cellular ingrowth. The controlled rate of expansion is provided through the incorporation of ethylenically unsaturated monomers with ionizable functional groups (e.g., amines, carboxylic acids). For example, if acrylic acid is incorporated into the cross-linked network, the hydrogel is incubated in a low pH solution to protonate the carboxylic acid groups. After the excess low pH solution is rinsed away and the hydrogel dried, the hydrogel can be introduced through a microcatheter filled with saline at physiological pH or with blood. The hydrogel cannot expand until the carboxylic acid groups deprotonate. Conversely, if an amine-

containing monomer is incorporated into the cross-linked network, the hydrogel is incubated in a high pH solution to deprotonate amines. After the excess high pH solution is rinsed away and the hydrogel dried, the hydrogel can be introduced through a microcatheter filled with saline at physiological pH or with blood. The hydrogel cannot expand until the amine groups protonate.

[0045] In another embodiment, the material forming the expansile element 1 may be an environmentally responsive hydrogel, similar to those described in U.S. Patent No. 6,878,384; however, an ethylenically unsaturated, and preferably non-ionic, macromer replaces or augments at least one monomer or polymer. The Applicants surprisingly have discovered that hydrogels prepared in accordance with this embodiment can be softer and/or more flexible in their unexpanded state than those prepared in accordance with U.S. Patent No. 6,878,384. The Applicants also have discovered that ethylenically unsaturated and non-ionic macromers (e.g., poly(ethylene glycol) and derivatives thereof) may be used not only to prepare a softer unexpanded hydrogel; but, in combination with monomers or polymers containing ionizable groups, one that also may be treated to be made environmentally responsive. The surprising increase in unexpanded flexibility enables the hydrogels to be, for example, more easily deployed in an animal or deployed with reduced or no damage to bodily tissues, conduits, cavities, etceteras.

[0046] The hydrogels prepared from non-ionic macromers in combination with monomers or polymers with ionizable functional groups still are capable of undergoing controlled volumetric expansion in response to changes in environmental parameters. These hydrogels may be prepared by combining in the presence of a solvent: (a) at least one, preferably non-ionic, macromer with a plurality of ethylenically unsaturated moieties; (b) a macromer or polymer or monomer having at least one ionizable functional group and at least one ethylenically unsaturated moiety; and (c) a polymerization initiator. It is worthwhile to note that with this type of hydrogel, a cross-linking agent may not be necessary for cross-linking since, in certain embodiments, the components selected may be sufficient to form the hydrogel. As hereinbefore described, a porosigen may be added to the mixture and then removed from the

resultant hydrogel to provide a hydrogel with sufficient porosity to permit cellular ingrowth.

[0047] The non-ionic macromer-containing hydrogels' controlled rate of expansion may be provided through the incorporation of at least one macromer or polymer or monomer having at least one ionizable functional group (e.g., amine, carboxylic acid). As discussed above, if the functional group is an acid, the hydrogel is incubated in a low pH solution to protonate the group. After the excess low pH solution is rinsed away and the hydrogel dried, the hydrogel can be introduced through a microcatheter, preferably filled with saline. The hydrogel cannot expand until the acid group(s) deprotonates. Conversely, if the functional group is an amine, the hydrogel is incubated in a high pH solution to deprotonate the group. After the excess high pH solution is rinsed away and the hydrogel dried, the hydrogel can be introduced through a microcatheter, preferably filled with saline. The hydrogel cannot expand until the amine(s) protonates.

[0048] More specifically, in one embodiment, the hydrogel is prepared by combining at least one non-ionic macromer having at least one unsaturated moiety, at least one macromer or monomer or polymer having at least one ionizable functional group and at least one ethylenically unsaturated moiety, at least one polymerization initiator, and a solvent. Optionally, an ethylenically unsaturated cross-linking agent and/or a porosigen also may be incorporated. In one embodiment, concentrations of the non-ionic macromers in the solvent range from about 5% to about 60% (w/w). In another embodiment, concentrations of the non-ionic macromers in the solvent range from about 20% to about 30% (w/w). In one embodiment, concentrations of the non-ionic macromers in the solvent range are about 25% (w/w). In one embodiment the non-ionic macromer is poly(ethylene glycol), its derivatives, and combinations thereof. Derivatives include, but are not limited to, poly(ethylene glycol) di-acrylamide, poly(ethylene glycol) di-acrylate, and poly(ethylene glycol) dimethacrylate. Poly(ethylene glycol) di-acrylamide is a preferred derivative of poly(ethylene glycol) and has a molecular weight ranging from about 8,500 grams/mole to about 12,000 grams/mole. The macromer may have less than 20 polymerization sites, more preferably less than 10 polymerization sites, more preferably about five or less polymerization sites, and more preferably from

about two to about four polymerization sites. Poly(ethylene glycol) di-acrylamide has two polymerization sites.

[0049] Preferred macromers or polymers or monomers having at least one ionizable functional group include, but are not limited to compounds having carboxylic acid or amino moieties or, derivatives thereof, or combinations thereof. Sodium acrylate is a preferred ionizable functional group-containing compound and has a molecular weight of 94.04 g/mole. In one embodiment, concentrations of the ionizable macromers or polymers or monomers in the solvent range from about 5% to about 60% (w/w) In another embodiment, concentrations of the ionizable macromers or polymers or monomers in the solvent range from about 20% to about 30% (w/w). In one embodiment, concentrations of the ionizable macromers or polymers or monomers in the solvent are about 27% (w/w). In some embodiments, at least about 10%-50% of the ionizable macromers or polymers or monomers selected should be pH sensitive. In other embodiments at least about 10%-30% of the ionizable macromers or polymers or monomers selected should be pH sensitive. In one embodiment no free acrylamide is used in the macromer-containing hydrogels of the present invention.

[0050] When used, the cross-linking agent may be any multifunctional ethylenically unsaturated compound, preferably N, N'-methylenebisacrylamide. If biodegradation of the hydrogel material is desired, a biodegradable cross-linking agent may be selected. The concentrations of the cross-linking agent in the solvent should be less than about 1% w/w, and preferably less than about 0.1% (w/w).

[0051] As described above, if a solvent is added, it may be selected based on the solubilities of the macromer(s) or monomer(s) or polymer(s), cross-linking agent, and/or porosigen used. If a liquid macromer or monomer or polymer solution is used, a solvent may not be necessary. A preferred solvent is water, but a variety of aqueous and organic solvents may be used. In one embodiment, concentrations of the solvent range from about 20% to about 80% (w/w). In another embodiment, concentrations of the solvent range from about 40% to about 60% (w/).

[0052] Crosslink density may be manipulated through changes in the macromer or monomer or polymer concentration, macromer molecular weight, solvent concentration

and, when used, cross-linking agent concentration. As described above, the hydrogel may be cross-linked via reduction-oxidation, radiation, and/or heat. A preferred type of polymerization initiator is one that acts via reduction-oxidation. Suitable polymerization initiators include, but are not limited to, N,N,N',N'-tetramethylethylenediamine, ammonium persulfate, azobisisobutyronitrile, benzoyl peroxides, 2,2'-azobis(2-methylpropionamidine) dihydrochloride, derivatives thereof, or combinations thereof. A combination of ammonium persulfate and N,N,N',N'-tetramethylethylenediamine is a preferred polymerization initiator for use in the macromer containing embodiments of the invention.

[0053] After polymerization is complete, the hydrogels of the present invention may be washed with water, alcohol or other suitable washing solution(s) to remove any porosigen(s), any unreacted, residual macromer(s), monomer(s), and polymer(s) and any unincorporated oligomers. Preferably this is accomplished by initially washing the hydrogel in distilled water.

[0054] Porosity may be imparted into the solid hydrogel through the use of porosigens such as sodium chloride, ice crystals, or sucrose. Polymerization of the monomer solution around the solid particles in suspension and subsequent removal of the solid particles from the hydrogel can provide a hydrogel with sufficient porosity to permit cellular ingrowth. A preferred porosigen is sodium chloride with particles less than 10 microns in diameter. Preferred sodium chloride concentrations in the monomer solution range from 0.2 to 0.4 g sodium chloride per g monomer solution.

[0055] The hydrogels of the present invention may be made environmentally-responsive by protonating or deprotonating the ionizable functional groups present on the hydrogel network, as discussed above. Once the hydrogel has been prepared and, if needed, washed, the hydrogel may be treated to make the hydrogel environmentally-responsive. For hydrogel networks where the ionizable functional groups are carboxylic acid groups, the hydrogel is incubated in a low pH solution. The free protons in the solution protonate the carboxylic acid groups on the hydrogel network. The duration and temperature of the incubation and the pH of the solution influence the amount of control on the expansion rate. In general, the duration and temperature of the incubation are

directly proportional to the amount of expansion control, while the incubation solution pH is inversely proportional thereto.

[0056] It has been determined that incubation solution water content also affects expansion control. In this regard, higher water content enables greater hydrogel expansion and is thought to increase the number of protonation-accessible carboxylic acid groups. An optimization of water content and pH is required for maximum control on expansion rate. Expansion control, among other things, has an effect on device positioning/repositioning time. Typically, a positioning/repositioning time of about 0.1 to about 30 minutes is preferred for hydrogel devices in accordance with the present invention.

[0057] After incubation, the excess treating solution is washed away and the hydrogel material is dried. A hydrogel treated with the low pH solution has been observed to dry down to a smaller dimension than an untreated hydrogel. This effect is desirable since devices containing these hydrogels may be delivered through a microcatheter.

[0058] For hydrogel networks where the ionizable functional groups are amine groups, the hydrogel is incubated in a high pH solution. Unlike carboxylic acid functional groups, deprotonation occurs on the amine groups of the hydrogel network at high pH. Aside from incubation solution pH, the incubation is carried out similarly to that of the carboxylic acid containing hydrogels. In other words, the duration and temperature of the incubation and the pH of the solution are directly proportional to the amount of expansion control. After incubation is concluded, the excess treating solution is washed away and the hydrogel material is dried.

[0059] In a preferred embodiment, the expansile element 1 is an expansile hydrogel comprised of (a) at least one, preferably non-ionic, ethylenically unsaturated macromer or monomer or polymer having at least two cross-linkable groups; (b) at least one monomer and/or polymer which has at least one cross-linkable groups, and at least one moiety that is sensitive to changes in an environmental parameter; and (c) a polymerization initiator. In some embodiments, the monomers and polymers may be water soluble, while in other embodiments they may be non-water soluble. Suitable

polymers for component (a) include poly(ethylene glycol), poly(ethylyene oxide), poly(vinyl alcohol), poly(propylene oxide), poly(propylene glycol), poly(ethylene oxide)-co-poly(propylene oxide), poly(vinyl pyrrolidinone), poly(amino acids), dextrans, poly(ethyloxazoline), polysaccharides, proteins, glycosaminoglycans, and carbohydrates, and derivatives thereof. The preferred polymer is poly(ethylene glycol) (PEG), especially for component (a). Alternatively, polymers that biodegrade partly or completely may be utilized.

