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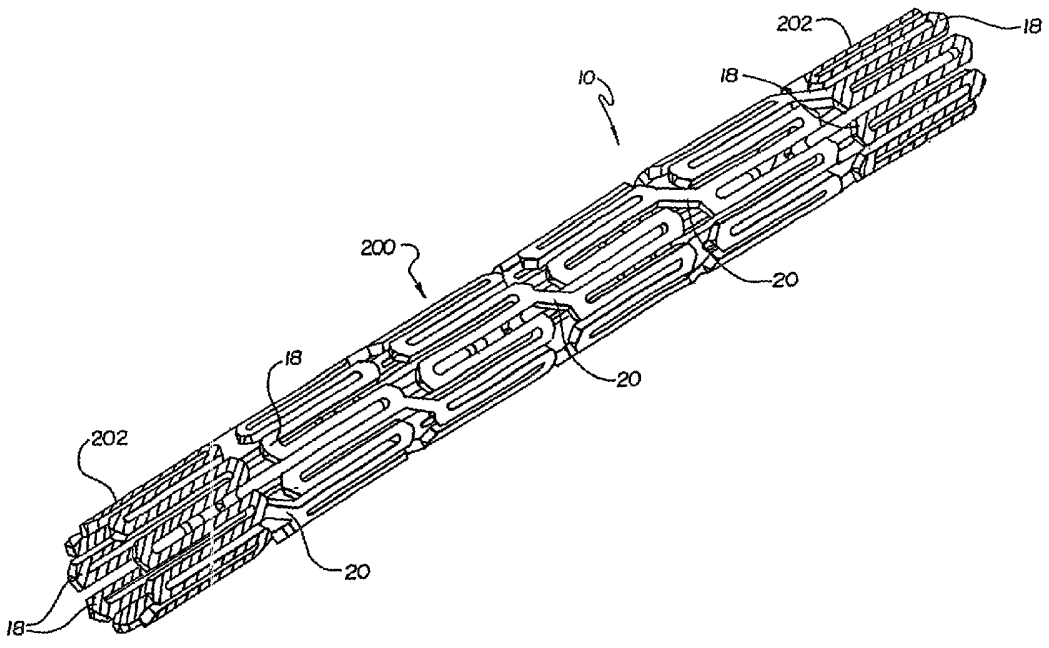
(54) Title: CUSTOMIZED MATERIAL FOR IMPROVED RADIOPACITY



(57) Abstract: A method for obtaining diagnostic information about a region of a living being, the region having a medical device with a radiopaque portion disposed therein. An X-ray beam having a first energy level in excess of the K-absorption edge of the radiopaque portion of the medical device is directed at the region to obtain a first image information and radiographically locate the medical device within the living being and an X-ray beam having second energy level at or below the K-absorption edge is applied to the region to obtain a second image information.

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CUSTOMIZED MATERIAL FOR IMPROVED RADIOPACITY

Background of the Invention

Stents are placed or implanted within a blood vessel for treating stenoses, strictures or aneurysms therein. They are implanted to reinforce collapsing, partially occluded, weakened, or dilated sections of a blood vessel. They have also been implanted in other bodily vessels including arteries, veins, biliary ducts, urethras, fallopian tubes, bronchial tubes, the trachea and the esophagus.

Stents are typically either self-expanding or mechanically expandable via the application of radially outward force from within the stent, as by inflation of a balloon. Hybrid stents, e.g., stents which are both self-expanding and mechanically expandable are also known.

Stents may be produced from a wide variety of materials. Typically, radiopaque materials are incorporated into stents to facilitate visualizing them as they are delivered to desired bodily locations. The radiopaque material may be provided in the form of a coating, in the form of one or more marker bands which are attached to the stent or may be incorporated into the basic structure of the stent as by blending a radiopaque metal with a structural metal. The entirety of the stent may be radiopaque or only desired portions of the stent may be radiopaque, for example, the proximal and distal ends of the stent. In the case of a bifurcated stent, it may be desirable for the region of sidebranch access to be radiopaque.

While rendering regions of a stent radiopaque facilitates imaging the stent during delivery, the radiopacity of the stent may hinder visualizing the contents of the stent subsequent to expansion of the stent. Visualizing flow of a bodily fluid through a stent may be necessary in cases where restenosis has occurred subsequent to implantation of the stent.

The darkness of the radiopaque region of the stent obscures the contents of the stent from the fluoroscopic image.

There remains a need to provide novel methods of imaging stents which allow for viewing the stent under fluoroscopy but which also allow for visualizing the contents of the stent.

All U.S. patents, 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, a brief summary of the claimed embodiments of the invention is set forth below. Additional details of the summarized embodiments of the invention and/or additional embodiments of the invention may be found in the Detailed Description of the Invention below.

A brief abstract of one or more embodiments of the invention is provided as well for the purposes of complying with 37 C.F.R. 1.72.

Summary of the Invention

In one embodiment, the invention is directed to a method of obtaining diagnostic information about a region of a living being, the region having a medical device including a radiopaque portion disposed therein. The radiopaque portion of the medical device is characterized by a K-absorption edge. In accordance with the method, an X-ray beam having a first energy level in excess of the K-absorption edge of the radiopaque portion of the medical device is applied to the region to obtain a first image information and radiographically locate the medical device within the living being. An X-ray beam having a second energy level at or below the K-absorption edge is applied to the region to obtain a second image information. Desirably, the step involving radiographically locating the

medical device precedes the step of obtaining the second image information using an X-ray beam having a second energy level at or below the K-absorption edge.

