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(54) Title: GRAFTS AND STENT GRAFTS HAVING A RADIOPAQUE MARKER

(57) Abstract: A graft device comprising a layer of synthetic non-metallic material having a first surface and a second surface spaced apart from the first surface. The device further, includes a radiopaque marker at least partially embedded in the layer.

TITLE: GRAFTS AND STENT GRAFTS HAVING A RADIOPAQUE MARKER

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GRAFTS AND STENT GRAFTS HAVING A RADIOPAQUE MARKER

Priority Data and Incorporation by Reference

[0001] This application claims benefit of priority to U.S. Provisional Patent Application No. 60/734,725 filed November 9, 2005 which is incorporated by reference in its entirety.

Technical Field

[0002] The present invention relates generally to medical devices, and more particularly to a radiopaque marker for implantable devices.

Background of the Invention

[0003] Unless specifically defined, the terms "Radio-opaque" or "Radiopaque" have same meaning. Stents, artificial grafts, and related endoluminal devices are currently used by medical practitioners to treat tubular body vessels or ducts that become so narrowed (stenosed) that flow of blood or other biological fluids is restricted. Such narrowing (stenosis) occurs, for example, as a result of the disease process known as arteriosclerosis. While stents are most often used to "prop open" blood vessels, they can also be used to reinforce collapsed or narrowed tubular structures in the respiratory system, the reproductive system, bile or liver ducts or any other tubular body structure.

[0004] Vascular grafts made of polytetrafluoroethylene (PTFE) are typically used to replace or repair damaged or occluded blood vessels within the body. However, they may require additional means for anchoring the graft within the blood vessel, such as sutures, clamps, or similarly functioning elements to overcome retraction. Stents have been used in combination with grafts to provide endovascular prostheses which are capable of maintaining their fit against blood vessel walls. The use of grafts along with stents also serves to overcome a problem found with stents where smooth muscle cells and other tissues can grow through the stent's mesh-like openings, resulting in restenosis of the vessel.

[0005] PTFE has proven unusually advantageous as a material from which to fabricate blood vessel grafts or prostheses, because PTFE is extremely biocompatible, causing little or no immunogenic reaction when placed within the human body. In its preferred form, expanded PTFE (ePTFE), the material is light, porous and readily colonized by living cells so that it becomes a permanent part of the body. The process of making ePTFE of vascular graft grade is well known to one of ordinary skill in the art. Suffice it to say that the critical step in this process is the expansion of PTFE into ePTFE. This expansion represents a controlled longitudinal stretching in which the PTFE is stretched to several hundred percent of its original length. Examples of ePTFE grafts are shown and described in U.S. Patent Nos. 5,641,443; 5,827,327; 5,861,026; 5,641,443; 5,827,327; 6,203,735; 6,221,101; 6,436,135; and 6,589,278, each of which is incorporated in its entirety by reference. Grafts made from materials other than ePTFE that have been utilized include, for example, Dacron mesh reinforced umbilical tissues, bovine collagen, polyester knitted collagen, tricot knitted polyester collagen impregnated, and polyurethane (available under the trademark Vectra®).

[0006] Stent grafts are a prosthetic device designed to maintain the patency of various vessels in the body, including the tracheobronchial tree. The device may include a balloon expandable stent encapsulated with ePTFE or alternatively a self-expanding Nitinol stent encapsulated with ePTFE and pre-loaded on a flexible delivery system. One example of the latter is known commercially as "Fluency®," which is marketed by C.R. Bard Peripheral Vascular Inc. Examples of such stent-graft is shown and described in U.S. Patent Nos. 6,053,941; 6,124,523; 6,383,214; 6,451,047; and 6,797,217, each of which is incorporated in its entirety by reference. The field of covering stents with polymeric coatings and ePTFE in particular has been substantially explored by those skilled in the art. One popular way of covering the stent with ePTFE material is to encapsulate it within two layers of ePTFE which

are subsequently fused together by heat in places where the two layers are in contact through openings in the stent wall. This provides a solid one-piece device that can be expanded and contracted without an ePTFE layer delaminating.

[0007] Implantation of a graft or an encapsulated stent into the vasculature of a patient involves very precise techniques. Generally, the device is guided to the diseased or damaged portion of a blood vessel via an implantation apparatus that deploys the graft or the encapsulated stent at the desired location. In order to pinpoint the location during deployment, the medical specialist will generally utilize a fluoroscope to observe the deployment by means of X rays. Deployment of an encapsulated stent at an unintended location can result in immediate trauma, as well as increasing the invasiveness associated with multiple deployment attempts and/or relocation of a deployed device. In addition, visualization of the implanted device is essential for implantation, follow-up inspection and treatment. Accordingly, in order to implant the encapsulated stent using fluoroscopy, some portion of the stent, graft or implantation device should be radiopaque.

[0008] Stents that are implanted and expanded within a blood vessel using a balloon catheter can be located by fluoroscopy because the balloon catheter can have radiopaque features incorporated therein that may be used as a visual marker. However, if the balloon moves after expansion of the stent, correct placement of the stent, in the absence of a radiopaque marker incorporated into the stent, cannot be confirmed. A self-expanding stent can be generally delivered to the damaged or diseased site via a constraining member in the form of a catheter or sheath and can be deployed by removing the constraining member. In order to direct the delivery device and the self-expanding stent to the precise location for deployment, the radiopacity must be incorporated into the device or the constraining member to confirm the correct placement within the vessel.

[0009] In addition to visually verifying the location of the implanted stent or graft, it may be necessary to visually verify the orientation of the graft or stent, and/or visually determine if the implant has been twisted or kinked. A properly configured radiopaque marker can facilitate meeting these visual needs. Moreover, radiopaque markers incorporated into the material of a graft or encapsulated stent can provide an alternative to exposed "spoon" type markers that can contact areas of the blood vessel being treated.

Disclosure of Invention

[00010] A preferred embodiment according to the present invention provides a graft device comprising a layer of synthetic non-metallic material having a first surface and a second surface spaced apart from the first surface. The device further includes a radiopaque marker at least partially embedded in the layer. In one embodiment, the radiopaque marker is about twenty to sixty percent (20-60 %) tantalum powder. Alternatively, the radiopaque marker is about 20% to about 60% Barium Sulfate.

[0010] In another preferred embodiment, a graft device comprises a layer of synthetic non-metallic material having a first surface and a second surface spaced apart from the first surface. The device further includes a radio-opaque ink printed on at least one of the first and second surfaces of the synthetic non-metallic material.

[0011] In another embodiment, the marker preferably has a color so as to be visible to the naked eye as well as being radio-opaque. In one preferred embodiment, radio-opaque material Barium Sulfate material is mixed with biocompatible dye or pigment to make a colored as well as radio-opaque marker.

