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(54) METHODS AND APPARATUS FOR THE IDENTIFICATION AND STABILIZATION OF VULNERABLE PLAQUE

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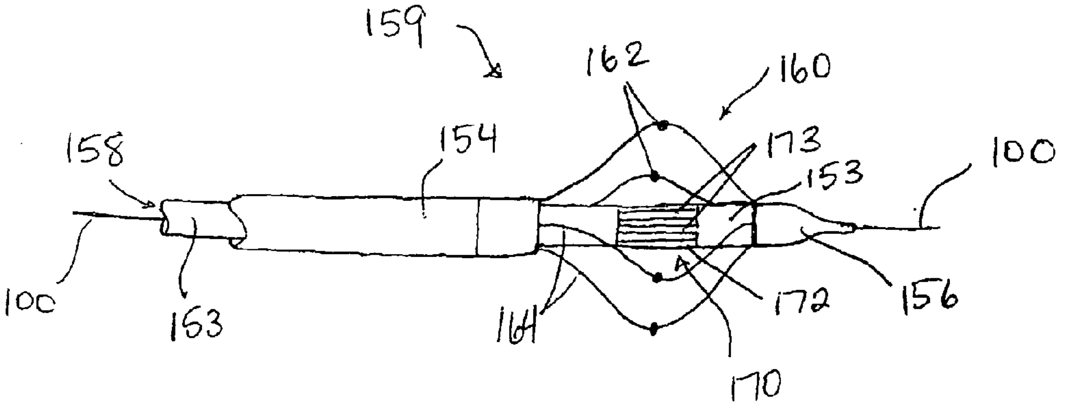
(57) ABSTRACT

The present invention provides methods and apparatus for identifying and stabilizing vulnerable plaque via multi-functional catheters having both thermography and imaging capabilities. It is expected that correlating imaging and thermography data will facilitate improved identification of vulnerable plaque. Apparatus of the present invention may also be provided with optional stabilization elements for stabilizing vulnerable plaque, as well as optional embolic protection. Methods of using apparatus of the present invention are provided.



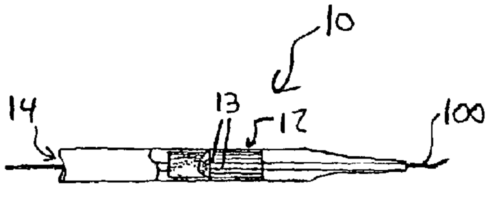


FIG. 1 (PRIOR ART)

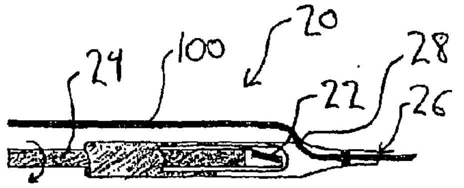


FIG. 2 (PRIOR ART)

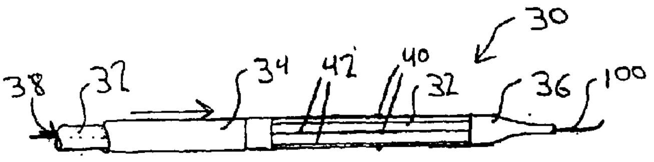


FIG. 3A (PRIOR ART)

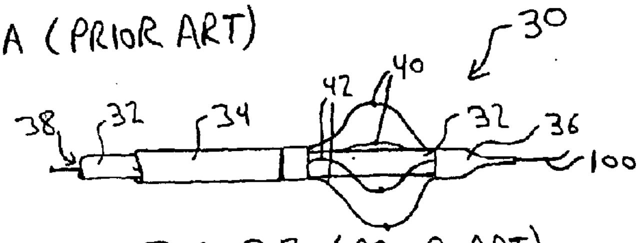


FIG. 3B (PRIOR ART)

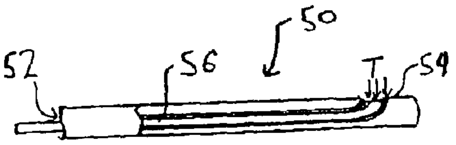


FIG. 4 (PRIOR ART)

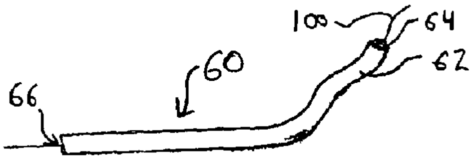


FIG. 5 (PRIOR ART)

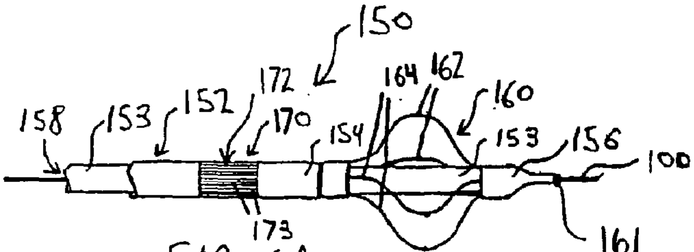


FIG. 6A

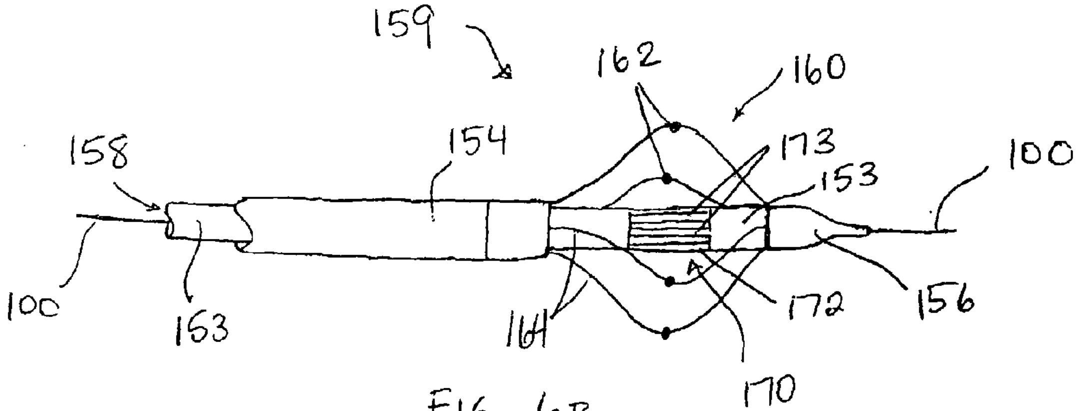


FIG. 6B

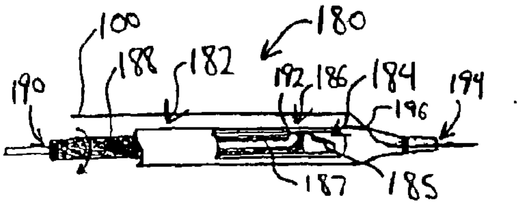


FIG. 7

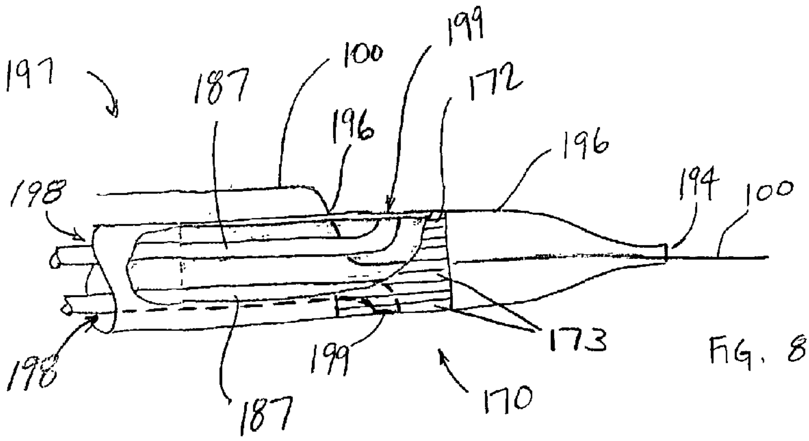


FIG. 8A

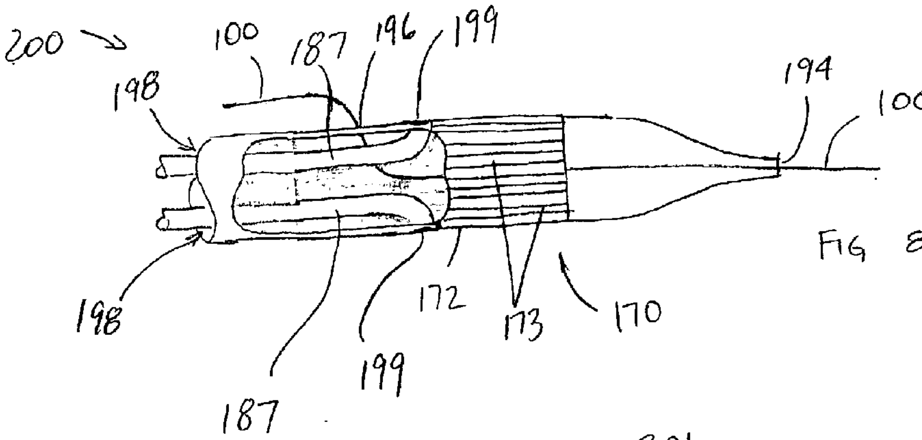


FIG 8B

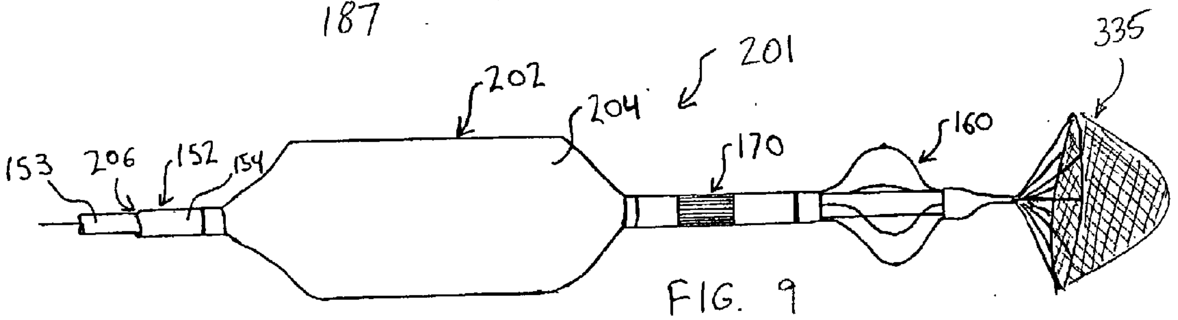


FIG. 9

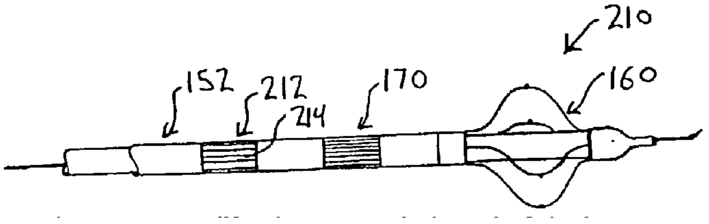


FIG. 10

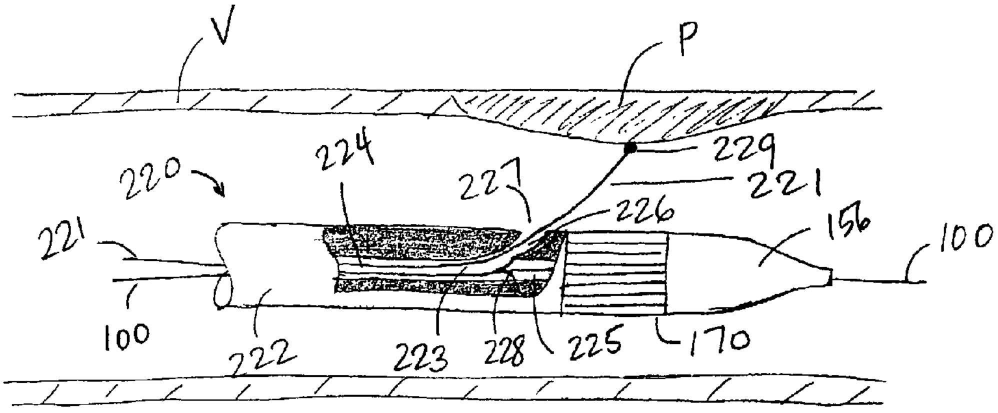
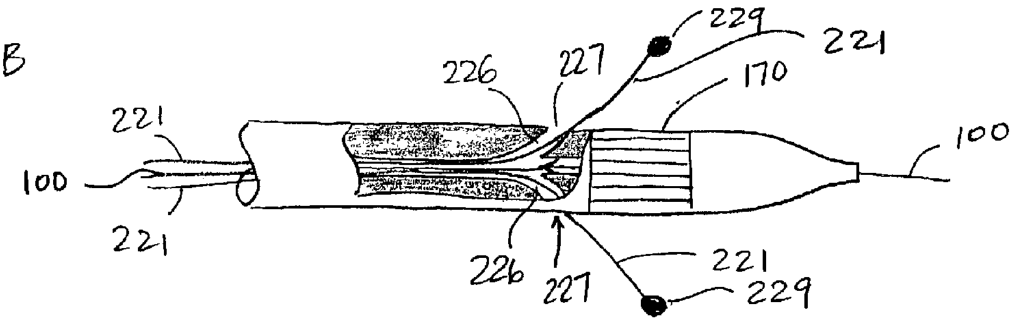