In another embodiment, the invention is directed to a method of implanting a medical device which is expandable in a living body and monitoring flow through the medical device. The method comprises the steps of delivering the medical device on a catheter to a desired location in a living body, locating the medical device by imaging the medical device with an X-ray beam having a first energy level in excess of the K-absorption edge of the radiopaque portion of the medical device, manipulating the catheter to expand the expandable medical device and visualizing flow of a bodily fluid comprising a contrast agent through the medical device by imaging the medical device with an X-ray beam having a second energy level at or below the K-absorption edge of the medical device.

In yet another embodiment of the invention, the invention is directed to a method for radiographic imaging of a region of a body having a medical device with a radiopaque portion therein where the radiopaque portion has a K-absorption edge. The method comprises the steps of:

a) generating a plurality of X-ray beams with predetermined different energy spectra, at least one of the plurality of X-ray beams having a mean energy in excess of the K-absorption edge, at least one of the plurality of X-ray beams having a mean energy no greater than the K-absorption edge,

b) illuminating the region with each of the plurality of beams; and

c) acquiring a radiographic image of the region during illumination by each of the plurality of beams.

In yet another embodiment, the invention is directed to a stent having a flowpath

therethrough. At least a portion of the stent comprises an amount of a radiopaque material which is characterized by an attenuation curve having a K-absorption edge. The amount of radiopaque material is chosen such that when an X-ray beam having a mean energy in excess of the K-absorption edge energy is directed at the stent and a radiographic image acquired, the radiopaque material is visible in the image and radiographically obscures any fluid in the flowpath of the stent, and when an X-ray beam having a mean energy slightly below the K-absorption edge energy is directed at the stent, the radiopaque material is substantially transparent.

The invention is also directed to a method of designing a stent comprising the steps of selecting a stent structure, selecting a radiopaque material which is characterized by an attenuation curve having a K-absorption edge, selecting at least one portion of the stent structure which will be provided with the radiopaque material and calculating an amount of the radiopaque material which must be provided in the selected portion of the stent structure such that the selected portion of the stent structure will be radiographically visible when an X-ray beam having a mean energy in excess of the K-absorption edge energy is directed at the stent and such that the selected portion of the stent structure will be substantially radiographically transparent when an X-ray beam having a mean energy slightly below the K-absorption edge energy is directed at the stent.

The invention is further directed to a method of manufacturing a stent comprising the steps of selecting a stent structure, selecting a radiopaque material which is characterized by an attenuation curve having a K-absorption edge, selecting at least one portion of the stent structure which will be provided with the radiopaque material, calculating an amount of the radiopaque material which must be provided in the selected portion of the stent structure

such that the selected portion of the stent structure will be radiographically visible when an X-ray beam having a mean energy in excess of the K-absorption edge energy is directed at the stent and such that the selected portion of the stent structure will be substantially radiographically transparent when an X-ray beam having a mean energy slightly below the K-absorption edge energy is directed at the stent, and constructing a stent having the selected stent structure and comprising the selected radiopaque material in the selected portion of the stent, the radiopaque material present in the calculated amount.

The invention is also directed to a method of monitoring a treatment of a selected bodily region. The method comprises the steps of delivering a therapeutic agent to a desired bodily region, the therapeutic agent comprising a radiopaque material characterized by a K-absorption edge, generating a plurality of X-ray beams with predetermined different energy spectra, at least one of the plurality of X-ray beams having a mean energy in excess of the K-absorption edge, at least one of the plurality of X-ray beams having a mean energy no greater than the K-absorption edge, illuminating the region with each of said plurality of beams and, acquiring a radiographic image of the region during illumination by each of said plurality of beams.

The invention is also directed to stents and other medical devices made in accordance with the inventive methods disclosed herein.

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

Brief Description of the Drawings

Figure 1 is a graphical illustration of the attenuation of x-rays through various materials as a function of the energy of the x-rays. The attenuation coefficient is plotted on a logarithmic scale;

Figure 2 is a side-elevational view of a stent having a radiopaque proximal end and a radiopaque distal end;

Figure 3 is a side-elevational view of a stent having a radiopaque proximal end, a radiopaque distal end and a radiopaque region in a region of sidebranch access;

Figure 4 is a schematic showing an X-ray image of a stent in a vessel when an X-ray beam having a mean energy in excess of the K-absorption edge energy of the radiopaque material is directed at the stent; and

Figure 5 is a schematic showing an X-ray image of a stent in a vessel when an X-ray beam having a mean energy in slightly less than the K-absorption edge energy of the radiopaque material is directed at the stent.

Detailed Description of the Invention

While this invention may be embodied in many different forms, there are described in detail herein specific preferred embodiments of the invention. This description 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, like reference numerals in the figures shall refer to like features unless otherwise indicated.

Fluoroscopy is used for a variety of purposes including monitoring and aiding in the delivery and positioning of medical devices such as stents in desired bodily regions. To that end, medical devices in general and stents in particular are often provided with one or more radiopaque regions. Radiopaque regions of the medical device will absorb more energy than non-radiopaque regions of the medical device and hence, will appear as dark areas in a fluoroscopic image. Each material is characterized by its own attenuation curve.

Attenuation curves of a number of different materials are shown in Figure 1.