[0012] In yet another embodiment, a graft device comprises a stent frame, a synthetic non-metallic material that surrounds a portion of the stent frame, and a radiopaque strip embedded in the non-metallic material.

[0013] Another embodiment according to the present invention provides a method of forming a graft device. The method comprises extruding a synthetic non-metallic material so as to form a member having a first surface and a second surface spaced apart from the first surface. Extruding the non-metallic material includes extruding a radiopaque material at least partially embedded in the non-metallic material to form the device.

Brief Description of the Drawings

[0014] The accompanying drawings, which are incorporated herein and constitute part of this specification, illustrate exemplary embodiments of the invention, and, together with the general description given above and the detailed description given below, serve to explain the features of the invention. It should be understood that the preferred embodiments are examples of the invention as provided by the appended claims.

[0015] Figure 1 illustrates a cross-section of a preferred graft device.

[0016] Figure 2 illustrates a cross-section of a preferred device used in making the graft device of Figure 1.

[0017] Figures 3 is a perspective view of an illustrative embodiment of a stent graft having a longitudinal radiopaque marker.

[0018] Figures 3A is a cross-sectional view of the stent graft of Figure 3 along line 3A--3A.

[0019] Figure 3B is an exploded perspective view of the stent graft of Figure 3.

[0020] Figure 4 is a perspective view of another embodiment of a stent graft having a longitudinal radiopaque marker.

[0021] Figures 5 and 6 are additional embodiments of a graft device having a radiopaque marker,

[0022] Figure 7 is another embodiment of a graft device having a radiopaque marker.

[0023] Figure 8 is a fluoroscopic view of different embodiments of a bare stent and graft devices having a radiopaque marker.

Mode(s) For Carrying Out the Invention

[0024] Figures 1-8 illustrate the preferred embodiments. Shown in Figure 1 is a cross-section of one of the preferred embodiments of a graft device 100 having at least one radiopaque marker 106 embedded in an outer surface 104B of the device 100. Alternatively or in addition to, one or more radiopaque markers 102, 108 can be provided on the inner surface 104A, outer surface 104B or be dispersed or integrated with the graft material 104 of the device 100 between the inner surface 104A and the outer surface 104B.

[0025] The device 100 can be made from a graft material 104 which can be a non-metallic material. Specifically, the non-metallic material 104 can include a synthetic fiber or fabric material such as, for example, Dacron, polyester, PTFE, ePTFE, polyurethane, polyurethane-urea, siloxane, and combinations thereof with an appropriate amount of additives added therein such as, for example, bio-active agents. In the preferred embodiments, the graft material 104 is expanded polytetrafluoroethylene or "ePTFE."

[0026] The ePTFE material for graft 104 can be made by a variety of suitable techniques, one of which is described as follows. A compounding of a polymeric compound is generated by sifting PTFE resin with a suitable amount of lubricant such as, for example, Isopar H, at 15-35% by weight of the PTFE to enable the PTFE to flow through extrusion equipment. The combined PTFE resin and lubricant are then placed in a shaker device and shaken so that the lubricant coats and penetrates each of the PTFE resin particles. The thoroughly mixed combination of PTFE resin and lubricant is then incubated in a warming cabinet overnight which is maintained at a temperature of approximately eighty-five degrees Fahrenheit (85° F). The incubation period is believed to allow for a further and more equal dispersion of the lubricant throughout the PTFE resin.

[0027] If desired, the PTFE resin can be further mixed and heated as part of an optional compounding process. For example, the PTFE resin can be compounded with a suitable hydroxyapatite (HA) material to produce a graft configured for increased biocompatibility and bioactivity in order to, for example, promote endothelial cell growth for the maintenance of graft patency and the reduction of intimal hyperplasia.

[0028] The PTFE resin or its compound can be preformed into a compressed cylinder by series of process steps. First, the resin can be poured into an inner barrel of a preformer by directing it through a funnel which is fit to the outside of the inner barrel. Figure 2 illustrates a preferred embodiment of a divided preform barrel 40 which can be used in preforming a resin into a compressed cylinder. The divided preform barrel 40 preferably includes an outer hollow cylindrical member 42, an optional inner hollow cylindrical member 44, and a central solid cylindrical member 46. The inner hollow cylindrical member 44 can be concentrically contained within the outer hollow cylindrical member 42. Details of a similar process are shown and described in U.S. Patent Nos. 5,827,327; 5,641,443; and 6,190,590, each of which is incorporated in its entirety by reference.

[0029] The PTFE resin can be poured within a first area 52 located between the outer hollow cylindrical member 42 and a solid cylindrical member 46. The first area 52 can be divided by one or more inner members 44 to define a secondary area 48 for receipt of any optionally added compound such as, for example, an HA compound material.

[0030] In one of the preferred embodiments, the outer hollow cylindrical member 42 has a radius greater than the radius of the inner hollow cylindrical member 44. The diameter of the components which comprise the preform barrel 40 will vary depending on the size and type of graft that is being produced. A preferred embodiment of the preform barrel 40 can have a radius of approximately 1.5 inches. The secondary area 48 between the inner hollow cylindrical member 44 and the central solid cylindrical member 46 can have a radius of

approximately 0.38 inches, the inner hollow cylindrical member 44 can have a wall thickness of approximately 0.07 inches, and the first area 52 located between the outer hollow cylindrical member 42 and the inner hollow cylindrical member 44 can have a radius of approximately 0.6 inches.

[0031] In addition, a radiopaque paste or resin can be partially or fully embedded in a portion of the outer or inner surfaces of the PTFE resin. Preferably, the radiopaque paste can be formed from a tantalum powder. Other radio-opaque materials which could be used include, but are not limited to, tungsten, gold, silver powder, Barium Sulfate and the like. The preferred radio-opaque material is also heat stable so that it can tolerate sintering temperature encountered during graft manufacturing. In one exemplary embodiment, the radio-opaque paste can be formed by mixing 4 grams of ePTFE, 6 grams of tantalum and 2 grams of Isopar-H to produce a mixture containing sixty percent (60%) tantalum. Preferably, substantially all lubricant is evaporated after extrusion and sintering as described herein. Further in the alternative, the radiopaque paste can be formed from a Barium Sulfate mixture. For example, the radiopaque paste can include an ePTFE paste mixed with twenty to forty percent (20-40%) Barium Sulfate. In a preferred embodiment, the radiopaque paste is formed into an elongated strip that can be disposed along the length of the outer surface of the PTFE resin. Alternatively or in addition to, the radiopaque paste can form a plurality of radiopaque elements that can be aligned along the outer surface of the PTFE resin along its length. The radiopaque paste can be formed into any shape or form. For example, the paste can be formed as sutures, threads and other small pieces such as disks disposed anywhere within the PTFE resin. The continuous or elongated strip of radiopaque material can provide the visual cues to the clinician viewing the stent under fluoroscopy such as, for example, location, orientation or kinking.