[0060] One embodiment comprises combining in the presence of a solvent (a) about 5% to about 50% of a non-ionic, ethylenically unsaturated macromer or monomer or polymer; (b) about 5% to about 60% of an ethylenically unsaturated monomer or polymer with at least one ionizable functional group; and, (c) a polymerization initiator. Suitable ionizable, ethylenically unsaturated monomers include acrylic acid and methacrylic acid, as well as derivatives thereof. One suitable monomer having at least one ionizable functional group is sodium acrylate. Suitable macromers with two ethylenically unsaturated moities include poly(ethylene glycol) di-acrylate and poly(ethylene glycol) di-acrylamide, and poly(ethylene glycol) di-acrylamide, which have molecular weights ranging between 400 and 30,000 grams/mole. The use of macromers with a plurality of ethylenically unsaturated groups permits the elimination of the cross-linker, as the cross-linker functions are performed by the multi-functional polymer. In one embodiment, the hydrogel comprises, about 5% to about 60% sodium acrylate, about 5% to about 50% poly(ethylene glycol) di-acrylamide.

[0061] A sodium acrylate/ poly(ethylene glycol) di-acrylamide hydrogel is used to enhance the mechanical properties of the previously-described environmentally responsive hydrogel. Since a sodium acrylate/poly(ethylene glycol) di-acrylamide hydrogel is softer than a sodium acrylate/acrylamide hydrogel (e.g., the one utilized in *Hydrogel Embolic System (HES)* made by MicroVention, Aliso Viejo, CA), devices incorporating it may be more flexible. Due to the relative stiffness of the HES, MicroVention recommends pre-softening the device by soaking in warm fluid or steaming the implant. In addition, devices made from acrylamide are relatively straight before pre-softening because the stiffness of the acrylamide-based hydrogel prevents the carrier member (for the HES, a microcoil) from assuming its secondary

configuration. Devices made from a sodium acrylate/poly(ethylene glycol) di-acrylamide hydrogel may not require pre-softening techniques such as soaking in warm fluid such as saline or blood or exposure to steam in order to form into a secondary configuration heat-set into the carrier member 2 or a similar carrier member. Thus, in embodiments comprising, for example, sodium acrylate and poly(ethylene glycol) di-acrylamide, a substantially continuous length of hydrogel disposed either within the lumen 3 of the carrier member 2 as shown in, for example, **Fig. 1** or on a carrier element such as those shown in the Martinez '981 application or Greene '261, will form into the secondary configuration pre-formed into the carrier member without pre-treatment (e.g. exposure to steam, fluid, or blood). This makes the device easier to use because it allows elimination of the pre-treatment step and the device may be safer when deployed into the patient because a softer device is less likely to cause damage to the lesion.

[0062] **Examples**

[0063] 3 g of acrylamide, 1.7 g of acrylic acid, 9 mg of bisacrylamide, 50 mg of N,N,N',N'-tetramethylethylenediamine, 15 mg of ammonium persulfate, and 15.9 g water were combined and polymerized in a 0.020 inch tube. The tubularized polymer was removed from the tubing to prepare Hydrogel 1 in accordance with U.S. Patent No. 6,878,384.

[0064] 4.6 g of poly(ethylene glycol) diacrylamide, 3.3 g of sodium acrylate, 100 mg of N,N,N',N'-tetramethylethylenediamine, 25 mg of ammonium persulfate, and 15.9 g water were combined and polymerized in a 0.020 inch tube. The tubularized polymer was removed from the tubing to prepare Hydrogel 2, in accordance with a macromer-containing hydrogel embodiment of the present invention.

[0065] A large platinum microcoil for the above examples has a 0.014 inch outer diameter and a 0.0025 inch filar. A small platinum microcoil has a 0.010 inch outer diameter and a 0.002 inch filar.

[0066] 8.3 g of poly(ethylene glycol) diacrylamide, 9.0 g of sodium acrylate, 155 mg of N,N,N',N'-tetramethylethylenediamine, 20 mg of ammonium persulfate, and 15.9 g water were combined and polymerized in a 0.025 inch tube. The tubularized polymer

was removed from the tubing to prepare Hydrogel 3, in accordance with a macromer-containing hydrogel embodiment of the present invention.

[0067] The Hydrogel 3 is distinct from the Hydrogel 1 and 2 examples. The Hydrogel 3 has a reduced stiffness relative to Hydrogel 1 and it further does not require pretreatment prior to use. Such pretreatment can sometimes require soaking in warm fluid or steaming to achieve a desired flexibility. Hydrogel 3 also allows for increased expansion compared with Hydrogel 2.

[0068] In another embodiment, monomers are used to impart moieties to the expansile element 1 that are suitable for coupling bioactive compounds, for example anti-inflammatory agents such as corticosteroids (e.g. prednisone and dexamethasone); or vasodilators such as nitrous oxide or hydralazine; or anti-thrombotic agents such as aspirin and heparin; or other therapeutic compounds, proteins such as mussel adhesive proteins (MAPs), amino acids such as 3-(3,4-dihydroxyphenyl)-L-alanine (DOPA), genes, or cellular material; see U.S Patent 5,658,308, WO 99/65401, *Polymer Preprints* 2001,42(2), 147 Synthesis and Characterization of Self-Assembling Block Copolymers Containing Adhesive Moieties by Kui Hwang *et. al.*, and WO 00/27445; the disclosures of which are hereby incorporated by reference. Examples of moieties for incorporation into hydrogel materials include, but are not limited to, hydroxyl groups, amines, and carboxylic acids.

[0069] In another embodiment, the expansile element 1 may be rendered radiopaque by incorporation of monomers and/or polymers containing, for example, iodine, or the incorporation of radiopaque metals such as tantalum and platinum.

[0070] In some embodiments, the carrier member 2 is a flexible, elongate structure. Suitable configurations for the carrier member 2 include helical coils, braids, and slotted or spiral-cut tubes. The carrier member 2 may be made of any suitable biocompatible metal or polymer such as platinum, tungsten, PET, PEEK, Teflon, Nitinol, Nylon, steel, and the like. The carrier member may be formed into a secondary configuration such as helix, box, sphere, flat rings, J-shape, S-shape or other complex shape known in the art. Examples of appropriate shapes are disclosed in Horton 5,766,219; Schaefer Appl. No. 10/043,947; and Wallace 6,860,893; all hereby incorporated by reference.

[0071] As previously described, some embodiments of the instant invention may comprise polymers that are sufficiently soft and flexible that a substantially continuous length of the expansile element 1 will form into a secondary configuration similar to the configuration originally set into the carrier member 2 without pre-softening the device or exposing it to blood, fluid, or steam.

[0072] In some embodiments, the carrier member 2 incorporates at least one gap 7 that is dimensioned to allow the expansile element 1 to expand through the gap (one embodiment of this configuration is shown in **Figs. 1-2)**. In other embodiments, the carrier member 2 incorporates at least one gap 7 that allows the expansile element 1 to be exposed to bodily fluids, but the expansile element 1 does not necessarily expand through the gap (one embodiment of this configuration is shown in **Fig. 8**). In other embodiments, no substantial gap is incorporated into the carrier member 2. Rather, fluid is allowed to infiltrate through the ends of the device or is injected through a lumen within the delivery system and the expansile element 1 expands and forces its way through the carrier member 2.

[0073] In one embodiment shown in **Fig. 1**, the expansile element 1 comprises an acrylamide or poly(ethylene glycol)-based expansile hydrogel. The carrier member 2 comprises a coil. At least one gap 7 is formed in the carrier member 2. The expansile element 1 is disposed within the lumen 3 defined by the carrier member 2 in a generally coaxial configuration. A tip 4 is formed at the distal end of the device 11 by, for example, a laser, solder, adhesive, or melting the hydrogel material itself. The expansile element 1 may run continuously from the proximal end to the distal end, or it may run for a portion of the device then terminate before reaching the distal or proximal end, or both.

[0074] As an example, in one embodiment the device is dimensioned to treat a cerebral aneurysm. Those skilled in the art will appreciate that the dimensions used in this example could be re-scaled to treat larger or smaller lesions. In this embodiment, the expansile element 1 is about 0.006”-0.007” before expansion and about 0.02” after expansion. The expansile element is, for example, approximately 52% sodium acrylate, 48% poly(ethylene glycol) di-acrylamide with a molecular weight about 8000

grams/mole. About 0.4 g/g sodium chloride (about 10 micron particle size) is used as a porosigen and about 0.6 mg/mL ammonium persulfate and 7 mg/mL tetramethylethylene diamine is used as an initiator. The carrier member 2 in this embodiment is a microcoil in the range of about 0.012"-0.0125" in diameter and has a filar between about 0.002"-0.00225". In one embodiment, the carrier member 2 comprises at least one gap 7 between 1 to 3 filar sizes long. In another embodiment, the carrier member 2 comprises at least one gap 7 that is about 2 filars long. In one embodiment the size of the gap 7 is between about 0.0015 inches and 0.0075 inches long. In another embodiment, the size of the gap 7 is between 0.00225 inches and 0.00750 inches long.

[0075] A coupler 13 is placed near the proximal end to allow the implant 11 to be detachably coupled to a delivery system or pushed or injected through a catheter. Examples of delivery systems are found in co-pending Appl. No. 11/ 212,830 to Fitz, US6,425,893 to Guglielmi, US4,994,069 to Ritchart, US6,063,100 to Diaz, and US5,690,666 to Berenstein; the disclosures of which are hereby incorporated by reference.

[0076] In this embodiment, the implant 11 is constructed by formulating and mixing the hydrogel material as previously described in order to form the expansile element 1. The carrier member 2 is wound around a helical or complex form, and then heat-set by techniques known in the art to form a secondary diameter ranging from 0.5 mm to 30 mm and a length ranging from 5 mm to 100 cm. After processing, washing, and optional acid treatment, the expansile element 1 is threaded through the lumen 3 of the carrier member 2. The distal end of the expansile element 1 is then tied, for example by forming a knot, to the distal end of the carrier member 2. Adhesive, such as UV curable adhesive or epoxy, may be used to further enhance the bond between the expansile element 1 and the carrier member 2 and to form the distal tip 4. Alternatively, the tip may be formed by, for example, a laser weld or solder ball.

[0077] In some embodiments, the size of the gap 7 and the ratio of expansion, loops or folds 12 may form as shown in **Fig. 7** as the expansile element 1 expands. It is desirable to prevent these loops or folds 12 from forming. This can be done by

stretching the expansile element 1 either before placing it within the carrier member 2 or after the distal end of the expansile element 1 is secured to the carrier member 2. For example, once the distal end of the expansile element 1 is secured to the carrier member 2, the expansile element 1 is stretched such that its initial diameter of 0.010" is reduced to between about 0.006: - 0.007" before placing it within the carrier member 2. After stretching, the expansile element 1 may be trimmed to match the length of the carrier member 2 and then bonded near the proximal end of the carrier member 2 by, for example, tying a knot, adhesive bonding, or other techniques known in the art.

[0078] Once the implant 11 has been constructed, it is attached to a delivery system previously described by methods known in the art. The device may also be exposed to, for example, e-beam or gamma radiation to cross-link the expansile element 1 and to control its expansion. This is described in U.S. Patent No. 6,537,569 which is assigned to the assignee of this application and hereby incorporated by reference.

[0079] Previously, the secondary dimensions of prior devices (e.g. HES) are generally sized to a dimension 1-2 mm smaller than the dimension (i.e. volume) of the treatment site due to the relative stiffness of these devices. The increased flexibility and overall design of the implant 11 of the instant invention allows the secondary shape of the implant 11 to be sized to a dimension approximately the same size as the treatment site, or even somewhat larger. This sizing further minimizes the risk of the implant moving in or slipping out of the treatment site.