A number of different materials are typically used to provide a medical device with radiopacity. One such material is gold. As shown in Figure 1, gold as illustrated by curve 100 has a higher attenuation coefficient than stainless steel, as shown in curve 105 and various tissues and hence will appear darker than stainless steel and various tissues in a radiographic image.

Certain materials that exhibit radiopacity are characterized by a discontinuity. As shown in attenuation curve 100 in Figure 1, gold has a discontinuity 102 in its attenuation coefficient as a function of the incident energy of the photons directed at the gold. This discontinuity is referred to as a K-absorption edge. At the K-absorption edge, there is a precipitous change in the attenuation of radiation directed at the metal.

It has been found that this discontinuity may be exploited in a variety of imaging methods. This discontinuity has also been found useful in the design and manufacture of medical devices including stents.

In one embodiment, the invention is directed to a method of obtaining diagnostic information about a region of a living being, the region having a medical device including a radiopaque portion disposed therein. The radiopaque portion of the medical device is characterized by a K-absorption edge. In accordance with the method, an X-ray beam having a first energy level in excess of the K-absorption edge of the radiopaque portion of the medical device is applied to the region to obtain a first image information and radiographically locate the medical device within the living being. An X-ray beam having a second energy level at or below the K-absorption edge is applied to the region to obtain a second image information. Desirably, the step involving radiographically locating the

medical device can precede the step of obtaining the second image information using an X-ray beam having a second energy level at or below the K-absorption edge.

Desirably, the medical device is a stent. An example of a stent is shown at 200 in Figure 2. Stent 200 may be self-expanding or balloon expandable. The entirety of the stent may be radiopaque or only certain portions of the stent may be radiopaque. For example, as shown in Figure 2, one or both ends 202 of stent 200 are radiopaque, as indicated by the darkened regions of the stent. Another example of a stent is shown at 200 in Figure 3. In addition to having optional radiopaque regions 202 at the proximal and distal ends of the stent, stent 200 of Figure 3 has a region 204 of sidebranch access which is radiopaque. Adjacent regions can be non-radiopaque. Other suitable medical devices for use in the inventive methods include embolic agents and aneurysm fillers including liquid, gel, spherical and metallic coils, components of catheter tips, vena cava filters, and polymeric medical devices containing radiopaque elements with k-absorption shifts. An example of a vena cava filter is disclosed in U.S. Patent No. 6,126,673. Embolic agents are disclosed in U.S. Patent No. 5,637,086.

Any suitable, biocompatible radiopaque material may be used in the radiopaque portion of the medical device. Suitable radiopaque materials include but are not limited to one or more metals selected from the group consisting of gold, platinum and tantalum. The radiopaque material may also be an alloy comprising at least 10% tungsten by weight. An example of the latter is L-605. Other suitable materials for the radiopaque portion of the medical device or for the entirety or selected portions of the medical device include one or more inventive materials for stents such as titanium-tantalum alloys, tantalum-niobium alloys, and stainless steel alloys comprising at least one of platinum, gold, tantalum, and

rhenium. Desirably, one or more of these materials are present in at least one of the first and second ends of the medical device.

The method may prove to be of particular value in obtaining information about the flow of a bodily fluid through a stent where the stent is located in a bodily vessel, the vessel having restenosed in the region of interest.

Desirably, in the practice of the inventive methods, the first and second energy levels are chosen such that the attenuation of the X-ray beam having the first energy level by the radiopaque portion is at least three times greater than the attenuation of the X-ray beam having the second energy level by the radiopaque portion.

As a non-limiting example of one of the inventive methods disclosed herein, a medical device such as a stent is delivered via catheter to a desired bodily location. The stent includes at least one radiopaque portion provided by a metal such as gold. Energy in excess of the K-absorption edge of the radiopaque portion of the stent is applied to the desired bodily location to obtain a first image information and radiographically locate the stent within the living being. An X-ray beam having a second energy level at or below the K-absorption edge of the metal is applied to the desired bodily location to obtain a second image information. The second energy level is chosen so that the radiopaque material does not obscure the contents of the stent. Thus, where the stent is implanted within a blood vessel and a contrast agent is included in the blood, the flow of blood through the radiopaque regions of the stent may be visualized, notwithstanding the presence of the radiopaque material, as a result of operating at an energy slightly below the K-absorption edge of the radiopaque metal. Desirably, energy at approximately 5 keV below the absorption edge is used.

In another embodiment, the invention is directed to a method of implanting a medical device which is expandable in a living body and monitoring flow through the medical device. The medical device may be any of those disclosed herein or any other suitable medical device. The method comprises the steps of delivering the medical device on a catheter to a desired location in a living body, locating the medical device by imaging the medical device with an X-ray beam having a first energy level in excess of the K-absorption edge of the radiopaque portion of the medical device, manipulating the catheter to expand the expandable medical device and visualizing flow of a bodily fluid comprising a contrast agent through the medical device by imaging the medical device with an X-ray beam having a second energy level at or below the K-absorption edge of the medical device.

Where the medical device is a balloon expandable stent, the manipulating step includes expanding a medical balloon disposed within the catheter to expand the stent. Where the stent is self-expandable, the manipulating step includes removing a restraining device, for example a sheath, from about the stent so that the stent is free to self-expand. It is noted that the term "stent" as used herein is intended to include within its scope stents, grafts and stent-grafts. Other suitable medical devices include, but are not limited to vena cava filters, embolic agents and aneurysm fillers including liquid, gel, spherical and metallic coils, components of catheter tips, and polymeric medical devices containing radiopaque elements with k-absorption shifts.

