US007727153B2

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Fritz et al.

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(45) **Date of Patent: Jun. 1, 2010**

(54) **ULTRASONIC BLOOD VESSEL MEASUREMENT APPARATUS AND METHOD**

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(73) Assignee: **SonoSite, Inc.**, Bothell, WA (US)

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 821 days.

(21) Appl. No.: **10/975,616**

(22) Filed: **Oct. 28, 2004**

(65) **Prior Publication Data**

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Related U.S. Application Data

(63) Continuation-in-part of application No. 10/682,699, filed on Oct. 9, 2003, now Pat. No. 6,835,177, which is a continuation-in-part of application No. 10/407,682, filed on Apr. 7, 2003, now Pat. No. 6,817,982.

(51) **Int. Cl.**
A61B 5/06 (2006.01)

(52) **U.S. Cl.** **600/449**; 600/407; 600/410; 600/425; 600/431; 600/437; 600/473; 600/476; 382/128; 382/130; 382/131; 382/168; 382/286

(58) **Field of Classification Search** 600/407, 600/408, 410, 425, 431, 436, 473, 476, 479, 600/437, 438, 442, 443, 462; 382/128, 130–131, 382/168–172, 286–288
See application file for complete search history.

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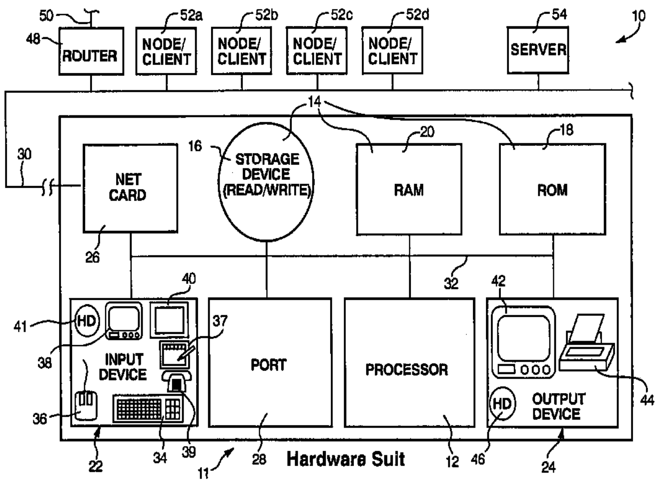
Primary Examiner—Brian Casler
Assistant Examiner—James Kish
(74) *Attorney, Agent, or Firm*—Fulbright & Jaworski L.L.P.

(57) **ABSTRACT**

Disclosed are systems and methods for identifying various tissue structure aspects, such as boundaries of arterial walls, within an image, such as an ultrasound image. Various measurements may be made using information with respect to the identified aspects of tissue structure. For example, intima-media thickness measurements may be made. Additionally or alternatively, tissue structure aspects, such as plaque within an artery, may be characterized, such as by determining a density thereof. Various information, such as measurement datums, used in identification of aspects of tissue structure in one image may be stored and applied to subsequent images, such as images of a video sequence.

66 Claims, 29 Drawing Sheets



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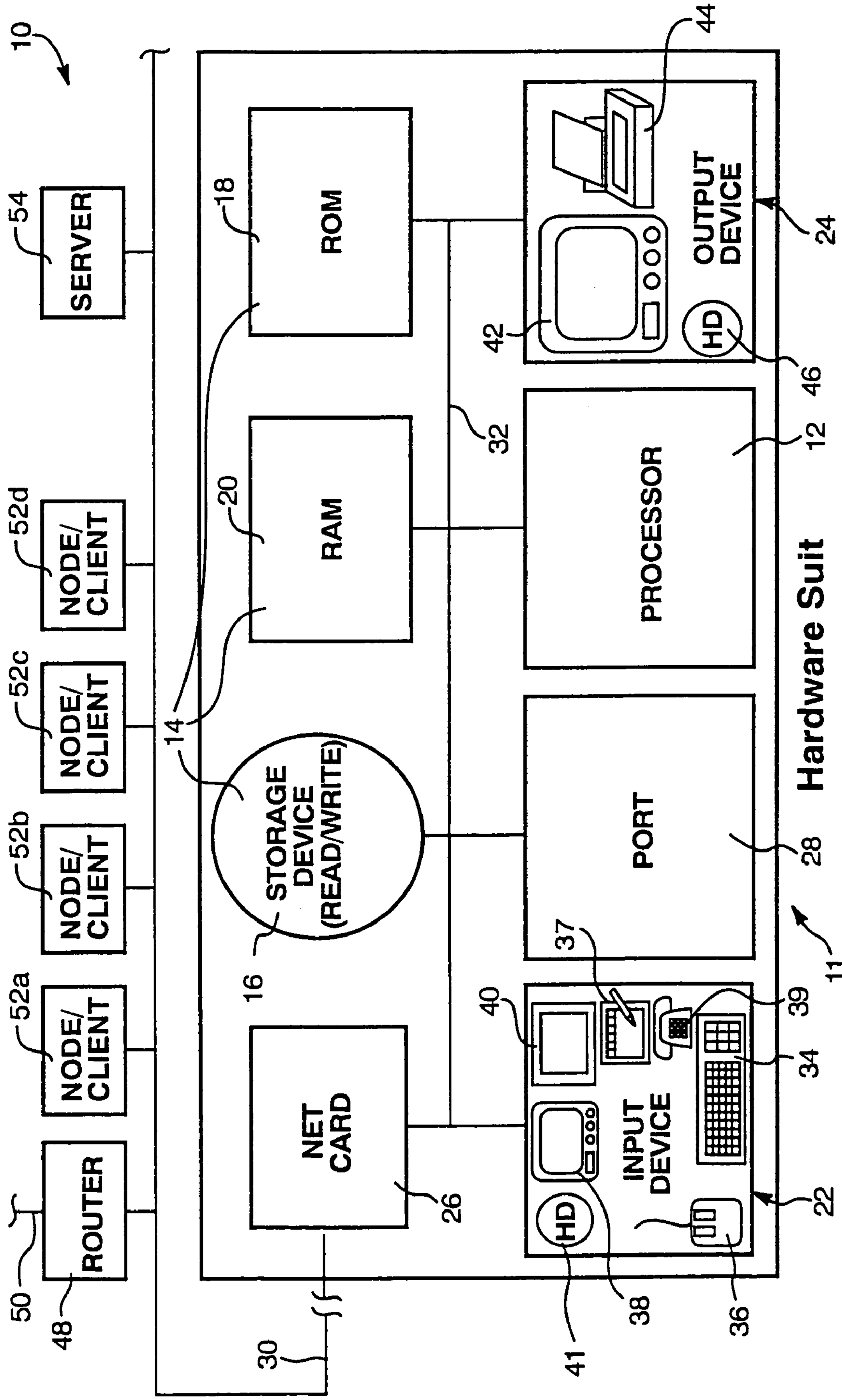


