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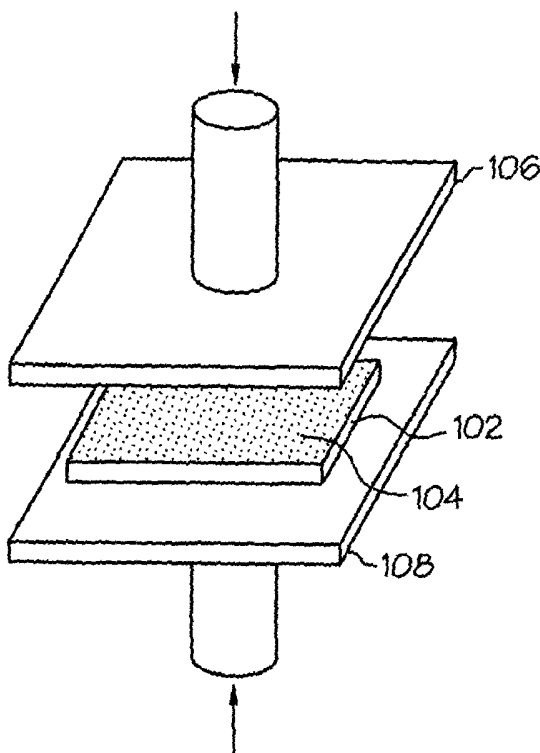
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(54) Title: METHOD FOR ENHANCING SHEET OR TUBING METAL STENT RADIOPACITY



(57) Abstract: A radiopaque stent may be prepared by providing a stent preform (102), providing a particulate radiopaque material (104) on at least a portion of the stent preform, pressing the particulate radiopaque material into a desired portion of the stent preform and processing the stent preform into a stent.

WO 03/011191 A1

METHOD FOR ENHANCING SHEET OR TUBING METAL STENT RADIOPACITY

BACKGROUND OF THE INVENTION

Metal stents are commonly fabricated from stainless steel or nitinol sheet
5 metal or tubing. Radiopacity of the bare metal stent is determined by the radiographic
density of the stent material and the thickness of the stent wall. For small diameter stents
such as coronary stents and other stents with a diameter of less than 12 mm, the bare
metal stents may not necessarily have enough radiopacity for imaging purposes.

There are a number of different methods for providing and enhancing
10 radiopacity in stents. One method of enhancing stent radiopacity involves depositing a
thin surface layer of more radiographically dense material such as gold on the surface of
the stent. The layer may be deposited via plating, ion deposition or any other suitable
technique. Deposition methods, however, may be frustrated by poor adhesion and the
resultant delamination of the deposited layer. Furthermore, the deposited layer may
15 affect stent properties and biocompatibility adversely if it has low elongation properties
or contains impurities.

Another method for providing radiopacity in stents such as wire stents is
to make the stent wire of a composite construction with a radiographically dense core
material such as tantalum or platinum and a casing of structural material such as stainless
20 steel or Elgiloy.

Another method for providing a stent with radiopacity is to add an
immiscible highly radiopaque agent in with the stent metal during ingot melting. With
this method, however, the radiopaque constituent may be drawn out to a stringer
morphology during sheet metal or tubing fabrication and become a structural weakpoint
25 within the material.

Yet another method for providing a stent with radiopacity involves
providing a radiopaque plug of material in the stent. Typically, the stent will be provided
with one or more openings in which the radiopaque material is inserted.

There remains a need for novel methods of providing radiopacity in stents
30 which do not have the adhesion problems associated with plating and which do not
change the metallurgy of the base metal of the stent.

All US patents and applications and all other published documents

mentioned anywhere in this application are incorporated herein by reference in their entirety.

Without limiting the scope of the invention in any way, the invention is briefly summarized in some of its aspects below. Additional details of the invention
5 and/or additional embodiments of the invention may be found in the Detailed Description of the Invention below.

A brief abstract of the some of the aspects of the technical disclosure in the specification is provided as well for the purposes of complying with 37 C.F.R. 1.72.

10 SUMMARY OF THE INVENTION

In one embodiment, the invention is directed to a method of preparing a stent. The method comprises the steps of providing a stent preform and providing a particulate radiopaque material on at least a portion of the stent preform. The particulate radiopaque material is pressed into a desired portion of the stent preform and the stent
15 preform processed into a stent. The stent preform may be in the form of a sheet or a tube during the pressing step. In the former case, the stent preform may be rolled during the processing step to form a coil stent or opposing longitudinal edges may be secured one to the other to form a stent. The stent preform may be provided with a stent pattern prior to or subsequent to the pressing step.

20 In accordance with the invention, the processing step may include the step of heat treating the stent preform. The stent preform may be heated to a temperature above ambient temperature and less than the melting points of the stent preform and the particulate radiopaque material.

Desirably, the particulate radiopaque material is in the form of an element
25 having an atomic weight of at least 43. Suitable particulate radiopaque materials include particulate tantalum, particulate tungsten, particulate platinum, particulate iridium, particulate gold, particulate bismuth, particulate zirconium and alloys thereof.

The particulate radiopaque material, optionally, may be coated or compounded with a diffusion activating substance such as, for example, boron. The
30 particulate radiopaque material may be provided in a number of different forms including mixed with a binder, in the form of a dry powder, or in the form of a slurry.

Desirably, the particulate radiopaque material will be of -325 mesh or

smaller. Also desirably, the particulate radiopaque material will be characterized by an average particle size of 5 microns and, more desirably, 1.5 microns or less.

The stent preform may be made of metal or polymeric material.

Typically, the stent will be made of a metal such as stainless steel, Elgiloy, titanium or
5 any of its alloys or nitinol. Other biocompatible metals may also be used.

In accordance with the invention, the pressing step may be accomplished using platens, tube drawing equipment, a rolling mill, a pressure chamber or any other suitable device for applying pressure to the stent preform. The thickness of the stent preform may remain substantially unchanged as a result of the pressing or may be
10 decreased.

The pressing step may be repeated one or more times and, optionally, an additional quantity of the particulate radiopaque material may be placed on the stent preform in between or during the pressing steps.

Optionally, to increase bonding of the particulate radiopaque material, the
15 stent precursor may be provided with a rough surface prior to depositing the radiopaque material. Also, the radiopaque material may be jet blasted against the stent precursor during the pressing step.

It is within the scope of the invention for a portion of the stent to be rendered radiopaque or for the entirety of the stent to be rendered radiopaque. For
20 example, only the inner surface or the outer surface of the stent may be rendered radiopaque or only a portion of the first end of the stent and/or only a portion of the second end of the stent may be rendered radiopaque.

The invention is also directed to a medical device comprising a plurality of radiopaque regions including a first radiopaque region and a second radiopaque
25 region, where the first and second radiopaque portions are of different radiopacities. The first and second radiopaque regions may be adjacent one another or may be separated from one another. The difference in radiopacity may be achieved by providing an amount of radiopaque material per unit area in the first region which exceeds the amount of radiopaque material provided per unit area in the second region. The difference in
30 radiopacity may also be achieved by providing a first radiopaque material in the first region and a second radiopaque material in the second region which is of different chemical composition from the first radiopaque material. Desirably, the medical device

is a stent.

The invention is further directed to medical devices in general and stents in particular made in accordance with any of the inventive methods disclosed herein.