[0032] The assembly of PTFE resin and radiopaque paste markers can then be compressed. The materials are compressed by placing the assembly into the preform barrel 40 on a suitable press such as, for example, shown in Figure 3 of U.S. Patent No. 5,827,327. The press used during the compression of the polymeric compound is driven by a suitable power drive, which forces a top member toward a bottom member to compress the material within the divided preform barrel 40. Hollow cylindrical tubes of varying thickness are used to compress the material within the divided preform barrel 40 by slidably reciprocating around the inner hollow cylindrical member 44, the outer hollow cylindrical member 42, and the center solid cylindrical member 46 of the divided preform barrel 40. After compressing the materials contained within the preform barrel 40, the inner cylindrical member 44 (if used), the outer cylindrical member 42, and the center solid cylindrical member 46 of the divided preform barrel 40 are removed to obtain a compressed cylinder of material. Alternatively, the dividers within the preform barrel may be removed prior to compression, without disturbing the interface between the different compounds, and then compressed to form a billet for extrusion. The compressed cylinder of material, or billet, can be co-extruded via a suitable device such as, for example, the extruder shown in Figure 4 of U.S. Patent No. 5,827,327. Briefly, the compressed cylinder of material is placed within an extrusion barrel. Force is applied to a ram, which in turn expels pressure on the compressed cylinder of material. The pressure causes the compressed cylinder of material to be extruded around a mandrel, through an extrusion die, and issue as a tubular extrudate. The tubular extrudate can be expanded to increase the porosity or alter the elasticity of the extrudate. After extrusion or expansion, the extrudate can be sintered in accordance with the expansion and sintering procedures undertaken with PTFE grafts which are known to those skilled in the art.

[0033] In one embodiment, a PTFE billet can include an optional HA lumenal layer 102 formed with a first outer strip of tantalum paste 106 and a second outer strip of Barium

Sulfate paste 108. The billet can be extruded through a suitable extruder at a pressure from about 500 to about 2000 psi. The reduction ratio (i.e., wall thickness of billet to extruded graft thickness) for the billet can be from about 50 to about 350. Table 1 below shows a preferred composition of a PTFE billet by weight.

[0034] **Table 1**

Ref. Number	Formulation	PTFE Resin Weight (g)	Tantalum Weight (g)	Barium Sulfate Weight (g)	Hydroxy-apatite (g)	Lube Weight (g)
102	*HA luminal layer*	200		-	50	60
106	*Tantalum line*	4	6	-	-	2
108	*Barium Sulfate Line**	4	-	6	-	2
-	*PTFE base*	500			-	100

* The Barium Sulfate is preferably mixed with 10-200 milligrams (mg.) cobalt blue (CAS no. 1345-16-0) to induce blue color.

[0035] The billets can be extruded to form various tubes 1 to 30 millimeters (mm.) in diameter, preferably 5 mm. to 6 mm. in diameter for peripheral vascular graft applications. More preferably, the diameter measured is the inner diameter of the tube. Each extruded tube can be expanded to various lengths to introduce different degrees of porosity in the PTFE material, thereby providing the expanded PTFE or ePTFE. The expanded tubes can be sintered at a suitable sintering temperature to cause the tube to maintain essentially the desired porosity and improve the physical characteristics of the expanded ePTFE. The expansion can potentially reduce the radio-opacity of the extruded material. In general, higher expansion gives reduced radio-opacity and/or visibility to the naked eye. It is preferred to add sufficient radio-opaque material or pigment material to produce a colored marking after expansion so that the graft shows adequate radio-opacity when viewed using medical x-ray imaging equipment. The sintering temperature can be similar to that of standard ePTFE graft processing, which can be from about 200 degrees Fahrenheit to 400 degrees Fahrenheit, and preferably about 300 degrees Fahrenheit. Other techniques to provide for the graft device

100 are shown and described in U.S. Patent Nos. 5,628,786; 6,053,943; and 6,203,735 and U.S. Patent Application Publication Nos. 2004/0164445; 2004/0232588; and 2004/0236400, each of which is incorporated in its entirety by reference.

[0036] In one embodiment, Barium Sulfate as a radio-opaque material is mixed with a biocompatible coloring agent to produce a blue color marking. Many biocompatible coloring agents or their mixtures can be used to produce desired color or shade. Black, blue or green colors are most preferred. Tantalum or tungsten metal provide black color as well as radio-opaque properties. In such case, no coloring agent may be needed. Many biocompatible coloring agents may be used, but colors that withstand high sintering temperature without substantial degradation are preferred. The preferred colored materials include, but are not limited to, cobalt blue, (Phthalocyaninato(2-)) copper, Chromium-cobalt-aluminum oxide, titanium oxide or mixtures thereof and the like.

[0037] Again referring to Figure 1, a tube preferably extruded by the process described above can form the lumenal graft device 100. The graft device 100 further preferably includes one or more elongated radiopaque markers or strips 106, 108 embedded in a first inner surface 104A, a second surface 104B or in the material 104 between the first and second surfaces 104A, 104B. More specifically, extrusion of the PTFE resin and the radiopaque marker provides for the device 100 with an ePTFE layer 104 with first surface 104A and second surface 104B. In a preferred embodiment, the device 100 includes at least one elongated portion 106 of radiopaque material on the outer surface 104B in which the radiopaque material is made of either tantalum powder or Barium Sulfate. The elongated portion 106 further preferably forms a continuous strip that runs along the length of the device 10. Alternatively, the graft device 100 can have one or more radiopaque elements, in any orientation line provided by the device 100 to improve visibility in a suitable imaging technique (e.g., x-ray imaging). More specifically, the radiopaque material can form a series

of radiopaque elements (not shown) aligned along the length of the outer surface 104B of the device 100.

[0038] Referring now to Figures 3-3A, shown is a preferred embodiment of an encapsulated stent or "stent-graft" 10. The stent-graft 10 can generally include a tubular member 12 having an interior surface 14 and an exterior surface 16 which are contained between first and second ends 18, 20. An elongated radiopaque marker 6 is preferably provided on the exterior surface 16. As illustrated in FIGS. 3, 3A and 3B, the tubular member 12 preferably includes a balloon or pressure expandable tubular shaped support member 22 which is loaded over a first biocompatible flexible tubular member 24 that is held on a mandrel (not shown). A second biocompatible flexible tubular member 26 is then preferably loaded over the first biocompatible tubular member/support member combination 22, 24. The tubular shaped support member 22 preferably includes a stent similar to that shown or described in any one of U.S. Pat. Nos. 4,733,665; 6,053,941; 6,053,943; 5,707,386; 5,716,393; 5,860,999; and 6,572,647 each of which is incorporated in its entirety by reference. The stent utilized for the member 22 can be balloon expandable stent, self-expanding stent or memory-shaped plastic stent. The tubular members 24, 26 are preferably fused together to encapsulate the support member 22.