Hardware Suit

FIG. 1

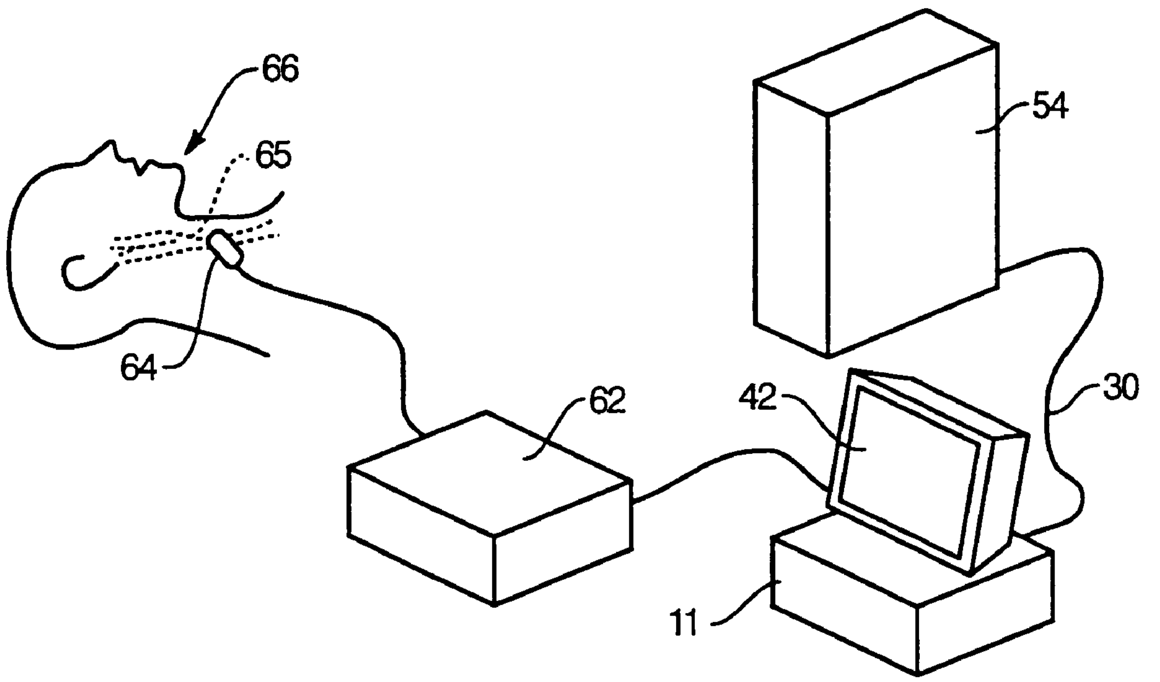


FIG. 2

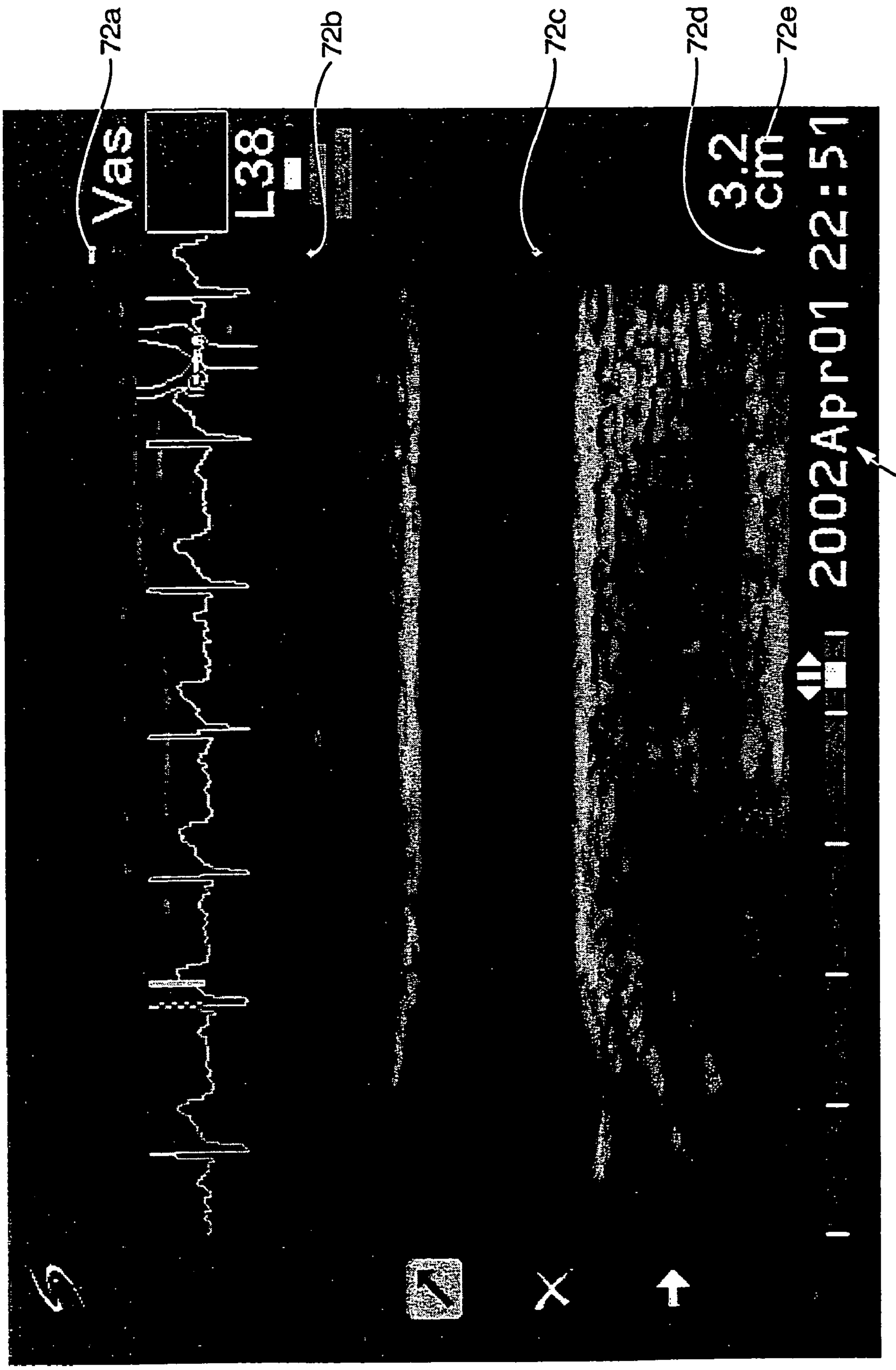


FIG. 3

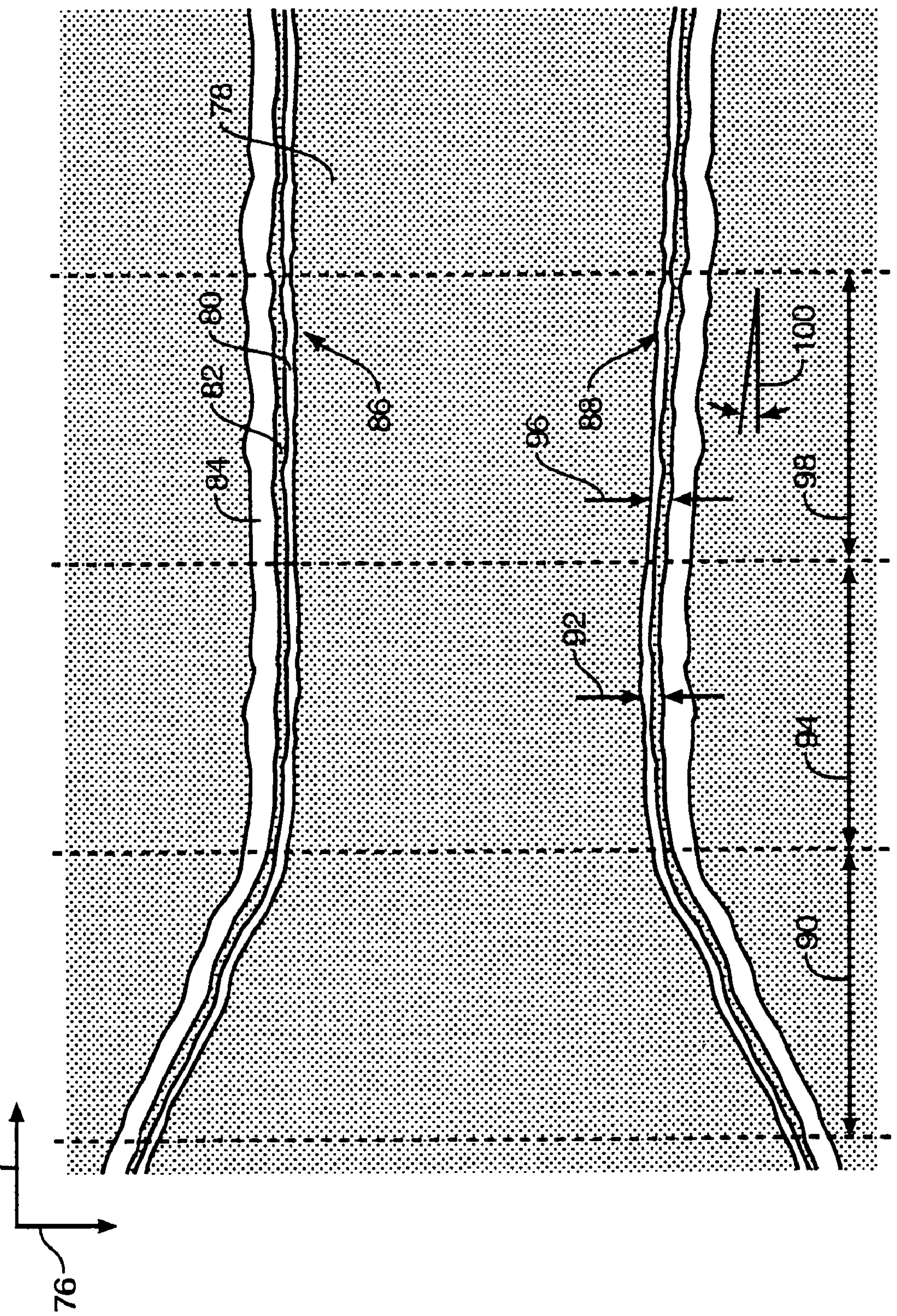


FIG. 4

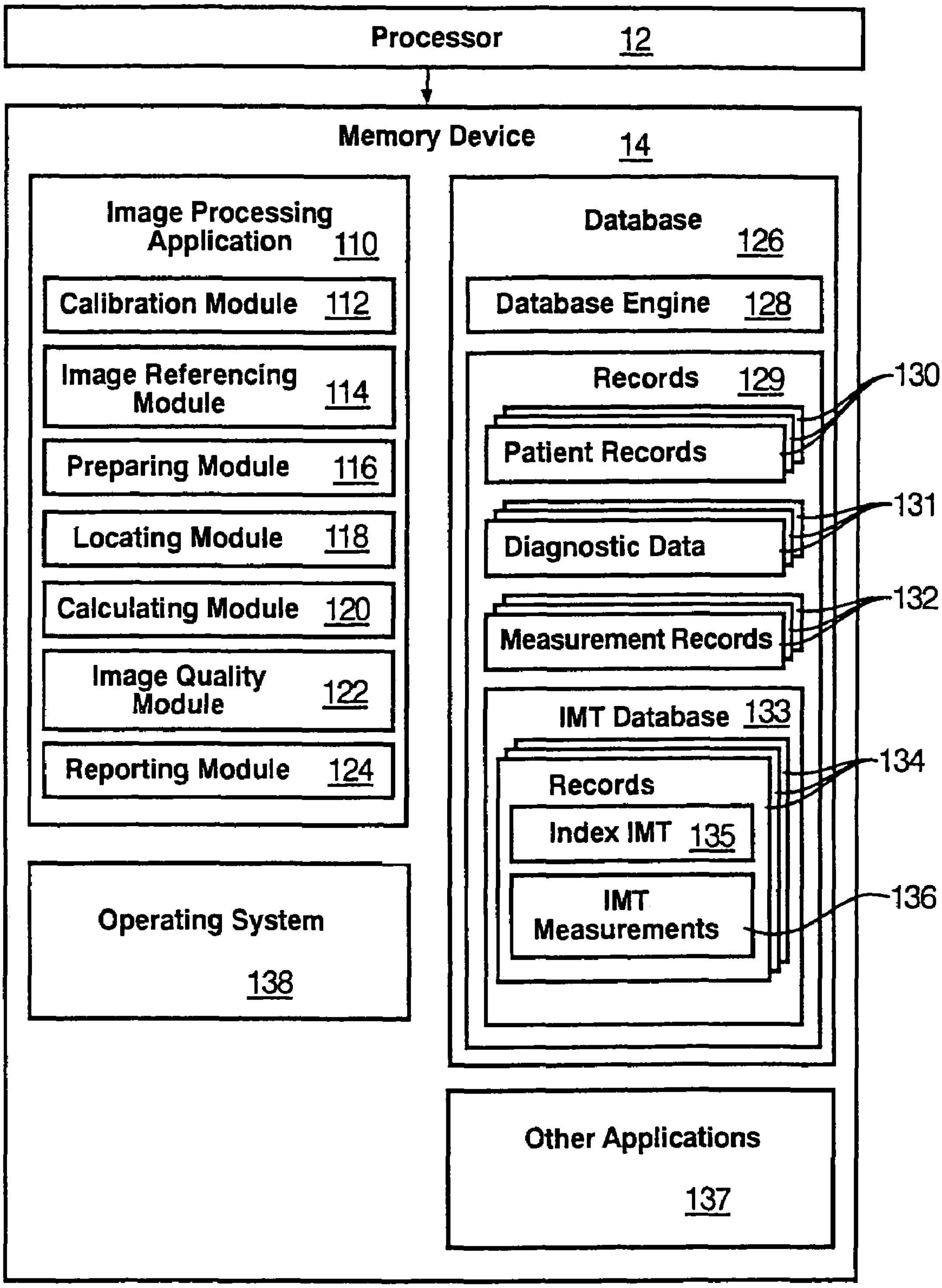

Processor 12
Memory Device 14
Image Processing Application 110
Calibration Module 112
Image Referencing Module 114
Preparing Module 116
Locating Module 118
Calculating Module 120
Image Quality Module 122
Reporting Module 124
Operating System 138
Database 126
Database Engine 128
Records 129
130
Patient Records
131
Diagnostic Data
132
Measurement Records
IMT Database 133
134
Records
Index IMT 135
136
IMT Measurements
Other Applications 137

FIG. 5

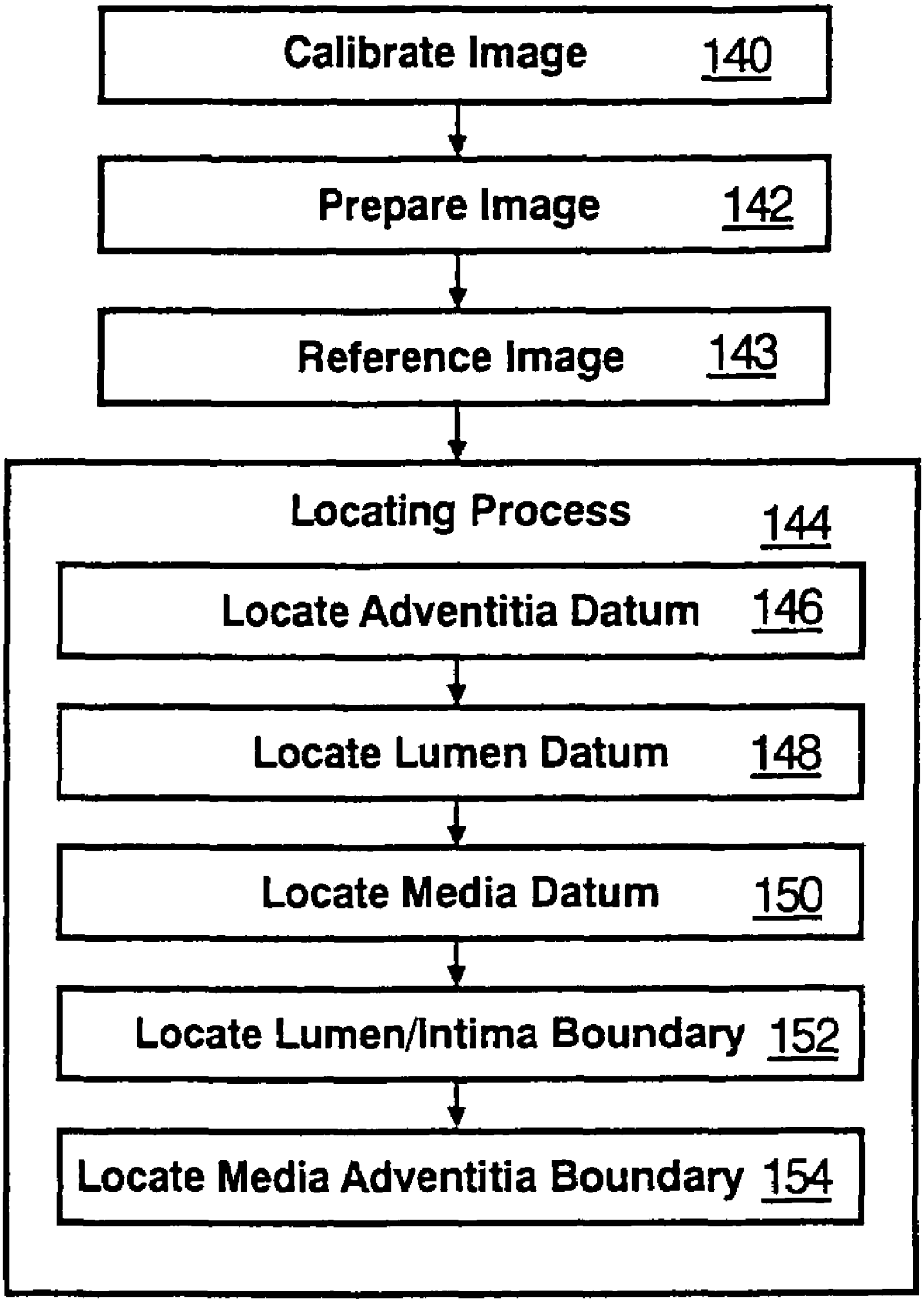

Calibrate Image 140
Prepare Image 142
Reference Image 143
Locating Process 144
Locate Adventitia Datum 146
Locate Lumen Datum 148
Locate Media Datum 150
Locate Lumen/Intima Boundary 152
Locate Media Adventitia Boundary 154