Additional details and/or embodiments of the invention are discussed
5 below.

BRIEF DESCRIPTION OF THE FIGURES

Fig. 1 is a schematic illustration of a stent precursor with particulate radiopaque material thereon immediately before being pressed between two platens.

10 Fig. 2 is a schematic illustration of the stent precursor of Fig. 1 subsequent to being pressed.

Fig. 3 is a transverse cross-sectional view of the stent precursor of Fig. 2 taken along line 3-3.

15 Fig. 4 is a side view of a stent precursor with particulate radiopaque material thereon as it is being drawn through a rolling mill.

Fig. 5 is a side view of a stent precursor with particulate radiopaque material being disposed thereon immediately prior to being drawn through a rolling mill. The stent precursor is reduced in thickness as a result of being drawn through the mill.

20 Fig. 6 is a side view similar to that of Fig. 5 differing in that the stent precursor is not substantially reduced in thickness as a result of being drawn through the rolling mill.

Fig. 7 is a transverse cross-sectional view of a stent precursor in the form of a sheet which is being rolled into a stent.

25 Fig. 8 is a side view of an inventive radiopaque stent formed by joining opposing edges of the stent precursor of Fig. 7.

Fig. 9 is a perspective view of an inventive radiopaque coil stent.

Fig. 10 is a side view illustrating a tubular stent precursor with radiopaque material disposed thereon as it is being drawn through a drawing die. The diameter of the tube is decreased as a result of being drawn.

30 Fig. 11 is a side view illustrating a tubular stent precursor with radiopaque material disposed thereon as it is being drawn through a drawing die. The diameter of the tube is substantially unchanged as a result of being drawn.

Fig. 12 is a cross-sectional view of an inventive die.

Fig. 13 is a side view of an inventive stent having radiopaque regions of different radiopacity.

Fig. 14 is a side view of another inventive stent having radiopaque regions
5 of different radiopacity.

Fig. 15 is a perspective view of yet another inventive stent having radiopaque regions of different radiopacity.

DETAILED DESCRIPTION OF THE INVENTION

10 While this invention may be embodied in many different forms, there are shown in the drawings and described in detail herein specific embodiments of the invention. The present disclosure is an exemplification of the principles of the invention and is not intended to limit the invention to the particular embodiments illustrated.

For the purposes of this disclosure, unless otherwise indicated, identical
15 reference numerals used in different figures refer to the same component.

In one embodiment, the invention is directed to a method of preparing a stent comprising the steps of providing a stent preform, providing a particulate radiopaque material on at least a portion of the stent preform, pressing the particulate radiopaque material into a desired portion of the stent preform and processing the stent
20 preform into a stent.

The stent preform may be in the form of a sheet or a tube with or without a stent pattern therein. The stent preform may be made of metal in part or in its entirety or of polymeric material in part or in its entirety. Suitable metals include stainless steel, Elgiloy, titanium or any of its alloys, nitinol and any other known stent metal. Suitable
25 polymeric materials include certain polymeric materials, particularly engineering plastics such as thermotropic liquid crystal polymers, PTFE and bioabsorbable polymers such as Poly-L-Lactide.

As shown in Fig. 1, stent preform 102 is in the form of a sheet. Preform 102 is provided with a particulate radiopaque material 104 using any suitable technique.
30 For example, the particulate material may be dusted onto the stent preform, poured onto the stent preform or jet blasted dry or in liquid onto the preform. Other techniques for applying the particulate radiopaque material to the stent preform include vacuum sputter

deposition, and vacuum or gas plasma spray deposition.

Particulate radiopaque material 104 is then pressed into stent preform using any suitable device capable of applying pressure to the stent preform. As shown in Fig. 1, stent preform 102 is disposed between a top platen 106 and a bottom platen 108 and the platens pressed together. As a result of the pressure applied to the stent preform, as shown in Figs. 2 and 3, the radiopaque material 104 is pressed into the stent preform 102 and the stent preform rendered radiopaque. The process of adding additional radiopaque material and pressing the material into the preform optionally may be repeated as necessary until a sufficient amount of radiopaque material has been applied to the stent preform.

It is desirable to press the particulate radiopaque material into the surface of the substrate or stent precursor so that a substantial quantity of the particulate radiopaque material does not subsequently separate from the surface of the stent precursor or stent during manufacturing and use. In order to form a secure attachment of the particulate radiopaque material to the surface, the particulate radiopaque material is desirably pressed into the surface of the stent precursor by indenting or displacing the stent precursor material or by deforming the particulate radiopaque material onto the surface such that it flows into and around the topographic features of the substrate. Without being bound by theory, it is believed that as a result of the pressing operation the particulate radiopaque material is mechanically attached to the surface. High pressure and/or temperature could also be used to allow diffusion of elements between the particulate radiopaque material and the substrate forming a metallurgical bond.

In order to press the particulate radiopaque material into the surface of the substrate, sufficient pressure must be applied to the pressing platens or between the die and workpiece to deform the particulate radiopaque material or the substrate material. Desirably, the pressure that is applied will be greater than the yield strength of the particulate radiopaque material in order for the particulate radiopaque material to be deformed onto the surface topography of the substrate. For example, the die pressure or pressure from platens to press tantalum powder into a substrate surface such as 316 alloy stainless steel will be 190 MPa (28 ksi). The room temperature yield strength of recrystallized pure tantalum metal is 190 MPa (28 ksi). The upper limit in pressure for this operation would be the ultimate tensile strength (UTS) of the substrate material to

prevent fracture of it. For example, the UTS of annealed 316 alloy stainless steel strip is 485 MPa (70 ksi), so the pressing operation for tantalum powder and 316 stainless steel should be in the range of 190 to 485 MPa (28 to 70 ksi) at room temperature.

When pressing a hard particulate radiopaque material, for example, tantalum carbide or tantalum boride, into a softer substrate, for example, annealed 316 stainless steel strip, the pressure should be sufficiently high to cause the particulate radiopaque material to indent into the substrate and deform the substrate material. Desirably, the pressure will be above the yield strength of the substrate material and below the yield strength of the particulate radiopaque material. These same considerations of material properties and pressing pressures may be applied to other material systems such as, for example, pressing platinum powder onto nitinol substrate.

The pressing operation may also be performed at lower pressures by heating the materials to an elevated temperature so as to reduce the flow stresses of the materials. Desirably, the materials would be heated to a temperature less than about 150C to avoid oxidation of the surface. Surface oxidation may reduce the effectiveness of any subsequent diffusion bonding heat treatments, because the oxide would act as a diffusion barrier between the two materials. Where it is desirable to heat the materials to higher temperatures, the pressing may be carried out in a chamber containing an inert gas (for example argon or nitrogen) or in a vacuum chamber to prevent oxidation.

Typically, in a room temperature pressing operation, pressure will be applied for a period of about 1 second to about 30 seconds. Once the necessary pressure level is reached, the material flow will be nearly instantaneous. It may prove necessary to hold the pressure application for a longer period of time where pressing temperatures in the creep regime of the materials (for slow creep flow) are used. Thus, for example, where temperatures at about $\frac{1}{4}$ to $\frac{1}{3}$ the melting point of the particulate radiopaque material and substrate materials are used, the pressing time may range from the order of 1 minute to 3 hours or more. At pressing temperatures above about $\frac{1}{3}$ the melting point of the materials, the pressing time required for material flow would be on the order of 1-30 seconds as the material flow would be nearly instantaneous.