[0039] The tubular members 24, 26 of stent-graph 10 are preferably formed in a manner substantially similar to the extruded graph device 100 described above. In particular, the first and second biocompatible flexible tubular members 24, 26 are preferably made by extruding a billet of expanded polytetrafluoroethylene (ePTFE). Alternatively, the first and second biocompatible flexible tubular members 24, 26 may also be made of unexpanded polytetrafluoroethylene (PTFE). The tubular member 26 is preferably extruded along with a radiopaque material to form at least one elongated radiopaque marker 6 embedded in the outer surface of the tubular member 26. Alternatively or in addition to, the tubular member

24 can also be extruded along with a radiopaque material to form at least one elongated radiopaque marker embedded in the outer surface of the tubular member 24. Further, the pressure expandable tubular shaped support member 22 may be made of any material having the strength and elasticity to permit radial expansion and resist radial collapse such as silver, titanium, stainless steel, gold, and any suitable plastic material capable of maintaining its shape and material properties at various sintering temperatures for PTFE or ePTFE.

[0040] Shown in Figure 3A is a cross-sectional view of the stent-graft 10 of Figure 3 prior to fusing the graft or tubular members 24, 26 to the expansion member 22. The first biocompatible flexible tubular member 24, preferably made of unsintered ePTFE, forms the innermost layer or luminal surface of the stent-graft 10, and covers the lumen 28 of the stent-graft 10, thereby providing a smooth, inert biocompatible blood flow surface. The tubular support member 22, preferably a stent or similarly constructed structure, forms the middle layer located at the center of the stent-graft 10. Finally, the second biocompatible flexible tubular member 26, which is also preferably made of unsintered ePTFE, forms the outermost layer or abluminal surface of the stent-graft 10.

[0041] To form the stent-graft 10, the tubular shaped members 24, 22, and 26 can be loaded onto one another. Pressure is applied to the graft/stent/graft assembly in order to fuse the first and second biocompatible flexible tubular members 24, 26 to one another through the openings contained within the tubular support member 22. Where the tubular support member 22 is a stent frame, the first and second ePTFE tubular members 24, 26 are fused to one another through the openings between the struts of the stent. The graft/stent/graft assembly is then heated at sintering temperatures to form a physical bond between the ePTFE layers. The resulting prosthesis is an unexpanded stent encapsulated within ePTFE layers, or specifically, an unexpanded stent having ePTFE layers on its luminal and abluminal surfaces in which the stent and ePTFE layers are inseparable. Alternatively, the prosthesis can include

hydroxyapatite on both its luminal and abluminal surfaces. Further, the ePTFE layers may also be fused or joined together around the ends of the unexpanded stent thereby entirely encasing the stent within ePTFE in both the radial and longitudinal directions. The resulting stent-graft 10 can be loaded onto a suitable delivery device such as, for example, U.S. Patent No. 6,756,007, which is incorporated in its entirety by reference. The stent-graft 10 may advantageously be used in a variety of medical applications including intravascular treatment of stenoses, aneurysms or fistulas; maintaining openings in the urinary, biliary, tracheobronchial, esophageal, renal tracts, vena cava filters; repairing abdominal aortic aneurysms; or repairing or shunting damaged or diseased organs such as, for example, Transjugular Intrahepatic Portosystemic Shunt (TIPS).

[0042] Procedures like TIPS can use an alternative embodiment of the stent-graft 10 as shown in Figure 4. Shown in Figure 4 is a stent-graft 10' having a bare stent portion 12' embedded in a stent-graft, encapsulated or covered portion 14', i.e., a "hybrid" stent-graft. A surgical procedure using the hybrid or stent-graft 10' may require determination of where the covered portion 14' ends during the procedure in order to allow blood flow through the uncovered stent-graft portion 12'. The encapsulated portion 14' of the hybrid stent graft 10' is preferably formed in a manner substantially similar for forming the stent-graft 10 as described above so as to include extrusion of at least an outer ePTFE or PTFE member 26' with an elongated radiopaque material to form the radiopaque marker 6'. Accordingly, the radiopaque marker or strip 6' on the covered portion 14' of the stent 10' provides a medical practitioner with a visual cue as to the actual position of the covered portion while the implantable prosthesis is inside a mammalian body. In addition, the radiopaque marker or strip 6' provides by its proximity, the position of the uncovered portion 12' of the hybrid stent-graft 10' to determine placement of the entire stent-graft 10' during and subsequent to a

surgical procedure. Moreover, the radiopaque strip 6' can eliminate the need for "spoon" or bead-type markers used at the non-encapsulated ends of the stent 10'.

[0043] Referring to Figures 5 and 6, shown are alternative embodiments of a graft, namely vascular bypass grafts 200 and 300 having a radiopaque elongation, marker, or strip embedded in the outer surface. Vascular bypass graft 200 is configured for desired blood flow characteristics for applications above the knees, whereas bypass graft 300 is configured for blood flow characteristics below the knee. Regardless of the structural configurations and applications of the bypass grafts 200 and 300, the grafts 200, 300 can be preferably formed by extruded ePTFE material along with a radiopaque paste as described above to provide the elongated radiopaque markers or strips 204, 304. That is, a radiopaque paste can be embedded or incorporated by extrusion with the synthetic non-metallic material (e.g., Dacron, polyester, PTFE, ePTFE, polyurethane, polyurethane-urea, siloxane, and combinations thereof) to form grafts 200 and 300 with a radiopaque strip 204, 304 along at least one of the luminal and abluminal surfaces of the grafts (200 or 300). The material or combinations of materials used (e.g., Dacron, polyester, PTFE, ePTFE, polyurethane, polyurethane-urea, siloxane, and combinations thereof) can include surface modifying additives or other materials. Examples of various grafts are shown and described in U.S. Patent Nos. 6,203,735; 6,039,755; and 6,790,226, each of which is incorporated in its entirety by reference.