FIG. 11A

FIG. 11B



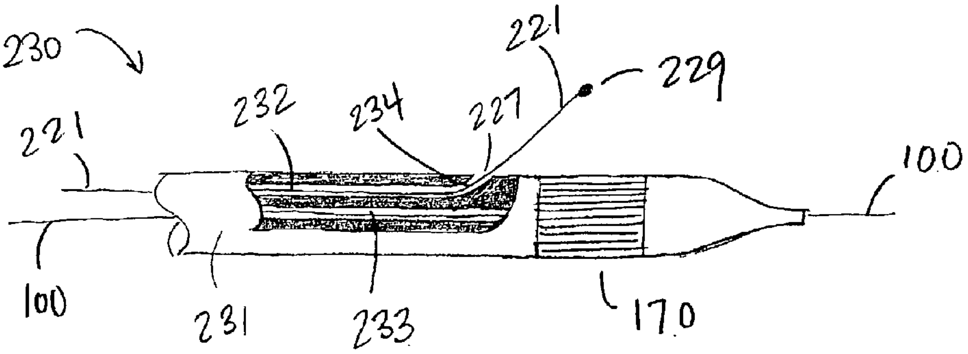


FIG. 11C

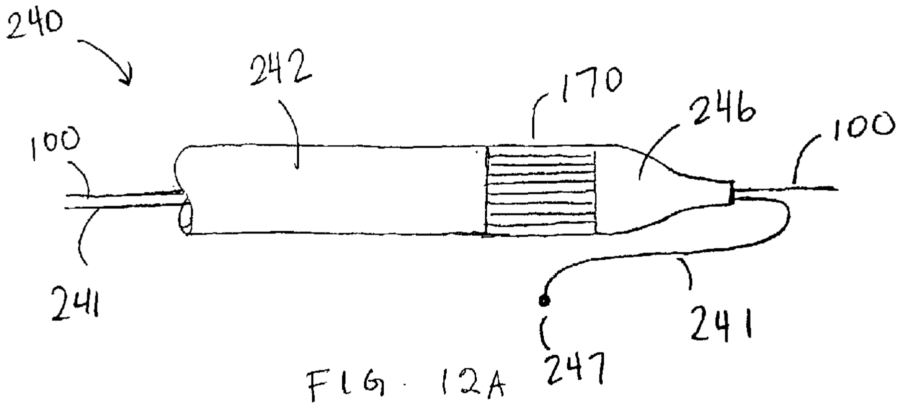


FIG. 12A

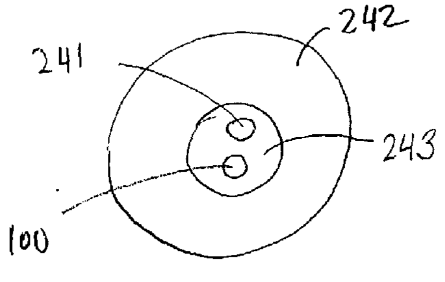


FIG. 12B

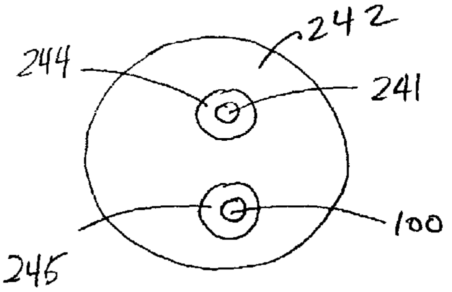


FIG. 12C

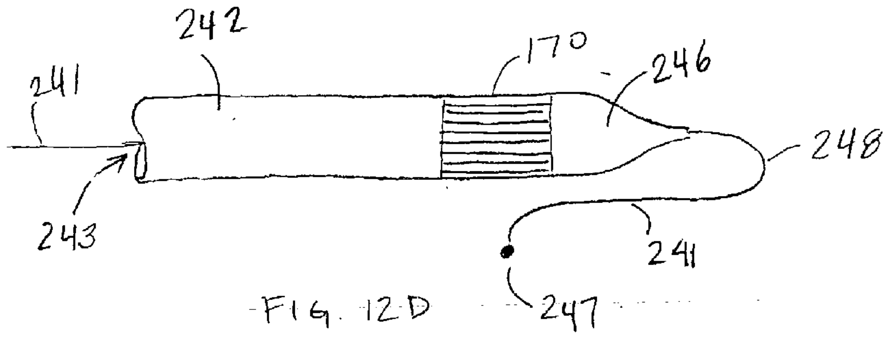


FIG. 12D

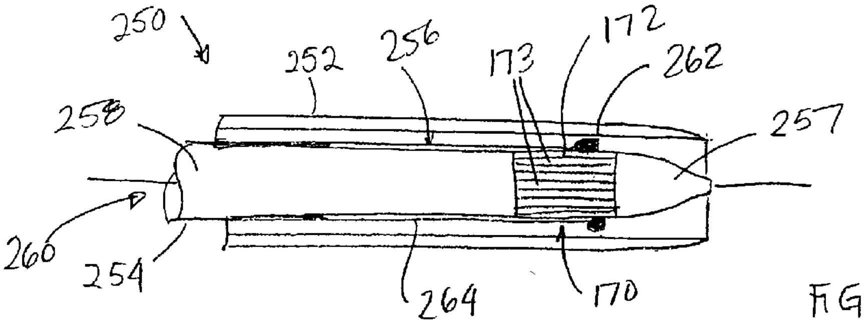


FIG. 13A

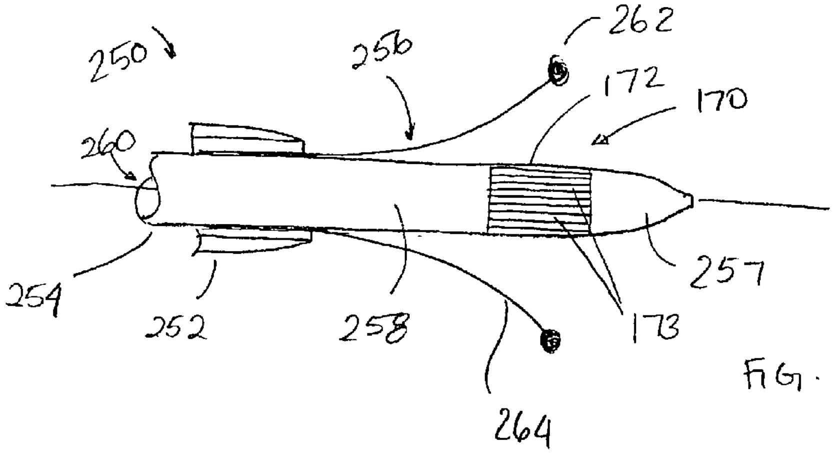


FIG. 13B

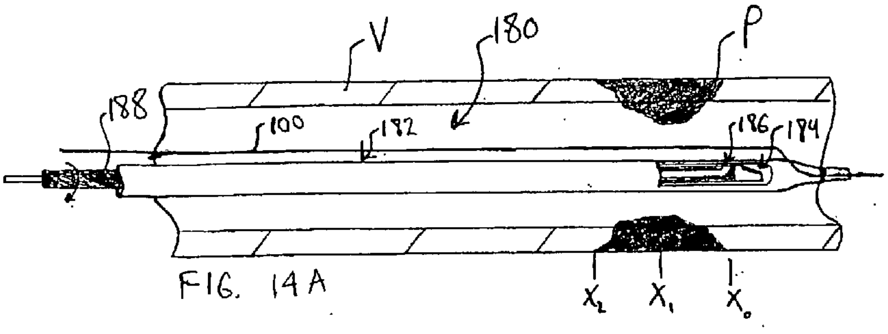


FIG. 14A

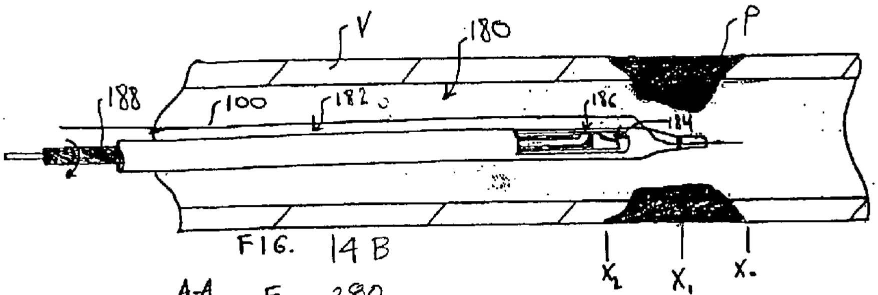


FIG. 14B

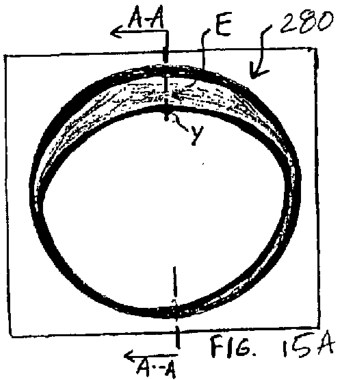


FIG. 15A

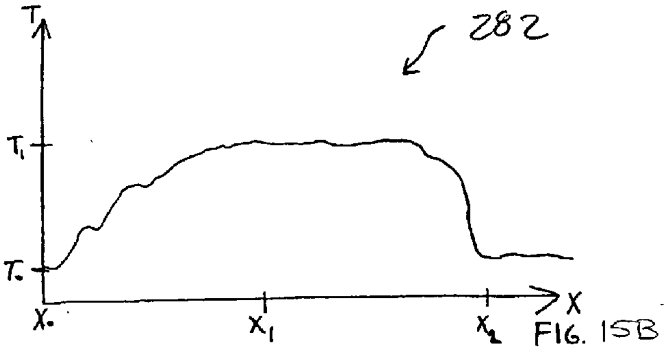


FIG. 15B

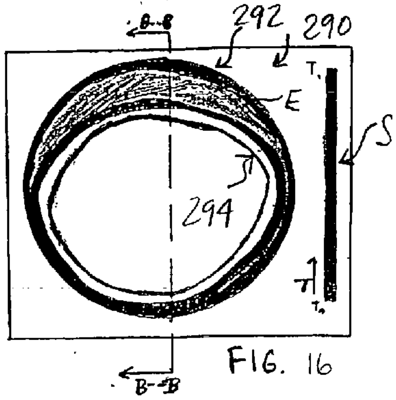


FIG. 16

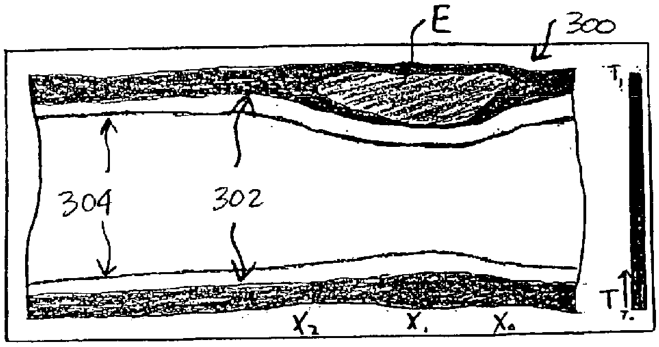


FIG. 17

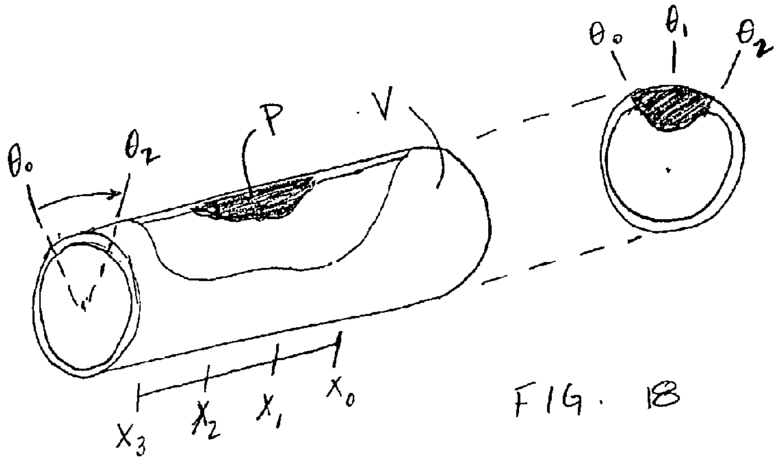


FIG. 18

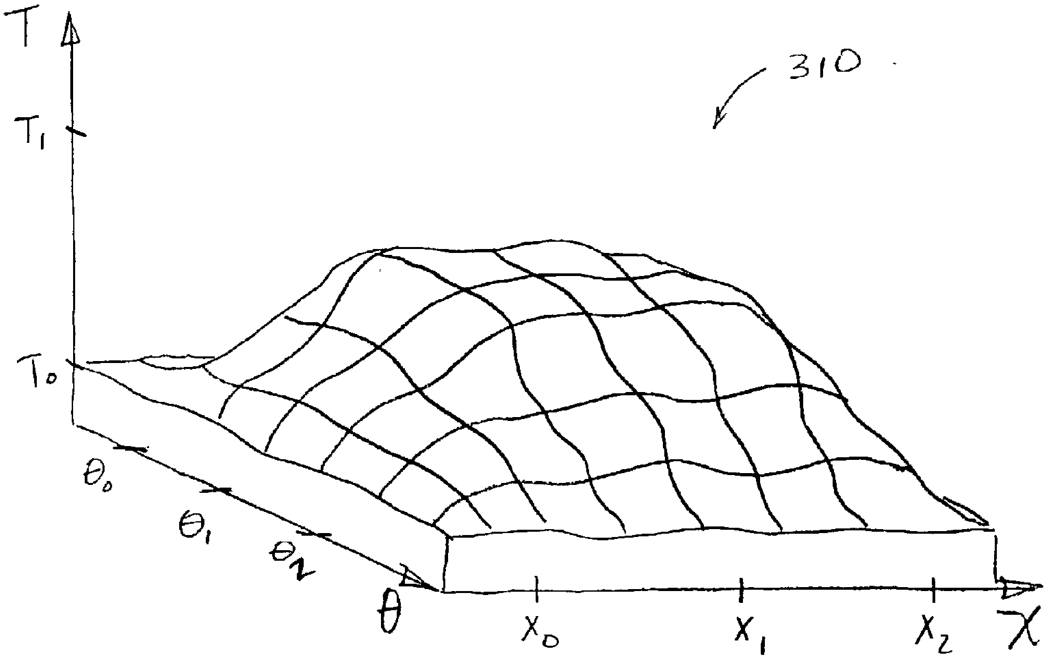
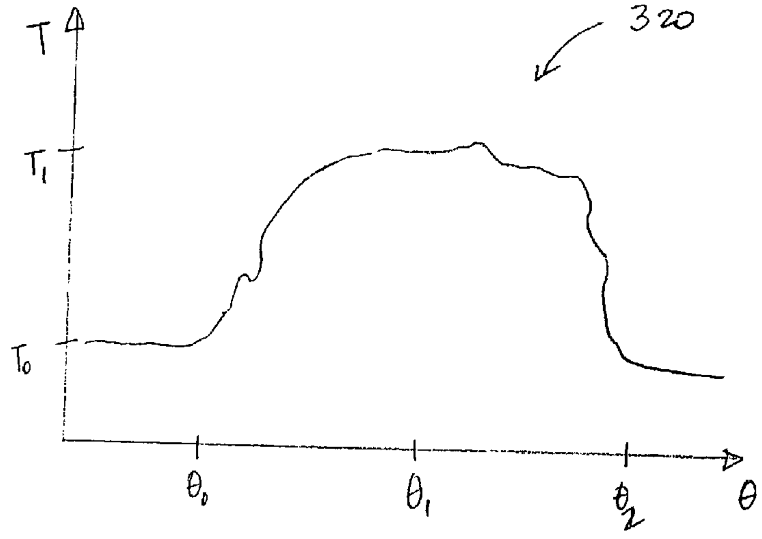


FIG. 19


320
T
T_1
T_0
θ_0
θ_1
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θ

FIG. 20

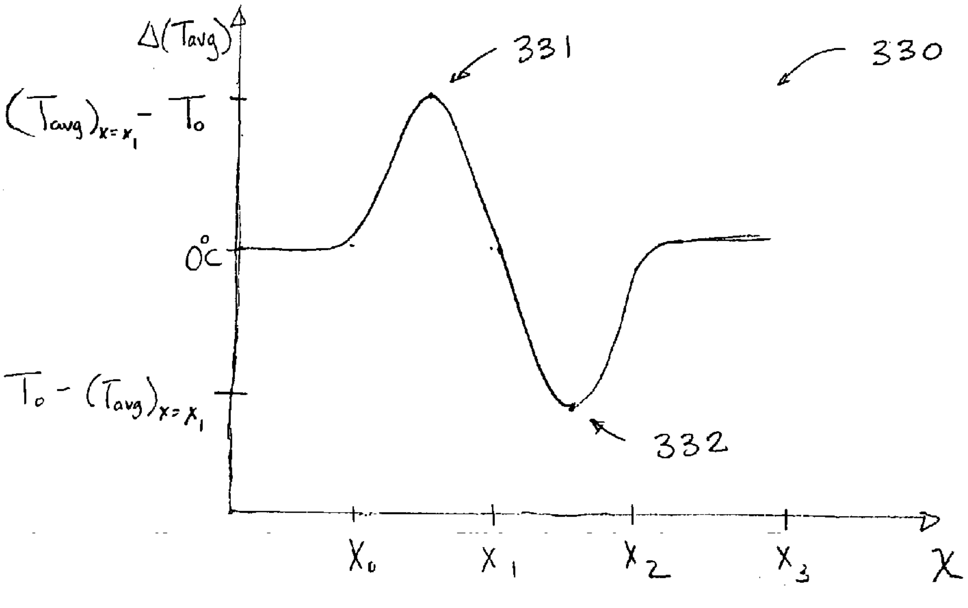
$\Delta(T_{avg})$
331
330
$(T_{avg})_{x=x_1} - T_0$
0°C
$T_0 - (T_{avg})_{x=x_1}$
332
X_0
X_1
X_2
X_3
X

FIG. 21

METHODS AND APPARATUS FOR THE IDENTIFICATION AND STABILIZATION OF VULNERABLE PLAQUE

FIELD OF THE INVENTION

[0001] The present invention relates to methods and apparatus for identifying and stabilizing vulnerable plaque, and for characterizing plaque. More particularly, the present invention relates to specialized catheters having both an imaging element and a thermographer for improved identification of vulnerable plaque. Apparatus of the present invention may in addition include an optional stabilization element for stabilizing the plaque.