In yet another embodiment of the invention, the invention is directed to a method for radiographic imaging of a region of a body having a medical device with a radiopaque portion therein where the radiopaque portion has a K-absorption edge. The method comprises the steps of:

a) generating a plurality of X-ray beams with predetermined different energy spectra, at least one of the plurality of X-ray beams having a mean energy in excess of the K-absorption edge, at least one of the plurality of X-ray beams having a mean energy no greater than the K-absorption edge,

b) illuminating the region with each of said plurality of beams; and

c) acquiring a radiographic image of the region during illumination by each of said plurality of beams.

Desirably, the image acquired during the illumination step with the X-ray beam having a mean energy in excess of the K-absorption edge is used to locate the medical device, for example, a stent, and the image acquired during the illumination step with the X-ray beam having a mean energy at or below the K-absorption edge is used to visualize flow of a bodily fluid through the medical device.

The medical device may be any of the devices disclosed herein. Suitably, the medical device will be a stent.

The method may prove to be of particular value where the stent is in a bodily vessel and the vessel has restenosed in a region of the bodily vessel containing the stent.

In yet another embodiment, the invention is directed to a stent having a flowpath therethrough, such as that shown at 200 in Figure 2. At least a portion of stent 200 comprises an amount of a radiopaque material which is characterized by an attenuation curve having a K-absorption edge. As shown by way of example in Figure 2, both ends 202 of the stent comprise a radiopaque material. The radiopaque material may be any of those disclosed herein or any other suitable radiopaque material. The amount of radiopaque material is chosen such that when an X-ray beam having a mean energy in excess of the K-absorption

edge energy of the radiopaque material is directed at the stent and a radiographic image acquired, the radiopaque material is visible in the image and radiographically obscures any fluid in the flowpath of the stent. When an X-ray beam having a mean energy slightly below the K-absorption edge energy is directed at the stent, the radiopaque material is substantially transparent. Thus, the flow of a bodily fluid comprising a contrast agent such as iodinated nonionic contrast, ionic contrast or barium-based contrast may be visualized. In Figure 4, a schematic is provided showing an X-ray image of stent 200 in vessel 302 when an X-ray beam having a mean energy in excess of the K-absorption edge energy of the radiopaque material is directed at the stent. Stent 200 appears dark in the image. Figure 5 shows an X-ray image of the same stent 200 when an X-ray beam having a mean energy slightly below the K-absorption edge energy of the radiopaque material is directed at the stent. The surrounding blood which has a contrast agent is more readily visible in Figure 5.

The invention is also directed to a method of designing a stent comprising the steps of selecting a stent structure, selecting a radiopaque material which is characterized by an attenuation curve having a K-absorption edge, selecting at least one portion of the stent structure which is to be provided with the radiopaque material and calculating an amount of the radiopaque material which must be provided in the selected portion of the stent structure such that the selected portion of the stent structure will be radiographically visible when an X-ray beam having a mean energy excess of the K-absorption edge energy is directed at the stent and such that the selected portion of the stent structure will be substantially radiographically transparent when an X-ray beam having a mean energy slightly below the K-absorption edge energy is directed at the stent.

The invention is further directed to a method of manufacturing a stent comprising the

steps of selecting a stent structure, selecting a radiopaque material which is characterized by an attenuation curve having a K-absorption edge, selecting at least one portion of the stent structure which will be provided with the radiopaque material, calculating an amount of the radiopaque material which must be provided in the selected portion of the stent structure such that the selected portion of the stent structure will be radiographically visible when an X-ray beam having a mean energy excess of the K-absorption edge energy is directed at the stent and such that the selected portion of the stent structure will be substantially radiographically transparent when an X-ray beam having a mean energy slightly below the K-absorption edge energy is directed at the stent, and constructing a stent having the selected stent structure and comprising the selected radiopaque material in the selected portion of the stent, the radiopaque material present in the calculated amount.

The inventive methods disclosed herein may also be applied to designing and manufacturing other medical devices such as embolic agents and aneurysm fillers including liquid, gel, spherical and metallic coils, components of catheter tips, vena cava filters, and polymeric medical devices containing radiopaque elements with k-absorption shifts.

The invention is also directed to a method of monitoring a treatment of a selected bodily region. The method comprises the steps of delivering a therapeutic agent to a desired bodily region, the therapeutic agent comprising a radiopaque material characterized by a K-absorption edge, generating a plurality of X-ray beams with predetermined different energy spectra, at least one of the plurality of X-ray beams having a mean energy in excess of the K-absorption edge, at least one of the plurality of X-ray beams having a mean energy no greater than the K-absorption edge, illuminating the region with each of said plurality of beams and, acquiring a radiographic image of the region during illumination by each of said plurality of

beams. Desirably, the amount of the therapeutic agent present at the selected bodily region is calculated from the images. Using this technique, the location of the radiopaque treatment agent may be monitored by imaging the region with the radiopaque treatment agent at an energy slightly above the K-absorption edge and any other radiopaque substance in the region may then be imaged by reducing the energy to below that of the K-absorption edge of the radiopaque treatment agent.