FIG. 6

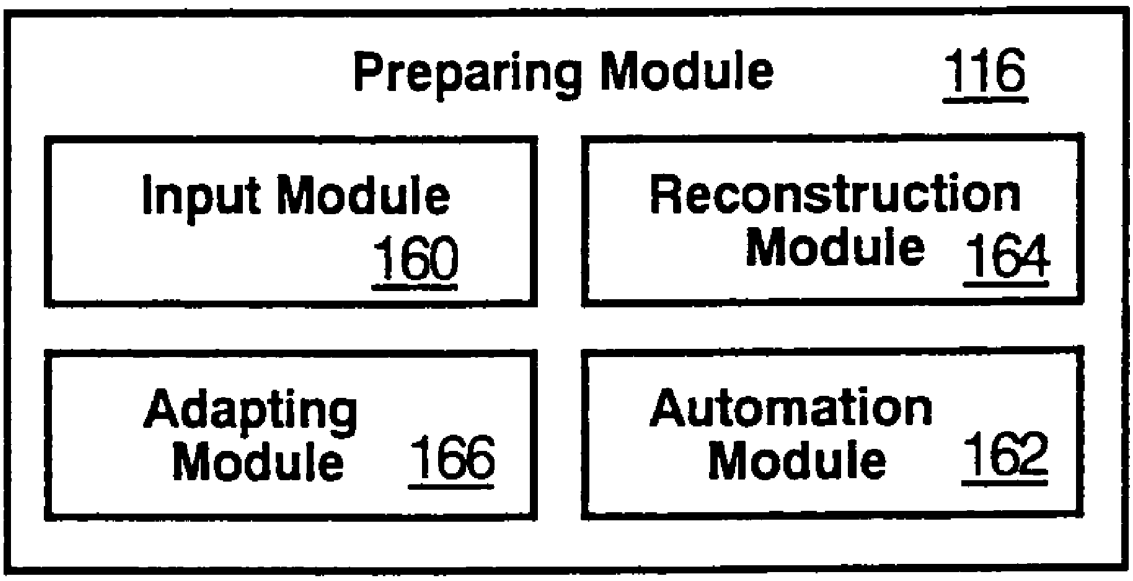

Preparing Module 116
Input Module 160
Reconstruction Module 164
Adapting Module 166
Automation Module 162

FIG. 7

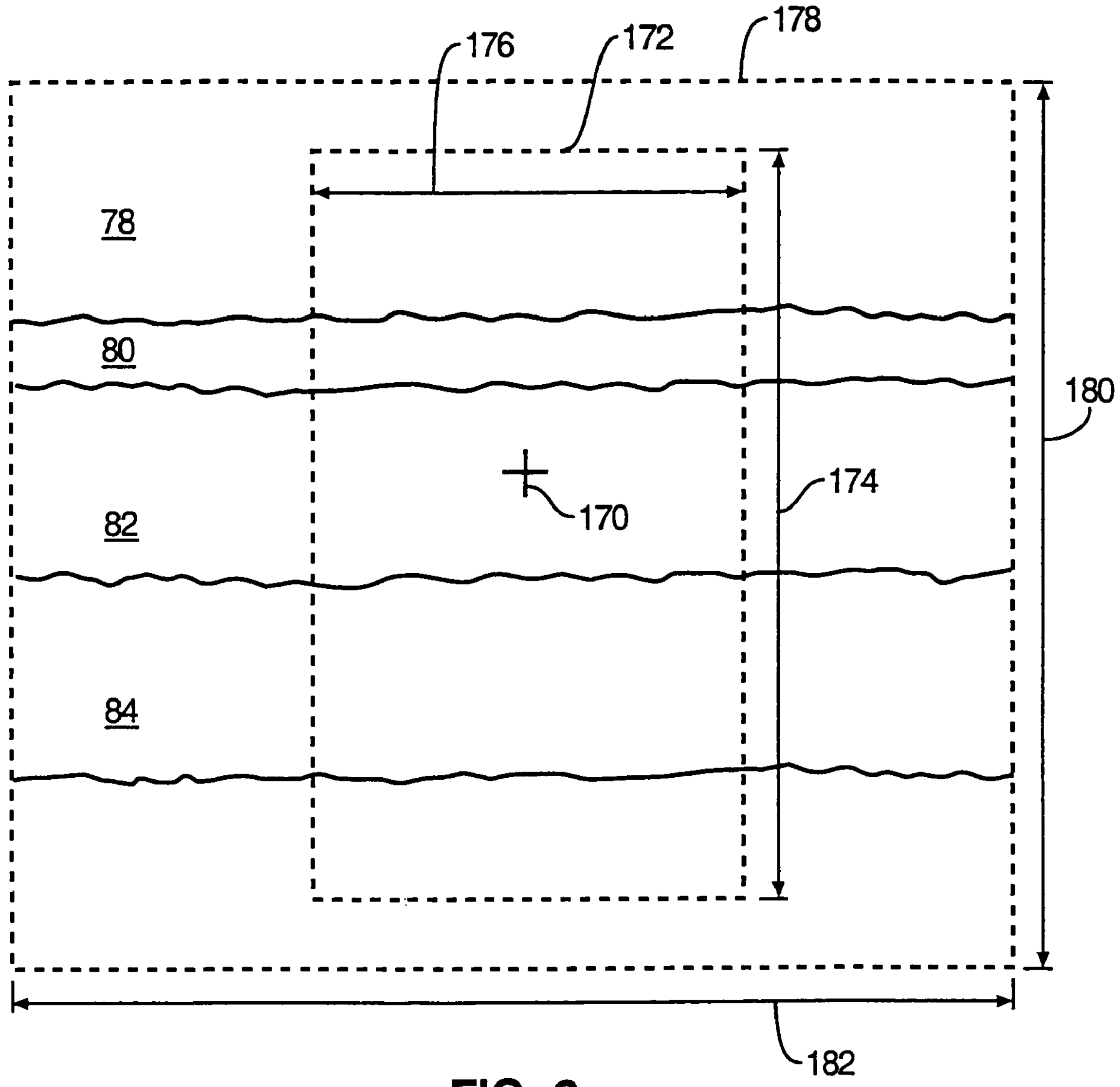


FIG. 8

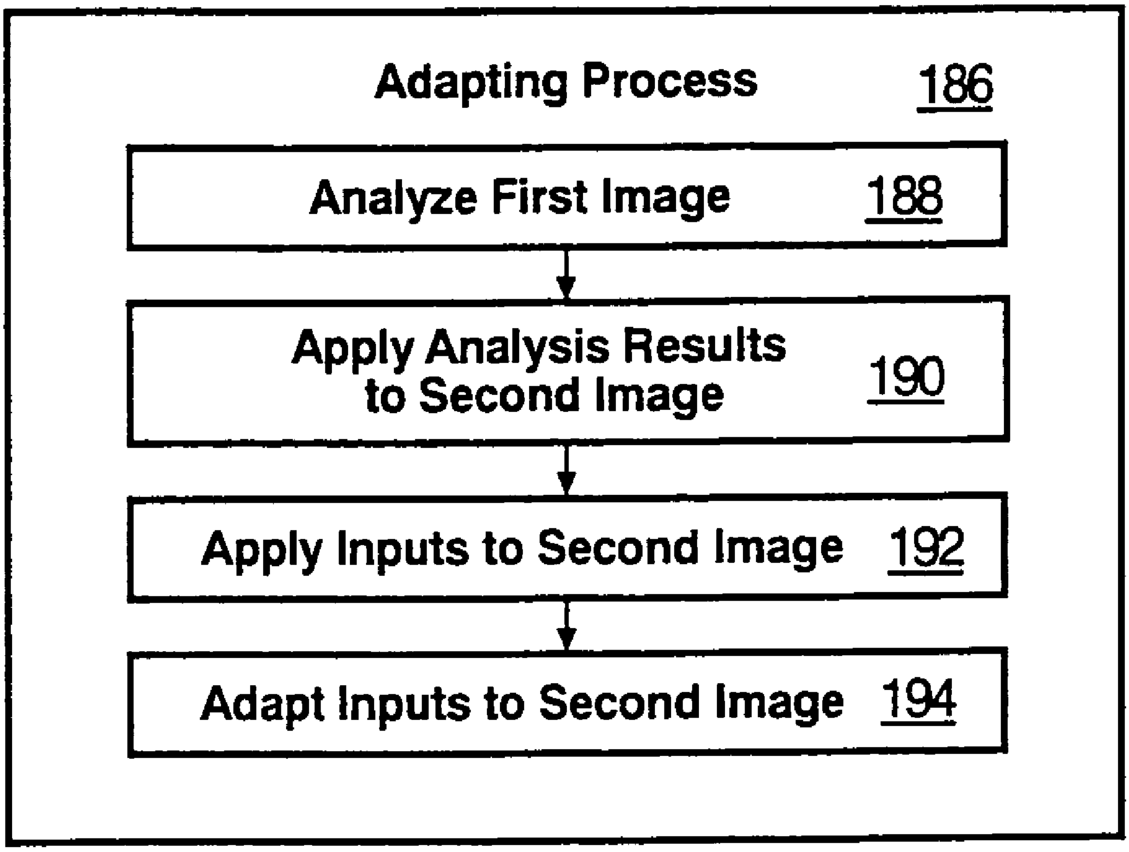

Adapting Process 186
Analyze First Image 188
Apply Analysis Results to Second Image 190
Apply Inputs to Second Image 192
Adapt Inputs to Second Image 194