The pressing step may occur at cold temperatures as low as -200C, at ambient temperatures or at elevated temperatures of up to 100C less than the melting point of the stent material. Thus, the pressing step may occur at temperatures as high as

1275C for 316 stainless steel, 1200C for nitinol, and 1568C for titanium. Pressing at the lower end of the temperature range may, in particular, be desirable when working with nitinol in the soft martensitic phase. At low temperatures, the martensitic phase of the metal is soft and the radiopaque powder can indent more easily into the metal. On the high end, pressing at a temperature of about 100C below the melting point of the metal is the highest temperature to which the workpiece may be heated without risking some melting. Pressing stainless steel or titanium will be easier at a high temperature because these metals are softer at higher temperatures. With metals that are easily oxidized, it is particularly desirable to press at ambient temperature to avoid oxidation of the base metal and the creation of a hard oxide surface layer. The presence of a hard oxide surface layer would not only necessitate the use of additional pressure in the pressing step but would also render it more difficult for the atoms of the powdered material, once pressed into the oxide layer, to diffuse through the oxide layer into the base metal to achieve a metallurgical bond, as discussed above.

Where a polymeric material is used for the stent precursor, the particulate radiopaque material may be heated during application so that it melts or softens the polymer to cause encapsulation of the particulate radiopaque material by the polymer.

The pressing may also be accomplished, as shown in Fig. 4, by applying pressure to stent preform 102 through the use of a roller 112. As shown in Fig. 4, the radiopaque material is applied prior to rolling. In another embodiment, as shown in Fig. 5, particulate radiopaque material 104 may be applied to stent preform 102 during the rolling operation via applicator 113. In this way, the particulate radiopaque material is pressed into the stent preform immediately after being deposited on the preform.

In the embodiment of Fig. 5, the particulate radiopaque material is pressed into the stent preform with sufficient pressure to reduce the thickness of the stent preform. It is also within the scope of the invention to use a roller without causing a substantial reduction in the thickness of the stent preform, as shown in Fig. 6.

In either case, the preform may be pressed a single time or any desirable number of times. Optionally, additional particulate radiopaque material may be added to the stent preform at any point during the process. Where multiple pressing steps are involved and additional particulate radiopaque material is added, the additional particulate radiopaque material is desirably added between pressing steps.

Yet another method for pressing the radiopaque material into the stent preform involves placing the preform in a pressure chamber and pressurizing the chamber.

It is also within the scope of the invention to combine any of the above
5 techniques. For example, pressing of the stent with platens may be followed by the application of pressure to the stent preform with rollers.

Subsequent to pressing, any desired stent pattern may be provided in the stent preform by any suitable technique. For example, a desired stent pattern may be etched into the stent preform or may be cut into the stent preform. Chemical etching
10 techniques, laser cutting techniques, mechanical cutting techniques or any other suitable technique may be used to provide the stent pattern in the stent preform.

After the desired pattern has been provided in the stent, stent preform 102 may then be rolled into a tube and opposing longitudinal edges 110 and 112 secured one to the other via any suitable technique including welding (laser or otherwise), riveting
15 and adhesive bonding, as shown in Fig. 7, to form stent 116, as shown in Fig. 8. The stent preform may also be rolled to form a coil stent, as shown generally at 116 in Fig. 9, without securing the longitudinal edges to one another. Stent 116 as shown in Fig. 9 does not include any openings therein. The coil stent of Fig. 9 may optionally be provided with any suitable stent pattern by removing material from the stent preform.

20 In yet another embodiment, the stent preform may be in the form of a sheet which has already been provided with a desired stent pattern prior to pressing radiopaque material therein. Subsequent to applying and pressing the radiopaque material, the stent preform may be rolled, as described above, and the longitudinal edges optionally secured to one another.

25 In yet another embodiment of the invention, as shown in Fig. 10, stent preform 102 may be in the form of a tube. The tube may optionally have a stent pattern cut therein or the stent pattern may be provided subsequent to rendering the stent preform radiopaque.

In accordance with the invention, particulate radiopaque material is
30 applied to the tubular stent preform and the stent preform is drawn through die 114. Desirably, the particulate radiopaque material is provided to stent preform 102 immediately before being drawn through die 114. Die 114 has an opening 116

therethrough. Opening 116 may be of non-constant diameter, as shown in Fig. 10 or may be of constant diameter, as shown in Fig. 11. In the latter case, there is substantially no reduction in the outer diameter of tubular stent preform 102. In the former case, where a die with a tapered diameter is used, the outer diameter of the stent preform is reduced as
5 a result of being drawn through the die.

In the embodiments of Figs. 10 and 11, the particulate radiopaque material is applied to the stent preform in the form of a slurry immediately prior to being drawn through the die.

It is also within the scope of the invention to use an inventive die such as
10 that shown at 114 in Fig. 12. Die 114 includes one or more channels 152 which terminate in openings in the inner wall surface 154 of the die. The particulate radiopaque material, desirably in the form of a slurry, may be pumped into die 114 from an outside source in communication with the one or more channels 152. The invention also contemplates the presence of optional reservoir 156 in fluid communication with the one
15 or more channels 152.

The radiopaque material may also be pressed into the stent preform via rotary swaging in which one or more dies rotate around and impact the surface of the stent preform to press the radiopaque powder into it.

In accordance with the invention, the particulate radiopaque material may
20 be in the form of particulate tantalum, particulate tungsten, particulate platinum, particulate iridium, particulate gold, particulate bismuth, particulate barium, particulate zirconium and alloys thereof. Examples of suitable alloys include a platinum/nickel alloy (10% nickel) and a platinum/iridium alloy (20% iridium). More generally, the particulate radiopaque material may be in the form of an elemental material having an atomic weight
25 of at least 43 or an alloy thereof. As the atomic weight of the particulate radiopaque material is increased, the amount of the radiopaque material which is necessary to achieve the desired degree of radiopacity decreases.

Typically, the particulate radiopaque material will be applied in a layer having a thickness of 1 to 5 microns. Thinner layers may be applied when radiopaque
30 materials with high atomic weights are used. As radiopaque materials with lower atomic weights are used, thicker layers of radiopaque material may be desirable.

Suitably, the particulate radiopaque material will be in the form of a

powder of -325 mesh or smaller. More desirably, powders ranging in size from -325 mesh to -1250 mesh will be used. Most desirably, powders of approximately -625 mesh will be employed.

Typically, the particulate radiopaque material will have an average
5 particle size of 10 microns or less. Desirably, the particulate radiopaque material will have an average particle size of 5 microns or less and more desirably, 1.5 microns or less.

Any of the above materials may be provided in powdered form. Examples
of currently available powders that may be used in the present invention include -325
10 mesh tantalum of 99.995% purity with an average particle size of 10 microns or less available from Cerac, Inc. Milwaukee, WI and -325 mesh tantalum boride of 99.5% purity with an average particle size of 10 microns or less.

The particulate radiopaque material may be provided in the form of a dry
powder or may be provided in the form of a slurry. In the latter case, the slurry may be
formed by mixing the particulate radiopaque material with a liquid such as water or a
15 drawing lubricant. A soap or water soluble cutting or forming fluid lubricant may be used to suspend the particulate radiopaque material in the water or other liquid. Emulsifiable oil cutting fluids, liquid handsoap and castile soap may be used for this purpose.