BACKGROUND OF THE INVENTION

[0002] Vulnerable plaque is commonly defined as plaque having a lipid pool with a thin fibrous cap, which is often infiltrated by macrophages. Vulnerable plaque lesions generally manifest only mild to moderate stenoses, as compared to the large stenoses associated with fibrous and calcified lesions. While the more severe stenoses of fibrous and calcified lesions may limit flow and result in ischemia, these larger plaques often remain stable for extended periods of time. In fact, rupture of vulnerable plaque is believed to be responsible for a majority of acute ischemic and occlusive events, including unstable angina, myocardial infarction, and sudden cardiac death.

[0003] The mechanism behind such events is believed to be thrombus formation upon rupture and release of the lipid pool contained within vulnerable plaque. Thrombus formation leads to plaque growth and triggers acute events. Plaque rupture may be the result of inflammation, or of lipid accumulation that increases fibrous cap stress. Clearly, prospective identification and stabilization of vulnerable plaque is key to effectively controlling and reducing acute ischemic and occlusive events.

[0004] A significant difficulty encountered while attempting to identify and stabilize vulnerable plaque is that standard angiography provides no indication of whether or not a given plaque is susceptible to rupture. Furthermore, since the degree of stenosis associated with vulnerable plaque is often low, in many cases vulnerable plague may not even be visible using angiography.

[0005] A variety of techniques for identifying vulnerable plaque are being pursued. These include imaging techniques, for example, Intravascular Ultrasound ("IVUS"), Optical Coherence Tomography ("OCT"), and Magnetic Resonance Imaging ("MRI"). Two primary IVUS techniques have been developed. The first is commonly referred to as rotational IVUS, which uses an ultrasound transducer that is rotated to provide a circumferential image of a patient's vessel. The second technique is commonly referred to as phased-array IVUS, which uses an array of discrete ultrasound elements that each provide image data. The image data from each element is combined to form a circumferential image of the patient's vessel.

[0006] Rotational IVUS systems are marketed by Terumo Corporation of Tokyo, Japan, and the Boston Scientific Corporation of Natick, Mass., and are described, for example, in U.S. Pat. No. 6,221,015 to Yock, which is incorporated herein by reference. Phased-array IVUS systems are marketed by JOMED Inc., of Rancho Cordova, Calif., and are described, for example, in U.S. Pat. No. 6,283,920 to Eberle et al., as well as U.S. Pat. No. 6,283,921 to Nix et al., both of which are incorporated herein by reference. Optical Coherence Tomography systems are developed by Lightlab Imaging, LLC., of Westford, Mass., and are described, for example, in U.S. Pat. No. 6,134,003 to Tearney et al., which is incorporated herein by reference. U.S. Pat. No. 5,699,801 to Atalar et al., which also is incorporated herein by reference, describes methods and apparatus for Magnetic Resonance Imaging inside a patient's vessel.

[0007] A primary goal while characterizing plaque-type via an imaging modality is identification of sub-intimal lipid pools at the site of vulnerable plaque. In an IVUS study entitled, "Morphology of Vulnerable Coronary Plaque: Insights from Follow-Up of Patients Examined by Intravascular Ultrasound Before an Acute Coronary Syndrome" (Journal of the American College of Cardiology, 2000; 35:106-11), M. Yamagishi et al., concluded that, "the risk of rupture is high among eccentric lesions with a relatively large plaque burden and a shallow echolucent zone." IVUS allows characterization of the concentricity or eccentricity of lesions, as well as identification of echolucent zones, which are indicative of lipid-rich cores. However, while IVUS and other advanced imaging modalities may provide a means for identifying vulnerable plaque and selecting patients likely to benefit from aggressive risk factor interventions, such imaging modalities typically require a significant degree of skill, training and intuition on the part of a medical practitioner in order to achieve a proper diagnosis.

[0008] In addition to imaging techniques, biological techniques also have been proposed for identifying vulnerable plaque. Biological techniques typically rely on characterization of material properties of the plaque. Biological techniques include thermography, biological markers, magnetic resonance, elastography and palpography. Biological markers typically attempt to 'tag' specific tissue types, for example, via chemical receptors, with markers that allow easy identification of tissue type. Magnetic resonance operates on the principal that different tissue types may resonate at different, identifiable frequencies. Techniques combining Magnetic Resonance Imaging and biological markers have also been proposed in which superparamagnetic iron oxide nanoparticles are used as MRI contrast media. It is expected that vulnerable plaque will preferentially take up the nanoparticles by virtue of macrophage infiltration, leaking vasa vasorum, and permeable thin cap (M. AbouQamar et al., Poster Abstract, Transcatheter Cardiovascular Therapeutics, 2001, Washington, D.C.).

[0009] Elastography and palpography seek to characterize the strain modulus, or other mechanical properties, of target tissue. Studies have shown that different plaque types exhibit different, identifiable strain moduli, which may be used to characterize plaque type. Elastography is described, for example, in U.S. Pat. No. 5,178,147 to Ophir et al., which is incorporated herein by reference. Palpography is described, for example, in U.S. Pat. No. 6,165,128 to Cespedes et al., which also is incorporated herein by reference.

[0010] Thermography seeks to characterize tissue type via tissue temperature. Tissue temperature may be characterized via thermographers of various types, including, for example, thermistors, thermosensors, thermocouples, thermometers, spectrography, spectroscopy, and infrared. Tissue characterization via thermographers has been known for some time; for example, U.S. Pat. No. 4,960,109 to Lele et al., which is incorporated herein by reference, describes a multi-function probe for use in hyperthermia therapy that employs at least one pair of temperature sensors.

[0011] It has been observed that vulnerable plaque results in a temperature increase at a vessel wall of as much as about 0.1° C. to over 2.0° C., and is typically at least 0.3° C. A review of thermographic apparatus and techniques for plaque characterization is provided by C. Stefanadis in "Plaque Thermal Heterogeneity—Diagnostic Tools and Management Implications" (Expert Presentation, Transcatheter Cardiovascular Therapeutics, Washington, D.C.). Thermography apparatus and methods are also provided in Greek Patent No. 1003158B to Diamantopoulos et al., Greek Patent No. 1003178B to Toutouzas et al., and Greek Utility Model No. 98200093U to Diamantopoulos et al., all of which are incorporated herein by reference. U.S. Pat. No. 5,445,157 to Adachi et al., which is incorporated herein by reference, describes a thermographic endoscope including an infrared image-forming device. U.S. Pat. No. 5,871,449 to Brown and U.S. Pat. No. 5,935,075 to Casscells et al., both incorporated herein by reference, describe catheters capable of detecting infrared radiation.

[0012] Although passing reference is made in the Abstract of the Casscells patent to using the infrared detection system with or without ultrasound, no ultrasound apparatus is described. If ultrasound were to be used, it would presumably be applied using known techniques, i.e. extravascularly or via a secondary, stand-alone IVUS catheter. Using extravascular ultrasound or a secondary, stand-alone IVUS catheter, in conjunction with an infrared catheter is expected to increase the complexity, time, and cost associated with identifying vulnerable plaque.

[0013] For the purposes of the present invention, in addition to temperature characterization, thermography includes characterization of tissue pH, for example, via Near-Infrared ("NIR") Spectroscopy. T. Khan et al., have shown that inflamed regions of plaque exhibit lower pH, and that NIR Spectroscopy may be used to measure such pH ("Progress with the Calibration of A 3-French Near Infrared Spectroscopy Fiberoptic Catheter for Monitoring the pH Of Atherosclerotic Plaque: Introducing a Novel Approach For Detection of Vulnerable Plaque," Poster Abstract, Transcatheter Cardiovascular Therapeutics, 2001, Washington, D.C.). Thus, plaque temperature and plaque pH are inversely correlated to one another. Thermography further may include other spectroscopic tissue characterization, such as tissue composition.

[0014] Although thermography is a promising new technique for identifying vulnerable plaque, it has several drawbacks. First, since thermography doesn't provide image data, it is expected that medical practitioners will have difficulty determining proper locations at which to use a thermographer in order to characterize plaque type. Thus, secondary, stand-alone imaging apparatus may be required in order to adequately identify and characterize plaque. Requiring separate imaging and thermography apparatus is expected to increase complexity, time and cost associated with identifying vulnerable plaque. Additionally, thermography provides no indication of the eccentricity of a plaque or of the presence or magnitude of lipid pools disposed in the plaque, both of which have been shown to indicate the presence of vulnerable plaque.

[0015] U.S. Pat. No. 5,924,997 to Campbell and PCT Publication WO 01/74263 to Diamantopolous et al., both of which are incorporated herein by reference, describe or suggest vascular catheters providing ultrasound imaging and temperature detection. The Campbell reference contemplates thermography catheters having a lumen in which a standard ultrasonography catheter may be advanced. It is expected that the cross-sectional profile of such catheters would significantly limit their clinical applicability. Moreover, the catheters described in the Campbell patent do not appear to have any "window" for passage of the IVUS signals; thus, it is expected that such composite thermography/IVUS catheters would provide reduced bandwidth, fidelity, etc., as compared to stand-alone IVUS catheters. The Campbell reference also describes an integrated catheter having thermography and rotational IVUS, but does not clearly describe how such data could be correlated.

[0016] The device suggested in PCT Publication WO 01/74263 also has several drawbacks. That reference provides no enabling structure for coupling thermography data to IVUS images. Moreover, the PCT reference contemplates displaying imaging and thermography data in separate, positionally-linked windows, which is expected to increase difficulties in analyzing the data.

[0017] Both U.S. Pat. No. 5,924,997 and PCT Publication WO 01/74263 apparently do not acknowledge that patients may not have regions within their vasculature that are suspected of harboring vulnerable plaque. The added time, expense, etc., of using thermography in conjunction with IVUS or other imaging modalities may not be justified. Accordingly, it would be desirable to provide an imaging catheter through which separate thermography probes, e.g. functional measurement guide wires, optionally may be advanced, for example, only in patients suspected of harboring vulnerable plaque.

[0018] Another drawback associated with many of the prior art techniques for identifying and stabilizing vulnerable plaque is that identification and stabilization are typically achieved using separate apparatus. Stabilization techniques include both local and systemic therapy. Localized techniques include angioplasty, stenting, mild heating, photonic ablation, radiation, local drug injection, gene therapy, covered stents and coated stents, for example, drug-eluting stents. Systemic therapies include extreme lipid lowering; inhibition of cholesterol acyltransferase (Acyl-CoA, "ACAT"); matrix metalloproteinase ("MMP") inhibition; and administration of anti-inflammatory agents, anti-oxidants and/or Angiotensin-Converting Enzyme ("ACE") inhibitors.

[0019] Multi-functional devices have been proposed in other areas of vascular intervention. For example, U.S. Pat. No. 5,906,580 to Kline-Schoder et al., which is incorporated herein by reference, describes an ultrasound transducer array that may transmit signals at multiple frequencies and may be used for both ultrasound imaging and ultrasound therapy. PharmaSonics, Inc., of Sunnyvale, Calif., markets therapeutic ultrasound catheters, which are described, for example, in

U.S. Pat. No. 5,725,494 to Brisken et al., incorporated herein by reference. U.S. Pat. No. 5,581,144 to Corl et al., incorporated herein by reference, describes another ultrasound transducer array that is capable of operating at multiple frequencies.

[0020] In addition to multi-functional ultrasound devices, other multi-functional interventional devices are described in U.S. Pat. Nos. 5,571,086 and 5,855,563 to Kaplan et al., both of which are incorporated herein by reference. However, none of these devices, nor the multi-functional ultrasound devices discussed previously, are suited for rapid identification and stabilization of vulnerable plaque in accordance with the principles of the present invention.

[0021] In view of the drawbacks associated with previously known methods and apparatus for identifying and stabilizing vulnerable plaque, it would be desirable to provide methods and apparatus that overcome those drawbacks.

[0022] It would be desirable to provide methods and apparatus that reduce the skill and training required on the part of medical practitioners in order to identify and stabilize vulnerable plaque.

[0023] It would be desirable to provide methods and apparatus for identifying and stabilizing vulnerable plaque that reduce the cost, complexity and time associated with such procedures.

[0024] It would be desirable to provide methods and apparatus that are multi-functional.

[0025] It would be desirable to provide methods and apparatus that facilitate characterization of lesion eccentricity, echogenicity, temperature or pH, and tissue composition.

[0026] It would be desirable to provide methods and apparatus that combine imaging, thermography, NIR spectroscopy, biochemical sensing and/or optional vulnerable plaque stabilization elements in a single device.

[0027] It would be desirable to provide a variety of data characterization techniques.

[0028] It would be desirable to provide methods and apparatus for identifying and stabilizing vulnerable plaque that facilitate imaging and allow subsequent advancement of thermography apparatus through the imaging apparatus for detailed inspection of regions suspected of harboring vulnerable plaque.

SUMMARY OF THE INVENTION

[0029] In view of the foregoing, it is an object of the present invention to provide apparatus and methods for identifying and stabilizing vulnerable plaque that overcome drawbacks associated with previously known apparatus and methods.

[0030] It is an object to provide methods and apparatus that reduce the skill and training required on the part of medical practitioners in order to identify and stabilize vulnerable plaque.

[0031] It also is an object to provide methods and apparatus for identifying and stabilizing vulnerable plaque that reduce the cost, complexity and time associated with such procedures.

[0032] It is another object to provide methods and apparatus that are multi-functional.

[0033] It is yet another object to provide methods and apparatus that facilitate characterization of lesion eccentricity, echogenicity, temperature or pH, and tissue composition.

[0034] It is an object to provide methods and apparatus that combine imaging, thermography, NIR spectroscopy, biochemical sensing and/or optional vulnerable plaque stabilization elements in a single device.

[0035] It would be desirable to provide a variety of data characterization techniques.

[0036] It is an object to provide methods and apparatus for identifying and stabilizing vulnerable plaque that facilitate imaging and allow subsequent advancement of thermography apparatus through the imaging apparatus for detailed inspection of regions suspected of harboring vulnerable plaque.

[0037] These and other objects of the present invention are accomplished by providing apparatus for identifying vulnerable plaque comprising a catheter having both an imaging element and a thermographer. Providing both thermography and imaging in a single, multi-functional catheter is expected to decrease the cost and increase the accuracy of vulnerable plaque identification, as well as simplify and expedite identification, as compared to providing separate, stand-alone thermography and imaging. Apparatus of the present invention also may be provided with optional stabilization elements for stabilizing vulnerable plaque, thereby providing vulnerable plaque identification and stablization in a single device.