FIG. 9

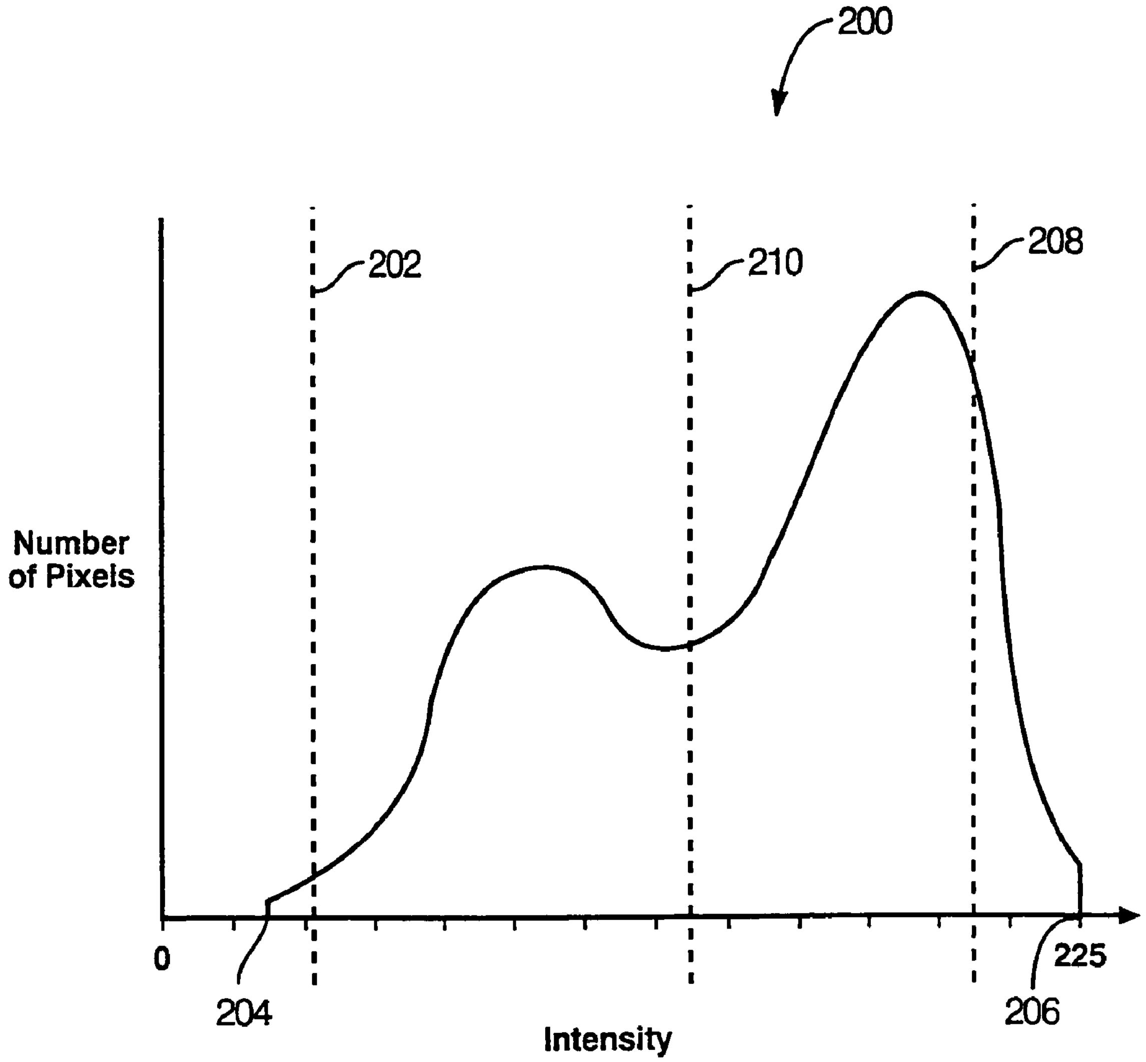


FIG. 10

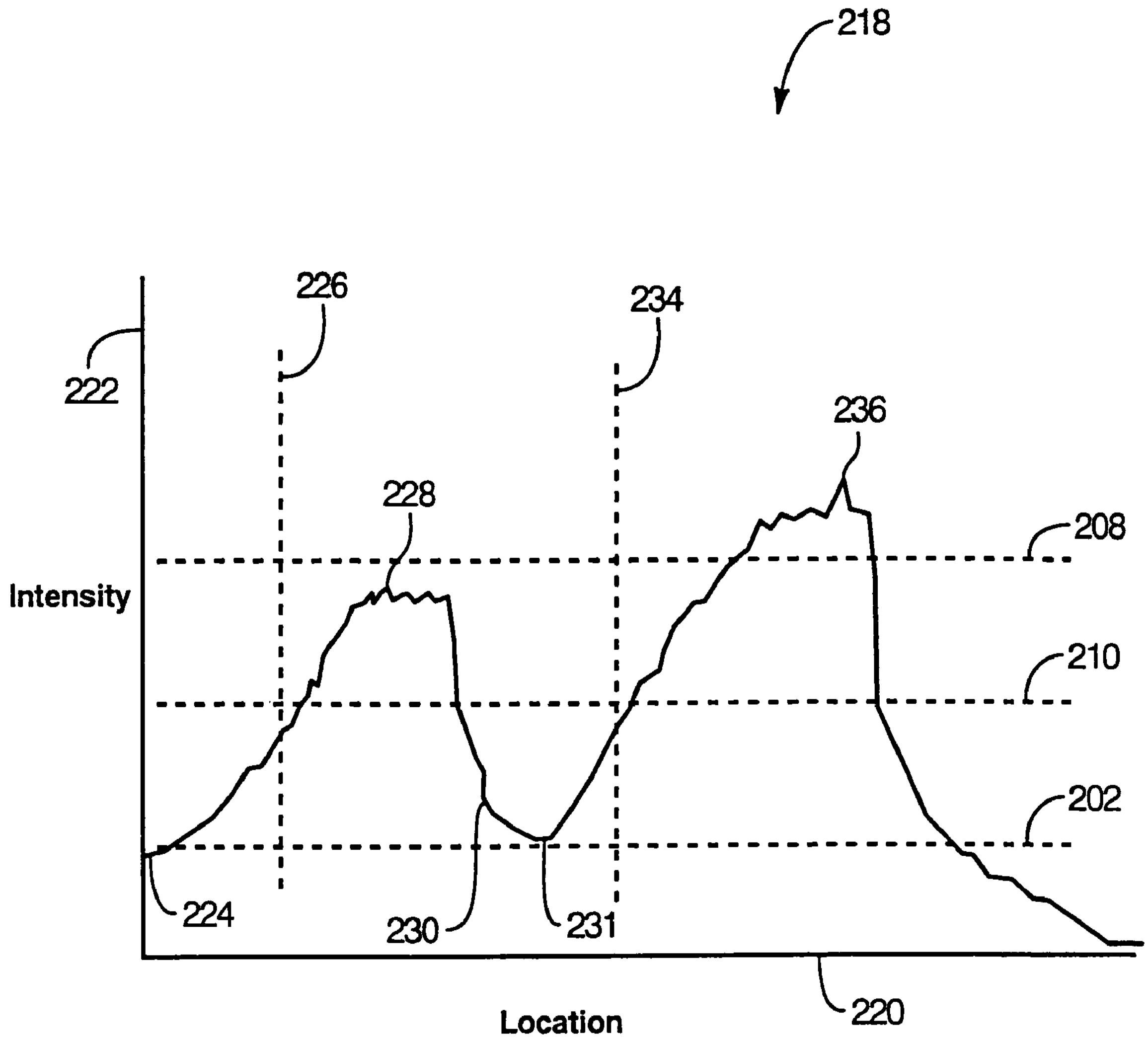

218
226
234
222
236
228
208
Intensity
210
202
224
230
231
Location
220

FIG. 11

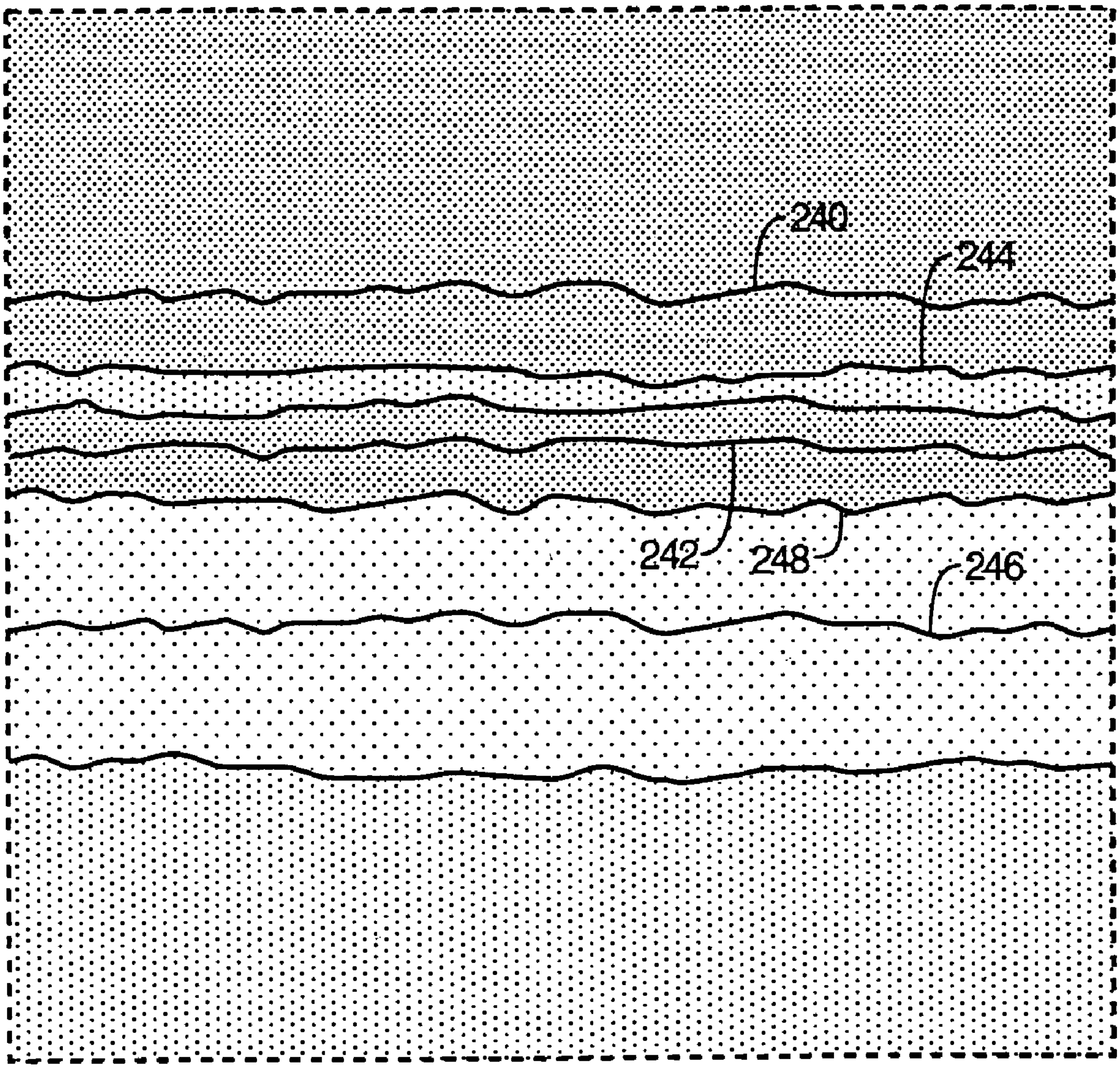


FIG. 12

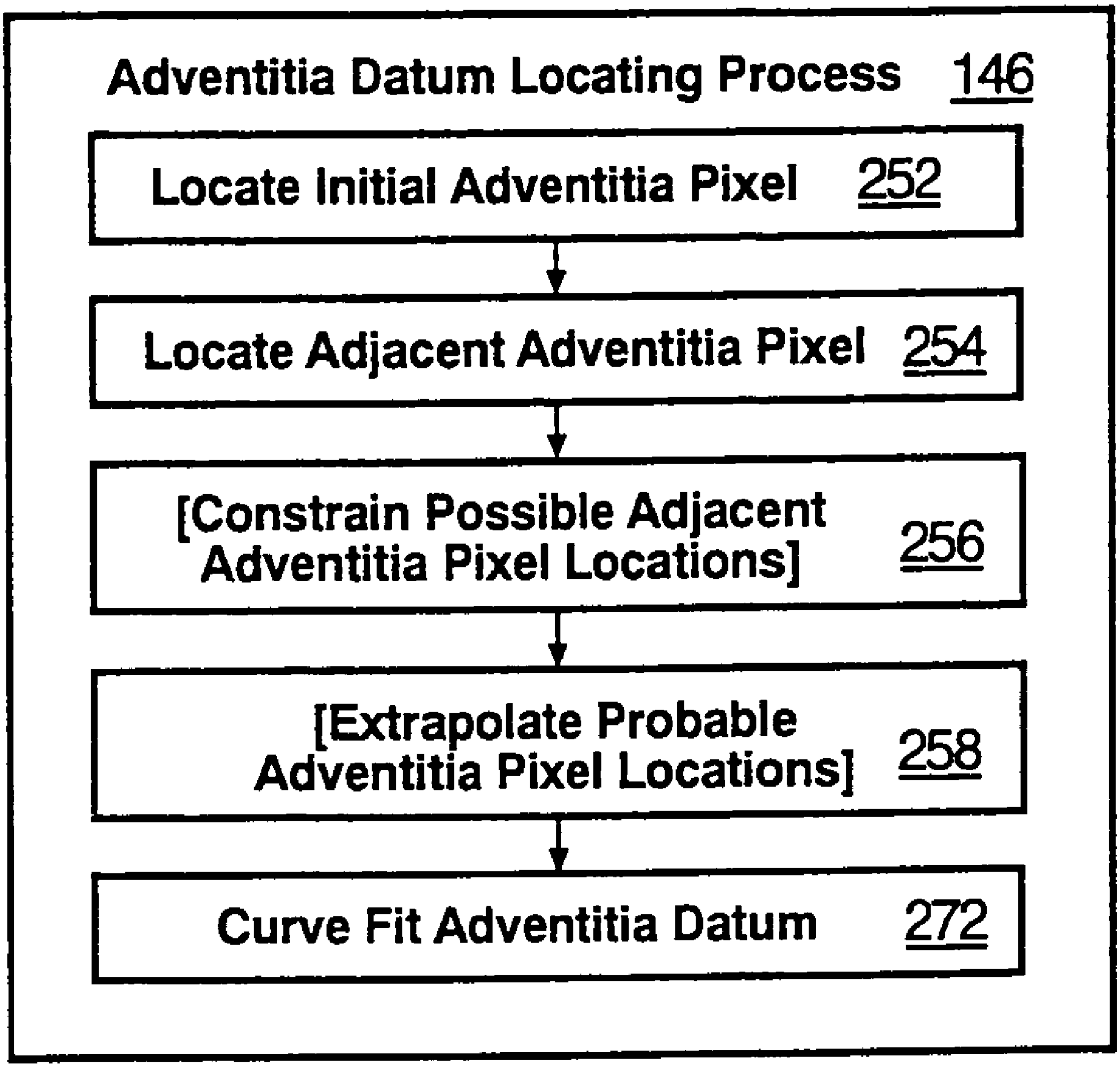

Adventitia Datum Locating Process 146
Locate Initial Adventitia Pixel 252
Locate Adjacent Adventitia Pixel 254
[Constrain Possible Adjacent Adventitia Pixel Locations] 256
[Extrapolate Probable Adventitia Pixel Locations] 258
Curve Fit Adventitia Datum 272