Retention of the particulate radiopaque material may be further facilitated
20 by providing the stent preform with a rough surface to entrap the radiopaque material. Desirable, the surface roughness of the stent preform will be from about 16 to 125 microinches (R_a). The surface may be roughened by techniques such as chemical milling, milling, laser machining, barrel finishing, grinding, grit blasting, shot peening or any other suitable technique.

25 The particulate radiopaque material may also be mixed with a paste or wax or other binder to temporarily bond the particulate radiopaque material to the preform prior to pressing. This would avoid having loose particles of material which detach from the stent preform and would ensure a uniform distribution of the particulate radiopaque material. The wax binder may be melted and the particulate radiopaque
30 material blended therein. The particulate material - wax blend may then be poured, sprayed, dipped or otherwise applied to the surface of the stent preform and allowed to solidify. Suitable waxes and pastes include paraffin waxes such as Ozokerite or a

Borneo type wax such as Aristowax. Ozokerite melts between 55C and 110C and is soluble in alcohol, benzol and naphtha. Any of these solvents may be used to remove the wax from the stent preform subsequent to pressing. Aristowax is a microcrystalline wax which melts at a temperature range between 40C and 90C. Yet another type of wax
5 which may be used is Ruhr wax which melts at a temperature range between 105C and 126C and has a low ash content (<50 ppm). These waxes may be burned off or melted off the stent preform. Desirably, the wax binder is melted or burned away from the metal after pressing so that the powder is held in place until the material is pressed. If the wax is removed prior to pressing, the powder may separate from the substrate thereby
10 eliminating the benefit of using the wax. The particulate radiopaque material may then be pressed into the stent preform using any suitable pressing technique. Optionally, the particulate radiopaque material may be hot rolled or pressed at a temperature where the binder is vaporized. The vaporized binder may then be evacuated.

Another technique for ensuring that the particulate radiopaque material
15 remains on the stent preform prior to pressing involves sandwiching the particulate radiopaque material between the stent preform and a layer of metal foil, wax paper or any other suitable substrate and feeding the assembly into the pressing equipment.

Optionally, the particulate radiopaque material may be coated or compounded with a diffusion activating substance, for example boron. An example of a
20 particulate radiopaque material coated or compounded with a diffusion activating substance is tantalum boride.

Any of the inventive embodiments disclosed herein may further comprise one or more additional heat treatment steps. The heat treatment steps may include annealing steps at higher temperatures and/or lower temperature treatment steps to allow
25 for diffusion bonding of the particulate material to the stent preform. The latter steps are desirably carried out at a temperature above ambient temperature and less than the melting points of the stent preform and the particulate radiopaque material. Desirably, the stent preform will be heat treated subsequent to pressing the radiopaque material into the stent preform.

30 It is within the scope for the entirety of the resulting stent to be rendered radiopaque or for only selected portions of the resulting stent to be rendered radiopaque. As an example of the latter, the particulate radiopaque material may be provided at only

the proximal and/or distal ends of the stent preform with the resulting stent being radiopaque only at the proximal and/or distal ends. As another example, where the resulting stent has sidebranch access, the stent may be rendered radiopaque in the region of sidebranch access by providing the particulate radiopaque material in the region of the stent preform corresponding to the region of sidebranch access in the finished stent. Yet another example involves selectively marking the middle of the stent preform and resulting stent.

It is also within the scope of the invention to provide the particulate radiopaque material in regions of different thickness on the stent preform so that the resulting stent has radiopaque regions of different thicknesses. The different radiopaque regions may be adjacent one another on the stent or separated by non-radiopaque portions of the stent. The variations in radiopacity may be achieved by varying the amount of the radiopaque material which is provided per unit area along one or more desired portions of the stent preform.

Providing radiopaque regions of different radiopacities may be desirable where there is a need to have portions of a stent, for example end portions, to appear clearly on a fluoroscopic image and where it is not critical if adjacent anatomy is blurred or obscured by the radiopaque region and where it is desirable to have other regions appear on a fluoroscopic image without blurring or obscuring nearby regions.

A stent having a radiopaque material of varying thickness may be provided by depositing layers of different thickness of particulate radiopaque material in different regions of the stent preform and pressing the stent preform as disclosed herein. For example, a first layer of particulate radiopaque material may be deposited in one or more desired regions of a stent preform and the preform pressed. Additional radiopaque material may then be deposited in selected regions of the stent preform and the preform pressed. The process may be repeated as necessary to build layers of radiopaque material of different thicknesses in different portions of the stent preform and ultimately, the stent.

Where an applicator is used to apply the particulate radiopaque material to the stent preform prior to rolling the preform or prior to drawing the preform through a die, the rate of delivery of the particulate radiopaque material to the stent preform may be varied to provide for layers of differing thickness of the particulate radiopaque material. The thickness of the layer of radiopaque material may also be controlled by varying the

rate at which the stent preform is drawn through the rollers or through the die with the rate of delivery of particulate radiopaque material remaining constant.

The inventive methods, in many of their embodiments, allow for radiopacity to be added to a stent preform via solid state processing techniques. The radiopacity is added to a stent preform by deforming discrete particles of radiopaque material into the surface of a stent preform. This technique overcomes many of the problems associated with plating techniques and with adding radiopacity in the molten state of the stent preform.

The invention is also directed to stents made in accordance with any of the inventive methods disclosed herein.

In one embodiment, the invention is directed to a stent having an exterior surface and an interior surface where particulate radiopaque material has been pressed only into the exterior surface of the stent.

In another embodiment, the invention is directed to a stent having an exterior surface and an interior surface where particulate radiopaque material has been pressed only into the interior surface of the stent.

In yet another embodiment, as shown in Fig. 13, the invention is directed to a stent 116 comprising a plurality of radiopaque regions including first radiopaque region 118 and second radiopaque region 120. The first and second radiopaque portions are of different radiopacities. First radiopaque region 118 is more radiopaque than second radiopaque region 120 as indicated by the difference in shading in the figure. In the stent of Fig. 13, the first and second radiopaque regions do not abut one another. The stent may also be provided in embodiments in which the first and second radiopaque regions are adjacent one. The radiopacity of the stent may taper over a given portion of the stent or may change abruptly. For example, as shown in Fig. 14, the amount of radiopaque material may gradually decrease from a maximum amount at the ends of the stent in region 118 to a decreased radiopacity in region 120 as indicated by the difference in shading in the figure. The remainder of the stent is not radiopaque. As shown in Fig. 15, ends 122 of stent 116 may be provided with a first amount of radiopaque material and a region of sidebranch access 124 may be provided with sufficient radiopaque material to be viewable in a fluoroscopic image but with less radiopaque material than is present in the ends of the stent, as indicated by the shading in the figure, to avoid blurring or

obscuring areas of the stent adjacent the region of sidebranch access.

The variable radiopacity may be achieved by varying the amount of radiopaque material per unit area in desired portions of the stent. The variable radiopacity may also be achieved by varying the radiopaque material that is applied to the
5 stent. For example, one region of the stent may comprise a first radiopaque material of a first atomic weight and another region of the stent may comprise a second radiopaque material of a second atomic weight different from the first atomic weight.