[0038] In a first embodiment of the present invention, a catheter is provided having a phased-array IVUS imaging system and a plurality of thermocouples. The plurality of thermocouples may be deployed into contact with an interior wall of a patient's body lumen, thereby providing temperature measurements along the interior wall that may be compared to IVUS images obtained with the imaging system to facilitate identification of vulnerable plaque. In a second embodiment, a catheter is provided with a rotational IVUS imaging system and a fiber optic infrared thermography system. The infrared system's fiber optic is preferably coupled to the rotating drive cable of the rotational IVUS imaging system, thereby providing a full circumferential temperature profile along the interior wall of the patient's body lumen. In a third embodiment, a catheter is provided having a phased-array IVUS imaging system and a fiber optic infrared thermography system. The infrared system preferably comprises a plurality of fiber optics to provide a full circumferential temperature profile along the interior wall of a patient's body lumen.

[0039] In a fourth embodiment, apparatus of the present invention is provided with, in addition to an imaging element and a thermographer, an optional stabilization element. The apparatus may further comprise an optional embolic protection device to capture emboli and/or other material released, for example, during stabilization of vulnerable plaque. The stabilization element may comprise an inflatable balloon. In a fifth embodiment, the stabilization element comprises a second ultrasound transducer that resonates at therapeutic ultrasound frequencies, as opposed to ultrasonic imaging frequencies. As yet another embodiment, the imaging element of the present invention comprises an ultrasound transducer that is capable of transmitting multiple frequencies that are suited to both ultrasonic imaging and ultrasonic therapy, thereby providing both vulnerable plaque imaging and stabilization in a single element.

[0040] In a sixth embodiment, a catheter, preferably comprising an imaging transducer, is provided having a side exit port disposed on a lateral surface of the catheter, the side exit port defining a distal termination of a bifurcation of a single lumen or one of two lumens disposed within the catheter through which a thermographer, for example, a functional measurement guide wire, a fiber optic spectroscopy probe, or a fiber optic infrared probe, may be advanced. The catheter also may comprise a plurality of bifurcations or lumens through which a plurality of thermographers may be advanced to facilitate acquisition of a full circumferential temperature profile along the interior wall of a patient's body lumen. The distal portion of the above-mentioned lumens comprise a curvature that directs advancement of the thermographer so that a distal working tip of the thermographer may be disposed in sensory proximity with the vessel wall to facilitate data acquisition.

[0041] Additionally, the direction provided by this curvature, along with the position of an optional imaging system disposed on the catheter distal the side exit port, e.g. an IVUS imaging system, permits the thermographer to be advanced within or immediately adjacent to the field of view of the imaging system, permitting simultaneous acquisition and real-time display of images and temperature data of the same or substantially the same axial or angular locations within the vessel. This eliminates the need to correlate and couple imaging and thermography data prior to display. Accordingly, a medical practitioner may immediately investigate potential areas within the vessel susceptible of harboring vulnerable plaque using the real-time images and temperature data. As an alternative to thermographers, higher resolution imaging probes or wires may be advanced through the side exit port to characterize vulnerable plaque. These include, for example, Optical Coherence Tomography probes or wires.

[0042] As yet another embodiment, rather than having a side exit port, the catheter may comprise a distal exit port disposed at the distal end of the catheter through which a thermographer of the present embodiment may be advanced. The thermographer may comprise a shape memory wire that may, upon advancement past the distal exit port, be everted to dispose the distal working end of the thermographer in sensory proximity with the vessel wall and in the field of view of the proximally disposed imaging system.

[0043] A still further embodiment comprises a catheter having a phased-array IVUS imaging system and a plurality of thermographers that are circumferentially disposed about the catheter and affixed thereto so that the distal portions of the thermographers radially self-expand away from the catheter when a delivery sheath is proximally retracted. Radial expansion of the plurality of thermographers permits each thermographer to contact the interior wall of a patient's body lumen.

[0044] Embodiments of the present invention may comprise one or more thermographers adapted to obtain the ambient temperature within the vessel. These thermographers may be disposed, for example, on the distal end of catheters made in accordance with the present invention. Additional locations will be apparent to those of skill in the art. Relative temperature increase or decrease at the vessel wall may then be determined by subtracting out the ambient temperature within the vessel.

[0045] These embodiments are provided only for the purpose of illustration. Additional embodiments will be apparent to those skilled in the art and are included in the scope of the present invention.

[0046] Imaging and thermographic data preferably are coupled in order to facilitate identification of vulnerable plaque. Coupling may be achieved using position indication techniques, for example, using an IVUS pullback system that is modified to simultaneously monitor the position of both the imaging element and the thermographer. IVUS pullback systems are described, for example, in U.S. Pat. No. 6,290,675 to Vujanic et al., U.S. Pat. No. 6,275,724 to Dickinson et al., U.S. Pat. No. 6,193,736 to Webler et al., and PCT Publication WO 99/12474, all of which are incorporated herein by reference. Additionally, relative distances between imaging elements and thermographers on catheters comprising both are preferably obtained prior to introduction of such catheters within a patient's vasculature. Measurement of such relative distances is expected to facilitate correlation of imaging and thermographic data.

[0047] Imaging data and thermographic data, coupled using position indication techniques and measured relative distances, preferably are simultaneously graphically displayed, for example, on a standard computer monitor. The coupled data preferably is displayed in a separate, yet overlaid fashion so that a medical practitioner may rapidly correlate temperature measurements obtained at a given position within the patient's body lumen to images obtained at that position. Rapid correlation is expected to simplify, expedite and increase the accuracy of vulnerable plaque identification, as well as facilitate plaque stabilization. The overlaid data may also be combined by, for example, color-coding the imaging data to represent temperature.

[0048] It is expected that additional data for additional vessel parameters also may be obtained, coupled and provided in the graphical display, for example, palpography, pressure, and pH data. Blood flow imaging, as described, for example, in U.S. Pat. Nos. 5,453,575 and 5,921,931 to O'Donnell et al., both of which are incorporated herein by reference, also may be provided.

[0049] In accordance with another aspect of the present invention, data for a vessel parameter may be displayed on an interactive 3-dimensional graph in which the data may be provided as a function of axial and angular position within the vessel. Selection of a particular value of one of the variables (e.g., vessel parameter data, axial position or angular position) may prompt display of a 2-dimensional graph in which the coordinate axes comprise the remaining two variables, or display of an image of the associated cross-section or side-section having the vessel parameter data overlaid thereon.

[0050] Vessel parameter data also may be conditioned to facilitate rapid bulk testing to narrow the region(s) of the vessel that may require additional analysis. Such conditioning may include computation and display of average vessel parameter values for a particular cross-section or side-section of the vessel, gradients of the individual or average vessel parameter values, and/or accentuation of shifts in individual or average vessel parameter data.

[0051] Methods of using the apparatus of the present invention also are provided.

BRIEF DESCRIPTION OF THE DRAWINGS

[0052] Further features of the invention, its nature and various advantages, will be more apparent from the following detailed description of the preferred embodiments, taken in conjunction with the accompanying drawings, in which like reference numerals apply to like parts throughout, and in which:

[0053] **FIG. 1** is a schematic cut-away view of a prior art phased-array IVUS catheter;

[0054] **FIG. 2** is a schematic cut-away view of a prior art rotational IVUS catheter;

[0055] **FIGS. 3A and 3B** are schematic side views of a prior art thermography catheter having a plurality of thermocouples, and shown in a collapsed delivery configuration and an expanded deployed configuration, respectively;

[0056] **FIG. 4** is a schematic cut-away view of a prior art thermography catheter having a side-viewing infrared thermographer;

[0057] **FIG. 5** is a schematic side view of a prior art thermography catheter having a steerable distal region with a thermocouple;

[0058] **FIG. 6A** is a schematic side view of a first embodiment of a catheter in accordance with the principles of the present invention having an imaging element and a thermographer;

[0059] **FIG. 6B** is a schematic side view of an alternative embodiment of the catheter of **FIG. 6A** in accordance with the principles of the present invention having an imaging element and a thermographer;

[0060] **FIG. 7** is a schematic cut-away view of a second embodiment of apparatus of the present invention having an imaging element and a thermographer;

[0061] **FIGS. 8A and 8B** are schematic cut-away side views of an alternative embodiment of the apparatus of **FIG. 7**;

[0062] **FIG. 9** is a schematic side view of a fourth embodiment of apparatus in accordance with the present invention having an optional stabilization element, as well as an optional embolic protection device;

[0063] **FIG. 10** is a schematic side view of a fifth embodiment of the present invention having an alternative stabilization element;

[0064] FIGS. **11A-11C** are schematic cut-away side views of a sixth embodiment of a catheter of the present invention having at least one side exit port for advancement of a thermographer;

[0065] FIGS. **12A-12D** are schematic side views and cross-sectional views of alternative embodiments of the present invention having an evertable thermographer;

[0066] **FIGS. 13A and 13B** are schematic side views of a further alternative embodiment of the present invention having self-expanding thermographers;

[0067] **FIGS. 14A and 14B** are schematic side views, partially in section, of the apparatus of **FIG. 7** disposed at a target site within a patient's vessel, illustrating a method of using the apparatus of the present invention;

[0068] **FIGS. 15A and 15B** are schematic views of graphical user interfaces that display imaging and thermographic data, respectively, obtained, for example, via the method of FIGS. **14**, with the thermographic data of **FIG. 15B** obtained along side-sectional view line A-A of **FIG. 15A**;

[0069] **FIG. 16** is a schematic view of a graphical user interface that couples and simultaneously displays imaging and thermographic data obtained along a cross-section of the patient's vessel;

[0070] **FIG. 17** is a schematic view of an alternative graphical user interface that simultaneously displays coupled imaging and thermographic data along side-sectional view line B-B of **FIG. 16**;

[0071] **FIG. 18** is a schematic perspective view of an illustrative vessel having a vulnerable plaque;

[0072] **FIG. 19** is a schematic view of a graphical user interface that displays illustrative thermographic data corresponding to the vessel of **FIG. 18** as a function of axial and angular position within a patient's vessel;

[0073] **FIG. 20** is a schematic view of a graphical user interface that displays illustrative thermographic data corresponding to the vessel of **FIG. 18** as a function of angular position; and

[0074] **FIG. 21** is a schematic view of a graphical user interface that displays gradients of average summation values of thermography data at multiple cross-sections of the vessel of **FIG. 18**.

DETAILED DESCRIPTION OF THE INVENTION

[0075] The present invention relates to methods and apparatus for identifying and stabilizing vulnerable plaque. More particularly, the present invention relates to specialized catheters having both an imaging element and a thermographer for improved identification of vulnerable plaque. Apparatus of the present invention may in addition include an optional stabilization element for stabilizing the plaque.

[0076] With reference to **FIG. 1, a** prior art phased-array Intravascular Ultrasound ("IVUS") catheter is described. Catheter **10** comprises phased-array ultrasound transducer **12** having a plurality of discrete ultrasound elements **13**. Catheter **10** further comprises guide wire lumen **14**, illustratively shown with guide wire **100** disposed therein. Catheter **10** also may comprise multiplexing circuitry, amplifiers, etc., per se known, which may be disposed on and/or electrically coupled to catheter **10**. Transducer array **12** of catheter **10** is electrically coupled to an imaging system (not shown), per se known, that provides excitation waveforms to the transducer array, and interprets and displays data received from the array.

[0077] **FIG. 2** depicts a prior art rotational IVUS catheter. Catheter **20** comprises ultrasound transducer **22** disposed on a distal region of rotatable drive cable **24**. Drive cable **24** is proximally coupled to a driver (not shown), e.g. an electric motor, for rotating the drive cable and ultrasound transducer **22**, thereby providing transducer **22** with a 360° view. Catheter **20** further comprises guide wire lumen **26** that opens in side port **28** distally of transducer **22**. Guide wire **100** is illustratively disposed within lumen **26**. As with transducer array **12** of catheter **10**, transducer **22** of catheter **20** is electrically coupled to an imaging system (not shown), per se known, that provides excitation waveforms to the transducer, and interprets and displays data received from the transducer.

[0078] As discussed hereinabove, it has been shown that sub-intimal lipid pools at the site of plaque, as well as the eccentricity of the plaque, are key indicators of vulnerable plaque susceptible to rupture. It has also been shown that IVUS may be used to determine the eccentricity of plaque, as well as to identify echolucent zones, which are indicative of lipid-rich cores. However, achieving proper identification of vulnerable plaque via IVUS or any of a host of other advanced imaging modalities (e.g. Magnetic Resonance Imaging or Optical Coherence Tomography) may require a significant degree of skill, training and intuition on the part of a medical practitioner.

[0079] With reference now to **FIG. 3, a** prior art thermography catheter is described. Catheter **30** comprises outer tube **34** coaxially disposed about inner tube **32**. Inner tube **32** comprises distal tip **36** and guide wire lumen **38**, in which guide wire **100** is illustratively disposed. Catheter **30** further comprises a plurality of thermocouples **40** disposed near its distal end. Each thermocouple comprises a wire **42** coupled proximally to the distal end of outer tube **34** and distally to distal tip **36** of inner tube **32**. The proximal and distal ends of each wire **42** are further electrically coupled to a processor (not shown) that captures and translates voltages generated by thermocouples **40** into temperature values, for example, via known calibration values for each thermocouple.

[0080] As seen in **FIG. 3**, catheter **30** is expandable from the collapsed delivery configuration of **FIG. 3A** to the expanded deployed configuration of **FIG.** 3B, by advancing outer tube **34** with respect to inner tube **32**. Such advancement causes thermocouples **40** to protrude from catheter **30** so that the thermocouples may contact the interior wall of a patient's body lumen. Catheter **30** is adapted for intravascular delivery in the collapsed configuration of **FIG.** 3A, and is adapted for taking temperature measurements at a vessel wall in the expanded configuration of **FIG. 3B**.

[0081] Referring to **FIG. 4**, another prior art thermography catheter is described. Catheter **50** comprises lumen **52**, which extends from a proximal end of catheter **50** to distal side port **54**. Fiber optic **56** is disposed within lumen **52** and is proximally coupled to an infrared thermography system (not shown). Catheter **50** thereby comprises a side-viewing fiber optic thermography catheter capable of measuring ambient temperature T near distal side port **54**.

[0082] By disposing side port **54** of catheter **50** within a patient's body lumen, the temperature of the patient's body lumen may be measured to facilitate identification of vulnerable plaque. However, a significant drawback of catheter **50** for identification of vulnerable plaque is that fiber optic **56** has only a limited field of view, and vulnerable plaque is typically eccentric, i.e. occurs predominantly on one side of a vessel. Thus, if side port **54** of catheter **50** were not rotated to the side of the vessel afflicted with vulnerable plaque build-up, it is expected that the ambient temperature T measured with catheter **50** would not reflect the presence of vulnerable plaque.

[0083] With reference to **FIG. 5**, yet another prior art thermography catheter is described. Catheter **60** comprises steerable distal end **62** having thermistor **64** coupled thereto. Thermistor **64** is proximally attached to a processor (not shown) that converts measurements taken with thermistor **64** into temperature measurements. Catheter **60** further comprises guide wire lumen **66** having guide wire **100** illustratively disposed therein.

[0084] Distal end **62** of catheter **60** may be positioned against a patient's body lumen to provide temperature measurements where thermistor **64** contacts the body lumen. However, a significant drawback of catheter **60** is that thermistor **64** only provides temperature measurements at a single point at any given time. It is therefore expected that eccentric vulnerable plaque will be difficult to identify with catheter **60**, especially if distal end **62** of catheter **60** is disposed against the unaffected, or mildly affected, side of a patient's vessel suffering from eccentric vulnerable plaque.