[0080] Prior implant devices, such as the HES device, currently provide the user with about 5 minutes of repositioning time. However, the implant 11 of the present invention increases the length of repositioning time. In some embodiments, the repositioning time during a procedure can be increased to about 30 minutes. In this respect, the user is provided with a longer repositioning time to better achieve a desired implant configuration

[0081] **Fig. 2** shows an implant 11 similar to that shown in **Fig. 1** after the expansile element 1 has expanded through the gap 7 to a dimension larger than the carrier member 2.

[0082] **Fig. 3** shows an implant 11 wherein multiple expansile elements 1 run somewhat parallel to each other through the carrier member 2. In one embodiment, this configuration is constructed by looping a single expansile element 1 around the tip 4 of the implant 11 and tying both ends of the expansile element 1 to the proximal end of the carrier member 2. In another embodiment, multiple strands of the expansile element 1 may be bonded along the length of the carrier member 2. The construction of these embodiments may also comprise stretching the expansile element 1 as previously described and/or forming gaps in the carrier member 2.

[0083] **Fig. 4** shows an embodiment wherein the implant 11 comprises a non-coil carrier member 2. In one embodiment, the carrier member 2 is formed by cutting a tube or sheet of plastic such as polyimide, nylon, polyester, polyglycolic acid, polylactic acid, PEEK, Teflon, carbon fiber or pyrolytic carbon, silicone, or other polymers known in the art with, for example; a cutting blade, laser, or water jet in order to form slots, holes, or other fenestrations through which the expansile element 1 may be in contact with bodily fluids. The plastic in this embodiment may also comprise a radiopaque agent such as tungsten powder, iodine, or barium sulfate. In another embodiment, the carrier member 2 is formed by cutting a tube or sheet of metal such as platinum, steel, tungsten, Nitinol, tantalum, titanium, chromium-cobalt alloy, or the like with, for example; acid etching, laser, water jet, or other techniques known in the art. In another embodiment, the carrier member 2 is formed by braiding, knitting, or wrapping metallic or plastic fibers in order to form fenestrations.

[0084] **Fig. 5** shows an implant 11 comprising a carrier member 2, an expansile element 1, and a stretch resistant member 10. The stretch resistant member 10 is used to prevent the carrier member 2 from stretching or unwinding during delivery and repositioning. The stretch resistant member 10 may be made from a variety of metallic or plastic fibers such as steel, Nitinol, PET, PEEK, Nylon, Teflon, polyethylene, polyolefin, polyolefin elastomer, polypropylene, polylactic acid, polyglycolic acid, and various other suture materials known in the art. Construction of the implant 11 may be by attaching the ends of the stretch resistant member 10 to the ends of the carrier member 2 as described by US6,013,084 to Ken and US5,217,484 to Marks both hereby incorporated by reference. Alternatively, the distal end of the stretch resistant member

10 may be attached near the distal end of the carrier member 2 and the proximal end to the stretch resistant member 10 attached to the delivery system as described in co-pending Appl. No. 11/ 212,830 to Fitz.

[0085] **Fig. 6** is an alternative embodiment comprising a stretch resistant member 10 wrapped around, tied to, or intertwined with the expansile element 1. This may occur over the length of the expansile element 1, or the wrapping or tying may be in only one area to facilitate bonding the expansile element 1 to the carrier element 2 by using the stretch resistant member 10 as a bonding element.

[0086] **Fig. 7** shows a loop or fold 12 of the expansile element 1 protruding outside the carrier element 2. In some embodiments, it may be desirable to avoid this condition by, for example, stretching the expansile element 1 as previously described. This would be done, for example, in embodiments configured for delivery through a small microcatheter to prevent the implant 11 from becoming stuck in the microcatheter during delivery. In other embodiments, slack may be added to the expansile element 1 so that the loop or fold will be pre-formed into the implant 11. This would be done in embodiments where, for example, a large amount of volumetric filling was necessary because the loops or folds would tend to increase the total length of the expansile element 1.

[0087] **Fig. 8** shows an embodiment wherein the expansile element 1 is configured to expand to a dimension larger than its initial dimension, but smaller than the outer dimension of the carrier member 2. This may be done by adjusting the ratio of, for example, PEG di-acrylamide to sodium acrylate in embodiments wherein the expansile element 1 comprises a hydrogel. Alternatively, a relatively high dose of radiation could be used to cross-link the expansile element 1, thus limiting its expansion. Embodiments such as shown in **Fig. 8** are desirable when filling is necessary and it is desirable to have a substrate for tissue growth and proliferation that the expansile element 1 provides. In an embodiment used to treat cerebral aneurysms, this configuration could be used as a ”filling” coil. In one embodiment, the expansile element 1 comprises a hydrogel incorporating a porosigen as previously described to provide a reticulated matrix to encourage cell growth and healing. Incorporating, for example, growth

hormones or proteins in the expansile element 1 as previously described may further enhance the ability of the implant 11 to elicit a biological response.

[0088] **Figs. 9-11** illustrate another preferred embodiment of an implant 11 according to the present invention. This implant is generally similar to the previously described embodiments, including an expansile element 1 that is disposed within a carrier member 2. Additionally, a stretch resistant member 10 is positioned along a longitudinal axis of the expansile element 1 and attached to the distal end of the carrier member 2. The stretch resistant member 10 is preferably located within or partially surrounded by the expansile element 1. Preferably, the stretch resistant member 10 is wrapped around a proximal portion of the carrier member 2 and attached near a heater coil 22 within a distal end of a delivery device 20, shown in **Fig. 11**.

[0089] As best seen in **Fig. 9**, the proximal end of the carrier member 2 can include a coiled region having a smaller diameter than the other coiled regions of the member 2. This smaller diameter coiled region allows the stretch resistant member 10 to be wrapped around the member 2 without extending outwards past the diameter of the other coiled regions of the member 2. Additionally, a covering material 5 can be further positioned over the smaller diameter coiled region without the loops of the stretch resistant member 10 being exposed. Preferably, this covering material 5 is a laser, solder, adhesive, or melted hydrogel material.

[0090] As seen best in **Fig. 9**, the spacing of the helical coils of the carrier member can vary along the length of the implant 11. For example, the coils can be located close to each other or touching each other near the proximal and distal ends while the center portion of the implant 11 can have coils with larger spaces between them. In other words, the gaps between the coils can be larger along most of the implant 11 and smaller near the ends of the implant 11.

[0091] In one embodiment, this implant 11 is created according to the following method. The expansile element 1 is created with hydrogel according to the previously described techniques in this specification. In one embodiment, the expansile element 1 is formed in a polymerization tube between about 0.025" and 0.032" ID. After polymerization, the polymerization tube is cut into segments that are dried under

vacuum. Once all water has been removed from the hydrogel, the dried hydrogel is pushed out of the polymerization tube using a mandrel. The hydrogel is then washed in water three times, swelling the hydrogel and removing sodium chloride and unreacted monomers.

[0092] This expanded hydrogel is then skewered along its longitudinal axis (i.e., along an axis of its length) using a microcoil (or similar elongated tool). This skewing creates a pathway along the approximate center of the hydrogel filament so that a stretch resistant member 10 can be later threaded through. Next, the skewered hydrogel is acid treated by immersion into a hydrochloric acid solution, protonating the carboxylic acid moieties of the sodium acrylate component of the polymer network. The skewered hydrogel is finally washed in alcohol to remove residual acid and dried under a vacuum.

[0093] A gapped platinum coil is used for member 2, having an outer diameter ranging from about 0.012" to about 0.018", filar ranging from about 0.0015" to about 0.0030", and gaps 7 ranging from about 0.0015" to about 0.0075". In another embodiment the gaps 7 range from about 0.00225" to about 0.00750". In one embodiment, this platinum coil has an outer diameter of about 0.012", a filar of about 0.002", and a gap 7 of about 0.004". In another embodiment, this platinum coil has an outer diameter of about 0.0125", a filar of about 0.00225", and a gap 7 of about 0.0045". This gapped platinum coil is wound over a mandrel and heat-set into a secondary helical shape. The platinum coil is cut to a desired implant length and bonded to a coupling marker band or coupler 13 via soldering, welding or adhesive (e.g., weld 15 in Figure 9).

[0094] The coil used to skewer the hydrogel filament is removed, and an about .0022" polyolefin stretch-resistant thread for the stretch resistant member 10 is threaded through the filament along the pathway left by the coil. The hydrogel filament, which now has an outer diameter of between about .010" to about .018" is stretched to an outer diameter between about .006" to about .012" and inserted into the gapped platinum body coil. While still under tension, the hydrogel filament is bonded to the body coil at both ends.

[0095] The stretch-resistant thread is knotted at the distal end of the platinum coil and wrapped around the open coil gaps at the proximal end (i.e., the end with coupler 13). Both ends of the implant 11 are covered with adhesive 4 and 5 to secure the stretch resistant member 10 and encapsulate the ends of the expansile element 1. Finally, the implant 11 is attached to a detachment pusher using the stretch resistant member 10 that protrudes from the proximal end of the implant 11.

[0096] During use of the implant 11 of this embodiment, the implant 11 is advanced via a detachment pusher 20 through a microcatheter (not shown). When the distal end of the microcatheter has reached a desired target area, the pusher 20 is advanced, thereby pushing the implant 11 out of the microcatheter. When the user wishes to detach the implant 11, a heater coil 22 is activated to break the stretch resistant member 10. Upon contact with the blood, the pH sensitive expansile element will expand to a final diameter between about .020" and .035", allowing the user about 5-10 minutes of working time.

[0097] In another embodiment of the invention, the implant 11 of Figure 9 includes a stretch-resistant member 10 composed of polyolefin and having an outer diameter of about .0022". The expansile element 1 is composed of a hydrogel of about 48% PEG 8000 diacrylamide and 52% sodium acrylate. The member 2 is a gapped platinum coil having an outer diameter between about .012" and .020" and more preferably about .012". The member 2 has a filar between about .0015" and .005" and more preferably about .002". The gap between winds of the member 2 is preferably about .003".

[0098] Figure 12 illustrates a preferred embodiment of an implant 11 similar to the previously described embodiment in which the gaps between winds of the member 2 are preferably between about .002" and .020". Additionally, the implant 11 contain one or more outer member 30 located at a proximal end of the implant 11, at a distal end of the implant, adjacent to the proximal or distal end of the implant, or at any combination of these locations. In the example of Figure 12, an outer member 30 is positioned at the proximal and distal ends of the implant 11.

[0099] In one example, the outer member 30 is preferably composed of platinum coil having a length between about .010" and .120" and more preferably between about

.040" and .080". The internal diameter of the outer member 30 is preferably between about .012" and .017" and more preferably between about .012" and .0125". The wire of the outer member 30 preferably has a filar between about .0015" and about .003" and more preferably about .0015".

[00100] In another example, the outer member 30 is composed of a slotted tube having a length between about .010" and .120 and more preferably between about .040" and .080". The internal diameter of the slotted tube is preferably between about .012" and .017" and more preferably between about .012" and .0125". The thickness of the slotted tube is preferably between about .001" and .003" and more preferably about .0015".