FIG. 13

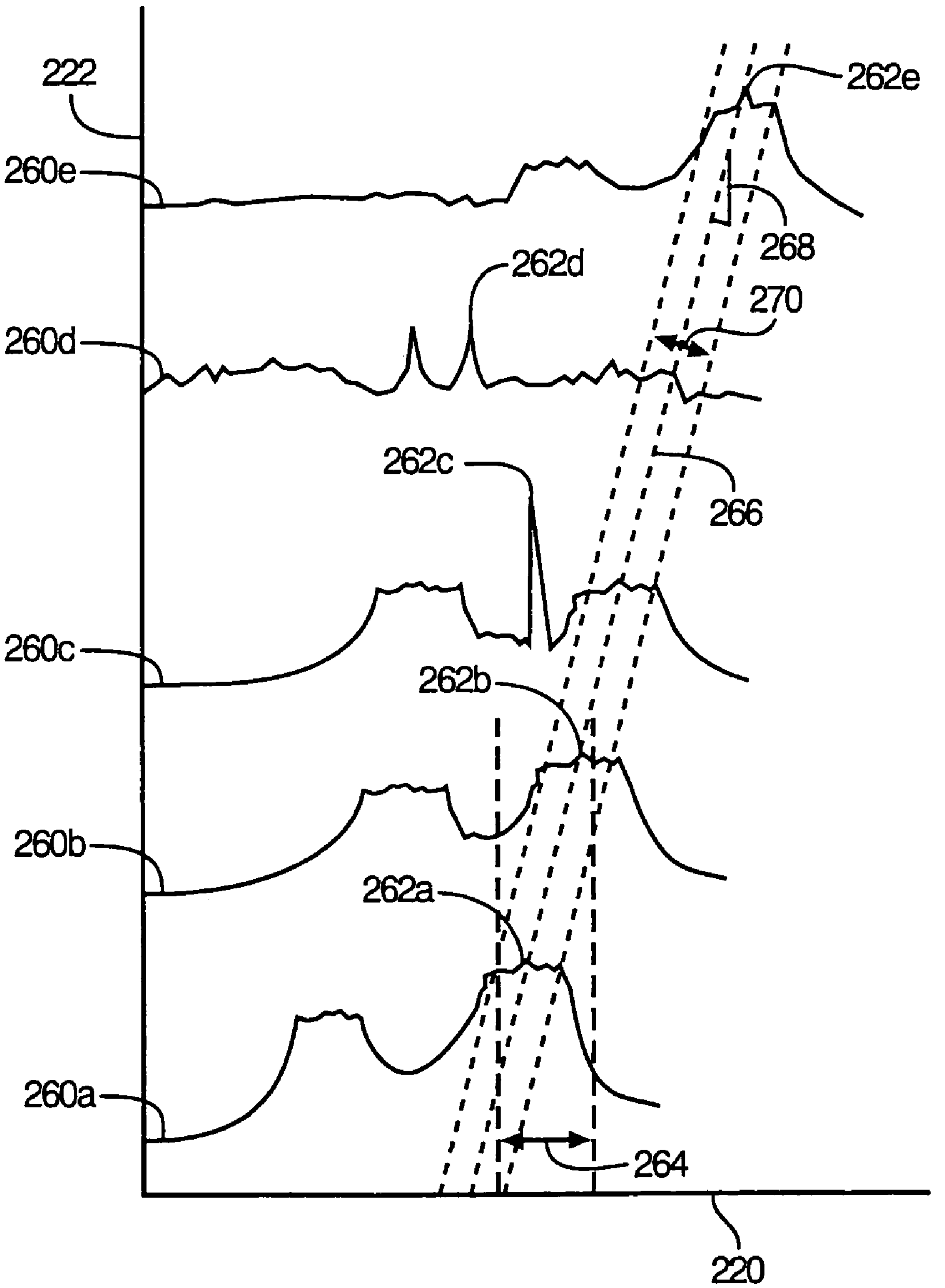

222
260e
262e
268
262d
270
260d
262c
266
260c
262b
260b
262a
260a
264
220

FIG. 14

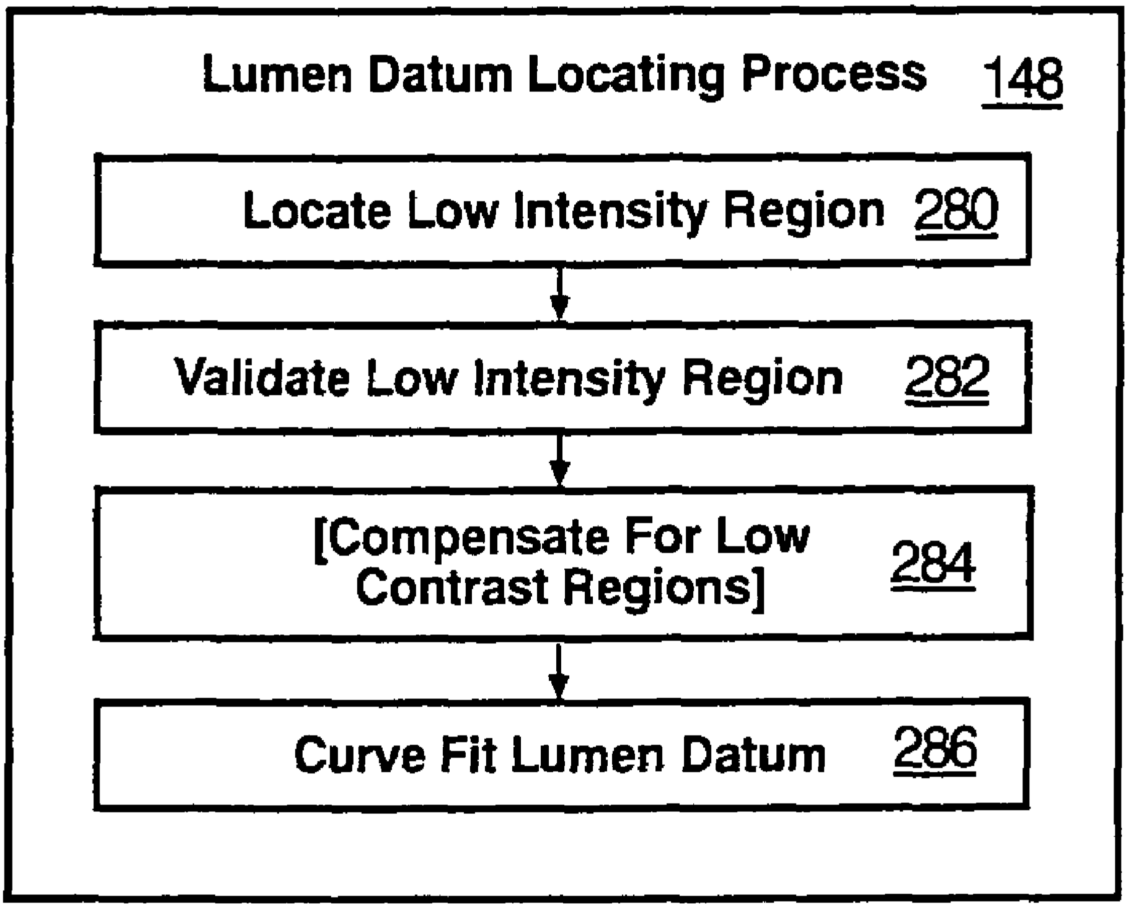

Lumen Datum Locating Process 148
Locate Low Intensity Region 280
Validate Low Intensity Region 282
[Compensate For Low Contrast Regions] 284
Curve Fit Lumen Datum 286

FIG. 15

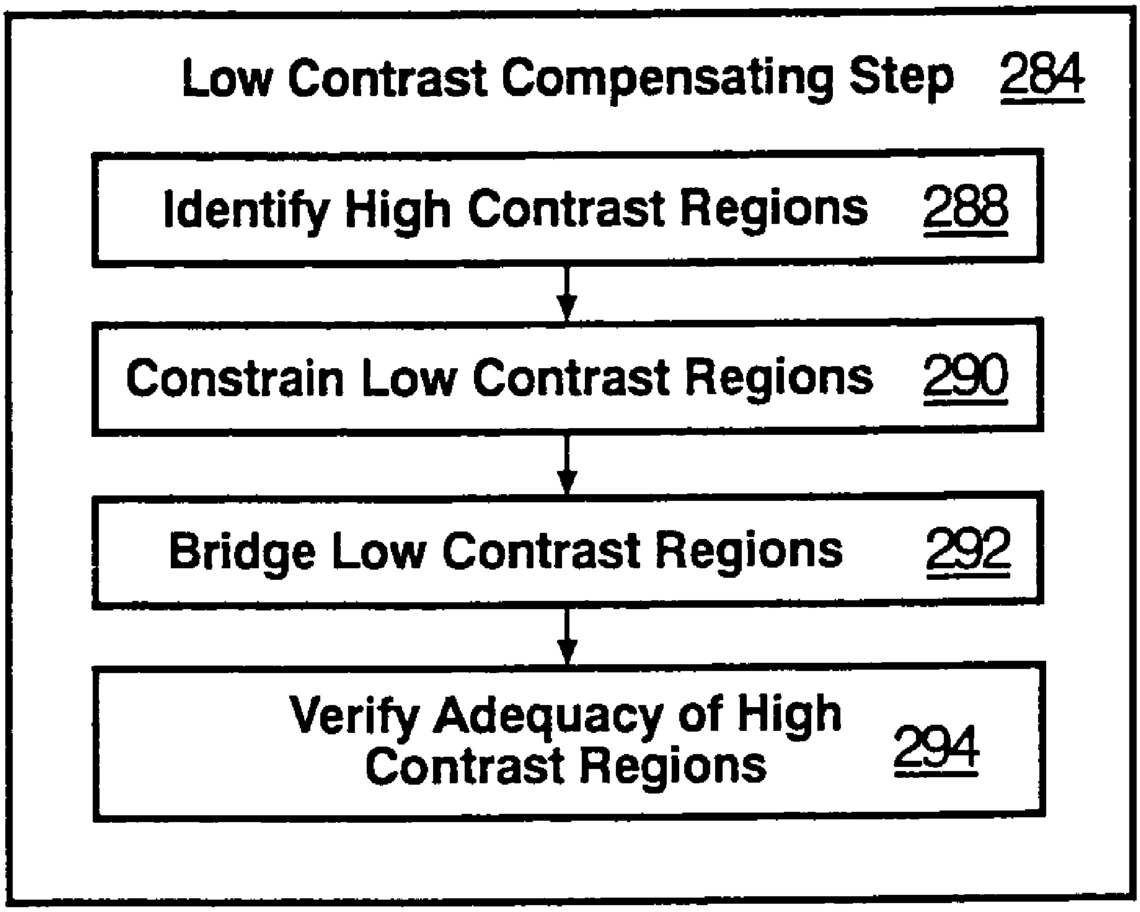

Low Contrast Compensating Step 284
Identify High Contrast Regions 288
Constrain Low Contrast Regions 290
Bridge Low Contrast Regions 292
Verify Adequacy of High Contrast Regions 294

FIG. 16

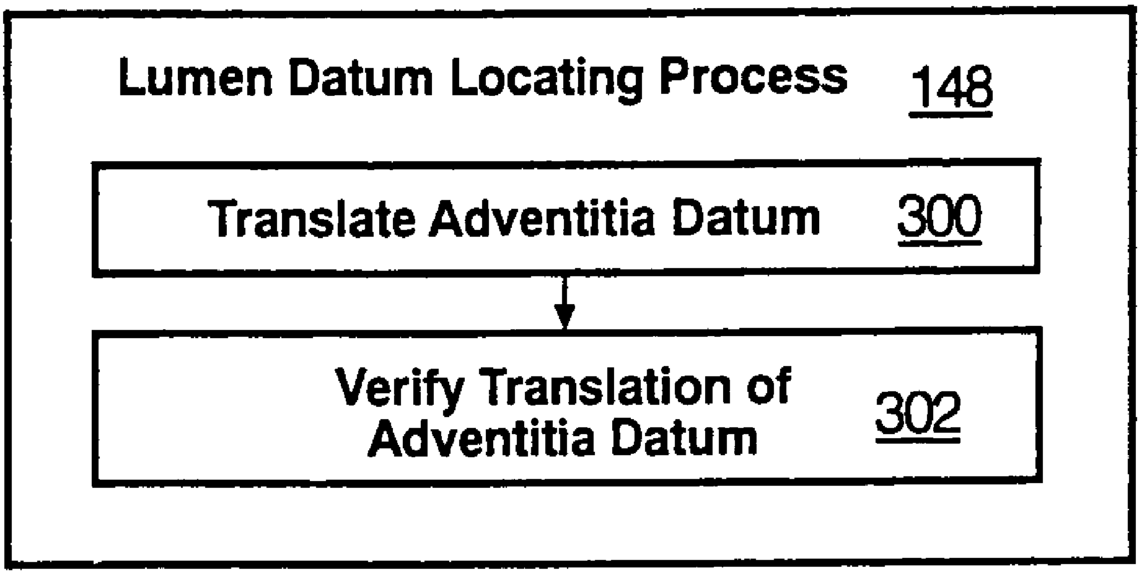

Lumen Datum Locating Process 148
Translate Adventitia Datum 300
Verify Translation of Adventitia Datum 302