[0044] Shown in FIG. 7 is another embodiment of the graft device 200. In the device 200, the graft material can be formed in a manner as previously described above using PTFE. However, the radiopaque marker 206 is not extruded with the graft material. Instead, the radio-opaque marker 206 is preferably printed on the extruded PTFE forming the tube of the device 200 by a suitable printing technique, such as, for example, engraving, mono-type, offset, cliché transfer, ink-jet or gliceé printing. The radio-opaque marker 206 can be a radio-

opaque ink such as, for example, the ink produced by CI Medical, Inc. of Norton Mass. Preferably, the radiopaque ink is tungsten based in which tungsten is mixed as a radio-opaque component into the ink. In one embodiment, an ink composition for an orientation line for an ePTFE surface includes a suitable polymeric binder that adheres well to an ePTFE surface, a biocompatible dye or pigment, a radiopaque material and a solvent that dissolves the polymeric binder. In addition, the ink composition may contain inorganic white solid materials such as titanium dioxide (to adjust ink shade) and a viscosity modifier. Although many pigments or dyes may be used to make the orientation line, pigments or dyes that have a long history of human implantation are most preferred. The preferred color compounds in the ink include, but are not limited to: (Phthalocyaninato(2-)) copper, D&C Blue No. 9, D&C Green No. 5, Chlorophyllin-copper complex, oil soluble, Chromium-cobalt-aluminum oxide, Ferric ammonium citrate, D&C Blue No. 5, FD&C Blue No. 2, D&C Green No. 6, Titanium dioxide, carbon, Iron oxide, and the like. (Phthalocyaninato(2-)) copper is the most preferred green compound. The color of the ink (e.g., black, blue, etc.) may be determined by viewing under a light having a temperature of about 6500 degrees Kelvin. Hence, in this embodiment, the lines are not only visible to the unaided human eyes, they are also visible to the human eyes with a suitable fluoroscope imager.

[0045] With reference to Figure 8, it has been demonstrated that various physical embodiments of the device can be viewed under fluoroscopic examination. In Figure 8, two graft devices 100A and 100B were provided along with a stent-graft 100c (commercially available under the trade name Fluency®) as referential datum for visibility under a fluoroscope imaging device through an Aluminum plate of 15 millimeters thickness. The reference stent-graft 100c was utilized with radiopaque ink that had 50% tantalum and 50% polycarbonate polyurethane as polymeric binder. The ink solution/dispersion was prepared by dissolving the polymer in tetrahydrofuran solvent. The dispersion was hand painted using a

paint brush to create a circular band on the stent graft surface. The band is slightly visible under fluoroscope so that the reference stent-graft 100c acts as referential datum as to the minimum radiopacity required. The aluminum plate is utilized to simulate the density of biological tissues by interposition of the plate (not shown) between the fluoroscope and the subject graft device. That is, the image of the reference stent-graft 100c in Figure 8 provides for an indication of the radiopacity of the stent as compared to the background environment on which the stent graft is placed in. Further, by having the Fluency stent graft in the image, a referential datum as to the effectiveness of the radiopaque line of the preferred embodiments is provided without resorting to observers with specialized training or machine visions. Consequently, as long as an ordinary observer can determine that the lines provided by the graft of the preferred embodiment in a fluoroscopic display medium has a darker or higher contrast image than the reference stent-graft 100c, then the radiopacity of the line would be deemed to be greater than a minimum level needed for the line to function as a radio-opaque marker in a mammalian body. Alternatively, a machine vision with the ability to recognize discrete levels of contrast can be utilized to provide an objective indicator of the effectiveness of the radiopacity of the radiopaque lines.

[0046] The graft device 100a was provided with two lines 106a and 108a where each line can be a combination of two different radiopaque materials: (1) Barium Sulfate and (2) Tantalum. Even though both lines are formed of different materials, both materials form generally similar solid black lines of radiopacity greater than the referential bare stent in a suitable imaging device, which is a black-and-white photographic print, as shown in Figure 8. Alternatively, graft 100b was provided with two lines 106b and 108b where 106b is made of 60% by weight Barium Sulfate material and a suitable colorant (e.g., cobalt blue). This line appears blue to the naked eye and is radio-opaque. The line 108B is made using 60% (by weight) of Tantalum powder and is black in color. The tantalum provides the black coloring

and generally no coloring agent is needed. These lines demonstrate that a clinician (or even an ordinary observer without any specialized training) would be able to observe and determine whether the graft device has been moved about in the body subsequent to implantation into an undesirable configuration by observing the orientation of such line on a fluoroscopic display medium (paper or graphical display monitor). For example, where the graft has twisted about its own axis, the display medium would show that the line forms a spiral, which is partly shown for graft 100A. Where the graft has rotated about an axis transverse to a longitudinal axis of the graft, i.e., a kink, the display medium would show an intersecting point rather than a smooth inflection curve, shown here in Figure 8 for graft 100B.

[0047] Although the graft device 100 has been described in relation to specific examples noted above, it should be emphasized that variations in the configuration or composition of ePTFE, radiopaque marker, stent framework, and other design parameters can be utilized with the graft device 100. For example, the weight percentage of either the tantalum powder or the Barium Sulfate in the graft device can vary. The percentage of radio-opaque composition in the graft will depend on the amount of radio-opacity needed for a given medical application and the amount of graft expansion subjected during manufacturing. The percentage of radio-opaque element such as tantalum or Barium Sulfate will very from 5% to 70% most preferably from 20% to 60% and even more preferably from 50-60 %. Finally, other types of bioactive agents can also be combined with the radiopaque materials described herein for the graft and the stent graft. The bioactive agents include (but are not limited to) pharmaceutic agents such as, for example, anti-proliferative/antimitotic agents including natural products such as vinca alkaloids (i.e. vinblastine, vincristine, and vinorelbine), paclitaxel, epidipodophyllotoxins (i.e. etoposide, teniposide), antibiotics (dactinomycin (actinomycin D) daunorubicin, doxorubicin and idarubicin), anthracyclines,