[00101] Figure 13 illustrates another preferred embodiment of the implant 11 that is generally similar to the previously described embodiment. However, this implant 11 further comprises a closed-wound platinum coil 32 disposed over the stretch-resistant member 10. Preferably, the stretch-resistant member 10 is composed of polyethylene and has an outer diameter of about .0009". The closed-wound platinum coil 32 preferably has an outer diameter of about .006" and has a wire filar of about .0015". The expansile element 1 is preferably composed of 48% PEG 8000 diacrylamide and 52% sodium acrylate. The member 2 is a gapped platinum coil having an outer diameter between about .012" and .020" and more preferably between about .014" and .015". The member 2 has a filar between about .0015" and .005" and more preferably about .002". The gap between winds of the member 2 is preferably between about .002" and .020" and more preferably .004".

[00102] Preferably, the implant 11 of Figure 13 is created by preparing expansile element 1 with hydrogel as previously described in this specification. Prior to the acid treatment, the hydrated hydrogel is skewered with a platinum coil 32. Preferably, the platinum coil 32 is heat-set into a predetermined helical shape with a defined pitch and diameter prior to skewering. A stiff and preferably platinum-based mandrel is inserted into the platinum coil 32 to provide support during further treatments and construction of the implant 11.

[00103] Following the acid treatment of the hydrogel, the mandrel is removed from within the platinum coil 32 and replaced by stretch-resistant member 10 (e.g., a polyolefin monofilament). Optionally, both the mandrel and the platinum coil 32 can also be removed and replaced by the stretch-resistant member 10. The member 2 (e.g., a gapped platinum coil) is placed over the resulting subassembly and is sized appropriately to allow little or no free space within the internal diameter of the member 2. The member 2 can optionally be wound and heat-set into a preliminary and preferably helical shape of a defined pitch and diameter prior to placing over the hydrogel and platinum coil 32.

[00104] Once the member 2 has been placed, it is bonded to the hydrogel using adhesives at proximal and distal ends (preferably UV-cured adhesives). At this point, outer members 30 can optionally be located and bonded at one or more ends of the implant 11. The stretch-resistant member 10 is then secured at both ends of the implant 11 and the implant 11 is coupled to an electrical detachment mechanism as described elsewhere in this specification.

[00105] In one embodiment of the invention a vaso-occlusive device comprises an expansile polymer element having an outer surface, a carrier member that covers at least a portion of the outer surface of the expansile polymer element, and wherein no carrier is disposed within the outer surface of the expansile element.

[00106] In another embodiment, a vaso-occlusive device comprises a coil having a lumen and a hydrogel polymer having an outer surface wherein the hydrogel polymer is disposed within the lumen of the coil and wherein the hydrogel polymer does not contain a coil within the outer surface of the hydrogel polymer.

[00107] In another embodiment, a vaso-occlusive device comprises a carrier member formed into a secondary configuration and an expansile element, wherein the expansile element is made from a polymer formulated to have sufficient softness that the expansile element will substantially take the shape of the secondary configuration formed into the carrier member without pre-treatment.

[00108] In another embodiment, a vaso-occlusive device comprises a carrier member formed into a secondary configuration and a substantially continuous length of hydrogel, wherein the device will substantially take the shape of the secondary configuration formed into the carrier member without pre-treatment.

[00109] In another embodiment, a vaso-occlusive device comprises a microcoil having an inner lumen and an expansile element disposed within the inner lumen. In this embodiment the expansile element comprises a hydrogel selected from the group consisting of acrylamide, poly(ethylene glycol), Pluronic, and poly(propylene oxide).

[00110] In another embodiment, a vaso-occlusive device comprises a coil and a hydrogel polymer disposed at least partially within the coil wherein the hydrogel has an initial length and wherein the hydrogel polymer has been stretched to a second length that is longer than the initial length.

[00111] In another embodiment, a vaso-occlusive device comprises an expansile element and a carrier member defining an inner lumen, wherein the expansile element is disposed within the inner lumen of the carrier member and wherein the expansile element has been stretched to a length sufficient to prevent a loop of the expansile element from protruding through the carrier member.

[00112] The invention disclosed herein also includes a method of manufacturing a medical device. The method comprises providing a carrier member having an inner lumen and an expansile element, inserting the expansile element into the inner lumen of the carrier member, and stretching the expansile element.

[00113] In another embodiment, a vaso-occlusive device comprises an expansile element encapsulated by a carrier element, wherein said expansile element is comprised substantially entirely and substantially uniformly of material having an expansile property.

[00114] In another embodiment, a vaso-occlusive device comprises a carrier element and an expansile element wherein the carrier element has a secondary shape that is different from its primary shape and wherein the expansile element is sufficiently flexible in a normal untreated state to conform with the secondary shape of the carrier.

[00115] In another embodiment, a vaso-occlusive device includes a carrier and an expansile element wherein the expansile element is fixed to the carrier in a manner such that the expansile element is in a stretched state along the carrier.

[00116] In another embodiment, a vaso-occlusive device includes a carrier having a plurality of gaps along the carrier and an expansile element positioned along an inside envelope of the carrier and wherein the expansion of the expansile element is controlled such that the expansile element expands into the gaps but not beyond the external envelope of the carrier.

[00117] In another embodiment, a vaso-occlusive device includes a carrier member and an expansile element wherein the expansile element is comprised of multiple strands extending along the carrier.

[00118] In another embodiment, a vaso-occlusive device includes a carrier and an expansile member wherein the carrier is a non-coiled cylindrically shaped structure and wherein said expansile member is disposed inside said carrier.

[00119] In another embodiment, a vaso-occlusive device includes a carrier and an expansile member and a stretch resistant member; said expansile member and said stretch resistant member being disposed in an internal region of the carrier and wherein the stretch resistant member is in tension on said carrier.

[00120] The invention disclosed herein also includes a method of treating a lesion within a body. The method comprises providing a vaso-occlusive device comprising a carrier member and an expansile element wherein the carrier member is formed into a secondary configuration that is approximately the same diameter as the lesion and inserting the vaso-occlusive device into the lesion.

[00121] Although preferred embodiments of the invention have been described in this specification and the accompanying drawings, it will be appreciated that a number of variations and modifications may suggest themselves to those skilled in the pertinent arts. Thus, the scope of the present invention is not limited to the specific embodiments and examples described herein, but should be deemed to encompass alternative embodiments and equivalents.

[00122] Unless otherwise indicated, all numbers expressing quantities of ingredients, properties such as molecular weight, reaction conditions, and so forth used in the specification and claims are to be understood as being modified in all instances by the term "about." Accordingly, unless indicated to the contrary, the numerical parameters set forth in the specification and attached claims are approximations that may vary depending upon the desired properties sought to be obtained by the present invention. At the very least, and not as an attempt to limit the application of the doctrine of equivalents to the scope of the claims, each numerical parameter should at least be construed in light of the number of reported significant digits and by applying ordinary rounding techniques. Notwithstanding that the numerical ranges and parameters setting forth the broad scope of the invention are approximations, the numerical values set forth in the specific examples are reported as precisely as possible. Any numerical value, however, inherently contains certain errors necessarily resulting from the standard deviation found in their respective testing measurements.

[00123] The terms "a," "an," "the" and similar referents used in the context of describing the invention (especially in the context of the following claims) are to be construed to cover both the singular and the plural, unless otherwise indicated herein or clearly contradicted by context. Recitation of ranges of values herein is merely intended to serve as a shorthand method of referring individually to each separate value falling within the range. Unless otherwise indicated herein, each individual value is incorporated into the specification as if it were individually recited herein. All methods described herein can be performed in any suitable order unless otherwise indicated herein or otherwise clearly contradicted by context. The use of any and all examples, or exemplary language (e.g., "such as") provided herein is intended merely to better illuminate the invention and does not pose a limitation on the scope of the invention otherwise claimed. No language in the specification should be construed as indicating any non-claimed element essential to the practice of the invention.

[00124] Groupings of alternative elements or embodiments of the invention disclosed herein are not to be construed as limitations. Each group member may be referred to and claimed individually or in any combination with other members of the group or other elements found herein. It is anticipated that one or more members of a group may be

included in, or deleted from, a group for reasons of convenience and/or patentability. When any such inclusion or deletion occurs, the specification is deemed to contain the group as modified thus fulfilling the written description of all Markush groups used in the appended claims.

[00125] Certain embodiments of this invention are described herein, including the best mode known to the inventors for carrying out the invention. Of course, variations on these described embodiments will become apparent to those of ordinary skill in the art upon reading the foregoing description. The inventor expects skilled artisans to employ such variations as appropriate, and the inventors intend for the invention to be practiced otherwise than specifically described herein. Accordingly, this invention includes all modifications and equivalents of the subject matter recited in the claims appended hereto as permitted by applicable law. Moreover, any combination of the above-described elements in all possible variations thereof is encompassed by the invention unless otherwise indicated herein or otherwise clearly contradicted by context.

[00126] Furthermore, numerous references have been made to patents and printed publications throughout this specification. Each of the above-cited references and printed publications are individually incorporated herein by reference in their entirety.

[00127] In closing, it is to be understood that the embodiments of the invention disclosed herein are illustrative of the principles of the present invention. Other modifications that may be employed are within the scope of the invention. Thus, by way of example, but not of limitation, alternative configurations of the present invention may be utilized in accordance with the teachings herein. Accordingly, the present invention is not limited to that precisely as shown and described.

What is claimed is:

1. A device for implantation in an animal comprising:

a helical carrier member; and

a hydrogel having ionizable functional groups wherein said hydrogel comprises a macromer of about 48% poly(ethylene glycol) di-acrylamide and a pH sensitive component of about 52% sodium.

2. A device according to Claim 1 wherein said macromer is cross-linked with at least one ethylenically unsaturated compound.

3. A device according to Claim 1 wherein said macromer is cross-linked with N, N'-methylenebisacrylamide, derivatives thereof, or combinations thereof.

4. A device according to Claim 1 wherein said hydrogel includes pores created by a porosigen.

5. A device according to Claim 4 wherein said porosigen is about 0.4 g/g sodium chloride.

6. A device according to Claim 5 wherein said sodium chloride has a particle size of about 10 microns.

7. A device according to Claim 1 wherein said helical coil includes gaps ranging from about 0.0015" to about 0.00750".

8. A device according to Claim 7 wherein said gap comprises .003".

9. A device according to Claim 1 further comprising a stretch resistant member disposed within said hydrogel member and wrapped around at least a portion of said helical carrier member.

10. The implant device of Claim 1, wherein said helical carrier member comprises a coiled region having a first diameter and a coiled region having a second diameter.

11. The implant device of claim 1 wherein said hydrogel expands from a diameter of about is about .006"-.007" to a diameter of about .02" after expansion.

12. A device for implantation in an animal comprising:

a helical carrier member having gaps ranging from about 0.0015" to about 0.00750"; and

a hydrogel.

13. A device according to Claim 12 comprising a hydrogel having ionizable functional groups wherein said hydrogel comprises at least a macromer of about 48% poly(ethylene glycol) di-acrylamide and a pH sensitive component of about 52% sodium.

14. The implant device of claim 12, wherein said hydrogel includes pores created by a porosigen.

15. The implant device of claim 14, wherein said porosigen is about 0.4 g/g sodium chloride.

16. The implant device of claim 15, wherein said sodium chloride has a particle size of about 10 microns.

17. A device according to Claim 12 wherein said gap comprises .003".

18. A device according to Claim 12 further comprising a stretch resistant member disposed within said hydrogel member and wrapped around at least a portion of said helical carrier member.

19. The implant device of claim 12, wherein said helical carrier member comprises a coiled region having a first diameter and a coiled region having a second diameter.

20. The implant device of claim 12 wherein said hydrogel expands from a diameter of about is about .006”-.007” to a diameter of about .02” after expansion.