FIG. 17

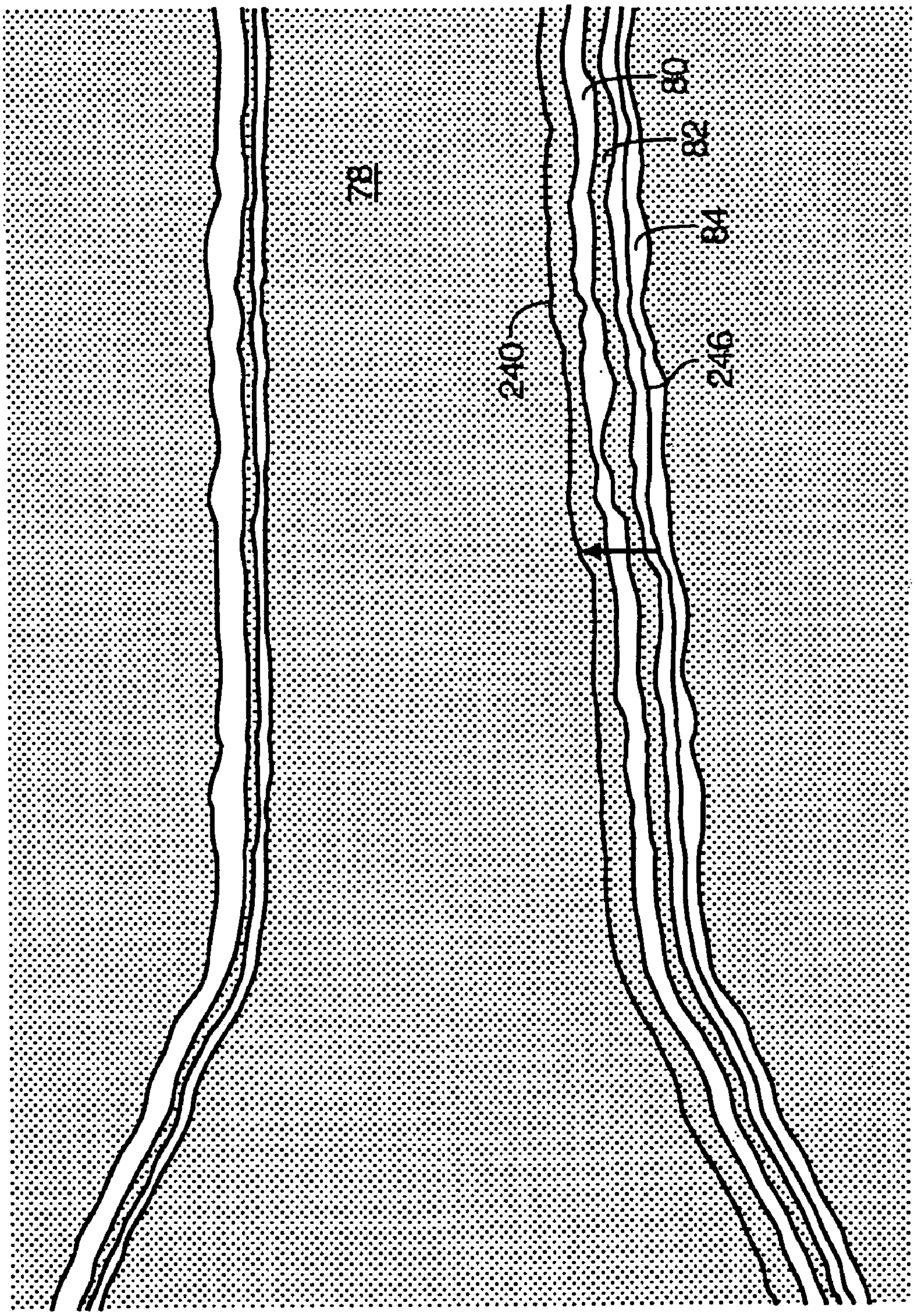


FIG. 18

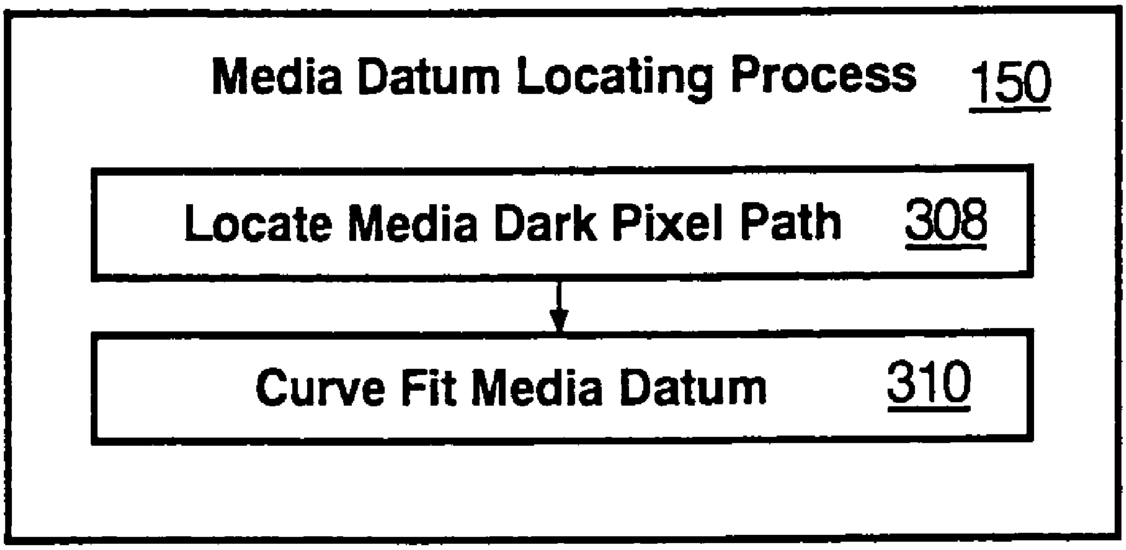

Media Datum Locating Process 150
Locate Media Dark Pixel Path 308
Curve Fit Media Datum 310

FIG. 19

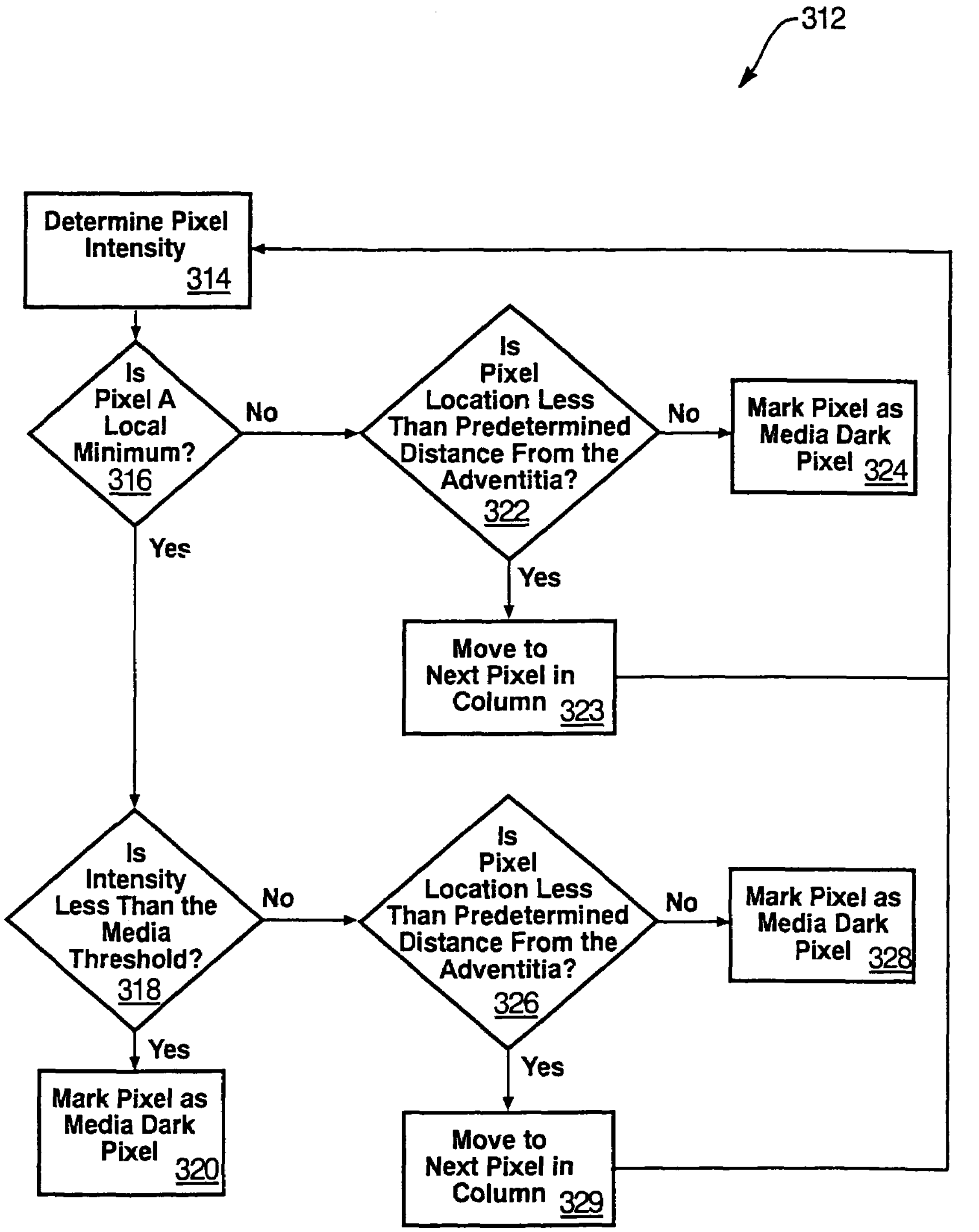

312
Determine Pixel Intensity 314
Is Pixel A Local Minimum? 316
No
Yes
Is Pixel Location Less Than Predetermined Distance From the Adventitia? 322
No
Mark Pixel as Media Dark Pixel 324
Yes
Move to Next Pixel in Column 323
Is Intensity Less Than the Media Threshold? 318
No
Is Pixel Location Less Than Predetermined Distance From the Adventitia? 326
No
Mark Pixel as Media Dark Pixel 328
Yes
Mark Pixel as Media Dark Pixel 320
Yes
Move to Next Pixel in Column 329

FIG. 20

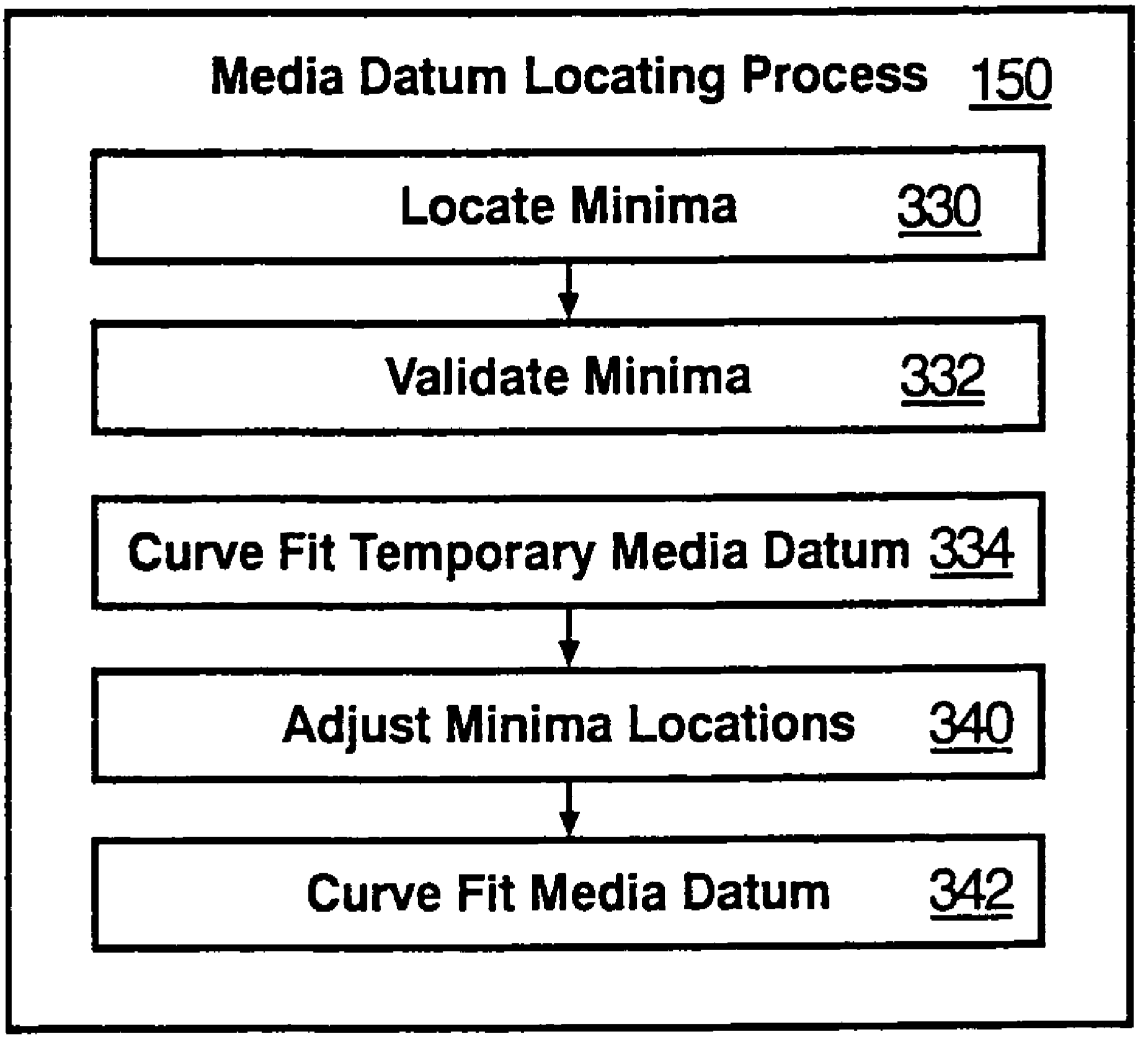

Media Datum Locating Process 150
Locate Minima 330
Validate Minima 332
Curve Fit Temporary Media Datum 334
Adjust Minima Locations 340
Curve Fit Media Datum 342