Therapeutic agents having radiopaque materials include cisplatin and cisplatin derivatives, bis-platinum complexes and other platinum complexes. Examples of cisplatin derivatives are disclosed in U.S. Patent No. 6,235,782. Examples of bis-platinum complexes are disclosed in U.S. Patent No. 6,022,892.

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 described herein which equivalents are also intended to be encompassed by the claims.

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 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 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 4 may be taken as alternatively dependent on claim 3; claim 5 may be taken as alternatively dependent from claim 2; claim 6 may be taken as alternatively dependent from any of claims 2-5, etc.).

This completes the description of the preferred and alternate embodiments of the invention. Those skilled in the art may recognize other equivalents to the specific embodiment described herein which equivalents are intended to be encompassed by the claims attached hereto.

What is claimed is:

1. A method of obtaining diagnostic information about a region of a living being, the region having a medical device disposed therein, the medical device including a radiopaque portion which is characterized by a K-absorption edge, the method comprising the steps of:

a) applying to the region an X-ray beam having a first energy level in excess of the K-absorption edge of the radiopaque portion of the medical device to obtain a first image information and radiographically locate the medical device within the living being; and

b) applying to the region an X-ray beam having second energy level at or below the K-absorption edge to obtain a second image information.

2. The method claim 1, wherein the radiopaque portion comprises a radiopaque metal.

3. The method of claim 2, wherein the radiopaque metal comprises one or more metals selected from the group consisting of gold, platinum and tantalum.

4. The method of claim 2, wherein the radiopaque metal is an alloy comprising at least 10% tungsten by weight.

5. The method of claim 4, wherein the radiopaque metal is L-605.

6. The method of claim 1, wherein the medical device is a stent.

7. The method of claim 6, wherein the radiopaque portion comprises a radiopaque metal.

8. The method of claim 7, wherein step a) is performed prior to step b).

9. The method of claim 8, wherein the stent is located in a bodily vessel and the vessel is restenosed in the region.

10. The method of claim 9, wherein the second image information contains information concerning the flow of a bodily fluid through the medical device.

11. The method of claim 7, wherein step b) is performed prior to step a).

12. The method of claim 6, wherein the entirety of the stent is radiopaque.

13. The method of claim 6, where only the first and/or seconds of the stent are radiopaque.

14. The method of claim 6, wherein the stent includes an opening for side branch access, the stent including a radiopaque section disposed about the opening.

15. The method of claim 1, wherein the first and second energy levels are chosen such that the attenuation of the X-ray beam having the first energy level by the radiopaque portion is at least three times greater than the attenuation of the X-ray beam having the second energy level by the radiopaque portion

16. A method of implanting a medical device which is expandable in a living body and monitoring flow through the medical device, the method comprising the steps of:

delivering the medical device on a catheter to a desired location in a living body;

locating the medical device by imaging the medical device with an X-ray beam having a first energy level in excess of the K-absorption edge of the radiopaque portion of the medical device;

manipulating the catheter to expand the expandable medical device;

visualizing flow of a bodily fluid comprising a contrast agent through the medical device by imaging the medical device with an X-ray beam having a second energy level at or below the K-absorption edge of the medical device.

17. The method of claim 16, wherein the medical device is a stent.

18. The method of claim 16, wherein the stent is balloon expandable and the manipulating step includes expanding a medical balloon disposed within the catheter.

19. The method of claim 17, wherein the stent is self-expandable and the

manipulating step includes removing a restraining device from about the stent so that the stent is free to self-expand.

20. A method for radiographic imaging of a region of a body having a medical device with a radiopaque portion therein, the radiopaque portion having a K-absorption edge, comprising:

a) generating a plurality of X-ray beams with predetermined different energy spectra, at least one of the plurality of X-ray beams having a mean energy in excess of the K-absorption edge, at least one of the plurality of X-ray beams having a mean energy no greater than the K-absorption edge,

b) illuminating the region with each of said plurality of beams; and

c) acquiring a radiographic image of the region during illumination by each of said plurality of beams.

21. The method of claim 20, wherein the medical device is a stent.

22. The method of claim 21, wherein the image acquired during the illumination step with the X-ray beam having a mean energy in excess of the K-absorption edge is used to locate the stent; and the image acquired during the illumination step with the X-ray beam having a mean energy at or below the K-absorption edge is used to visualize flow of a bodily fluid through the stent.

23. The method of claim 22, wherein the stent is in a bodily vessel and the vessel has restenosed in a region of the bodily vessel containing the stent.

24. A stent comprising an alloy selected from the group consisting of titanium-tantalum alloys, tantalum-niobium alloys, and stainless steel alloys comprising at least one of platinum, gold, tantalum, and rhenium.

25. The stent of claim 24, wherein the stent has a first end and a second end, at least one of which comprises the titanium-tantalum alloy.

26. A stent having a flowpath therethrough, at least a portion of the stent comprising an amount of a radiopaque material, the radiopaque material characterized by an attenuation curve having a K-absorption edge, the amount of radiopaque material such that when an X-ray beam having a mean energy in excess of the K-absorption edge energy is directed at the stent and a radiographic image acquired, the radiopaque material is visible in the image and radiographically obscures any fluid in the flowpath of the stent, and when an X-ray beam having a mean energy slightly below the K-absorption edge energy is directed at the stent, the radiopaque material is substantially transparent.