[0085] Although thermography is a promising new technique for identifying vulnerable plaque, the thermography devices described hereinabove have several drawbacks. Since thermography doesn't provide image data, it is expected that medical practitioners will have difficulty determining proper locations at which to use a thermographer in order to characterize plaque type. Thus, secondary, stand-alone imaging apparatus may be required in order to adequately identify and characterize plaque. Requiring separate imaging and thermography apparatus is expected to increase complexity, time and cost associated with identifying vulnerable plaque. Additionally, thermography provides no indication of the eccentricity of a plaque or of the presence or magnitude of lipid pools disposed in the plaque, both of which have been shown to indicate the presence of vulnerable plaque.

[0086] With reference now to **FIG. 6A, a** first embodiment of apparatus in accordance with the present invention is described that provides both an imaging element and a thermographer in a single device. By providing both imaging and thermography in a single device, the present invention combines positive attributes of stand-alone imaging systems and stand-alone thermographers described hereinabove, while reducing previously-described drawbacks associated with such stand-alone systems. Apparatus **150** of **FIG. 6A** comprises catheter body **152**, thermographer **160** and imaging element **170**.

[0087] Catheter body **152** comprises outer tube **154** coaxially disposed about inner tube **153**. Inner tube **153** comprises distal tip **156** and guide wire lumen **158**, in which guide wire **100** is illustratively disposed. Thermographer **160** comprises a plurality of thermocouples **162**. Any number of thermocouples **162** may be provided. Each thermocouple comprises a wire **164** coupled proximally to the distal end of outer tube **154** and distally to distal tip **156** of inner tube **153**. The proximal and distal ends of each wire **164** are further electrically coupled to a processor (not shown) that captures and translates voltages generated by thermocouples **162** into temperature values, for example, via known calibration values for each thermocouple.

[0088] Thermographer **160** optionally may also comprise thermosensor **161** disposed, for example, on distal tip **156**. Thermosensor **161** may be used to determine ambient temperature within a body lumen such as a blood vessel. This ambient temperature may be subtracted from temperature measurements obtained with thermocouples **162** so that changes in temperature, as opposed to absolute temperature, at a vessel wall may be examined.

[0089] Imaging element **170** comprises phased-array ultrasound transducer **172** having a plurality of discrete ultrasound elements **173**. Imaging element **170** optionally may comprise multiplexing circuitry, flexible circuitry or substrates, amplifiers, etc., per se known, which may be disposed on and/or electrically coupled to apparatus **150**. Transducer array **172** of imaging element **170** is electrically coupled to an imaging system (not shown), per se known, that provides excitation waveforms to the transducer array, and interprets and displays data received from the array. The imaging system coupled to imaging element **170** and the processor coupled to thermographer **160** are preferably combined into a single data acquisition and analysis system (not shown) for capturing and interpreting data received from apparatus **150**.

[0090] As with catheter **30** of **FIG. 3**, apparatus **150** is expandable from a collapsed delivery configuration to the expanded deployed configuration of **FIG. 6**A, by advancing outer tube **154** of catheter body **152** with respect to inner tube **153**. Such advancement causes thermocouples **162** of thermographer **160** to protrude from catheter body **152** so that the thermocouples may contact the interior wall of a patient's body lumen. Apparatus **150** is adapted for intravascular delivery in the collapsed configuration, and is adapted for taking temperature measurements at a vessel wall in the expanded configuration. Imaging via imaging element **170** may be achieved in either the collapsed delivery configuration or the expanded deployed configuration, thereby facilitating positioning of apparatus **150** at a stenosed region within a patient's vessel.

[0091] Thermographer **160** comprises multiple thermography sensors, illustratively in the form of thermocouples **162**, disposed radially about catheter body **152**. Temperature measurements obtained from these sensors may be displayed graphically as a 2-dimensional map or image, for example, as a cross-sectional temperature profile within a patient's vessel. Such a cross-sectional temperature profile may be compared with a cross-sectional image of the vessel obtained at the same location, for example, via imaging element **170**. Correlation of imaging and thermography data may be facilitated by determining the distance between imaging element **170** and thermographer **160** prior to use. By advancing or retracting catheter body **152**, correlated, 2-dimensional temperature and imaging data may be extended to 3-dimensions. Translation of catheter body **152** may be achieved, for example, using position indication techniques and/or a pullback system, per se known. Illustrative methods and apparatus for displaying thermographic and imaging data are provided hereinbelow with respect to FIGS. **14**-**21**.

[0092] Apparatus **150** is expected to provide significant advantages over prior art, stand-alone imaging and thermography catheters, such as catheters **10** and **30**, used either alone or in combination. Specifically, apparatus **150** is expected to decrease the complexity of obtaining both temperature and imaging data at a target site, as well as to facilitate correlation of such data. Additionally, apparatus **150** is expected to reduce the cost of obtaining both temperature and imaging data, as compared to providing both a stand-alone imaging system and a stand-alone thermography system.

[0093] Since vascular lumens commonly afflicted with vulnerable plaque, such as the coronary arteries, are often very small, it is expected that difficulty may be encountered while trying to simultaneously position separate imaging and thermography catheters at the site of vulnerable plaque; furthermore, a stand-alone thermography catheter may block imaging of portions of the vessel wall. Apparatus **150** overcomes these drawbacks. Additionally, apparatus **150** is expected to reduce the skill required on the part of a medical practitioner to identify vulnerable plaque via IVUS, by providing a secondary indication of vulnerable plaque in the form of temperature measurements. Likewise, apparatus **150** is expected to increase the likelihood of proper vulnerable plaque identification via thermography, by providing a secondary indication of vulnerable plaque in the form of IVUS imaging that allows examination of plaque eccentricity and echogenicity. Additional advantages of the present invention will be apparent to those of skill in the art.

[0094] An alternative embodiment of catheter **150** of **FIG. 6A** is illustrated in **FIG. 6B**. As with catheter **150**, catheter **159** also comprises catheter body **152**, thermographer **160** comprising a plurality of thermocouples **162**, and imaging element **170** comprising phased-array ultrasound transducer **172**. The difference between catheter **159** and catheter **150** resides in the configuration of thermographer **160** with respect to imaging element **170**. Specifically, while thermographer **160** of catheter **150** is disposed longitudinally distant from imaging element **170**, thermocouples **162** may be disposed at the same axial location as imaging element **170**.

[0095] In addition to the advantages discussed above with reference to catheter **150**, catheter **159** provides the further advantage of disposing thermocouples **162** within the field of view of phased-array ultrasound transducer **172**. This facilitates simultaneous acquisition, real-time viewing and correlation of both temperature and imaging data at the same axial and/or angular positions within vessel V, thereby eliminating the need to correlate and couple the temperature and imaging data prior to display. In particular, a medical practitioner may be able to view a real-time, cross-sectional image of the vessel with the temperature data instantly overlaid thereon. This permits the medical practitioner to immediately acquire knowledge of, and investigate potential areas within, the vessel suspected of harboring vulnerable plaque.

[0096] Referring now to **FIG. 7, a** second embodiment of apparatus in accordance with the present invention in described. Apparatus **180** comprises catheter **182** having imaging element **184** and thermographer **186**. Imaging element **184** comprises a rotational IVUS imaging element, and thermographer **186** comprises a rotational infrared thermographer.

[0097] Catheter **182** further comprises rotatable drive cable **188** having lumen **190** that distally terminates at side port **192**. Catheter **182** still further comprises guide wire lumen **194** that opens in side port **196** distally of drive cable **188**. Guide wire **100** is illustratively shown disposed in lumen **194**.

[0098] Thermographer **186** of catheter **182** comprises fiber optic **187** disposed within lumen **190** of drive cable **188**. Imaging element **184** of catheter **182** comprises ultrasound transducer **185** disposed on rotatable drive cable **188**. Drive cable **188** is proximally coupled to a driver (not shown), e.g. an electric motor, for rotating the drive cable, as well as ultrasound transducer **185** of imaging element **184** and fiber optic **187** of thermographer **186**, thereby providing imaging element **184** and thermographer **186** with a **3600** view. It will be evident to one of ordinary skill in the art that fiber optic **187** may comprise two or more fibers adjacently disposed, at least one fiber for transmitting a signal and at least one fiber for receiving the transmitted signal.

[0099] As with transducer **22** of catheter **20**, transducer **185** is electrically coupled to an imaging system (not shown), per se known, that provides excitation waveforms to the transducer, and interprets and displays data received from the transducer. Likewise, as with fiber optic **56** of catheter **50**, fiber optic **187** is proximally coupled to an infrared thermography system (not shown). Preferably, the imaging system of imaging element **184**, the infrared thermography system of thermographer **186**, and the driver coupled to drive cable **188**, are combined into a single data acquisition and analysis system (not shown) for capturing and interpreting data received from apparatus **180**. Alternatively, a subset of these elements may be combined. Determination of the distance between imaging element **184** and thermographer **186** prior to use is expected to facilitate correlation of imaging and thermography data.

[0100] Apparatus **180** provides many of the advantages described hereinabove with respect to apparatus **150**. Additionally, as compared to infrared thermography catheter **50**, described hereinabove with respect to **FIG. 4**, thermographer **186** of apparatus **180** provides significantly enhanced thermographic capabilities. Specifically, by coupling thermographer **186** to rotatable drive cable **188**, thermographer **186** is capable of providing a full circumferential temperature profile along the interior wall of a patient's body lumen, without necessitating potentially inaccurate manual rotation of the infrared thermographer by a medical practitioner. A stand-alone, rotatable infrared thermography catheter (not shown), similar to apparatus **180** but without imaging capabilities, is contemplated and is included in the scope of the present invention.

[0101] In an alternative embodiment of apparatus **180** of **FIG. 7**, imaging element **184**, comprising a rotational IVUS imaging element, is replaced with imaging element **170** of **FIG. 6**. Imaging element **170** comprises phased-array ultrasound transducer **172** having plurality of discrete ultrasound elements **173**. Apparatus **197** further comprises plurality of lumens **198** that distally terminate at plurality of side ports **199**.

[0102] Plurality of side ports **199** are disposed on a lateral surface of apparatus **197** at a longitudinal position that is coincident with that of ultrasound transducer **172** so that the circumferential orientation of discrete ultrasound elements **173** is interrupted at regular angular intervals to expose fiber optics **187** disposed within lumens **198**. This permits apparatus **197** to simultaneously acquire both circumferential temperature and imaging profiles at the same axial position within a patient's body lumen. As will be apparent to those of skill in the art, the plurality of lumens and side ports may comprise any number of lumens and side ports, including a single lumen and side port.

[0103] To provide a full circumferential image profile without the attendant interruptions of ultrasound elements **173**, side ports **199** may be shifted to a longitudinal position immediately adjacent to imaging element **170**, as illustrated in **FIG. 8B**. While this configuration does not permit simultaneous acquisition of temperature and imaging data at exactly the same axial position within a patient's body lumen, apparatus **200** allows simultaneous acquisition at substantially the same axial position. Specifically, the temperature data acquired by apparatus **200** corresponds to image data of the body lumen just proximal to the field of view of the imaging element. Accordingly, a medical practitioner may still obtain real-time viewing and correlation of both temperature and imaging data at approximately the same axial body lumen position for investigation of areas within the body lumen suspected of harboring vulnerable plaque.

[0104] In **FIG.** 8B, to facilitate correlation of temperature and imaging data at exactly the same axial position post-acquisition, the distance between side exit ports **199** and imaging element **170** preferably are provided or measured. The offset between the side ports and the imaging element may be subtracted out, for example, during data processing. Placing side exit ports **199** immediately adjacent imaging element **170** is expected to reduce artifacts within images obtained with the imaging element caused by placement of thermographers directly within the plane of view of the imaging element.

[0105] With reference to **FIG. 9, a** fourth embodiment of apparatus in accordance with the present invention is described that includes an optional stabilization element, in addition to an imaging element and a thermographer. The stabilization element is adapted to stabilize vulnerable plaque, thereby providing vulnerable plaque identification and stablization in a single device. Apparatus **201** comprises all of the elements of apparatus **150**, including catheter body **152**, thermographer **160** and imaging element **170**, and further comprises stabilization element **202**.

[0106] Stabilization element **202** comprises inflatable balloon **204**. Balloon **204** is inflatable from a collapsed delivery configuration to the deployed configuration of **FIG. 9** by suitable means, for example, via an inflation medium injected into the balloon through annulus **206** formed between the inner wall of outer tube **154** and the outer wall of inner tube **153** of catheter body **152**. Additional inflation techniques will be apparent to those skilled in the art.

[0107] It is expected that, once vulnerable plaque has been identified in a patient's vessel via thermographer **160** and/or imaging element **170**, stabilization element **202** may be positioned at the location of the identified vulnerable plaque. Stabilization element **202** may then be deployed, i.e. balloon **204** may be inflated, at the site of vulnerable plaque to stabilize the plaque, for example, by compressing, rupturing, scaffolding and/or sealing the plaque in the controlled environment of a catheterization laboratory. In addition to balloon **204**, stabilization element **202** may be provided with additional stabilization elements (not shown), for example, a stent, a covered stent, a stent graft, a coated stent or a drug-eluting stent, to further enhance stabilization of vulnerable plaque. Additional stabilization elements will be apparent to those of skill in the art.

[**0108**] In order to facilitate identification and stabilization of vulnerable plaque, the distances between stabilization element **202**, thermographer **160** and imaging element **170** are preferably provided or measured. Furthermore, the distances between the imaging, thermography and optional stabilization elements of all embodiments of the present invention are preferably provided or measured. This facilitates coupling of thermographic and imaging data, as well as proper positioning of optional stabilization elements.

[**0109**] Providing vulnerable plaque identification and stabilization elements in a single device, in accordance with the principles of the present invention, provides all of the benefits of apparatus **150** described hereinabove, as well as the additional advantage of not having to provide stand-alone apparatus for plaque stabilization. This, in turn, is expected to decrease the cost, time and complexity associated with identifying and stabilizing vulnerable plaque, as well as to decrease the crossing profile of such apparatus, as compared to stand-alone apparatus used concurrently. Further still, providing identification and stabilization in a single device is expected to simplify accurate placement of stabilization elements at the site of identified vulnerable plaque.

[**0110**] Referring now to **FIG. 10, a** fifth embodiment of the present invention having an alternative vulnerable plaque stabilization element, is described. Apparatus **210** comprises all of the elements of apparatus **150**, including catheter body **152**, thermographer **160** and imaging element **170**, and further comprises stabilization element **212**. Stabilization element **212** comprises therapeutic ultrasound transducer **214**, which is capable of resonating at, and transmitting, therapeutic ultrasound frequencies. Transducer **214** may comprise a single element or an array of elements. Transducer **214** is attached to an excitation unit (not shown) capable of causing resonance within the transducer. The excitation unit is preferably combined with the imaging system (not shown) of imaging element **170**.

[**0111**] Therapeutic ultrasound frequencies, at which therapeutic transducer **214** preferably is capable of resonating and transmitting, are typically described as low frequencies, for example, frequencies below 10,000,000 Hertz, or 10 Megahertz ("MHz"), and even more preferably frequencies below about 500,000 Hertz, or 500 Kilohertz ("kHz"). Conversely, transducer array **172** of imaging element **170** preferably is capable of resonating at, and transmitting, imaging ultrasound frequencies. Imaging ultrasound frequencies are typically described as high frequencies, for example, frequencies above about 10 Megahertz ("MHz"). These frequencies are provided only for the sake of illustration and should in no way be construed as limiting.