In addition to being directed to stents and methods of forming stents, the invention is directed more generally to methods of forming medical devices exhibiting
10 radiopacity. Desirably, the medical devices are implantable in the body, as in the case of stents. Other medical devices which may be provided in accordance with the inventive methods disclosed herein include vena cava filters, occlusion devices, device anchors, catheters and stent mounting hubs. An example of a vena cava filter is disclosed in US 6,126,673. An example of an occlusion device is disclosed in US 6,206,907. An
15 example of a device anchor is disclosed in US 6,231,581. An example of a catheter and hubs is disclosed in US 6,007,543.

EXAMPLE

Annealed 316L stainless steel tubing having an outer diameter of 0.25
20 inches and a wall thickness of 0.01 inches may be drawn so that the outer diameter is reduced to 0.20 inches with the wall thickness remaining approximately 0.01 inches thick. A slurry comprising particulate radiopaque material may be applied to the tubing to coat the tubing and the tubing drawn to an outer diameter of 0.15 inches and a wall thickness of 0.007 inches. Desirably, the die has an entrance angle such that the coating
25 is not skived off, but is instead pressed into the surface of the tubing within the die (as shown, for example, in Fig. 10). Additional slurry comprising the particulate radiopaque material may be applied to the tube and the tubing drawn to an outer diameter of 0.125 inches and a wall thickness of 0.005 inches. Next, the tubing is heated to 125C to evaporate the slurry from the surface of the tubing. The tubing is then annealed at 1100C
30 for 20 minutes in an inert gas or in hydrogen gas to soften the tube and facilitate diffusion bonding between the particulate radiopaque material and the stainless steel tubing. The tubing may be drawn down further in several steps to an outer diameter of 0.100 inches,

0.075 inches and finally to an outer diameter of 0.060 inches. The drawn tubing may then be annealed at 1025C for 5 minutes in an inert gas or hydrogen gas for a final recrystallization. A desired stent pattern may then be laser cut into the tubing and the surface of the tubing polished or otherwise finished resulting in a stent.

5 The above disclosure is intended to be illustrative and not exhaustive. This description will suggest many variations and alternatives to one of ordinary skill in this art. All these alternatives and variations are intended to be included within the scope of the claims where the term "comprising" means "including, but not limited to". Those familiar with the art may recognize other equivalents to the specific embodiments
10 described herein which equivalents are also intended to be encompassed by the claims.

 Further, the particular features presented in the dependent claims can be combined with each other in other manners within the scope of the invention such that the invention should be recognized as also specifically directed to other embodiments having any other possible combination of the features of the dependent claims. For
15 instance, for purposes of claim publication, any dependent claim which follows should be taken as alternatively written in a multiple dependent form from all prior claims which possess all antecedents referenced in such dependent claim if such multiple dependent format is an accepted format within the jurisdiction (e.g. each claim depending directly from claim 1 should be alternatively taken as depending from all previous claims). In
20 jurisdictions where multiple dependent claim formats are restricted, the following dependent claims should each be also taken as alternatively written in each singly dependent claim format which creates a dependency from a prior antecedent-possessing claim other than the specific claim listed in such dependent claim below (e.g. claim 3 may be taken as alternatively dependent from claim 1; claim 5 may be taken as
25 alternatively dependent on claim 4, claim 2 or claim 1, claim 6 may be taken as alternatively dependent from claim 4, claim 2 or claim 1; etc.).

 This PCT application claims priority from US Application No. 09/920,998, filed on August 2, 2001, the entire contents of which is hereby incorporated by reference.

30

CLAIMS

1. A method of preparing a stent comprising the steps of:
providing a stent preform;
providing a particulate radiopaque material on at least a portion of the stent
5 preform;
pressing the particulate radiopaque material into a desired portion of the stent
preform; and
processing the stent preform into a stent.
2. The method of claim 1 wherein the stent preform is in the form of a sheet during
10 the pressing step.
3. The method of claim 2 wherein the stent preform is rolled during the processing
step.
4. The method of claim 3 wherein a first edge of the stent preform is secured to the
second edge during the processing step.
- 15 5. The method of claim 3 wherein the stent preform is provided with a stent pattern
prior to the pressing step.
6. The method of claim 3 wherein the stent preform is provided with a stent pattern
subsequent to the pressing step.
7. The method of claim 1 wherein the stent preform is in the form of a tube during
20 the pressing step.
8. The method of claim 7 wherein the stent preform is provided with a stent pattern
prior to the pressing step.
9. The method of claim 7 wherein the stent preform is provided with a stent pattern
subsequent to the pressing step.
- 25 10. The method of claim 1 wherein the processing step includes the step of heat
treating the stent preform after the particulate radiopaque material has been disposed on
the stent preform.
11. The method of claim 10 wherein the particulate radiopaque material is coated or
compounded with a diffusion activating substance.
- 30 12. The method of claim 11 wherein the diffusion activating substance is boron.
13. The method of claim 10 wherein the stent preform is heated to a temperature
above ambient temperature and less than the melting points of the stent preform and the

- particulate radiopaque material.
14. The method of claim 1 wherein the particulate radiopaque material is selected from the group consisting of particulate tantalum, particulate tungsten, particulate platinum, particulate iridium, particulate gold, particulate bismuth, particulate zirconium, 5 particulate barium and alloys thereof.
15. The method of claim 1 wherein the particulate radiopaque material is selected from the group consisting of elements having an atomic weight of at least 43 and alloys thereof.
16. The method of claim 14 wherein the stent preform is made from metal.
- 10 17. The method of claim 16 wherein the metal is selected from the group consisting of stainless steel, titanium and nitinol.
18. The method of claim 1 wherein the stent preform is in the form of a sheet and the pressing step includes the steps of placing the stent preform between two platens and applying a force to the stent preform with one or more of the platens.
- 15 19. The method of claim 1 wherein the pressing step is repeated one or more times.
20. The method of claim 19 wherein an additional quantity of the particulate radiopaque material is placed on the stent preform in between or during the pressing steps.
21. The method of claim 1 wherein the pressing step is accomplished by directing the 20 stent preform through a rolling mill.
22. The method of claim 21 wherein the particulate radiopaque material is disposed on the stent preform prior to the step of pressing.
23. The method of claim 21 wherein at least some of the particulate radiopaque material is disposed on the stent preform during the pressing step.
- 25 24. The method of claim 1 wherein the stent preform has a thickness which is reduced during the pressing step.
25. The method of claim 1 wherein the stent preform has a thickness which is substantially unchanged by the pressing step.
26. The method of claim 1 wherein the particulate radiopaque material is 30 characterized by an average particle size of 5 microns or less.
27. The method of claim 1 wherein the particulate radiopaque material is of -325 mesh or smaller.