mitoxantrone, bleomycins, plicamycin (mithramycin) and mitomycin, enzymes (L-asparaginase which systemically metabolizes L-asparagine and deprives cells which do not have the capacity to synthesize their own asparagine); antiplatelet agents such as G(GP) II_b/III_a inhibitors and vitronectin receptor antagonists; anti-proliferative/antimitotic alkylating agents such as nitrogen mustards (mechlorethamine, cyclophosphamide and analogs, melphalan, chlorambucil), ethylenimines and methylmelamines (hexamethylmelamine and thiotepa), alkyl sulfonates-busulfan, nirtosoureas (carmustine (BCNU) and analogs, streptozocin), trazenes - dacarbazinine (DTIC); anti-proliferative/antimitotic antimetabolites such as folic acid analogs (methotrexate), pyrimidine analogs (fluorouracil, floxuridine, and cytarabine), purine analogs and related inhibitors (mercaptopurine, thioguanine, pentostatin and 2-chlorodeoxyadenosine {cladribine}); platinum coordination complexes (cisplatin, carboplatin), procarbazine, hydroxyurea, mitotane, aminoglutethimide; hormones (i.e. estrogen); anti-coagulants (heparin, synthetic heparin salts and other inhibitors of thrombin); fibrinolytic agents (such as tissue plasminogen activator, streptokinase and urokinase), aspirin, dipyridamole, ticlopidine, clopidogrel, abciximab; antimigratory; antisecretory (breveldin); anti-inflammatory: such as adrenocortical steroids (cortisol, cortisone, fludrocortisone, prednisone, prednisolone, 6α-methylprednisolone, triamcinolone, betamethasone, and dexamethasone), non-steroidal agents (salicylic acid derivatives i.e. aspirin; para-aminophenol derivatives i.e. acetominophen; indole and indene acetic acids (indomethacin, sulindac, and etodalac), heteroaryl acetic acids (tolmetin, diclofenac, and ketorolac), arylpropionic acids (ibuprofen and derivatives), anthranilic acids (mefenamic acid, and meclofenamic acid), enolic acids (piroxicam, tenoxicam, phenylbutazone, and oxyphenthatrazone), nabumetone, gold compounds (auranofin, aurothioglucose, gold sodium thiomalate); immunosuppressives: (cyclosporine, tacrolimus (FK-506), sirolimus (rapamycin), azathioprine, mycophenolate mofetil); angiogenic agents: vascular endothelial

growth factor (VEGF), fibroblast growth factor (FGF); angiotensin receptor blockers; nitric oxide donors; anti-sense oligionucleotides and combinations thereof; cell cycle inhibitors, mTOR inhibitors, and growth factor receptor signal transduction kinase inhibitors; retenoids; cyclin/CDK inhibitors; HMG co-enzyme reductase inhibitors (statins); and protease inhibitors.

[0048] Furthermore, the radiopaque marker, when configured as a strip or substantially straight line provides additional visual cues to the practitioner or clinician beyond graft location. Specifically, the straight line radiopaque marker can indicate whether there is any twisting of the graft during and subsequent to the implantation procedure. This feature is believed to be advantageous in that it allows for a clinician to determine with certainty whether the prosthesis has been implanted optimally in the body without kinking or twisting. That is, prior to the development of the prosthesis as described herein, movements of the arms and legs could cause the implanted prosthesis to kink or twist so as to restrict blood flow through the prosthesis without the clinician being aware of such adverse configurations after the implantation has been completed. The prosthesis, as described herein, allows the clinician to achieve an advantageous technique by ensuring that the prosthesis implanted by the clinician is properly configured inside the mammalian body. Alternatively, other types of indicia (e.g., date of manufacture, manufacture etc.,) can be provided by printing the radiopaque material onto the graft. The radio-opaque lines can also be encoded such as are used, for example, in bar coding of commercial goods. For example bar code, a series of black and white lines with certain thickness and heights can be interpreted by the machines as digital code which can be used in a computer database.

[0049] As used herein, the singular form of "a," "an," and "the" include the plural referents unless specifically defined as only one. While the present invention has been disclosed with reference to certain preferred embodiments, numerous modifications,

alterations, and changes to the described embodiments are possible without departing from the sphere and scope of the present invention, as defined in the appended claims. Moreover, where methods, processes and steps described above indicate that certain events occurring in certain order, those skilled in the art would recognize that the ordering of steps may be modified and that such modifications are within the variations of the described embodiments. Accordingly, it is intended that the present invention not be limited to the described embodiments, but that it have the full scope defined by the language of the following claims, and equivalents thereof.

We Claim:

1. A graft device comprising:

a layer of synthetic non-metallic material having a first surface and a second surface spaced apart from the first surface; and

a radiopaque marker at least partially embedded in the layer.

2. The graft device according to claim 1, wherein the radiopaque marker is fully embedded in the material.

3. The graft device according to any one of the above claims, wherein the radiopaque marker defines a portion of the first surface.

4. The graft device according to any one of the above claims, wherein the radiopaque marker defines a portion of the second surface.

5. The graft device according to claim 1, wherein the radiopaque marker is disposed between the first and second surfaces.

6. The graft device according to any one of the above claims, wherein the synthetic non-metallic material comprises a material selected from a group consisting essentially of Dacron, polyester, PTFE, ePTFE, polyurethane, polyurethane-urea, siloxane, and combinations thereof.

7. The graft device according to any one of the above claims, wherein the radiopaque marker is a paste having about 20% tantalum powder.

8. The graft device according to any one of the above claims, wherein the radiopaque marker is a paste having about 20% to about 40% Barium Sulfate.

9. The graft device according to claim 8 wherein the Barium Sulfate in mixed with a biocompatible coloring agent.

10. The graft device according to claim 9 wherein the coloring agent is green, blue or black colored.

11. The graft device according to claim 10 wherein the coloring agent is cobalt blue.

12. The graft device according to any one of claims 1-8, wherein the radiopaque marker comprises at least one line that extends along a substantial portion of the length of the graft.

13. The graft device according to claim 9, wherein the at least one line comprises two parallel lines that extends along a substantial portion of the length of the graft.

14. A graft device comprising:

a layer of synthetic non-metallic material having a first surface and a second surface spaced apart from the first surface; and

a radio-opaque ink printed on at least one of the first and second surfaces of the synthetic non-metallic material.

15. A device comprising:

a stent frame;

a synthetic non-metallic material that surrounds a portion of the stent frame, the synthetic non-metallic material having first and second surfaces; and

a radiopaque strip embedded in the non-metallic material.

16. A method of verifying orientation of a graft in a mammalian body subsequent to implantation of such graft in the mammalian body without an incision into the body, the method comprising:

directing electromagnetic energies at the implanted graft;

blocking some of electromagnetic energies through a portion of the graft; and

forming an image on a display medium that shows the portion as a line that extends along a substantial length of the graft.

17. A method of forming a graft device comprising:

extruding a synthetic non-metallic material so as to form a member having a first surface and a second surface spaced apart from the first surface,

wherein extruding includes extruding a radiopaque material at least partially embedded in the non-metallic material.

18. A method of verifying orientation of a graft in a mammalian body subsequent to implantation of such graft in the mammalian body without an incision into the body, the method comprising:

directing electromagnetic energies at the implanted graft;

blocking some of electromagnetic energies through a portion of the graft; and

forming an image on a display medium that shows the portion as a line that extends along a substantial length of the graft; and

contrasting the line to a reference datum.

19. The method of claim 18, wherein the contrasting includes contrasting the line to a reference stent-graft under the same electromagnetic energies.