[**0112**] It is expected that, once vulnerable plaque has been identified in a patient's vessel via thermographer **160** and/or imaging element **170**, stabilization element **212** may be positioned at the location of the identified plaque and activated, i.e. ultrasound transducer **214** may provide therapeutic ultrasound waves, to stabilize the plaque, for example, by compressing, rupturing, and/or sealing the plaque in the controlled environment of a catheterization laboratory. As with apparatus **201**, the distances between stabilization element **212**, thermographer **160** and imaging element **170** are preferably provided or measured in order to facilitate vulnerable plaque identification, as well as positioning of stabilization element **212** prior to activation.

[**0113**] In addition to therapeutic ultrasound transducer **214**, stabilization element **212** may be provided with additional stabilization elements (not shown), for example, contrast, tissue-tag or therapeutic agents, such as drug capsules, that rupture and are released upon exposure to ultrasound waves generated by therapeutic ultrasound transducer **214**. Additional stabilization elements will be apparent to those of skill in the art. Apparatus **210** is expected to provide many of the benefits described hereinabove with respect to apparatus **150** and apparatus **201**.

[**0114**] As yet another embodiment of the present invention, apparatus may be provided in which imaging element **170** and stabilization element **212** of apparatus **210** are replaced with a single ultrasonic transducer array that is capable of transmitting multiple frequencies suited to both ultrasonic imaging and ultrasonic therapy, thereby providing both vulnerable plaque imaging and stabilization in a single element. Techniques for providing an ultrasound transducer capable of resonating at multiple frequencies are provided, for example, in U.S. Pat. No. 5,906,580 to Kline-Schoder et al., as well as U.S. Pat. No. 5,581,144 to Corl et al., both of which are incorporated herein by reference.

[**0115**] Referring to **FIG. 11A, a** sixth embodiment of the present invention is described. Apparatus **220** comprises functional measurement wire **221** and catheter **222** having imaging element **170**. Wire **221** preferably comprises a thermographer such as a thermocouple, thermistor, or fiber optic infrared thermographer, but may comprise other diagnostic devices to measure, for example, pressure, flow velocity, pH or tissue composition. Further alternatives may include a secondary imaging device that provides a more detailed view than IVUS imaging element **170**, such as an Optical Coherence Tomography apparatus, high frequency ultrasound transducer, Near Infrared Spectroscopy fiber optic, or Magnetic Resonance Imaging apparatus, or may comprise a stabilization device such as an ablation device, therapeutic ultrasound transducer, drug delivery device, therapeutic agent and the like for local delivery to vulnerable plaque P.

[**0116**] Catheter **222** further comprises bifurcated lumen **223** having proximal portion **224** that branches into distal portion **225** and bifurcated portion **226**. Proximal portion **224** extends to the proximal end of catheter **222**, while distal portion **225** extends through distal end **156**. Bifurcated portion **226** terminates at side port **227** disposed on a lateral face of catheter **222**. Adjacent the junction of proximal portion **224**, distal portion **225** and bifurcated portion **226**, uni-directional valve **228** is disposed within distal portion **225** to prevent advancement of thermographer wire **221** into distal portion **225** while permitting advancement of catheter **222** over guide wire **100**. Guide wire **100** is illustratively shown disposed within proximal portion **224** and distal portion **225**, whereas wire **221** traverses proximal portion **224** and bifurcated portion **226**.

[0117] Advantageously, bifurcated portion **226** may be curved to direct advancement of wire **221** so that distal working tip **229** of wire **221** may be advanced into the field of view of imaging element **170**, which is disposed distal to side exit port **227**. Similar to catheter **159** of **FIG. 6**B, this facilitates simultaneous acquisition, real-time viewing and association of both temperature and imaging data respectively obtained by functional measurement wire **221** and imaging element **170** at the same axial and/or angular positions within vessel V, thereby eliminating the need to correlate and couple the temperature and imaging data prior to display. This permits a medical practitioner to view a real-time, cross-sectional image of the vessel with the associated temperature data overlaid thereon in real time. Furthermore, using the real-time images provided by imaging element **170** as a visual guide, wire **221** may be advanced into the field of view of imaging element **170**, and a medical practitioner may steer working tip **229** to a particular location of interest within vessel V for data acquisition, for example by rotating catheter **222** and/or wire **221**.

[0118] In accordance with another aspect of the present invention, bifurcated portion **226** may be curved to direct disposition of working tip **229** of wire **221** in sensory proximity with (i.e., contacting or adjacent to) target vascular tissue that is suspected of harboring vulnerable plaque P. This is especially significant since a variety of working tips **229** may require contact or close proximity with the vessel wall to obtain accurate or useful measurements. Such working tips include, for example, thermocouples and Optical Coherence Tomography probes (which may be unable to visualize through blood). Furthermore, pursuant to fluid dynamics theory, blood flow velocity is slowest near the wall of vessel V. Thus, positioning working tip **229** at or near the wall is expected to reduce unwanted migration of the tip due to pressure applied to the tip by blood flowing through the vessel.

[0119] Alternatively, bifurcated portion **226** may be curved to direct advancement of wire **221** so that distal working tip **229** is disposed in an axial position immediately adjacent to the field of view of imaging element **170**, and a radial position in sensory proximity with target vascular tissue. This reduces potentially undesirable imaging artifacts, such as incorporation of wire **221** and distal working tip **229** within the acquired images, that may result from advancement of distal working tip **229** within the field of view of imaging element **170**. Advantageously, a medical practitioner may still simultaneously obtain both temperature and imaging data at substantially the same axial position within a patient's body lumen, thereby permitting real-time viewing, analysis and/or diagnosis.

[0120] It will be evident to one of ordinary skill in the art that apparatus **220** may comprise more than one curved, bifurcated portion **226**. Additional bifurcated portions may be provided and disposed to radiate from proximal portion **224**, distally terminating at side exit ports **227** circumferentially disposed on a lateral face of catheter **222** (see **FIG. 11B**). The additional bifurcated portions may direct advancement of distal working tips **229** of additional wires **221** into or immediately adjacent to the field of view of imaging element **170**. This permits a medical practitioner to simultaneously obtain full circumferential temperature and imaging profiles along the interior wall of a patient's body lumen.

[0121] Advantageously, apparatus **220** provides for optional advancement of functional measurement wire **221**, without requiring such advancement. Many patients may not have regions within their vasculature that are suspected of harboring vulnerable plaque. For these patients, the added time, expense, etc., of thermography or other data collection in conjunction with IVUS or other imaging modalities may not be justified. Apparatus **220** allows for optional use of functional measurement wire **221**, for example, only in patients suspected of harboring vulnerable plaque.

[0122] In accordance with yet another aspect of the present invention, functional measurement wire **221** may be proximally removed from apparatus **220** once temperature or other data has been obtained, and successively replaced with other diagnostic, secondary imaging, and/or stabilization devices, examples of which are provided above. This permits a medical practitioner to initially locate vulnerable plaque P by simultaneous temperature and visual confirmation, and then obtain additional data about and/or a more detailed image of the plaque, or provide localized delivery of stabilization devices, while simultaneously viewing the interior of the vasculature to direct advancement of wire **221** or the replacement device. In this manner, apparatus **220** may be used to perform successive, multi-functional applications without removal of catheter **222** from the vessel site of interest.

[0123] Alternatively, rather than having bifurcated lumen **223**, apparatus **230**, illustrated in **FIG. 11**C, may instead comprise catheter **231** having separate wire lumen **232** and guide wire lumen **233**. As with apparatus **220** of **FIG. 10**A, wire lumen **232** permits thermographer wire **221** to exit catheter **231** via side port **227** disposed on a lateral face of catheter **231**. Distal portion **234** of wire lumen **232** is curved to permit working tip **229** of steerable wire **221** to be advanced within or immediately adjacent to the field of view of imaging element **170** and disposed in sensory proximity with (i.e., contacting or adjacent to) target vascular tissue that is suspected of harboring vulnerable plaque P. Furthermore, as with apparatus **220** in **FIG. 11**B, apparatus **230** may comprise additional wire lumens **232** disposed within catheter **231** that terminate at side exit ports circumferentially disposed on the lateral face thereof. Again, this allows additional functional measurement wires to be used in simultaneous acquisition of full circumferential temperature and imaging profiles.

[0124] Referring to FIGS. 12A-12C, an alternative embodiment of apparatus **220** and apparatus **230** of **FIG. 11** is described. Apparatus **240** comprises functional measurement wire **241** and catheter **242** having IVUS imaging element **170**. Alternative imaging elements will be apparent. Wire **241** preferably comprises a thermographer, but also may comprise or be exchanged for other diagnostic, secondary imaging and/or stabilization devices.

[0125] Unlike apparatus **220** and apparatus **230** of **FIG. 11**, catheter **242** comprises either single lumen **243**, as seen in **FIG. 12**B, or separate lumens **244** and **245**, as seen in **FIG. 12**C, through which wire **241** may exit catheter **242** through distal end **246**, instead of through side port **227** of **FIG. 11**. If catheter **242** comprises lumen **243**, both functional measurement wire **241** and guide wire **100** may be advanced therethrough. If catheter **242** comprises separate lumens **244** and **245**, wire **241** and guide wire **100** may be advanced through their respective lumens.

[0126] Functional measurement wire **241** of FIGS. **12**A-C preferably comprises a shape memory alloy wire, e.g., a nickel titanium alloy. When wire **241** is extended from catheter **242**, it adopts an everted curved shape that disposes distal working tip **247** of wire **241** within the field of view of imaging element **170**, which is disposed proximally of distal end **246**. In this everted configuration, a medical practitioner may rotate thermographer wire **241** and/or catheter **242** so that distal working tip **247** is in sensory proximity with target tissue P to obtain temperature (or other) data, using real-time images provided by imaging element **170** for visual guidance.

[0127] Once temperature data has been collected, wire **241** is retracted back into the lumen of catheter **242**, thereby returning wire **241** to its non-everted shape. In the non-everted state, wire **241** may be removed from catheter **242** and optionally replaced with another diagnostic, secondary imaging, or stabilization device that also may be everted upon exiting distal end **246** to permit disposition of the distal working tip of the replacement device within the field of view of imaging element **170**.

[0128] With reference to **FIG. 12**D, in an alternative embodiment of apparatus **240** of **FIG. 12**A, guide wire **100** may be eliminated. In this case, wire **241** initially may be inserted into vessel V as a straight wire. After catheter **242** is advanced along wire **241** to a general vessel location of interest, wire **241** may be extended to adopt an everted shape that disposes distal working tip **247** of guide wire **241** within the field of view of imaging element **107**. Wire **241** optionally may be provided with a removable sheath (not shown) to maintain the wire in a straight configuration for use as a guide wire while catheter **242** is advanced thereover, at which time the sheath may be removed and wire **242** may resume its everted shape.

[0129] Catheter **242** then may be concurrently advanced with wire **241** in its everted shape along vessel V, using curve **248** of everted guide wire **241** as an atraumatic bumper. In this manner, a medical practitioner may be able to identify potential sites of vulnerable plaque P by simultaneously viewing both real-time imaging and temperature data respectively provided by imaging element **170** and wire **241** for the same axial and/or angular locations within vessel V.

[0130] As in preceding embodiments, wire **241** may adopt an everted curved shape that disposes distal working tip **247** of wire **241** immediately adjacent to the field of view of imaging element **170**. This eliminates potentially undesirable imaging artifacts within the acquired images, such as the incorporation of wire **241** and working tip **247**, and yet still permits a medical practitioner to simultaneously obtain both temperature and imaging data at substantially the same axial position along a patient's body lumen for real-time viewing, analysis, and/or diagnosis.

[0131] Referring now to **FIG. 13**A, another alternative embodiment of the present invention is described. Apparatus **250** comprises delivery sheath **252** that may be distally tapered to provide an atraumatic tip for advancement of apparatus **250** through a patient's body lumen. Delivery sheath **252** is translatably and coaxially disposed around catheter **254**. As will be apparent to those of skill in the art, delivery sheath **252** may comprise, for example, a standard guiding catheter.

[0132] Catheter **254** of apparatus **250** comprises thermographer **256** and imaging element **170** disposed proximal of atraumatic distal tip **257**. Catheter **254** further comprises catheter body **258** having guide wire lumen **260**, within which guide wire **100** is illustratively disposed.

[0133] Thermographer **256** comprises a plurality of thermocouples **262** circumferentially disposed around catheter **254**. Any number of thermocouples **262** may be provided. Each thermocouple **262** comprises self-expanding wire **264** proximally coupled to catheter body **258**. The proximal end of each wire **264** is further electrically coupled to a processor (not shown) that captures and translates voltages generated by each thermocouple **262** into temperature values, for example, via known calibration values for each thermocouple.

[0134] Imaging element **170** comprises phased-array ultrasound transducer **172** having a plurality of discrete ultrasound elements **173** circumferentially disposed about catheter body **258** proximal of atraumatic distal tip **257**. Imaging element **170** optionally may comprise multiplexing circuitry, flexible circuitry or substrates, amplifiers, etc., per se known, which may be disposed on and/or electrically coupled to apparatus **250**. Transducer array **172** of imaging element **170** is electrically coupled to an imaging system (not shown), per se known, that provides excitation waveforms to the transducer array, and interprets and displays data received from the array. The imaging system coupled to imaging element **170** and the processor coupled thermographer **256** are preferably combined into a single data acquisition and analysis system (not shown) for capturing and interpreting data received from apparatus **250**.

[0135] Each wire **264** is proximally affixed to catheter body **258** and is distally unfettered so that apparatus **250** may expand from the collapsed delivery configuration of **FIG. 13A** to the expanded deployed configuration of **FIG. 13B**. More specifically, when delivery sheath **252** is proximally retracted relative to catheter **254** (or catheter **254** is distally advanced with respect to delivery sheath **252**), thermocouples **262** radially self-expand away from distal tip **257** to contact the interior wall of a patient's body lumen, remaining in the field of view of imaging element **170**. In order to provide visual guidance during positioning of apparatus **250** at a stenosed region within the patient's body lumen in the delivery configuration, distal tip **257** and imaging element **170** of catheter **254** may be disposed partially protruding from the distal end of delivery sheath **252**.

[0136] Alternatively, wires **264** may be configured so that, in the deployed configuration, thermocouples **256** contact the interior wall of the patient's body lumen immediately adjacent to the field of view of imaging element **170**. This permits thermographer **256** and imaging element **170** to simultaneously obtain both temperature and imaging data at substantially the same axial position within the patient's body lumen without incorporating imaging artifacts within the acquired images.

[0137] Of course, it will be evident to one of ordinary skill in the art that the catheter embodiments of **FIGS. 6 and 9-13** also may be provided as rapid exchange type catheters similar in configuration to that of **FIGS. 2, 7** and **8**. Specifically, rather than having guide wire lumens that span the entire longitudinal length of the catheter, the catheters of embodiments of the present invention may comprise a guide wire lumen, such as guide wire lumen **194** of **FIG. 7**, that proximally terminates at a side port disposed on a lateral face of the catheter. This permits a medical practitioner to rapidly exchange the catheters of the present invention with other therapeutic or diagnostic catheters.

[0138] With reference to **FIG. 14, a** method of using apparatus of the present invention is provided, illustratively using apparatus **180** described hereinabove. In **FIG. 14**, vessel V is afflicted with eccentric vulnerable plaque P that manifests only mild stenosis within vessel V. Catheter **182** of apparatus **180** is percutaneously advanced into vessel V, for example, over guide wire **100**, such that imaging element **184** and thermographer **186** are disposed distally of distal edge x_0 of vulnerable plaque P, as seen in **FIG. 14A**. Drive cable **188** is rotated via its driver (not shown) such that imaging element **184** and thermographer **186** are provided with a full 360° view.