FIG. 21

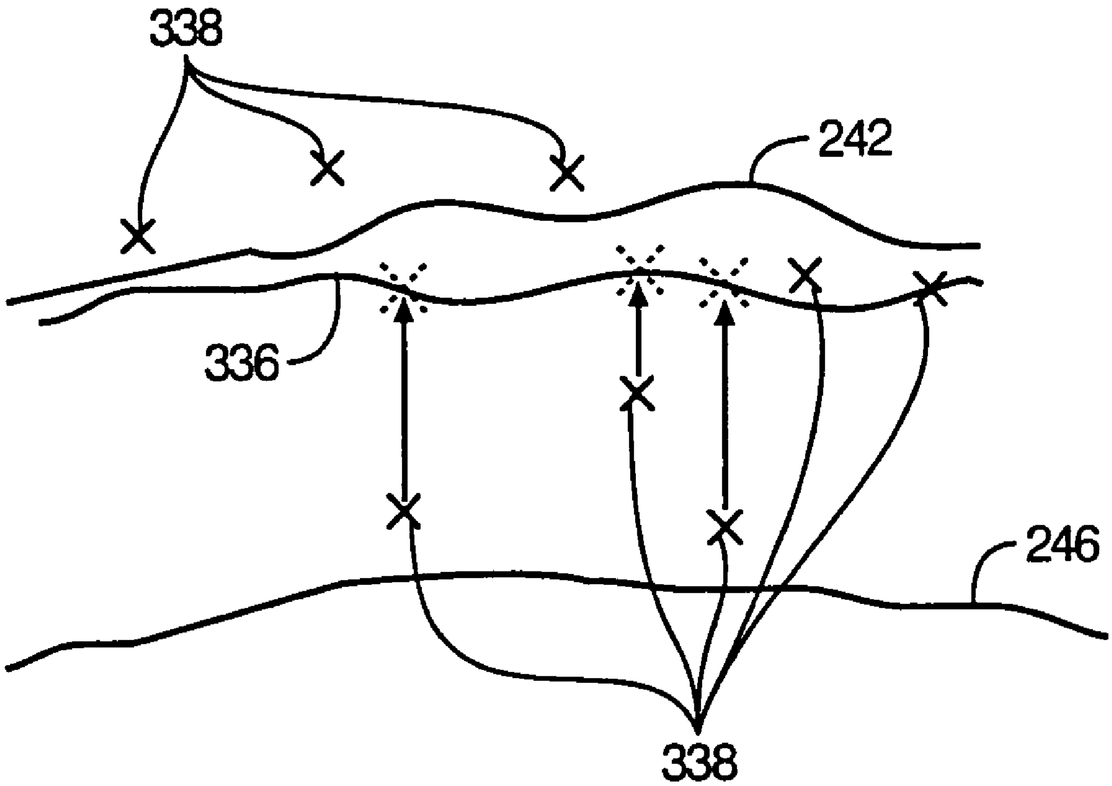


FIG. 22

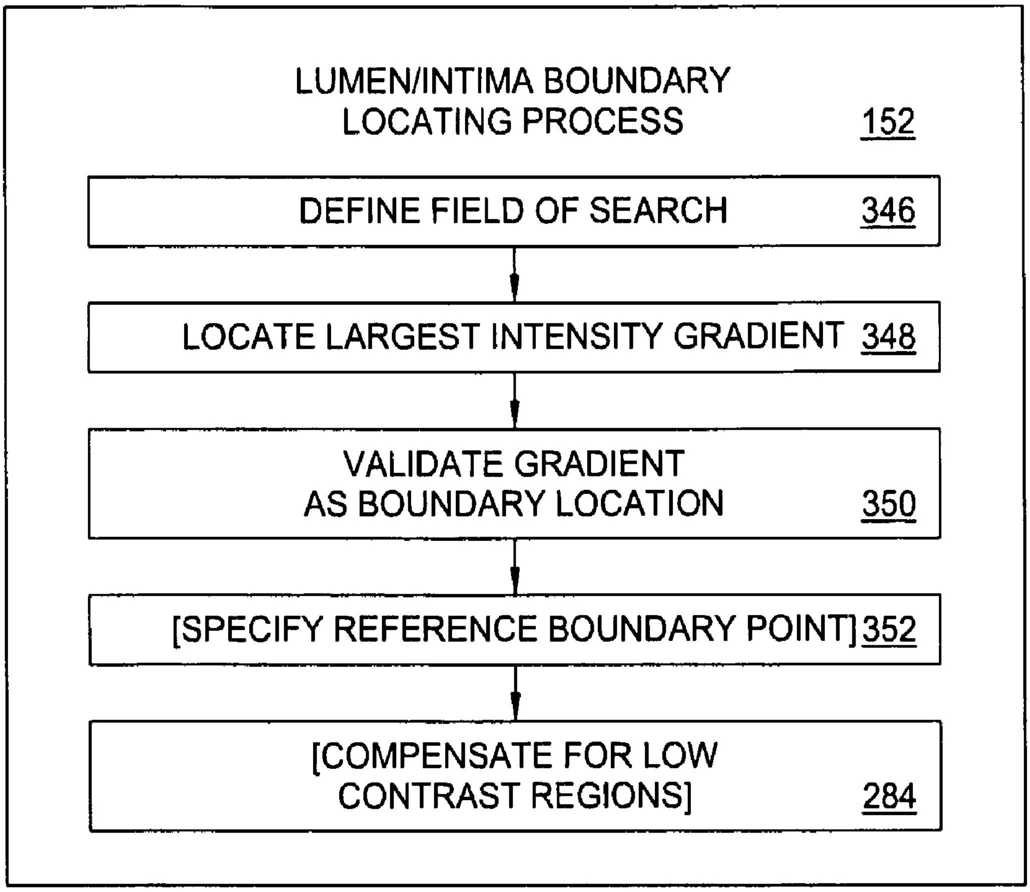

LUMEN/INTIMA BOUNDARY
LOCATING PROCESS 152
DEFINE FIELD OF SEARCH 346
LOCATE LARGEST INTENSITY GRADIENT 348
VALIDATE GRADIENT
AS BOUNDARY LOCATION 350
[SPECIFY REFERENCE BOUNDARY POINT] 352
[COMPENSATE FOR LOW
CONTRAST REGIONS] 284

FIG. 23

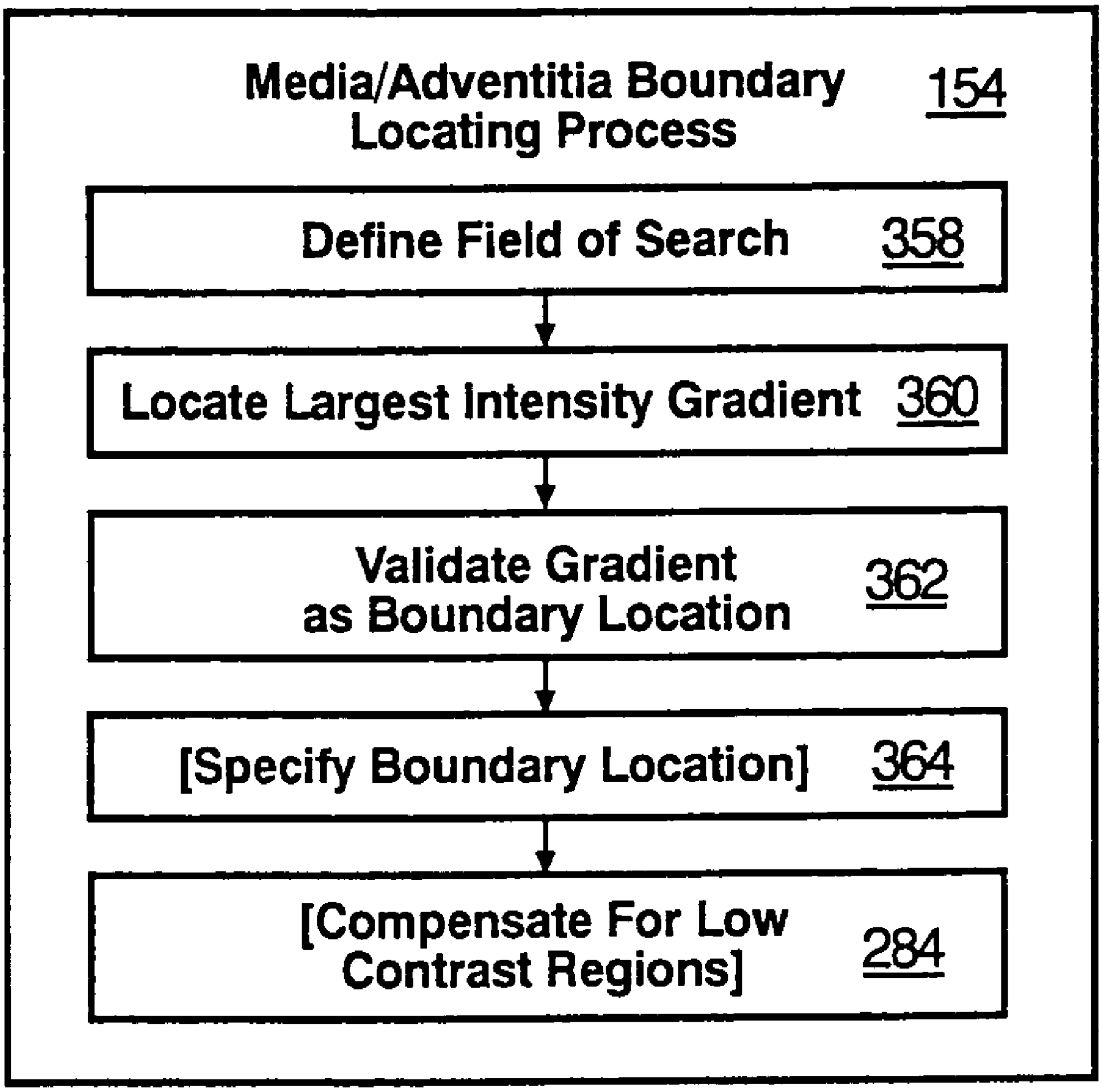

Media/Adventitia Boundary Locating Process
154
Define Field of Search
358
Locate Largest Intensity Gradient
360
Validate Gradient as Boundary Location
362
[Specify Boundary Location]
364
[Compensate For Low Contrast Regions]
284