21. An implant device comprising:

a helical carrier member having a gap comprising .003”;

a hydrogel member disposed within said helical carrier member; and,

a stretch resistant member disposed within said hydrogel member and wrapped around at least a portion of said carrier member;

wherein said hydrogel comprises a macromer of about 48% poly(ethylene glycol) di-acrylamide and a pH sensitive component of about 52% sodium acrylate.

22. The implant device of claim 21 wherein said hydrogel expands from a diameter of about is about .006”-.007” to a diameter of about .02” after expansion.

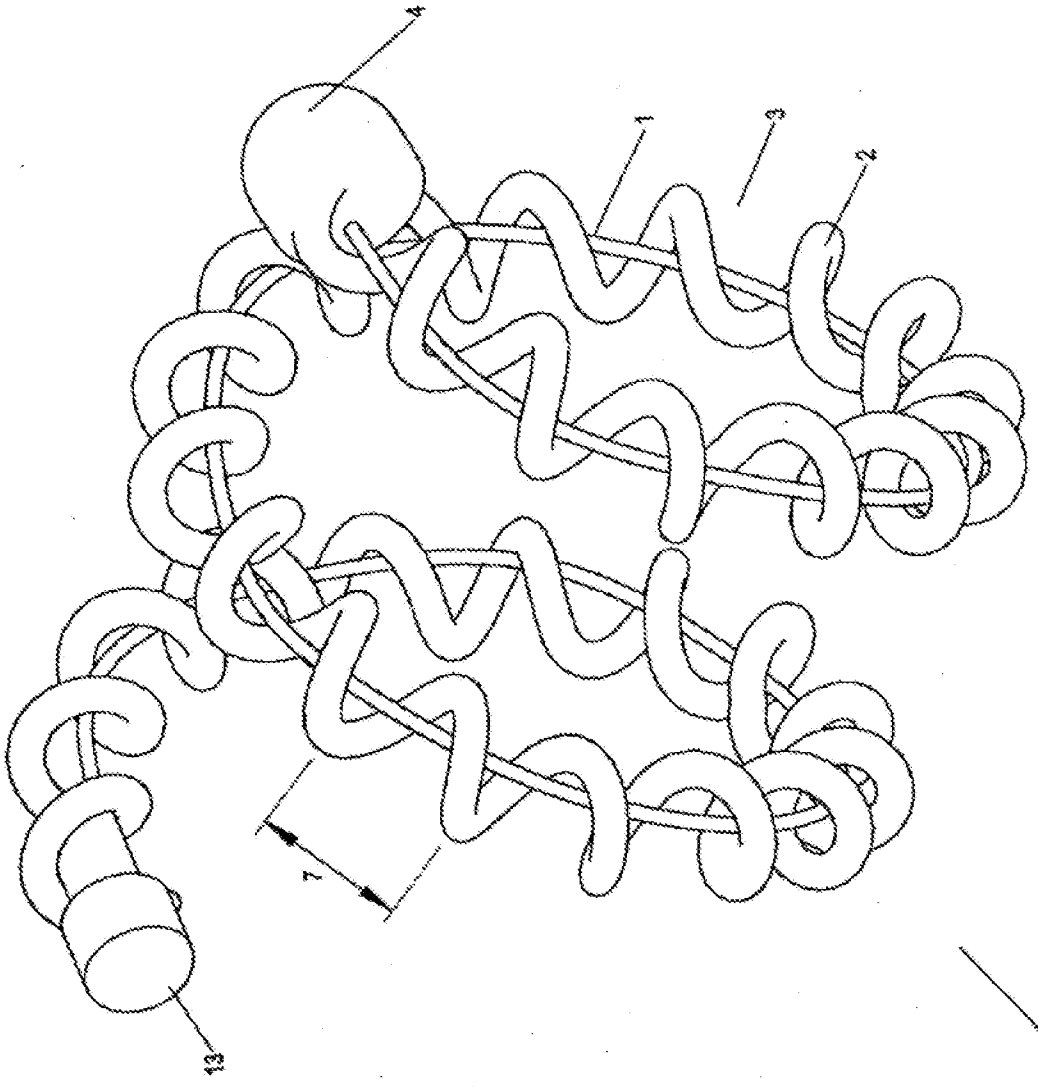

Fig. 1

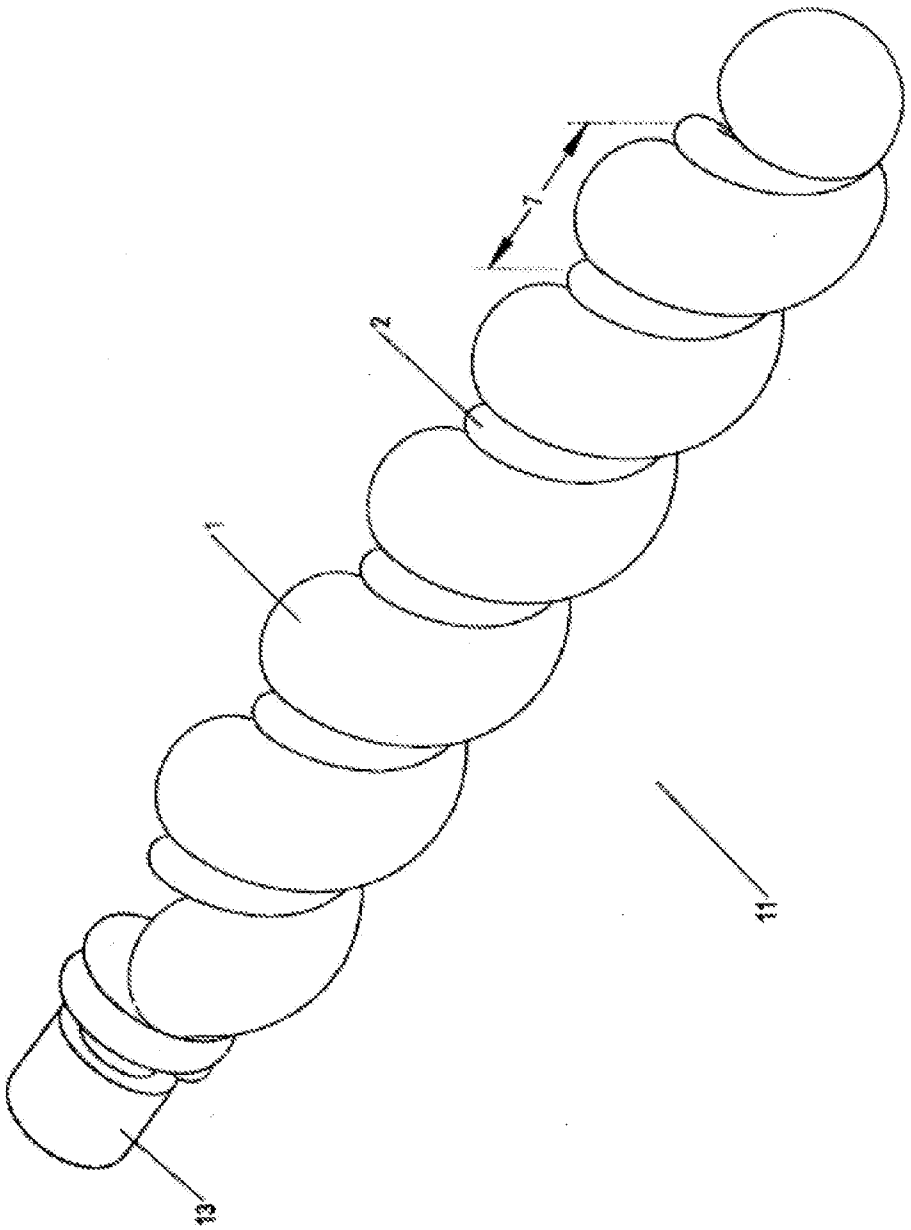

Fig. 2

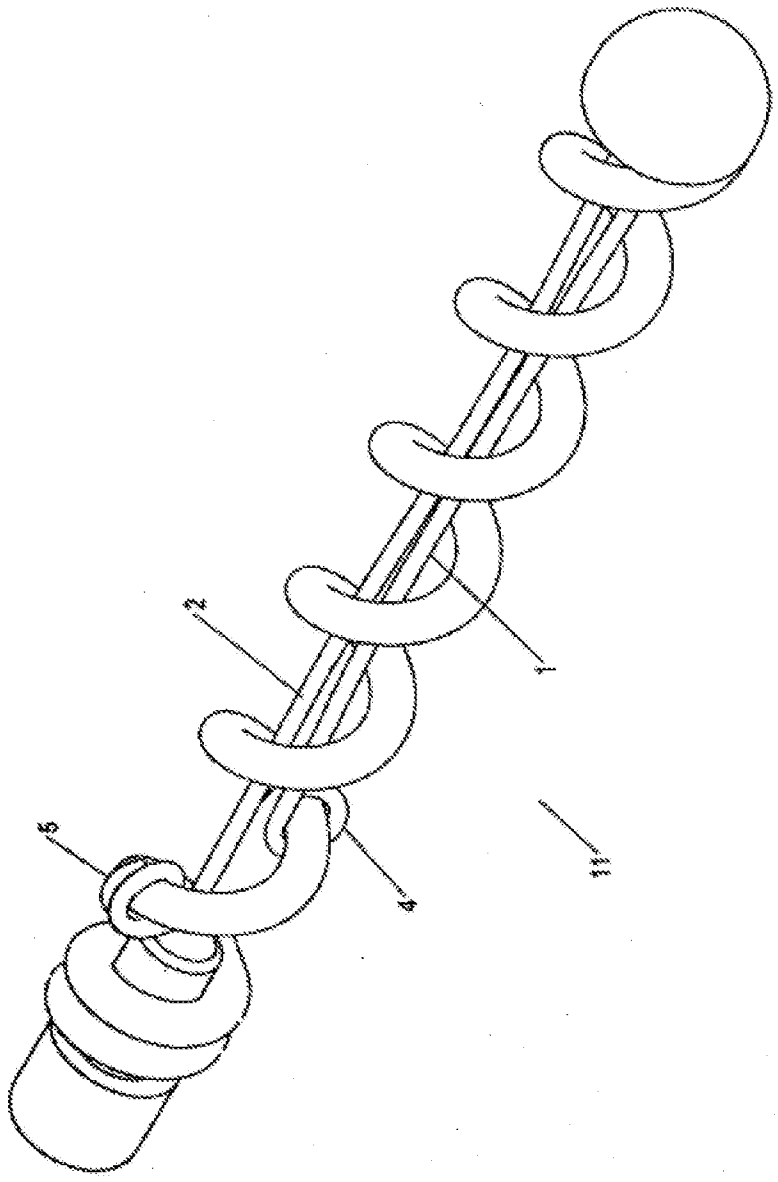

Fig. 3

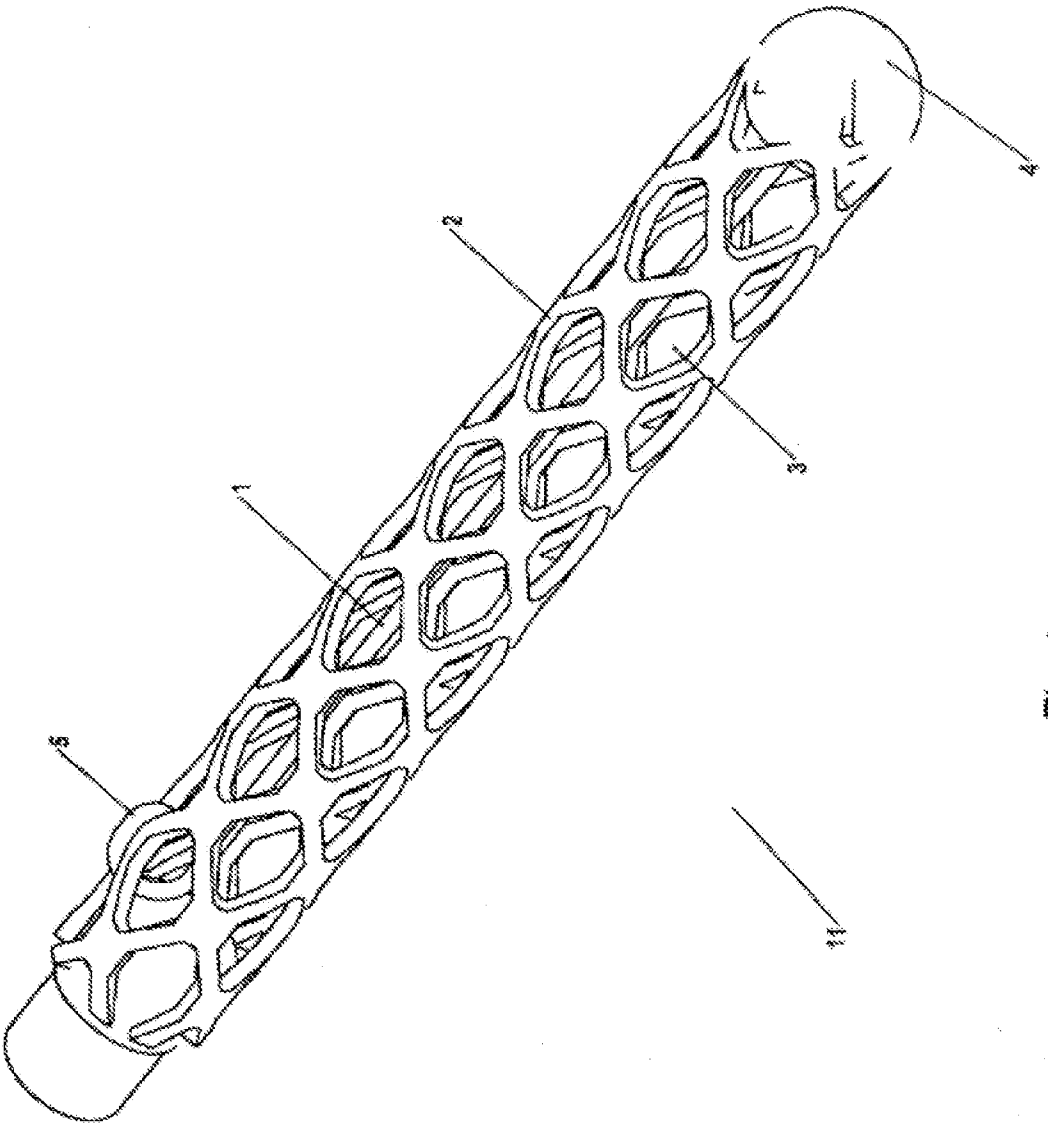

Fig. 4