28. The method of claim 1 wherein the particulate radiopaque material is provided mixed with a binder.
29. The method of claim 1 wherein the particulate radiopaque material is provided in the form of a dry powder.
- 5 30. The method of claim 1 wherein the particulate radiopaque material is provided in the form of a slurry.
31. The method of claim 1 wherein the stent precursor has a rough surface, the particulate radiopaque material disposed on the rough surface.
32. The method of claim 1 wherein the particulate radiopaque material is disposed in
10 a liquid.
33. The method of claim 32 wherein the liquid is jet blasted against the stent precursor during the pressing step.
34. The method of claim 1 wherein the stent has an outer surface and an inner surface, the entirety of the outer surface being radiopaque.
- 15 35. The method of claim 1 wherein the stent has an outer surface and an inner surface, the entirety of the inner surface being radiopaque.
36. The method of claim 1 wherein the stent has a first end and a second end, only a portion of the first end and only a portion of the second end being radiopaque.
37. The method of claim 1 wherein the stent precursor comprises a polymeric
20 material.
38. The method of claim 37 wherein the stent precursor is made entirely of a polymeric material.
39. The method of claim 37 wherein the stent precursor comprises a layer of polymeric material and the particulate radiopaque material is pressed into the polymeric
25 material during the pressing step.
40. The method of claim 37 wherein the particulate radiopaque material is pressed into the polymeric material.
41. The method of claim 1 wherein the particulate radiopaque material is blasted into the stent preform during the pressing step.
- 30 42. The method of claim 1 wherein the particulate radiopaque material is deposited on the stent preform via a method selected from the group consisting of vacuum deposition, grit blasting, plasma spraying and jet blasting prior to the pressing step.

43. An implantable medical device comprising a plurality of radiopaque regions including a first radiopaque region and a second radiopaque region, the first and second radiopaque portions of different radiopacities.
44. The implantable medical device of claim 43 in the form of a stent.
- 5 45. The implantable medical device of claim 44 wherein the first and second radiopaque regions are adjacent one another.
46. The implantable medical device of claim 44 wherein the first and second radiopaque regions do not abut one another.
47. The implantable medical device of claim 44 wherein the amount of radiopaque
10 material per unit area in the first region exceeds the amount of radiopaque material per unit area in the second region.
48. The implantable medical device of claim 44 wherein the first radiopaque region comprises a first radiopaque material and the second radiopaque material comprises a second radiopaque material of a different chemical composition from the first material.
- 15 49. An implantable medical device having a particulate radiopaque material pressed therein.
50. The implantable medical device of claim 49 in the form of a stent.
51. A method of preparing an implantable medical device comprising the steps of:
providing a medical device preform;
20 providing a particulate radiopaque material on at least a portion of the medical device preform;
pressing the particulate radiopaque material into a desired portion of the medical device preform; and
processing the medical preform into a medical device.