20. A graft device comprising:

a layer of synthetic non-metallic material having a first surface and a second surface spaced apart from the first surface; and

an orientation line disposed along at least one of the first and second surfaces, the orientation line having radiopaque marker and a coloring agent.

21. The graft device of claim 20, wherein the orientation line extends along the axial length of the non-metallic material.

22. The graft device of any one of claims 20-21, wherein the orientation line is one of a parallel pair of lines extending along the axial length of the non-metallic material.

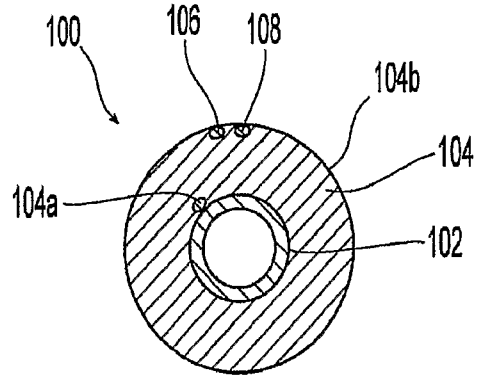

Fig. 1

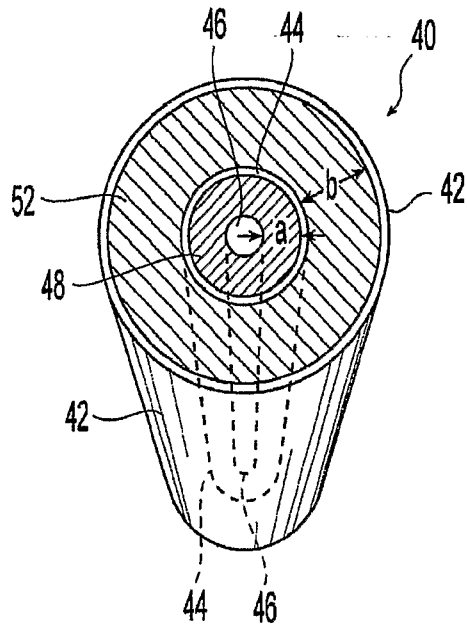

Fig. 2

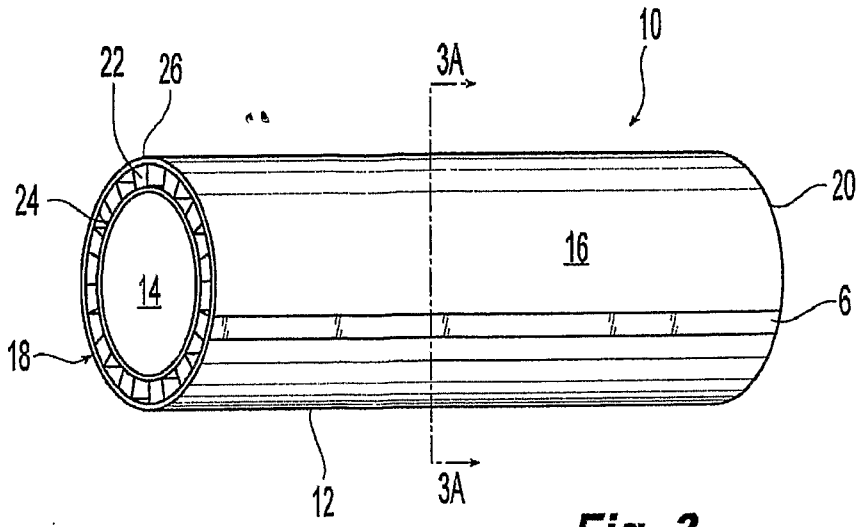

Fig. 3

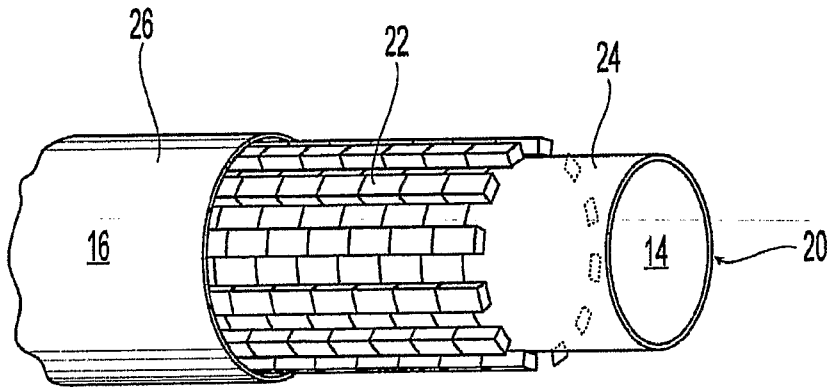

Fig. 3B

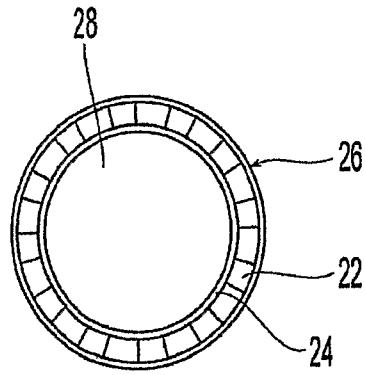

Fig. 3A

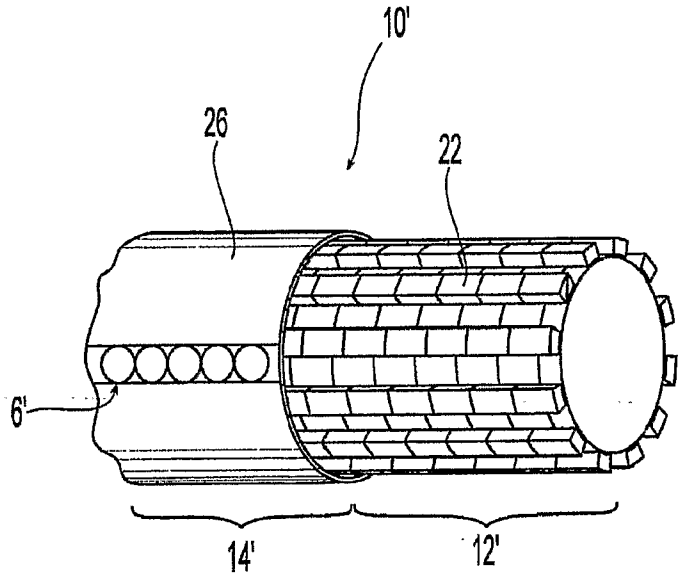

Fig. 4

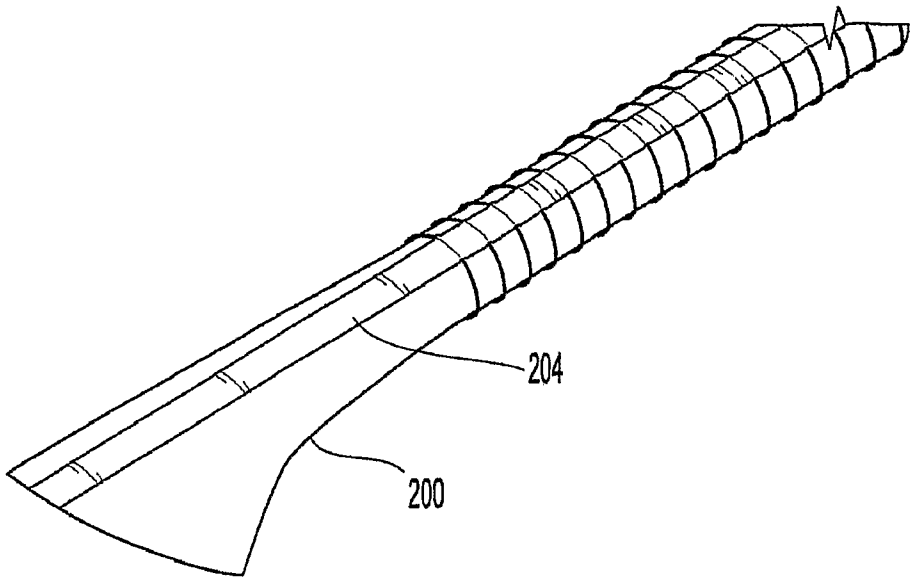

Fig. 5

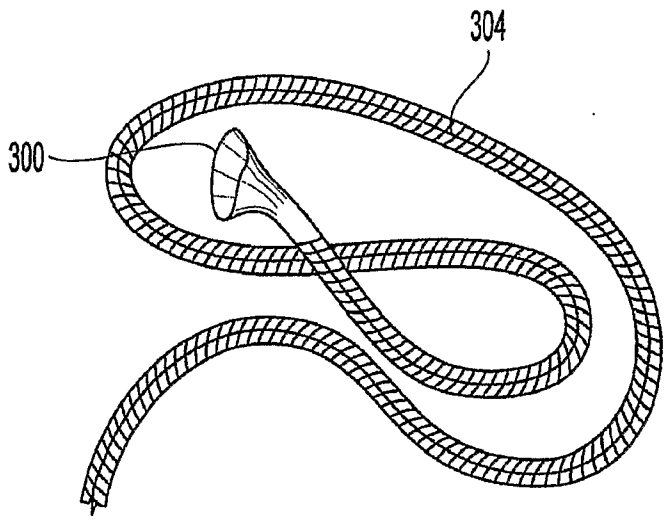

Fig. 6

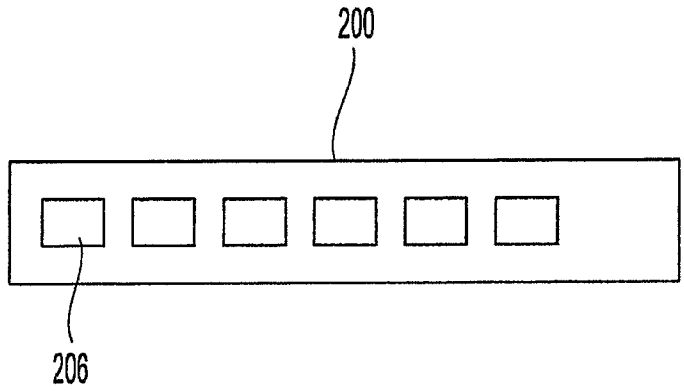

Fig. 7

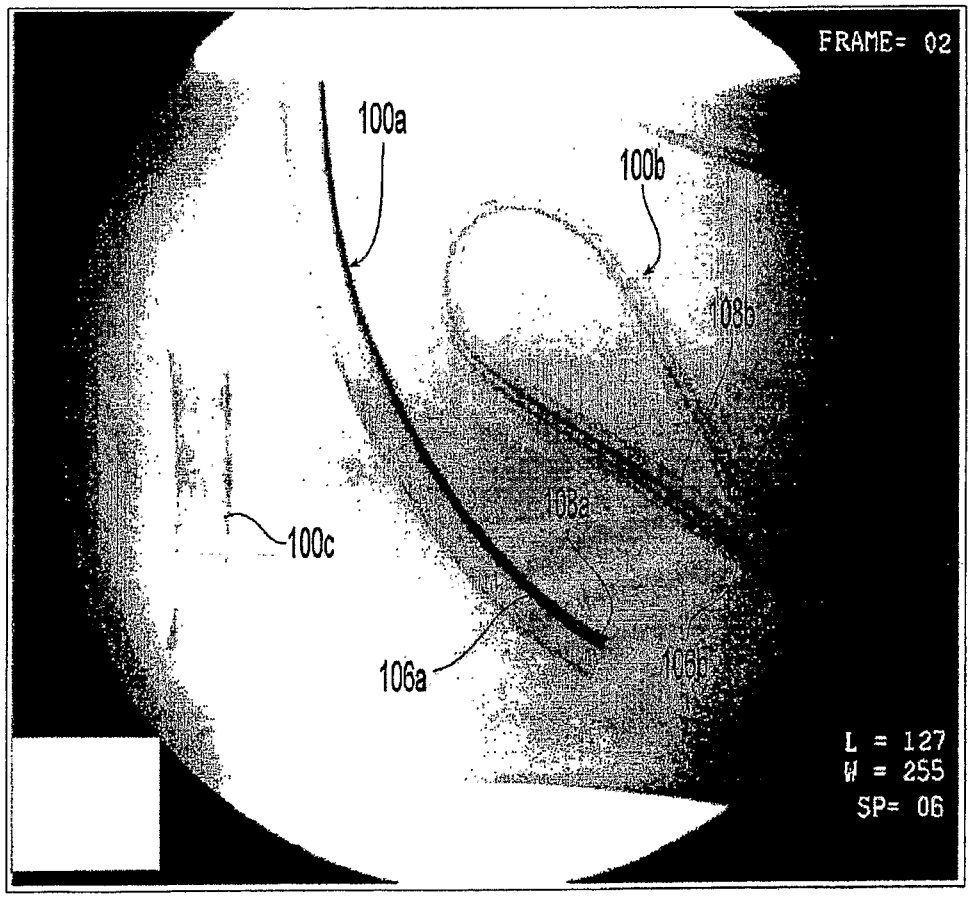

Fig. 8