[0139] Catheter **182** is then withdrawn proximally across the stenosis until imaging element **184** and thermographer **186** are disposed proximally of proximal edge x_2 of vulnerable plaque P, as seen in **FIG. 14B**. Imaging and thermography data are collected via imaging element **184** and thermographer **186**, respectively, during proximal retraction of catheter body **182** across the stenosis. Proximal retraction may be achieved manually or using a pullback system. Pullback systems are described, for example, in U.S. Pat. No. 6,290,675 to Vujanic et al., U.S. Pat. No. 6,275,724 to Dickinson et al., U.S. Pat. No. 6,193,736 to Webler et al., and PCT Publication WO 99/12474, all of which are incorporated herein by reference.

[0140] As will be apparent to those of skill in the art, catheter **182** alternatively may be advanced distally across vulnerable plaque P during data acquisition, or catheter **182** may be held stationary at a location of interest, for example, location x_1 in the middle of vulnerable plaque P. Additionally, when vulnerable plaque P has been identified, apparatus **180** optionally may be provided with stabilization elements capable of compressing, rupturing, sealing, scaffolding and/or otherwise treating the plaque in the controlled environment of a catheterization laboratory. Exemplary stabilization elements include balloon **204** of apparatus **201**, and therapeutic ultrasound transducer **214** of apparatus **210**. Additional stabilization elements will be apparent to those of skill in the art.

[0141] With reference now to **FIG. 15**, in conjunction with **FIG. 14**, graphical user interfaces for displaying and interpreting imaging and thermography data, collected, for example, using the methods of **FIG. 14**, are described. **FIG. 15A** provides cross-sectional IVUS image **280** formed from imaging data obtained at location x_1 within the patient's vessel V. Image **280** is eccentric and comprises echolucent zone E, which is indicative of a shallow lipid pool. Both the eccentricity and echogenicity of image **280** are indicative of vulnerable plaque P, with increased risk of rupture, at location x_1 within vessel V.

[0142] **FIG. 15B** displays temperature measurements T as a function of position x. Graphing temperature as a function of position requires that the position of the thermographer be recorded. Such position indication may be achieved, for example, using a pullback system, such as those described hereinabove.

[0143] In **FIG. 15**B, temperature measurements are obtained and graphed along angular position Y of section line A-A in **FIG. 15A** during proximal retraction of catheter **182** within vessel V from distal edge x_0 to location x_1 to proximal edge x_2 of vulnerable plaque P. The reference temperature within vessel V at locations proximal and distal of vulnerable plaque P is approximately T_0. All temperatures may be provided on an absolute scale, as in **FIG. 15**B, or temperatures may be provided as a relative change in temperature with respect to reference temperature T_0. Alternatively, an ambient reference temperature within the vessel may be obtained, for example, via thermosensor **161** of apparatus **150** of **FIG. 6**A, and all temperatures may be provided as a relative change with respect to the measured ambient temperature.

[0144] As seen in graph **282**, as catheter **182** is proximally retracted across vulnerable plaque P, the temperature at the interior wall of vessel V along point Y rises from reference temperature T_0 to local maximum temperature T_1. Temperature T_1 is obtained at location x_1 within vessel V. The temperature within the vessel recedes back to reference temperature To while catheter body **182** is further retracted from location x_1 to proximal edge x_2 of vulnerable plaque P. The increase in temperature from reference temperature T_0 to temperature T_1 in the region surrounding location x_1 within the vessel may be as much as about 0.1° C. to over 2.0° C., and is typically at least 0.3° C. This range is provided only for the purpose of illustration and should in no way be construed as limiting.

[0145] The increase in temperature from T_0 to T_1 is indicative of vulnerable plaque susceptible to rupture. By comparing and correlating the thermographic data of graph **282** of **FIG. 15B** to IVUS image **280** of **FIG. 15**A, identification of vulnerable plaque P is corroborated and confirmed. Thus, providing both imaging and thermography simplifies vulnerable plaque identification while reducing a level of skill required on the part of a medical practitioner in order to properly diagnose such plaque.

[0146] In addition to graphing temperature measurements as a function of position, temperature measurements alternatively may be displayed as dynamic, individual measurements (not shown) obtained at the current position of the thermographer. As yet another alternative, temperature measurements may be displayed for an entire vessel cross-section (see **FIG. 16**), such as a cross-section of temperature measurements obtained at location x_1. Cross-sections of thermography and imaging data at a given position may be compared to provide rapid and proper identification of vulnerable plaque.

[0147] Referring now to **FIG. 16, a** graphical user interface for concurrently displaying both imaging and thermography data is described. In **FIG. 16**, imaging and thermography data are correlated and coupled prior to display, for example, using position indication techniques and/or a pullback system, such as an IVUS pullback system that is modified to simultaneously monitor the position of both the imaging element and the thermographer. Determination of the distance between imaging elements and thermographers on integrated catheters of the present invention is also expected to facilitate coupling. Optional stablization elements also may be monitored via position indication techniques and/or a pullback system. IVUS pullback systems are described hereinabove.

[0148] In **FIG. 16**, imaging and thermography data, are simultaneously displayed on separate scales in a graphical, overlaid fashion, for example, on a standard computer monitor. Graphical user interface **290** comprises imaging cross-section **292** and thermography cross-section **294**. Both imaging cross-section **292** and thermography cross-section **294** were obtained at location x_1 within vessel V. Imaging cross-section **292** is eccentric and contains echolucent zone E, which is indicative of a shallow lipid pool.

[0149] Thermography cross-section **294** is displayed with reference to temperature intensity scale S that ranges between T_0 and T_1. Scale S may be provided as a color shift, an intensity shift, or a combination thereof. Furthermore the line width along thermography cross-section **294** may be altered to indicate changes in temperature. Additionally, the range of scale S may be extended beyond T_0 and T_1, or may be displayed as a change in temperature ΔT from a reference background temperature, such as T_0. Additional scales S will be apparent to those of skill in the art and are included in the present invention. As can be seen in **FIG. 16**, the intensity of thermography cross-section **294**, and thus the temperature within vessel V, increases along eccentric echolucent zone E of imaging cross-section **292**, which is indicative of vulnerable plaque.

[0150] Overlaying imaging and thermography data on separate scales facilitates rapid correlation of the temperature at a given position within vessel V to the image obtained at that position. Rapid correlation is expected to simplify, expedite and increase the accuracy of vulnerable plaque identification. As will be apparent to those skilled in the art, as an alternative to providing temperature and imaging data on separate scales within the same graphical user interface, the imaging data may be color-coded (not shown) to indicate temperature. Additional data may also be obtained, coupled and provided in the graphical display, for example, elastography or palpography data (not shown). Palpographic techniques are described, for example, in U.S. Pat. No. 6,165,128 to Cespedes et al., which is incorporated herein by reference. Blood flow imaging may also be provided (not shown). Blood flow imaging is described, for example, in U.S. Pat. Nos. 5,453,575 and 5,921,931 to O'Donnell et al., both of which are incorporated herein by reference.

[0151] Referring now to **FIG. 17**, an alternative graphical user interface that simultaneously displays coupled imaging and thermography data is described. Graphical user interface **300** overlays imaging and thermography data in a manner similar to interface **290** of **FIG. 16**. However, interface **300** displays data obtained along side-sectional view line B-B of **FIG. 16** during retraction or advancement of apparatus of the present invention across vulnerable plaque P. Retraction or advancement across plaque P is preferably achieved using a modified IVUS pullback system, as described hereinabove.

[0152] Graphical user interface **300** comprises imaging side-section **302** and thermography side-section **304**. Imaging side-section **302** is eccentric and comprises echolucent zone E, which is most pronounced in the region around location x_1 within vessel V. Likewise, thermography side-section **304** is of greatest intensity in the region around echolucent zone E of imaging side-section **302**. Concurrent analysis of imaging side-section **302** and correlated thermography side-section **304** is expected to facilitate improved identification of vulnerable plaque. As with the cross-sectional view of graphical user interface **290** of **FIG. 16**, image side-section **302** may alternatively be color-coded to indicate temperature (not shown). Furthermore, additional information, for example, palpography information or blood flow information, may be provided within the side-sectional view of graphical user interface **300**, in order to further facilitate plaque identification. The additional data, e.g. the palpography data or the blood flow data, is preferably obtained concurrently with imaging data, for example, via the imaging element.

[0153] As will be apparent to those of skill in the art, as an alternative to presenting imaging and thermographic data as side-sections and/or cross-sections, such data may be provided as partial or complete 3-dimensional reconstructions (not shown).

[0154] In accordance with another aspect of the present invention, temperature measurements (as well as imaging intensity or echogenicity, etc.) alternatively may be displayed on a 3-dimensional graph as a function of both axial vessel position and angular position. For example, **FIG. 19** illustratively provides 3-dimensional graph **310** having coordinate axes that correspond to temperature T, axial position x and angular position θ. Graph **310** illustratively provides temperature data that may be obtained by any of the embodiments of the present invention, for example, by catheter **182** of **FIG. 14** when catheter **182** is retracted and rotated in the manner described above within vessel V of **FIG. 18**. In particular, graph **310** provides illustrative temperature measurements along the vessel wall as a function of axial position x and angular position θ, approximately bounded by an area coincident with vulnerable plaque P. This area approximately is limited within the angular measurements θ_0 to θ_2, and axial positions x_1 to x_2. Clearly, an entire 360° angular view alternatively may be provided. The reference temperature within vessel V at locations peripheral to and outside of this area is approximately T_0. All temperatures may be provided as a relative change in temperature with respect to reference temperature T_0, or temperatures may be provided on an absolute scale, as in **FIG. 19**.

[0155] As seen in graph **310**, as catheter **182** is rotated and/or retracted across vulnerable plaque P, the temperature at the interior wall of vessel V increases from reference temperature T_0 to local maximum temperature T_1. The temperature within vessel V recedes back to reference temperature T_0 as catheter **182** is rotated and/or retracted past vulnerable plaque P.

[0156] In accordance with another aspect of the present invention, graph **310** may be interactive, allowing a medical practitioner to examine areas of interest, such as a local maximum or minimum, in greater detail by selecting indicia along the coordinate axes. For example, if angular position θ_1 is selected, a graphical user interface then may provide a 2-dimensional graph, such as graph **282** of **FIG. 15**B, of temperature measurements along the vessel wall at angular position **91**. Alternatively, selection of angular position θ_1 may provide a side-sectional view of vessel V with thermography data overlaid thereon, such as graphical user interface **300** of **FIG. 17**.

[0157] Likewise, upon selection of a specific axial position, a 2-dimensional graph of temperature along the vessel wall as a function of angular position θ may be provided at that specific axial position. For example, if axial position x_1

is selected on graph **310** of **FIG. 19**, graph **320** of **FIG. 20** may be provided. As may be seen from graph **320**, the temperature at the vessel wall at angular positions less than θ_0 and greater than θ_2 approximately equal reference temperature T_0, whereas the temperature at angular positions between θ_0 and θ_2 are approximately equivalent to local maximum temperature T_1. The higher temperature of the vessel between θ_0 and θ_2 is indicative of the presence of vulnerable plaque P with an increased risk of rupture. Alternatively, instead of graph **320**, selection of axial position x_1 may display a cross-sectional view of vessel V at axial position x_1 with the temperature data overlaid thereon, as illustrated in graphical user interface **290** of **FIG. 16**.

[0158] The user also may elect to obtain more detailed information about a specific temperature value. For example, selection of temperature T_1 on graph **310** of **FIG. 19** would provide a 2-dimensional graph, chart or table of the angular positions θ and axial positions x at which the temperature measured at the vessel wall equaled temperature T_1. The apparatus of the present invention then may be advanced to those identified positions for additional investigation.

[0159] Of course, one of ordinary skill in the art will recognize that, while the graphs and graphical user interfaces of FIGS. **15-20** display temperature measurements, other vessel parameters VP also may be displayed without departing from the present invention. As discussed previously, stiffness, strain and elasticity information may be obtained from elastography or palpography measurements. These parameters, along with blood flow imaging, pressure, pH and flow velocity, also may be displayed individually or simultaneously with combinations thereof. If these parameters are simultaneously displayed, the different datasets may be displayed in an overlaid fashion or as independent datasets. These vessel parameters are provided for illustrative purposes only and should in no way be construed as limiting.

[0160] In accordance with yet another aspect of the present invention, measurements of vessel parameter VP (e.g., temperature, strain, pressure and pH) may be provided as an average summation value along a cross-section or side-section of vessel V. Average summation values may be used in rapid bulk testing to narrow the region(s) within vessel V that require additional analysis. Mathematically, the average summation of vessel parameter VP may be computed, for example, as follows:

$$VP_{avg} = \left(\sum_{i=1}^{i=n} VP_i\right) \Big/ n \qquad \text{EQ. 1}$$

[0161] wherein VP is the vessel parameter of interest, such as temperature; n is the number of VP measurements taken along a given region of interest, such as a side-section or cross-section of vessel V; and i is the specific measurement of VP being examined.

[0162] As one of ordinary skill in the art will recognize, n will depend on the frequency of data acquisition, the number of imaging transducers or elements within an imaging transducer, the number of thermographers, etc., disposed within the apparatus of the present invention.

[0163] The value VP_{avg} may be displayed in a variety of ways, such as a numerical display, a color/intensity coded value in which the color/intensity is representative of the magnitude of the value and/or as an audio frequency in which the frequency increases with increasing magnitude of the value.

[0164] When VP_{avg} is calculated for multiple cross-sections or side-sections, a 2-dimensional graph may be presented in which the multiple VP_{avg} values are respectively displayed as a function of axial or angular position within vessel V.

[0165] To further facilitate rapid bulk testing, a number of methods may be used to accentuate atypical shifts or deviations in VP_{avg} values, which may be indicative of the presence of vulnerable plaque susceptible to rupture. A first method comprises raising each individual measurement of vessel parameter VP to a power, e.g., squared. The resultant average summation value may be calculated as follows:

$$VP_{shift\ indicator\ avg} = \left(\sum_{i=1}^{n} (VP_i)^2\right) \Big/ n \qquad \text{EQ. 2}$$

[0166] Alternatively, shifts in VP_{avg} values may be accentuated by multiplying each individual measurement of vessel parameter VP by a scaling factor C:

$$VP_{scaled\ avg} = \left(\sum_{i=1}^{i=n} C(VP_i)\right) \Big/ n \qquad \text{EQ. 3}$$

[0167] Yet another alternative method to accentuate shifts in VP_{avg} values subtracts out a normal value VP_{normal} from each individual measurement of vessel parameter VP as follows:

$$VP_{normalized\ avg} = \left(\sum_{i=1}^{i=n} (VP_i - VP_{normal})\right) \Big/ n \qquad \text{EQ. 4}$$

[0168] An illustrative value for VP_{normal} may comprise a reference value of vessel parameter VP, such as T_0 for temperature. When $VP_{normalized\_avg}$ is greater or less than zero, the cross-section or side-section corresponding to that $VP_{normalized\ avg}$ value may require additional examination.

[0169] Shifts in VP_{avg} may be further accentuated by raising the difference between each individual value of vessel parameter VP and VP_{normal} to a power, e.g., squared, as follows:

$$VP_{normalized\ shift\ indicator\ avg} = \left(\sum_{i=1}^{i=n} (VP_i - VP_{normal})^2\right) \Big/ n \qquad \text{EQ. 5}$$

[0170] An alternative method to further accentuate shifts in VP_{avg} comprises multiplying the difference between each individual value of vessel parameter VP and VP_{normal} by scaling factor C as follows:

$$VP_{normalized\ scaled\ avg}=\left[\sum_{i=1}^{i=n}(VP_i-VP_{normal})\right]\Big/n \qquad \text{EQ. 6}$$

[0171] As discussed with reference to EQ. 1, average summation values calculated using EQS. 2-6 may be provided as a numerical display, a color/intensity coded value, or an audio frequency.