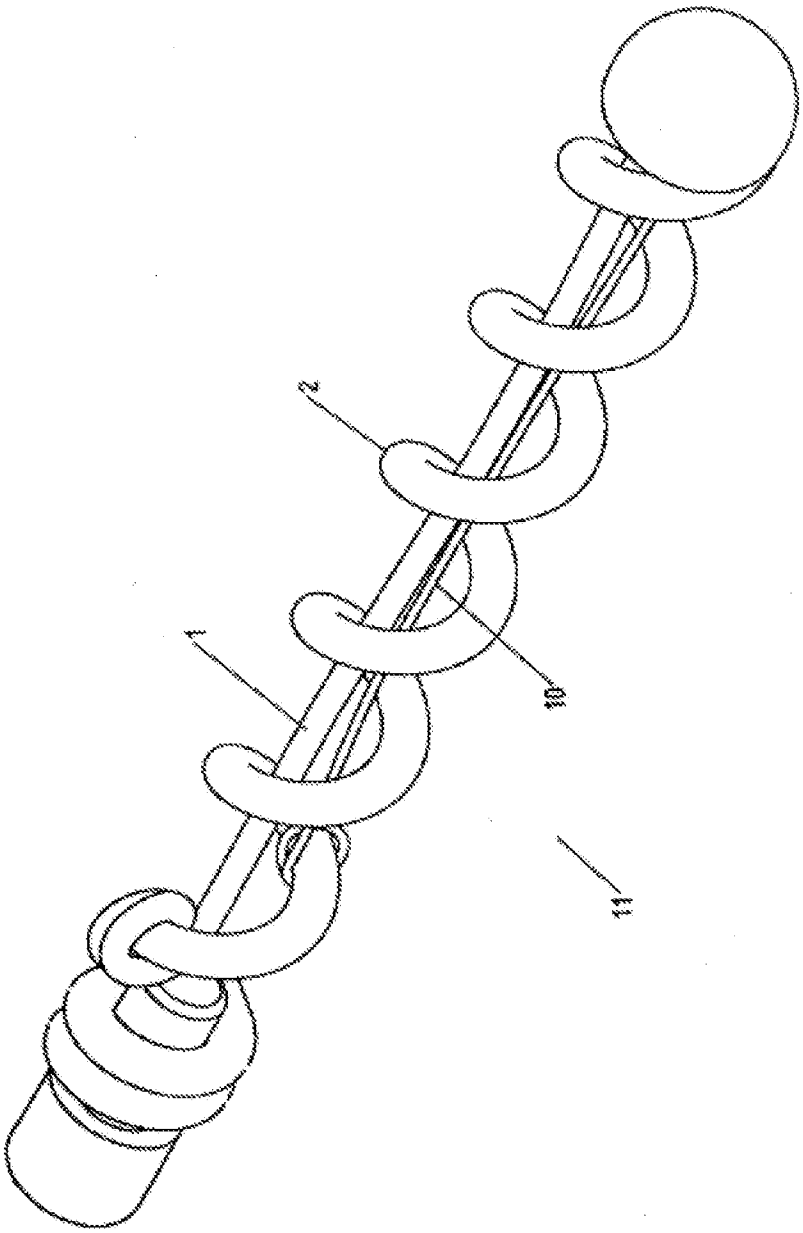

Fig. 5

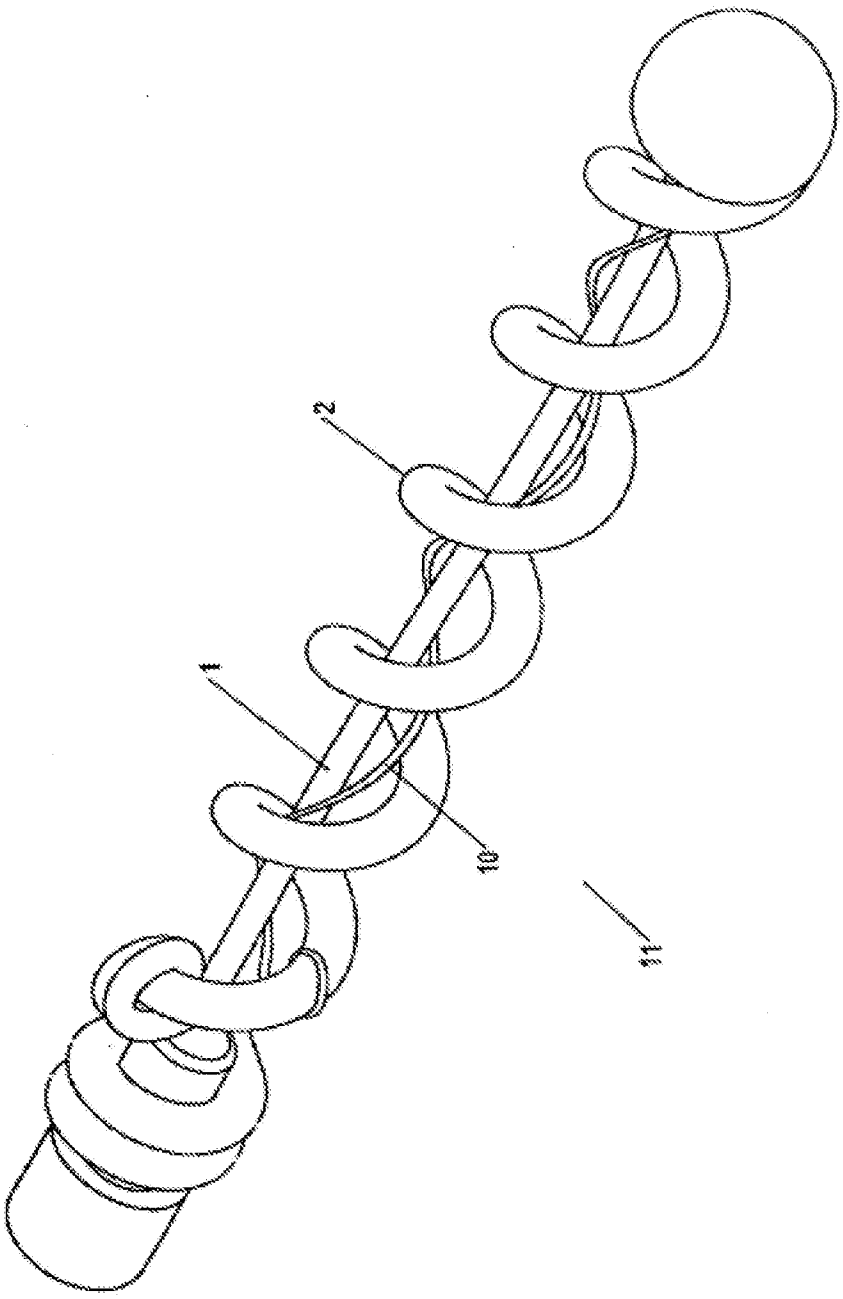

Fig. 6

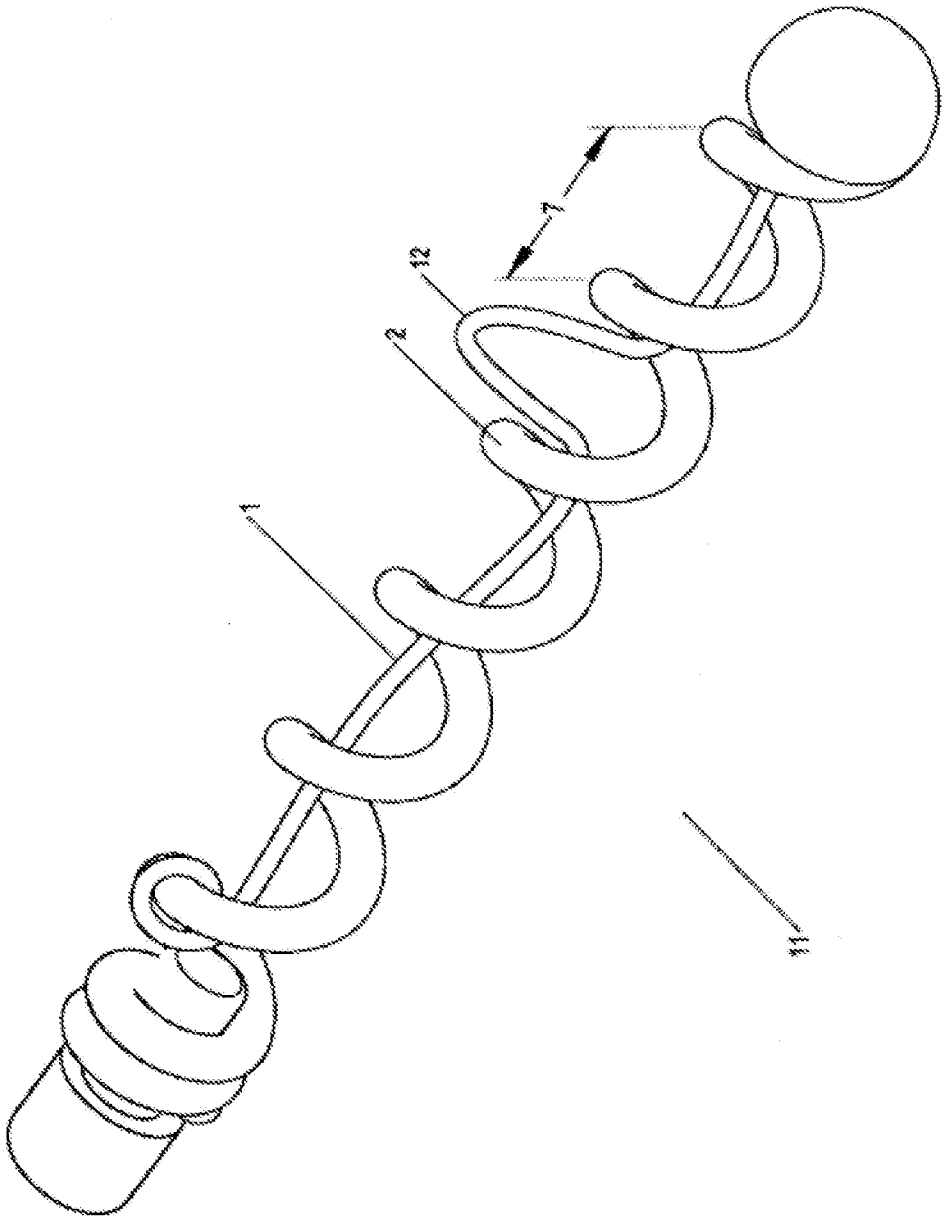

Fig. 7

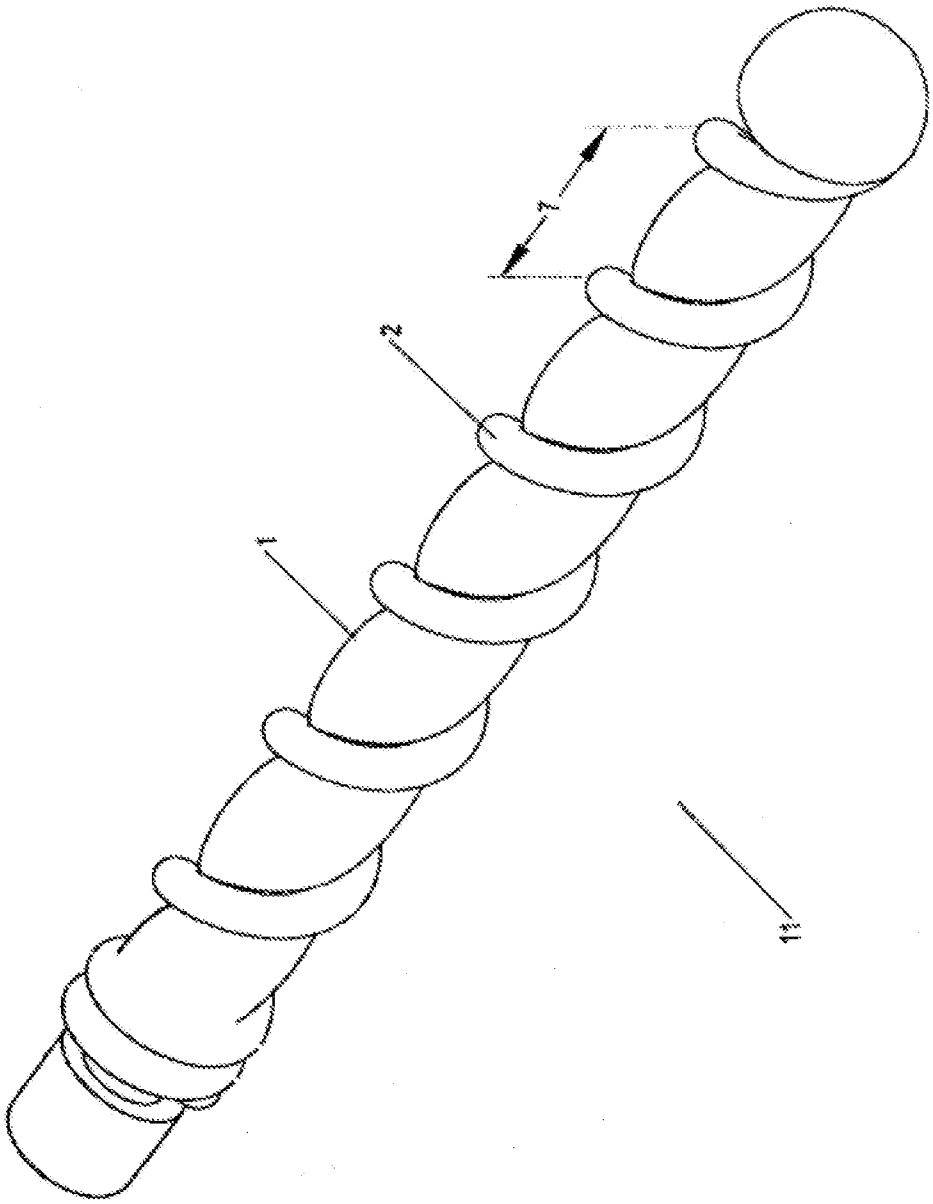

Fig. 8

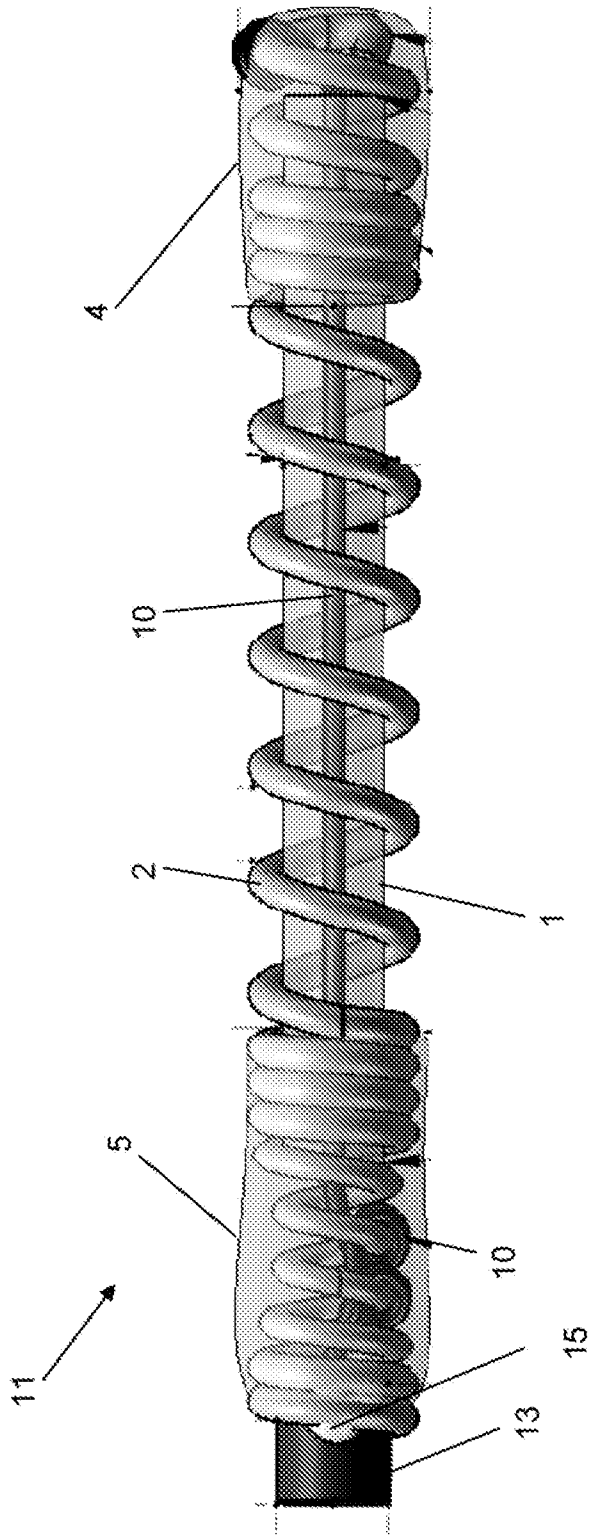

Fig. 9

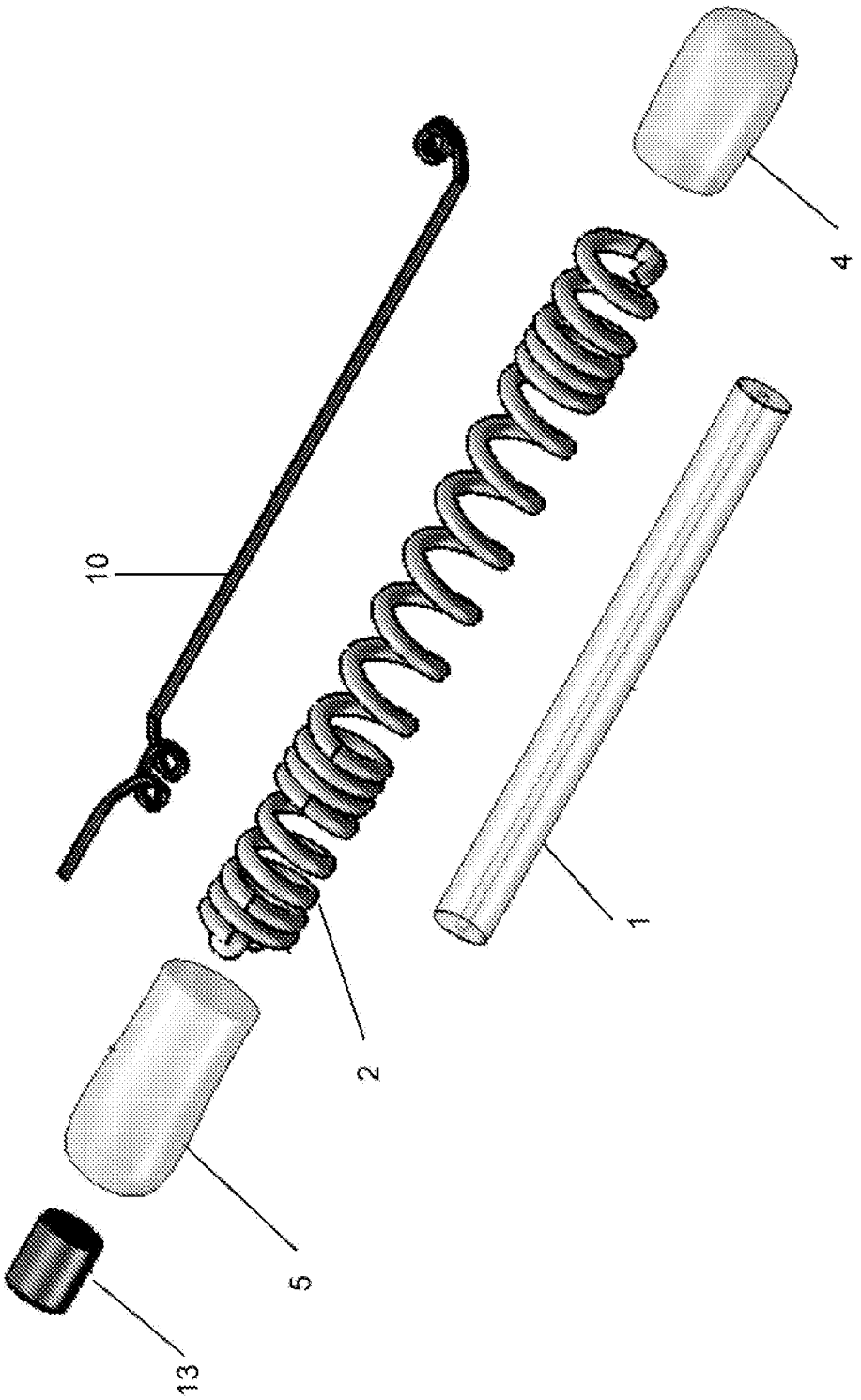

Fig. 10

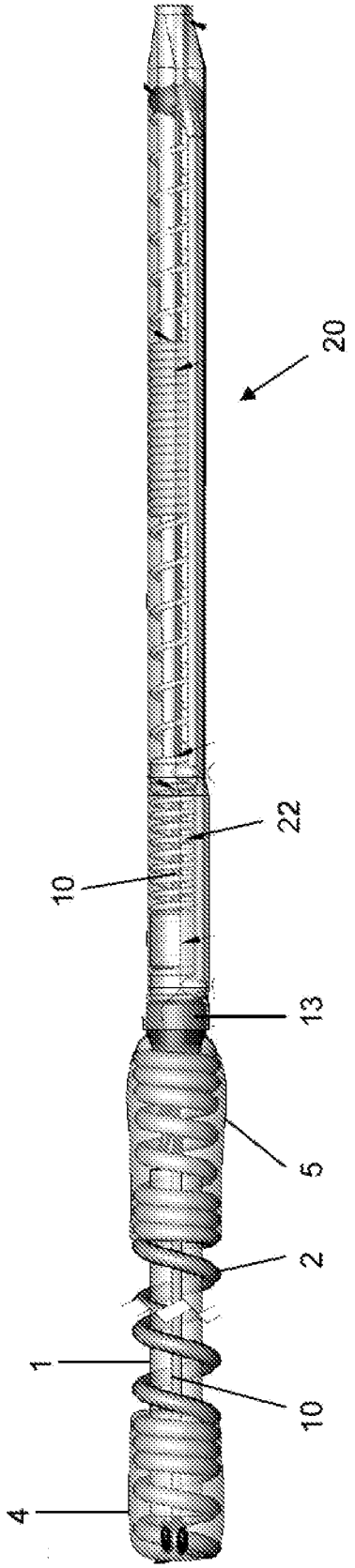

Fig. 11

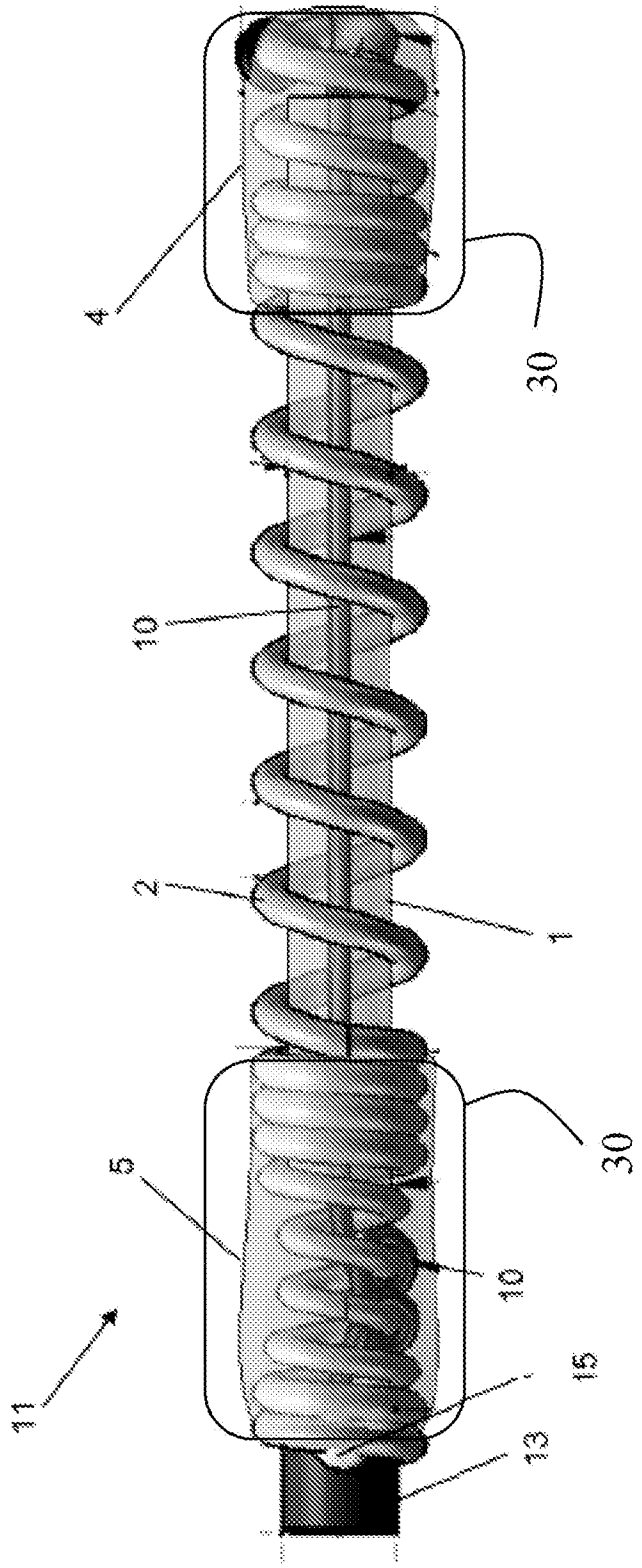

Fig. 12

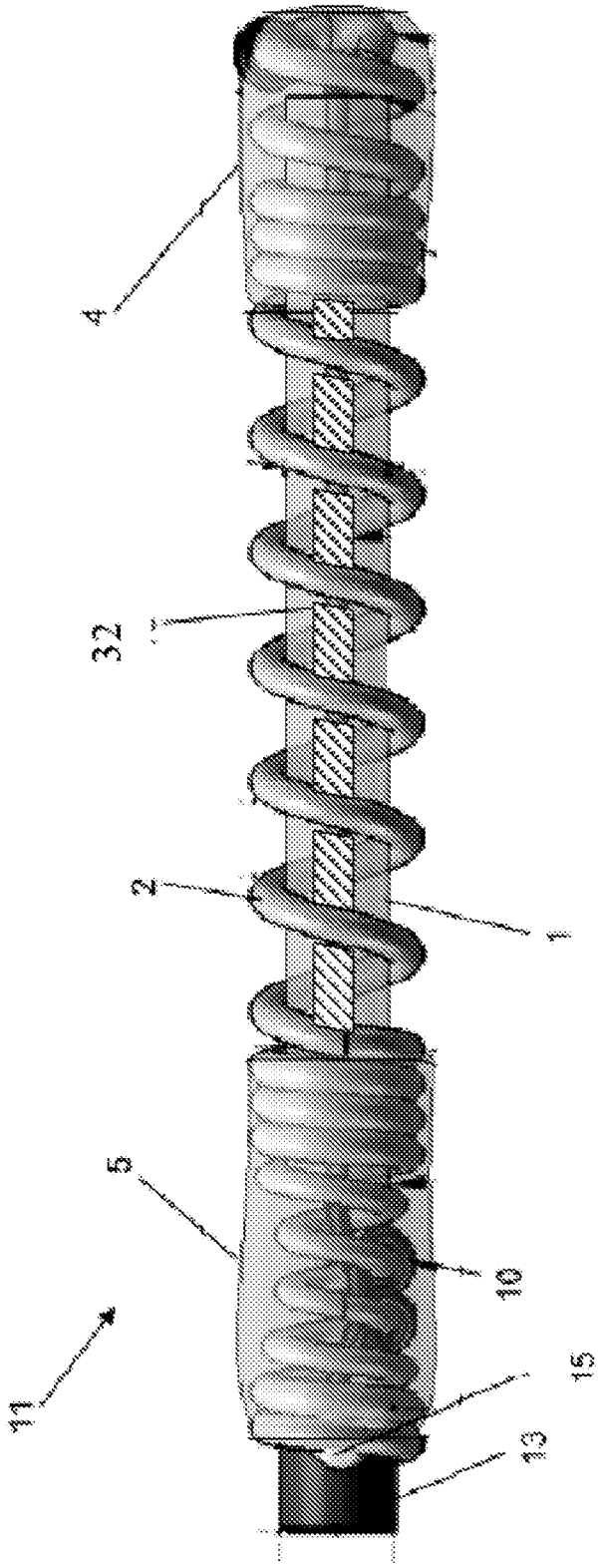

Fig. 13

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 10/53972

A. CLASSIFICATION OF SUBJECT MATTER
IPC(8) - A61B 1/267 (2010.01)
USPC - 600/192
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC(8): A61B 1/267 (2010.01)
USPC: 600/192

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
USPC: 128/831

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