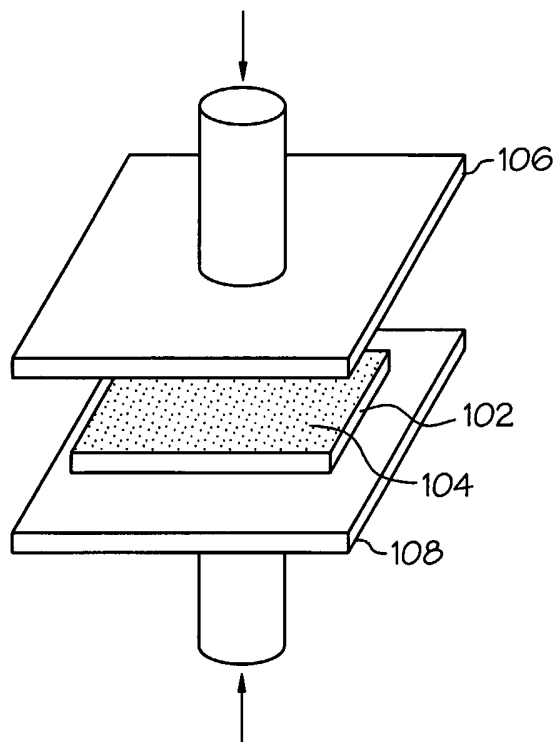


FIG. 1

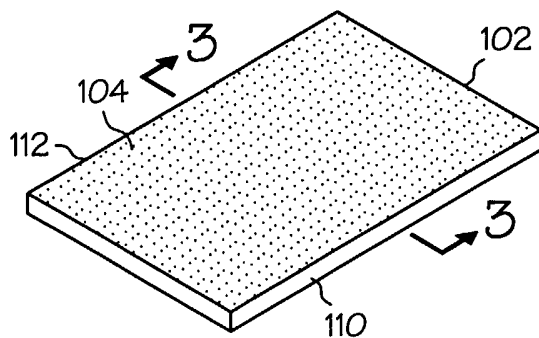


FIG. 2

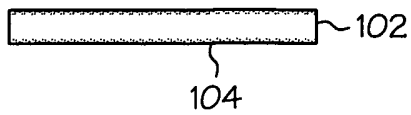


FIG. 3

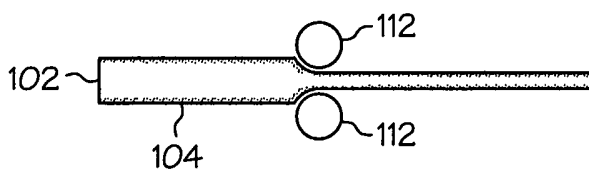


FIG. 4

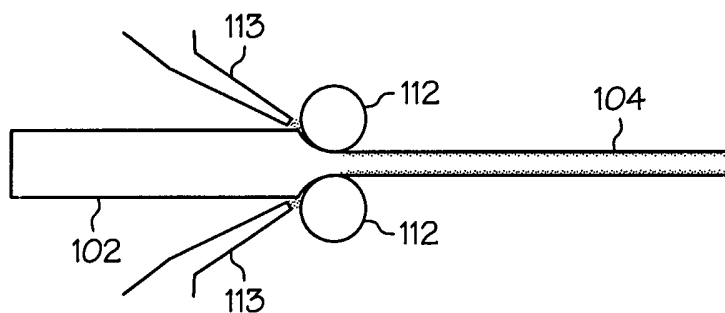


FIG. 5

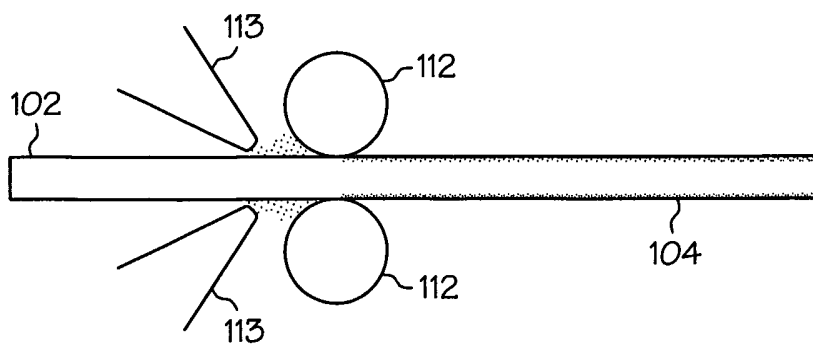


FIG. 6

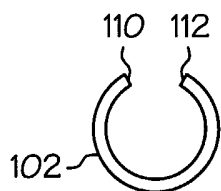


FIG. 7

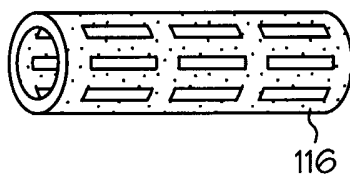


FIG. 8

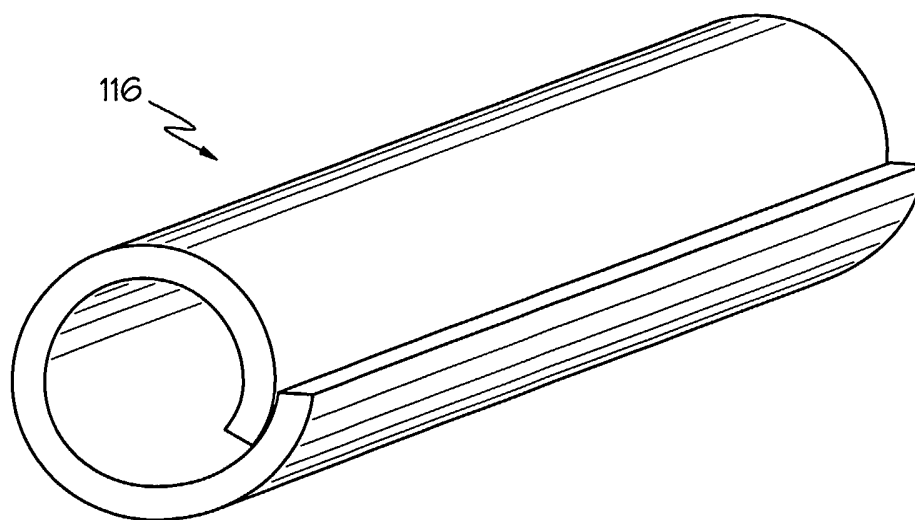


FIG. 9

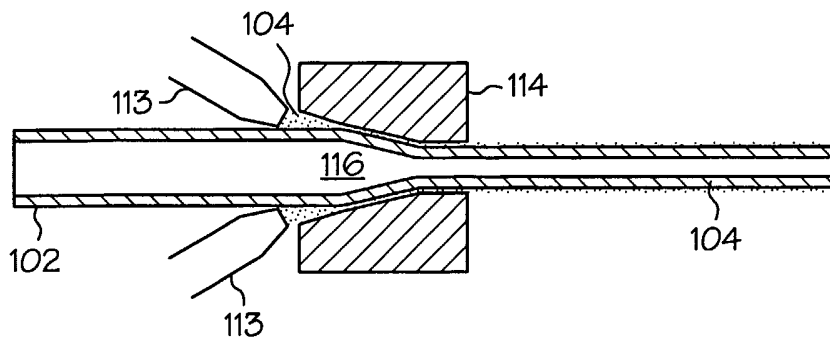


FIG. 10

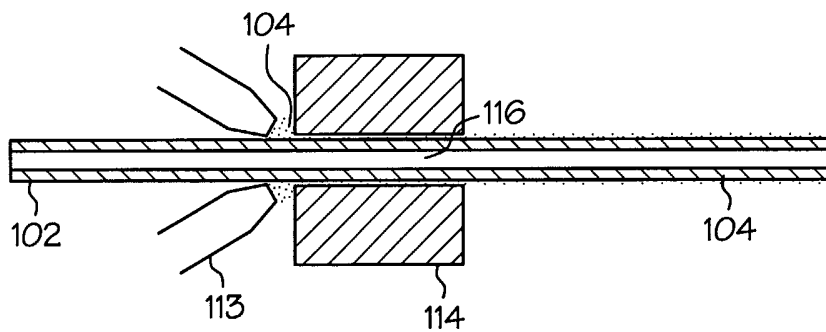


FIG. 11

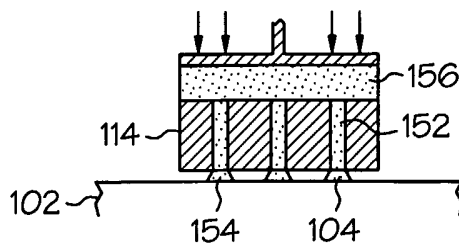


FIG. 12

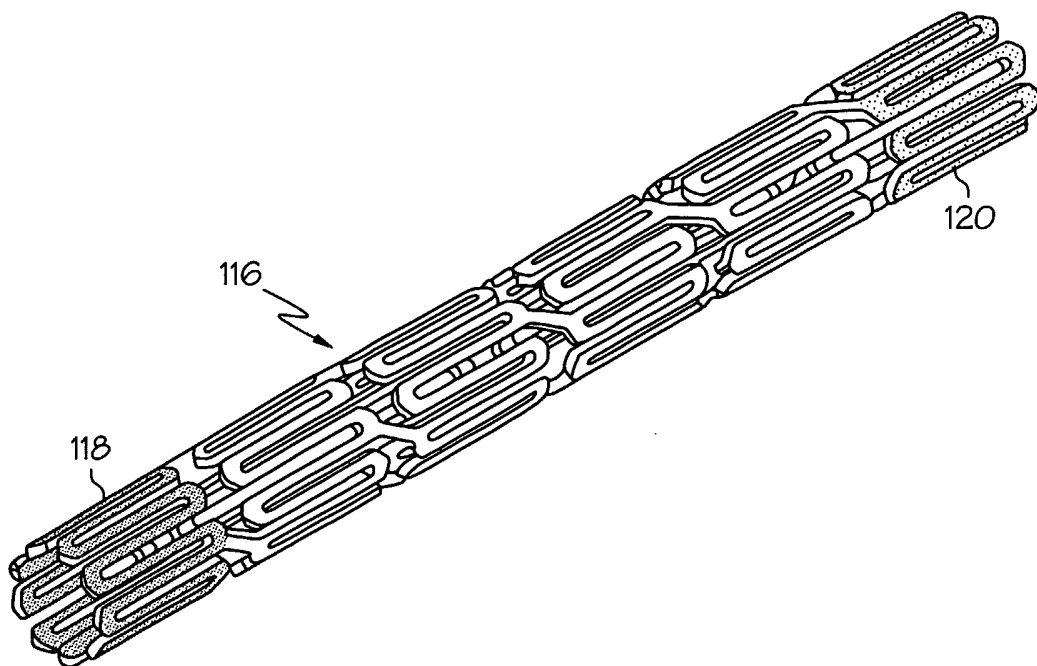


FIG. 13

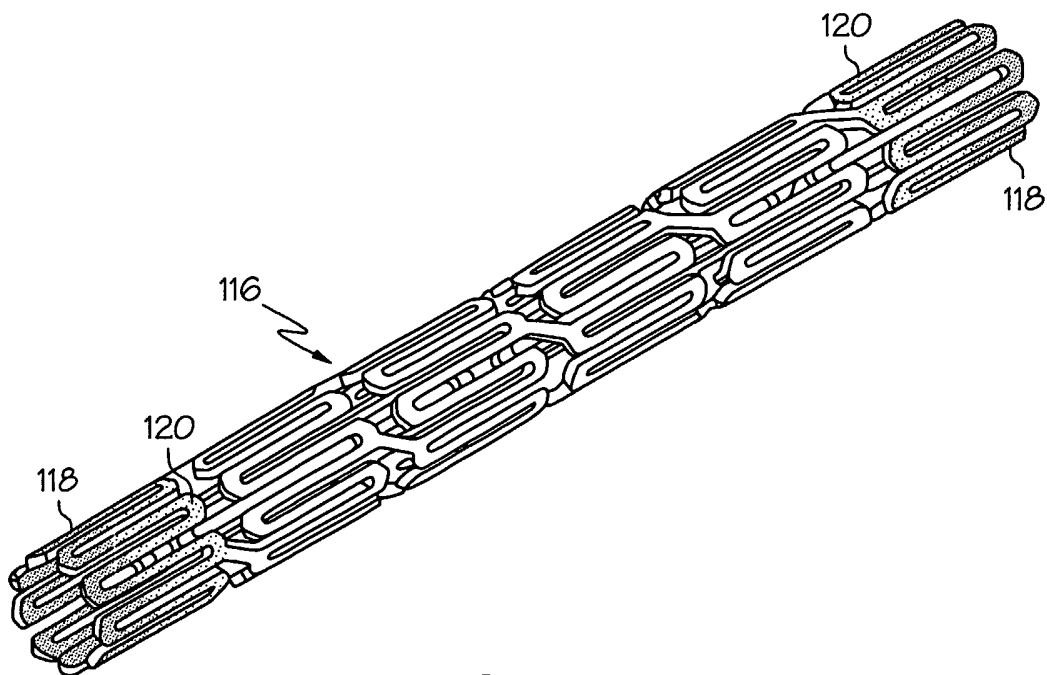


FIG. 14

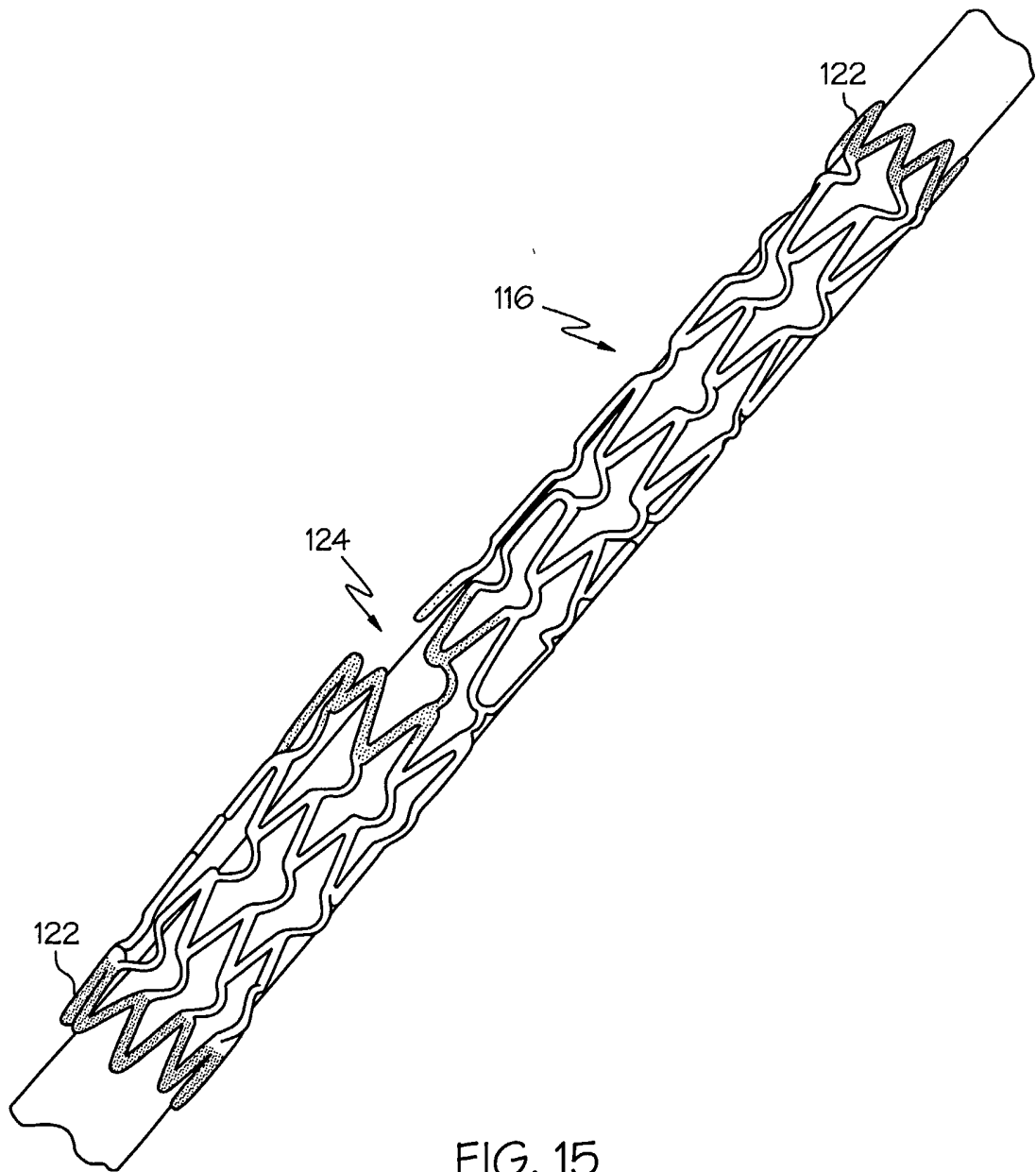


FIG. 15

INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 02/22916

A. CLASSIFICATION OF SUBJECT MATTER
 IPC 7 A61F2/06 A61B19/00

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 7 A61F A61B

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

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

EPO-Internal, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X Y A	<p>WO 00 54704 A (ADVANCED CARDIOVASCULAR SYSTEM) 21 September 2000 (2000-09-21)</p> <p>page 3, line 6 - line 29 page 8, line 1 -page 10, line 3 --- -/--</p>	<p>1,7,9, 10, 13-17, 19,21, 22,24, 34,49-51 36 2,8,11, 18,20, 25-32, 35,37, 38,41-43</p>



Further documents are listed in the continuation of box C.



Patent family members are listed in annex.

° Special categories of cited documents :

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document 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

14 October 2002