[0172] It also may be desirable to examine vessel parameter VP in a third dimension. Gradients may be calculated to detect rapid changes in the average summation values VP_{avg} between successive cross-sections or side-sections of vessel V. Large gradients may be indicative of areas within vessel V that require additional examination or the presence of vulnerable plaque P susceptible to rupture. To determine the change in average summation values VP_{avg} between successive cross-sections or side-sections of vessel V, the following calculation may be made:

$$\nabla(VP_{avg})=VP_{avg,p+1}-VP_{avg,p} \qquad \text{EQ. 7}$$

[0173] wherein p, the specific measurement of VP_{avg} being examined, ranges from 1 to m, wherein m is the number of cross-sections or side-sections for which VP_{avg} has been calculated along the length or angular section of vessel V that is of interest.

[0174] To display the gradients computed with EQ. 7, $\nabla(VP_{avg})$ may be graphed as a function of axial position x if values of $\nabla(VP_{avg})$ are calculated for successive cross-sections of vessel V, or as a function of angular position θ if values of $\nabla(VP_{avg})$ are calculated for successive side-sections of vessel V.

[0175] Graph **330** of **FIG. 21** illustrates EQ. 7, wherein temperature T is used as vessel parameter VP. Axial positions x_0-x_3 correspond to the same axial positions denoted in **FIG. 18**. Specifically, axial positions x_0 and x_2 respectively represent the distal and proximal ends of vulnerable plaque P, x_1 represents an axial location in the middle of vulnerable plaque P, and x_3 represents an axial position proximal to vulnerable plaque P. As discussed previously, the temperature at axial positions x_0, x_2 and X_3 are approximately equal to reference temperature T_0, whereas the temperature at axial position x_1 approximately equals elevated temperature T_1. Accordingly, T_{avg} of the cross-sections of vessel V that correspond to axial positions x_o, x_2 and x_3 would equal T_0, while T_{avg} of the cross-section at axial position x_1 (i.e., $(T_{avg})_{x=x1}$) would be greater than T_0. When EQ. 7 is applied to each axial position, illustrative results of which are shown on graph **330** of **FIG. 21**, gradient shifts **331** and **332** are noticeable between axial positions x_0 and x_2. In addition to visual confirmation from images provided by imaging element **184**, shifts **331** and **332** may be indicative and may provide notice of the presence of vulnerable plaque P in vessel V with increased risk of rupture.

[0176] As in EQ. 1, an average gradient value for $\nabla(VP_{avg})$ may be calculated for the length or angle of interest as follows:

$$\nabla(VP_{avg})_{avg}=\left[\sum_{p=1}^{p=m}(VP_{avg,p+1}-VP_{avg,p})\right]\Big/m \qquad \text{EQ. 8}$$

[0177] Furthermore, as in EQS. 2 and 5, shifts in gradients $\nabla(VP_{avg})$, such as shifts **331** and **332** of **FIG. 21**, may be accentuated by raising each gradient to a power, e.g., squared, as follows:

$$\nabla(VP_{avg})_{shift\ indicator}=(VP_{avg,p+1}-VP_{avg,p})^2 \qquad \text{EQ. 9}$$

[0178] Likewise, as in EQS. 3 and 6, shifts in gradients $\nabla(VP_{avg})$ also may be accentuated by multiplying each gradient by scaling factor C as follows:

$$\nabla(VP_{avg})_{scaled}=C(VP_{avg,p+1}VP_{avg,p}) \qquad \text{EQ. 10}$$

[0179] As discussed in reference to EQ. 7, the gradients calculated by EQS. 9 and 10 may be displayed on a 2-dimensional graph as a function of axial position x or angular position θ.

[0180] Of course, one of ordinary skill in the art will recognize that $\nabla(VP_{avg})_{shift\ indicator}$ of EQ. 9 and $\nabla(VP_{avg})_{scaled}$ of EQ. 10 may be averaged over a length or angle of vessel segment that is of interest to facilitate rapid determination of whether that vessel segment requires further examination. To calculate $\nabla(VP_{avg})_{shift\ indicator\ avg}$ or $\nabla(VP_{avg})_{scaled\ avg}$, EQ. 8 may be used in which $\nabla(VP_{avg})$ is replaced with $\nabla(VP_{avg})_{shift\ indicator}$ or $\nabla(VP_{avg})_{scaled}$, respectively.

[0181] It is also noted that the equations given above may be modified for use with individual measurements of vessel parameter VP. Specifically, to accentuate shifts in measurements of vessel parameter VP, and thereby facilitate rapid bulk testing, each measurement value may be raised to a power (e.g., squared), multiplied by scaling factor C, added to normal value $-VP_{normal}$, or modified by combinations thereof as follows:

$$VP_{shift\ indicator}=VP^2 \qquad \text{EQ. 11}$$

$$VP_{normalized}=VP-VP_{normal} \qquad \text{EQ. 12}$$

$$VP_{normalized\ shift\ indicator}=(VP-VP_{normal})^2 \quad \text{EQ. 13}$$

$$VP_{scaled}=C(VP) \qquad \text{EQ. 14}$$

[0182] The resultant modified vessel parameter may be displayed as a numerical display, a color/intensity coded value, and/or an audio frequency.

[0183] Gradients also may be calculated for a particular axial or angular section of interest by calculating the difference in successive values obtained for vessel parameter VP, as follows

$$\nabla VP=VP_{q+1}-VP_q \qquad \text{EQ. 15}$$

[0184] wherein q ranges from 1 to s, s being the number of measurements of vessel parameter VP that have been obtained at a particular axial or angular section of vessel V that is of interest. Furthermore, shifts in gradient values calculated using EQ. 15 may be accentuated to facilitate rapid bulk testing by using EQS. 11 and 14, wherein vessel parameter VP may be replaced by ∇VP. These gradients may be displayed in a 2-dimensional graph as a function of axial position x or angular position θ.

[0185] Furthermore, rapid bulk testing may further be facilitated if average summation values are provided for the above described gradients. Specifically, the following calculations may be made and displayed as a numerical display, a color/intensity coded value, or a radio frequency:

$$(\nabla VP)_{avg} = \left(\sum_{q=1}^{s} (VP_{q+1} - VP_q)\right) \Big/ s \tag{EQ. 16}$$

$$(\nabla VP)_{shift\ indicator\ avg} = \left(\sum_{q=1}^{s} (VP_{q+1} - VP_q)^2\right) \Big/ s \tag{EQ. 17}$$

$$(\nabla VP)_{scaled\ avg} = \left(\sum_{q=1}^{s} C(VP_{q+1} - VP_q)\right) \Big/ s \tag{EQ. 18}$$

[0186] It will be obvious to one of ordinary skill in the art that the above discussed values also may be determined as a function of radial dimension r. Likewise, the equations also may be applied to spherical and Cartesian coordinates, as well as any other coordinate system.

[0187] While preferred illustrative embodiments of the present invention are described hereinabove, it will be apparent to those of skill in the art that various changes and modifications may be made therein without departing from the invention. For example, the specific structure of the imaging elements, thermographers, and stabilization elements of the embodiments of FIGS. **6-11**, are provided only for the sake of illustration. Contemplated imaging elements include, but are not limited to, ultrasound transducers, linear-array ultrasound transducers, phased-array ultrasound transducers, rotational ultrasound transducers, forward-looking ultrasound transducers, radial-looking ultrasound transducers, magnetic resonance imaging apparatus, angiography apparatus, optical coherence tomography apparatus, and combinations thereof. Contemplated thermographers include, but are not limited to, thermocouples, thermosensors, thermistors, thermometers, spectrography devices, infrared thermographers, fiber optic infrared thermographers, ultrasound-based thermographers, spectroscopy devices, near infrared spectroscopy devices, and combinations thereof.

[0188] Contemplated stabilization elements include, but are not limited to, balloons, stents, coated stents, covered stents, stent grafts, eluting stents, drug-eluting stents, magnetic resonance stents, anastamosis devices, ablation devices, photonic ablation devices, laser ablation devices, RF ablation devices, ultrasound ablation devices, therapeutic ultrasound transducers, sonotherapy elements, coronary bypass devices, myocardial regeneration devices, sonotherapy devices, drug delivery devices, gene therapy devices, atherectomy devices, heating devices, localized heating devices, devices for heating in a range between about 38-44 degrees Celsius, cell apoptosis-inducing apparatus, growth factors, cytokines, plaque rupture devices, secondary-substance modifiers, therapeutic agents, contrast agents, drug capsules, tissue-type tags, extreme lipid lowering agents, cholesterol acyltransferase inhibitors, matrix metalloproteinase inhibitors, anti-inflammatory agents, antioxidants, angiotensin-converting enzyme inhibitors, radiation elements, brachytherapy elements, local drug injection elements, gene therapy elements, photodynamic therapy elements, photoangioplasty elements, cryotherapy elements, and combinations thereof. Additional imaging elements, thermographers, and optional stabilization elements will be apparent to those of skill in the art. The appended claims are-intended to cover all combinations of imaging elements, thermographers, and, optionally, stabilization elements that fall within the true spirit and scope of the present invention.

[0189] Furthermore, apparatus of the present invention may optionally be provided with an embolic protection device, such as distally-located expandable basket filter **335** of **FIG. 9**. Alternatively, embolic protection may be achieved with a proximally-located suction device. Embolic protection may be provided in order to capture emboli and/or other material released, for example, during stabilization of vulnerable plaque. Embolic protection devices are described, for example, in U.S. Pat. No. 6,348,062 to Hopkins et al., and U.S. Pat. No. 6,295,989 to Connors, III, both of which are incorporated herein by reference. Additional embolic protection devices, per se known, will be apparent to those of skill in the art. The appended claims are intended to cover all such changes and modifications that fall within the true spirit and scope of the invention.

What is claimed is:

1. A method for identifying vulnerable plaque within a body lumen of a patient, the method comprising:

providing apparatus comprising a catheter having a longitudinal axis, a phased-array IVUS imaging system, and a thermographer;

percutaneously advancing the catheter to a target region within the patient's body lumen;

disposing the thermographer within or immediately adjacent a field of view of the phased-array IVUS imaging system;

obtaining an image of the target region with the phased-array IVUS imaging system;

obtaining temperature data at the target region with the thermographer; and

assessing whether the target region includes vulnerable plaque by correlating the image and the temperature data obtained at the target region.

2. The method of claim 1, wherein disposing the thermographer further comprises removably advancing the thermographer through the catheter.

3. The method of claim 1, wherein providing apparatus comprising a thermographer further comprises providing a thermographer having a delivery configuration and a deployed configuration, the method further comprising deploying the thermographer from the delivery configuration to the deployed configuration.

4. The method of claim 1, wherein providing apparatus comprising a catheter further comprises providing a catheter having a lumen, the method further comprising advancing the thermographer through the lumen in a non-parallel direction to the longitudinal axis of the catheter.

5. The method of claim 1, further comprising reversibly disposing the thermographer in an everted configuration.

6. The method of claim 1, wherein assessing whether the target region includes vulnerable plaque further comprises simultaneously displaying the image and the temperature data.

7. The method of claim 1, wherein assessing whether the target region includes vulnerable plaque further comprises displaying the image and the temperature data in real-time.

8. The method of claim 1, wherein providing apparatus further comprises providing a stabilization element, the method further comprising stabilizing the vulnerable plaque with the stabilization element.

9. The method of claim 8, wherein stabilizing the vulnerable plaque further comprises removing the thermographer and advancing the stabilization element through the catheter.

10. A method for identifying vulnerable plaque within a body lumen of a patient, the method comprising:

providing apparatus comprising a catheter having a longitudinal axis, a lumen and an imaging element;

percutaneously advancing the catheter to a target region within the patient's body lumen;

obtaining an image of the target region with the imaging element;

removably advancing a thermographer through the lumen;

obtaining temperature data at the target region with the thermographer; and

assessing whether the target region includes vulnerable plaque by correlating the image and the temperature data obtained at the target region.

11. The method of claim 10, wherein removably advancing a thermographer further comprises removably advancing a thermographer within or immediately adjacent to a field of view of the imaging element.

12. The method of claim 10, wherein removably advancing a thermographer further comprises advancing the thermographer through the lumen in a non-parallel direction to the longitudinal axis of the catheter.

13. The method of claim 10, further comprising reversibly disposing the thermographer in an everted configuration.

14. The method of claim 10, wherein assessing whether the target region includes vulnerable plaque further comprises simultaneously displaying the image and the temperature data.

15. The method of claim 10, wherein assessing whether the target region includes vulnerable plaque further comprises displaying the image and the temperature data in real-time.

16. The method of claim 10, wherein providing apparatus further comprises providing a stabilization element, the method further comprising stabilizing the vulnerable plaque with the stabilization element.

17. The method of claim 16, wherein stabilizing the vulnerable plaque further comprises removing the thermographer and advancing the stabilization element through the lumen.

18. A method for identifying vulnerable plaque within a body lumen of a patient, the method comprising:

providing apparatus comprising a catheter having a longitudinal axis, an imaging element and a thermographer having a delivery configuration and a deployed configuration;

percutaneously advancing the catheter to a target region within the patient's body lumen;

obtaining an image of the target region with the imaging element;

disposing the thermographer in overlapping relationship with the imaging element along the longitudinal axis of the catheter when the thermographer is in the deployed configuration;

obtaining temperature data at the target region with the thermographer; and

assessing whether the target region includes vulnerable plaque by correlating the image and the temperature data obtained at the target region.

19. The method of claim 18, further comprising removably advancing the thermographer through the catheter.

20. The method of claim 18, wherein providing apparatus comprising a catheter further comprises providing a catheter having a lumen, the method further comprising advancing the thermographer through the lumen in a non-parallel direction to the longitudinal axis of the catheter.

21. The method of claim 18, further comprising reversibly disposing the thermographer in an everted configuration.

22. The method of claim 18, wherein assessing whether the target region includes vulnerable plaque further comprises simultaneously displaying the image and the temperature data.

23. The method of claim 18, wherein assessing whether the target region includes vulnerable plaque further comprises displaying the image and the temperature data in real-time.

24. The method of claim 18, wherein providing apparatus further comprises providing a stabilization element, the method further comprising stabilizing the vulnerable plaque with the stabilization element.

25. The method of claim 24, wherein stabilizing the vulnerable plaque comprises removing the thermographer and advancing the stabilization element through the catheter.

* * * * *

patsnap

专利名称(译)	用于识别和稳定易损斑块的方法和设备		
公开(公告)号	US20030199767A1	公开(公告)日	2003-10-23
申请号	US10/232428	申请日	2002-08-28
[标]申请(专利权)人(译)	CESPEDES EDUARDO IGNACIO MICHLITSCH KENNETHĴ		
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IPC分类号	A61B1/24 A61B5/00 A61B8/06 A61B8/12 A61B5/05 A61B6/00		
CPC分类号	A61B1/00082 A61B1/24 A61B5/0088 A61B5/01 A61B8/12 A61B5/6853 A61B5/6858 A61B5/6859 A61B8/06 A61B5/02007 A61B5/7425		
外部链接	Espacenet USPTO		

摘要(译)

本发明提供了用于通过具有热成像和成像能力的多功能导管识别和稳定易损斑块的方法和装置。预计相关的成像和热成像数据将有助于改善脆弱斑块的识别。本发明的装置还可以设置有可选的稳定元件，用于稳定易损斑块，以及可选的栓塞保护。提供了使用本发明的装置的方法。