27. The stent of claim 26, having a first end and a second end at least one of which comprises the radiopaque material.

28. The stent of claim 26, having an opening for side branch access, the radiopaque material disposed about the opening.

29. A method of designing a stent comprising the steps of:

selecting a stent structure;

selecting a radiopaque material which is characterized by an attenuation curve having a K-absorption edge;

selecting at least one portion of the stent structure which will be provided with the radiopaque material;

calculating an amount of the radiopaque material which must be provided in the selected portion of the stent structure such that the selected portion of the stent structure will be radiographically visible when an X-ray beam having a mean energy excess of the K-absorption edge energy is directed at the stent and such that the selected portion of the stent structure will be substantially radiographically transparent when an X-ray beam having a mean energy slightly below the K-absorption edge energy is directed at the stent.

30. A method of manufacturing a stent comprising the steps of:

selecting a stent structure;

selecting a radiopaque material which is characterized by an attenuation curve having a K-absorption edge selecting at least one portion of the stent structure which will be provided with the radiopaque material;

calculating an amount of the radiopaque material which must be provided in the

selected portion of the stent structure such that the selected portion of the stent structure will be radiographically visible when an X-ray beam having a mean energy excess of the K-absorption edge energy is directed at the stent and such that the selected portion of the stent structure will be substantially radiographically transparent when an X-ray beam having a mean energy slightly below the K-absorption edge energy is directed at the stent; and

constructing a stent having the selected stent structure and comprising the selected radiopaque material in the selected portion of the stent, the radiopaque material present in the calculated amount.

31. A method of monitoring a treatment of a selected bodily region comprising the steps of:

a) delivering a therapeutic agent to a desired bodily region, the therapeutic agent comprising a radiopaque material characterized by a K-absorption edge;

b) generating a plurality of X-ray beams with predetermined different energy spectra, at least one of the plurality of X-ray beams having a mean energy in excess of the K-absorption edge, at least one of the plurality of X-ray beams having a mean energy no greater than the K-absorption edge,

c) illuminating the region with each of said plurality of beams; and

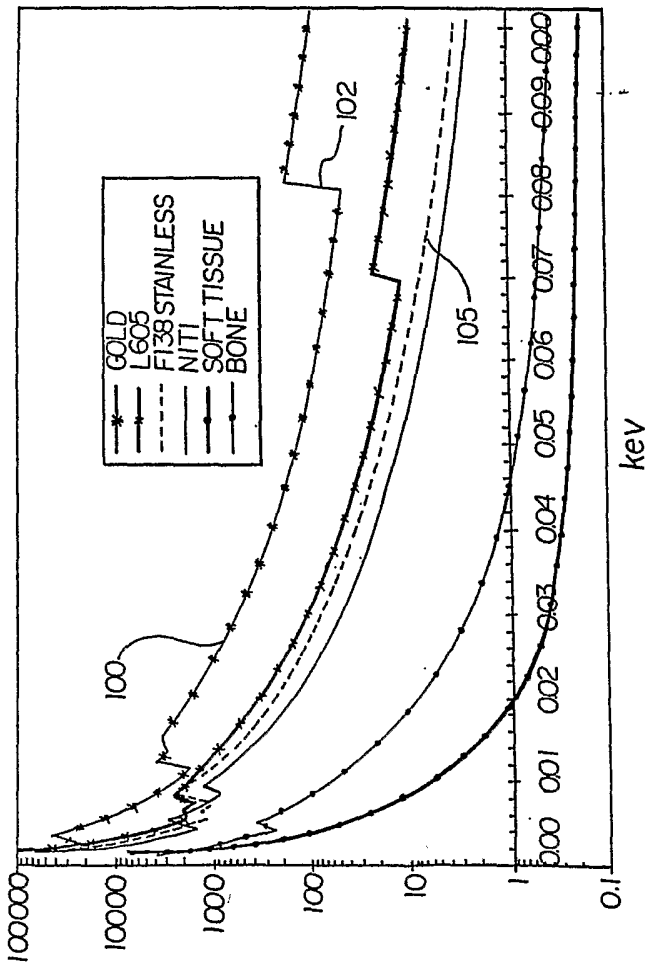
d) acquiring a radiographic image of the region during illumination by each of said plurality of beams.

32. The method of claim 31, wherein an amount of the therapeutic agent present

at the selected bodily region is calculated from the images.

33. The method of claim 31, the presence of therapeutic agent in the desired bodily region is ascertained from the image.

Fig. 1


GOLD
L605
F138 STAINLESS
NITI
SOFT TISSUE
BONE
100
102
105
100000
10000
1000
100
10
1
0.1
.000
.001
.002
.003
.004
.005
.006
.007
.008
.009
.010
kev