Date of mailing of the international search report

22/10/2002

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
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Authorized officer

Amaro, H

INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 02/22916

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X Y A	US 5 725 572 A (FRANTZEN JOHN J ET AL) 10 March 1998 (1998-03-10) column 4, line 1 -column 5, line 10 figures 1A-2B,5 ---	43, 44, 46, 47 36 45
P, X	WO 02 26162 A (ADVANCED CARDIOVASCULAR SYSTEM) 4 April 2002 (2002-04-04) page 3, line 10 - line 25 page 6, line 10 - line 19 page 7, line 4 - line 15 page 8, line 4 - line 8 page 9, line 8 - line 10 page 10, paragraph 2 page 12, line 6 - line 10 page 13, line 8 - line 11 page 14, paragraph 4 figures 1A-6C ---	1, 7, 8, 14, 16, 17, 19, 20, 25, 31, 32, 34, 36, 37, 39-44, 46, 47, 49-51
P, X	US 6 340 368 B1 (VERBECK MARCEL A E) 22 January 2002 (2002-01-22) column 3, line 1 - line 38 column 5, line 39 - line 58 figure 1 -----	43-46, 48

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claims: 1-42,49-51

Implantable medical device and method for preparing it.

2. Claims: 43-48

An implantable medical device comprising a plurality of radiopaque regions.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 02/22916

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

3. Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- The additional search fees were accompanied by the applicant's protest.
- No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCI/US 02/22916

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
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			WO 0226162 A2	04-04-2002

US 6340368	B1	22-01-2002	NONE	