PubWEST (PGPB,USPT,USOC,EPAB,JPAB); Google Scholar
Search terms used: (embolus OR embolization OR embolisation) (gel OR hydrogel) implant (helical OR helix OR helices) ("sodium chloride" OR NaCl) macromer polyethylene glycol di-acrylamide

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 2007/0299464 A1 (CRUISE et al.) 27 December 2007 (27.12.2007), entire document, especially: para [0002], [0010], [0013], [0014], [0039], [0043], [0044], [0054], [0059], [0064], [0068], [0078]	1-5, 7-15, 17-22
Y		6, 16
Y	US 2009/0232869 A1 (GREENE Jr., et al.) 17 September 2009 (17.09.2009), para [0101]	6, 16
A	US 2008/0208167 A1 (STANKUS et al.) 28 August 2008 (28.08.2008), entire document	1-22

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

* Special categories of cited documents:
"A" document defining the general state of the art which is not considered to be of particular relevance
"E" earlier application or patent but published on or after the international filing date
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
"O" document referring to an oral disclosure, use, exhibition or other means
"P" document published prior to the international filing date but later than the priority date claimed
"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
10 December 2010 (10.12.2010)	17 DEC 2010
Name and mailing address of the ISA/US Mail Stop PCT, Attn: ISA/US, Commissioner for Patents P.O. Box 1450, Alexandria, Virginia 22313-1450 Facsimile No. 571-273-3201	Authorized officer: Lee W. Young PCT Helpdesk: 571-272-4300 PCT OSP: 571-272-7774

Form PCT/ISA/210 (second sheet) (July 2009)