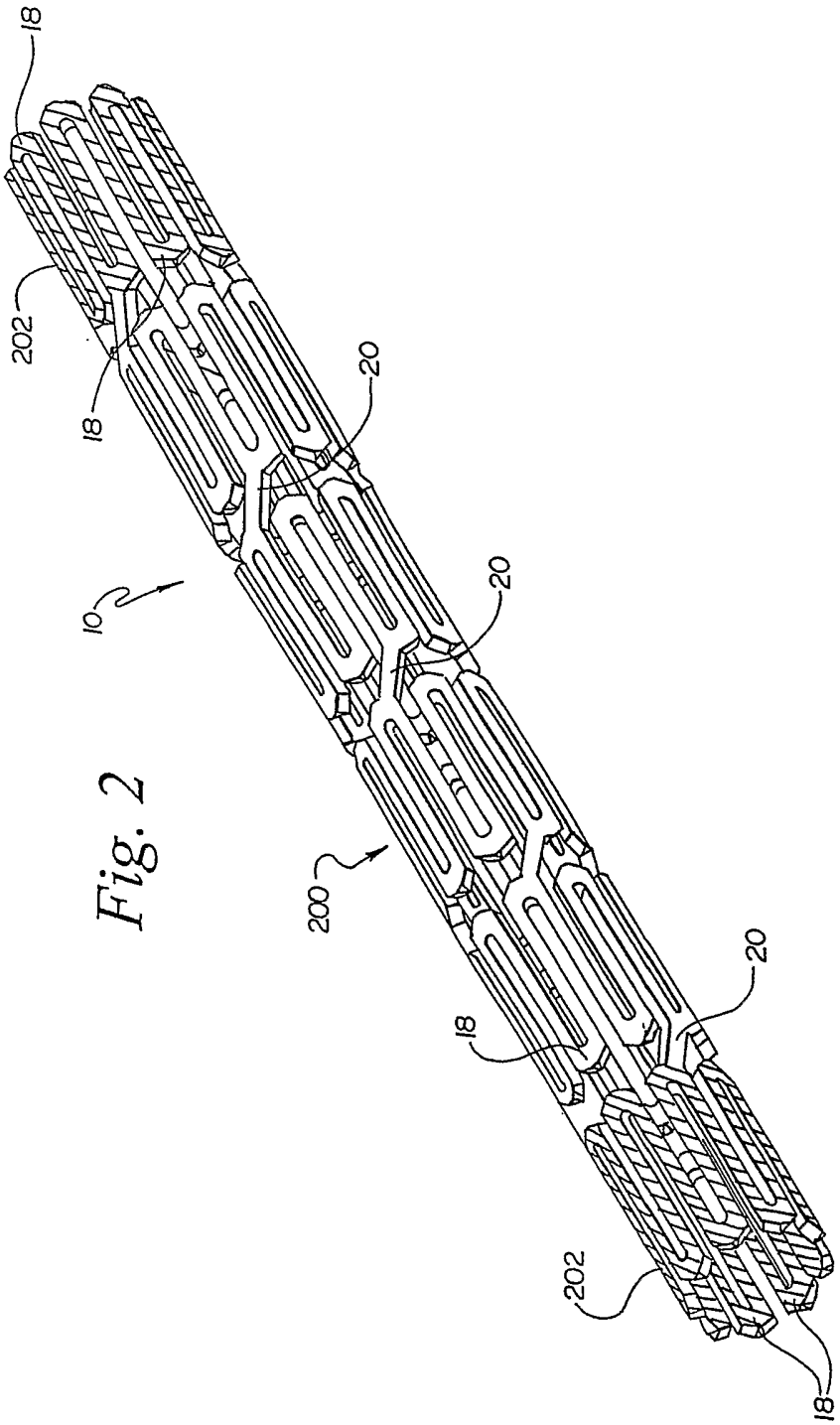


Fig. 2

Fig. 3

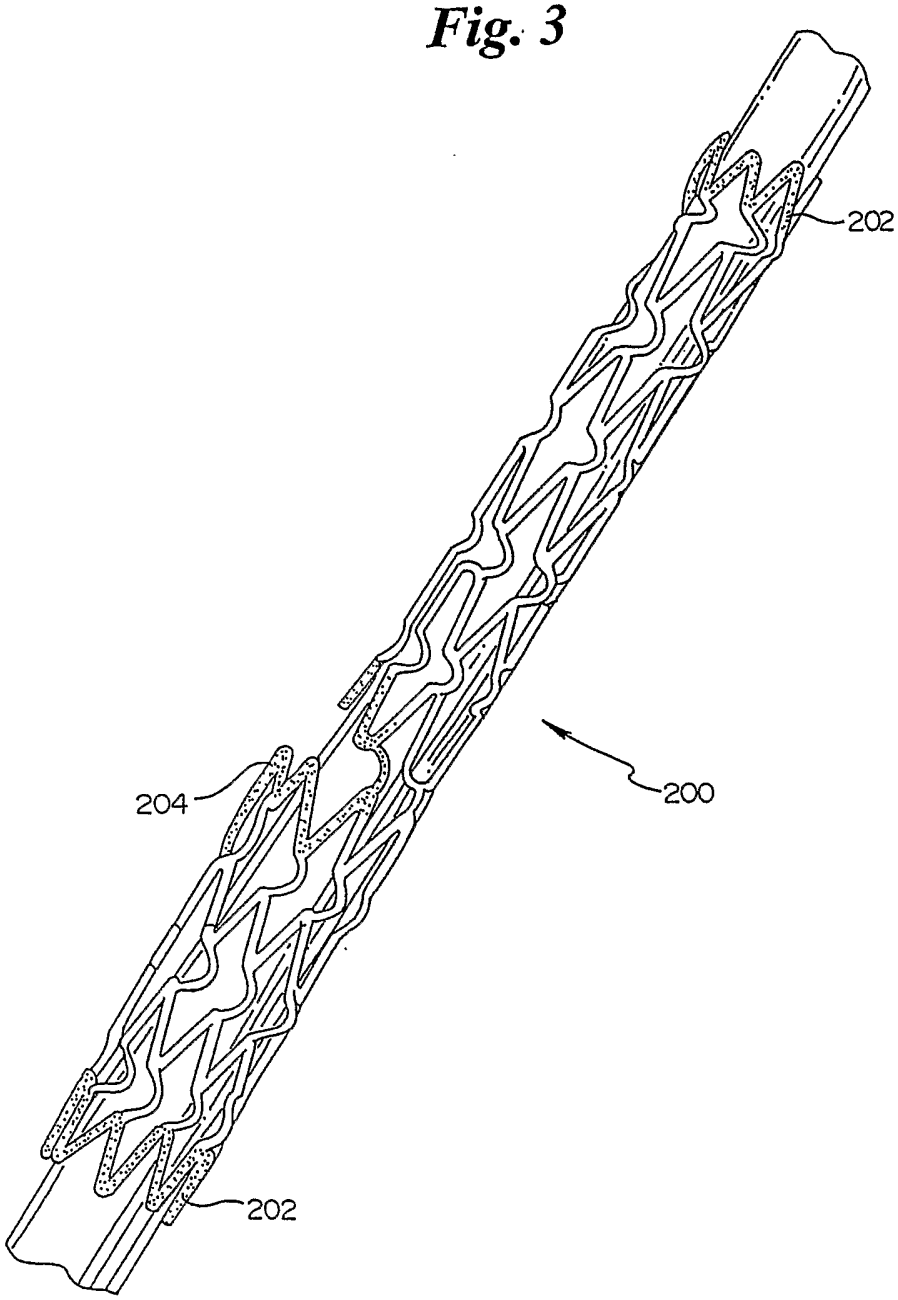


Fig. 4

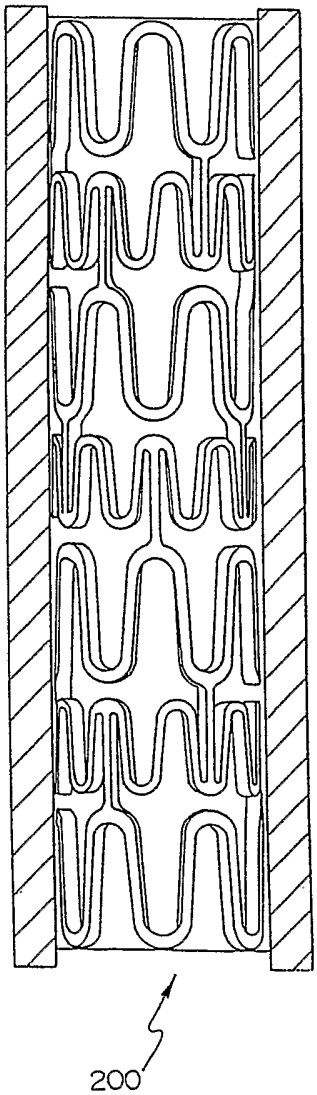
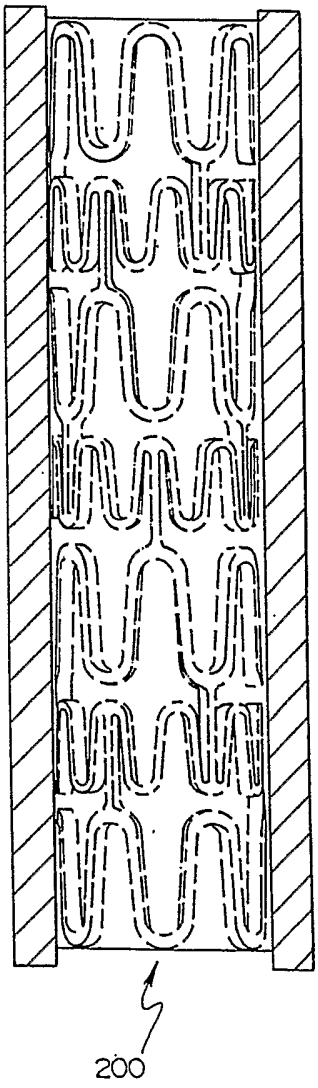


Fig. 5



INTERNATIONAL SEARCH REPORT

PCT/US 03/13421

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61B6/03 A61L31/02 A61F2/06

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 A61B A61L A61F A61N

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)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 02 05863 A (ADVANCED CARDIOVASCULAR SYSTEM) 24 January 2002 (2002-01-24) page 4, line 13 -page 5, line 8 page 7, line 17 -page 12, line 11; figure 6; tables 1,2 ---	24,25
P,X	WO 02 078764 A (SCIMED LIFE SYSTEMS INC) 10 October 2002 (2002-10-10) page 3, line 24 -page 5, line 8; figure 1B ---	24,25
A	US 2002/039401 A1 (SALB JESSE) 4 April 2002 (2002-04-04) abstract page 19, paragraph 209 -page 20, paragraph 220 -----	1,20

☐ 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	Date of mailing of the international search report
15 July 2003	23/07/2003

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk Tel. (+31–70) 340–2040, Tx. 31 651 epo nl, Fax: (+31–70) 340–3016	Artikis, T

INTERNATIONAL SEARCH REPORT

PCT/US 03/13421

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. [X] Claims Nos.: 16-19, 31-33
because they relate to subject matter not required to be searched by this Authority, namely:

Claims 16-19: Rule 39.1(iv) PCT Method for treatment of the human or animal body by surgery
Claims 31-33: Rule 39.1(iv) PCT Method for treatment of the human or animal body by surgery and therapy

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:

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

PCT/US 03/13421

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