FIG. 24

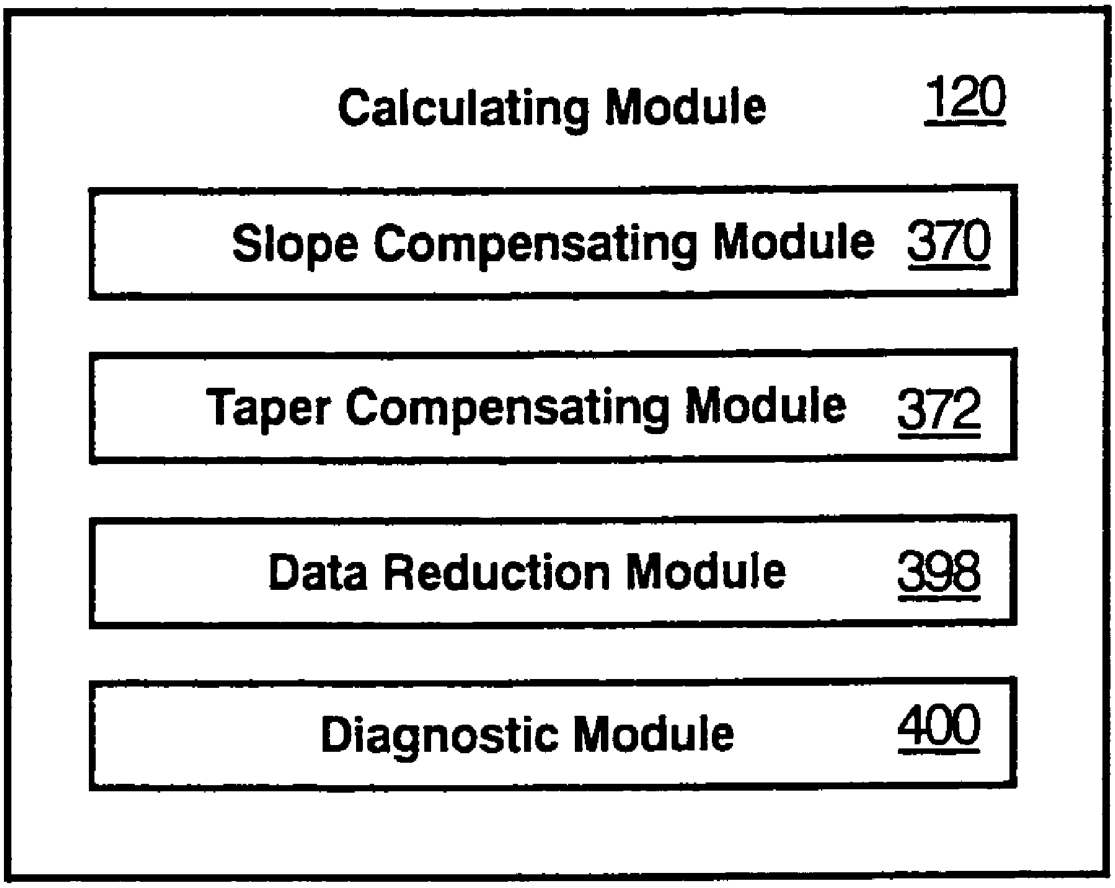

Calculating Module 120
Slope Compensating Module 370
Taper Compensating Module 372
Data Reduction Module 398
Diagnostic Module 400

FIG. 25

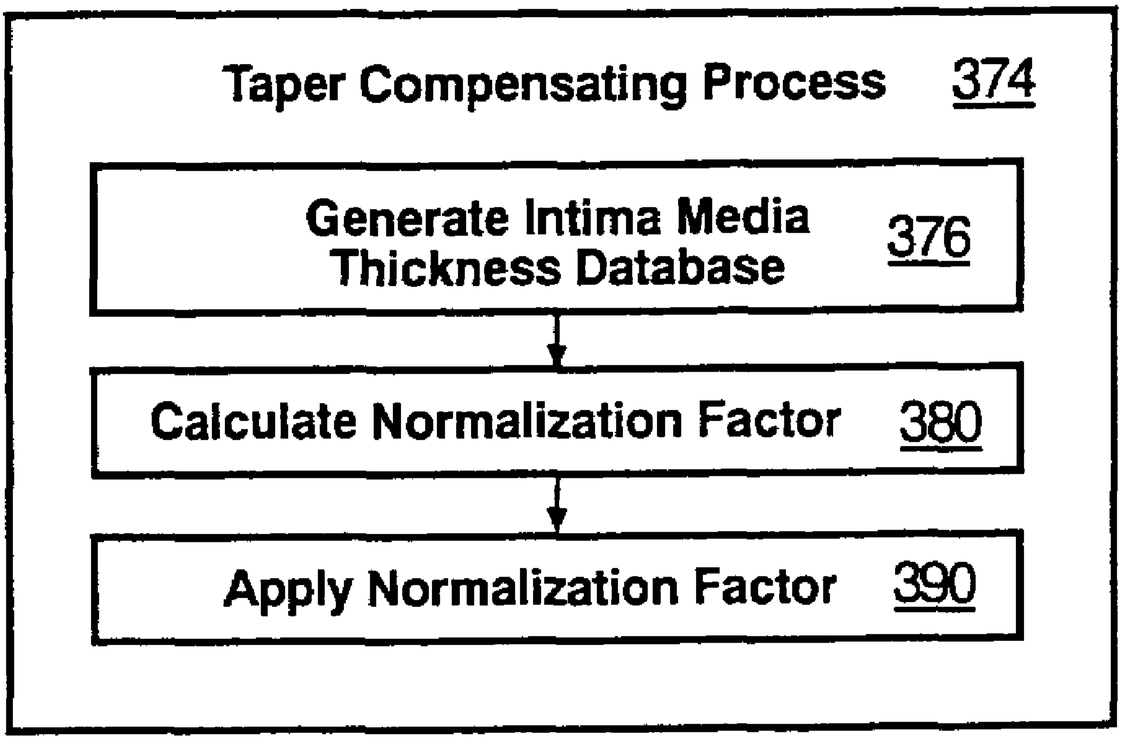

Taper Compensating Process 374
Generate Intima Media Thickness Database 376
Calculate Normalization Factor 380
Apply Normalization Factor 390

FIG. 26

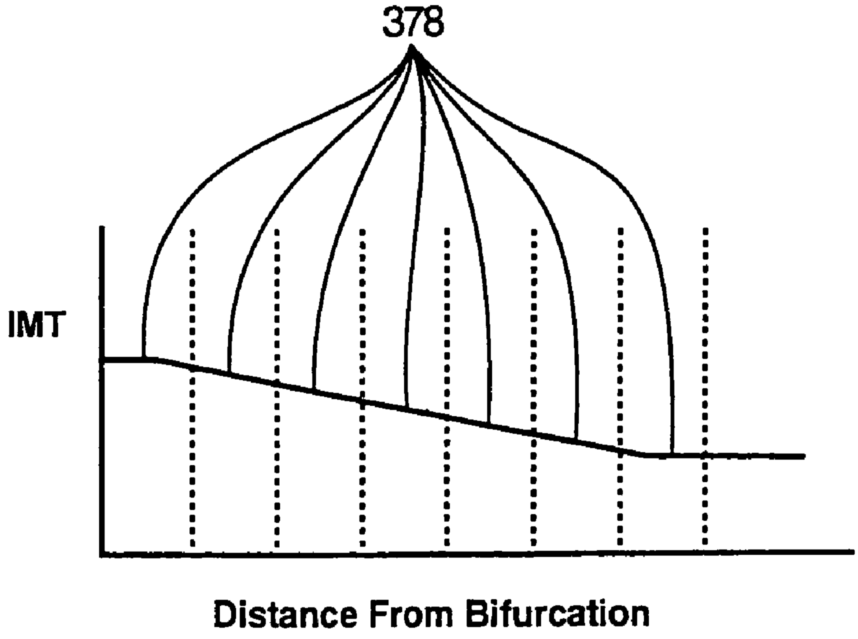

378
IMT
Distance From Bifurcation

FIG. 27

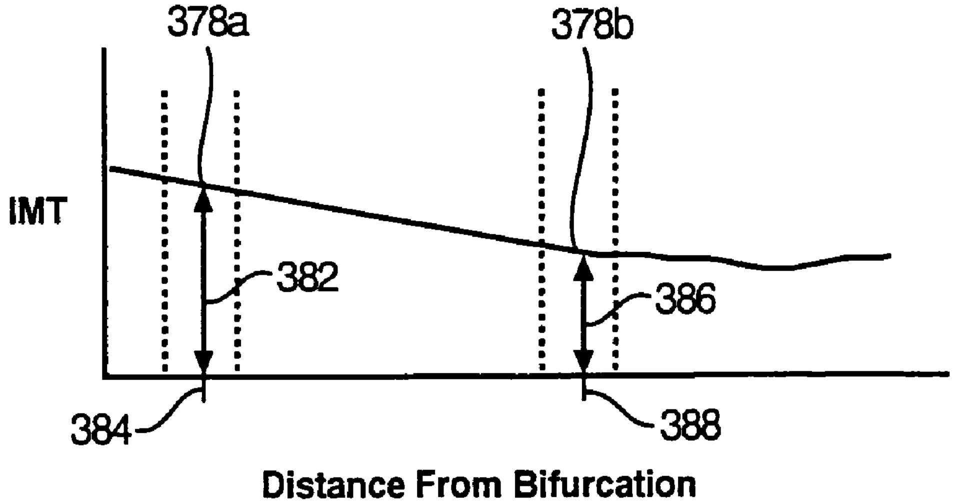

378a
378b
IMT
382
386
384
388
Distance From Bifurcation

FIG. 28

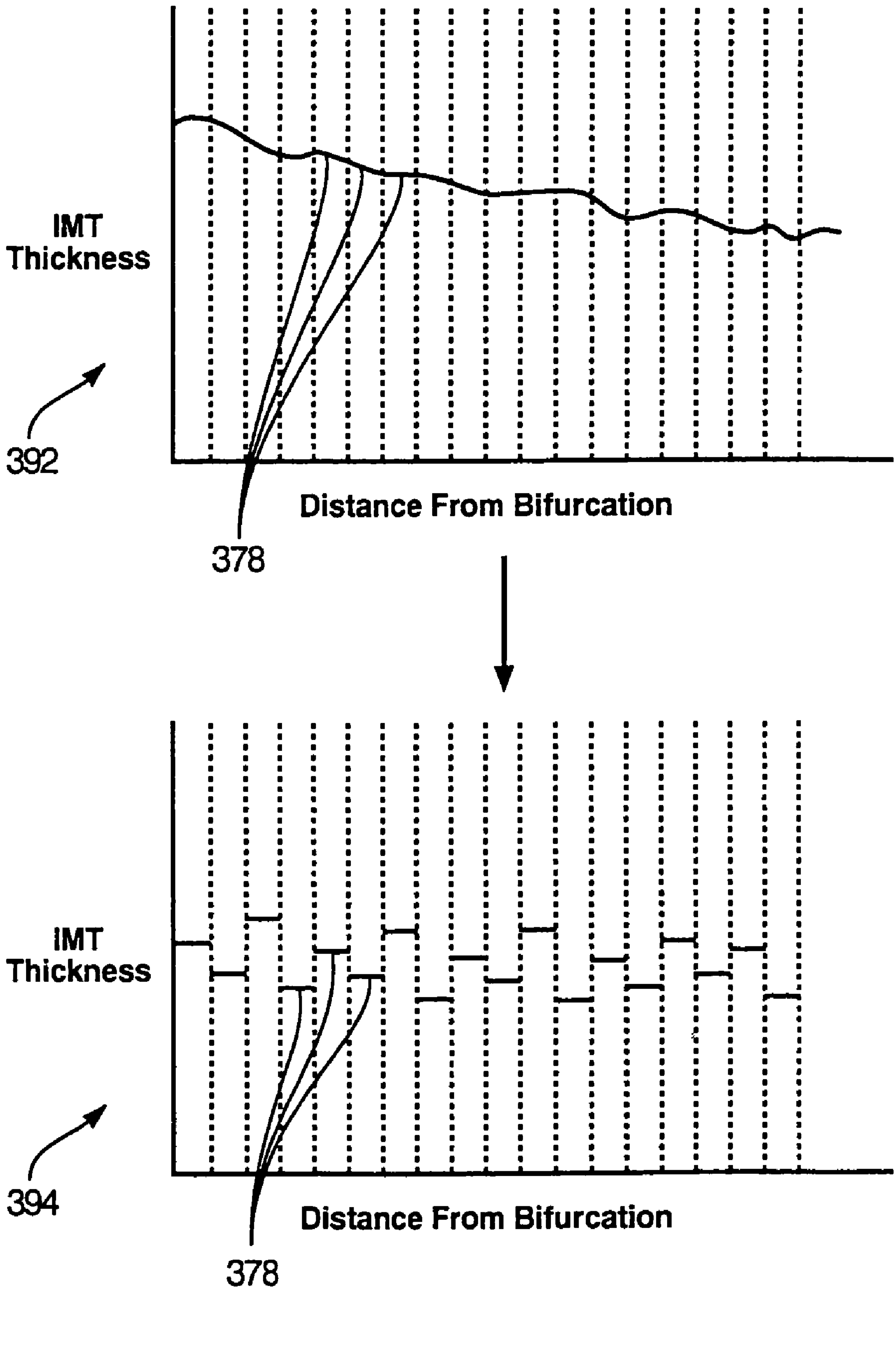

IMT
Thickness
Distance From Bifurcation
392
378
IMT
Thickness
Distance From Bifurcation
394
378

FIG. 29

FIG. 30

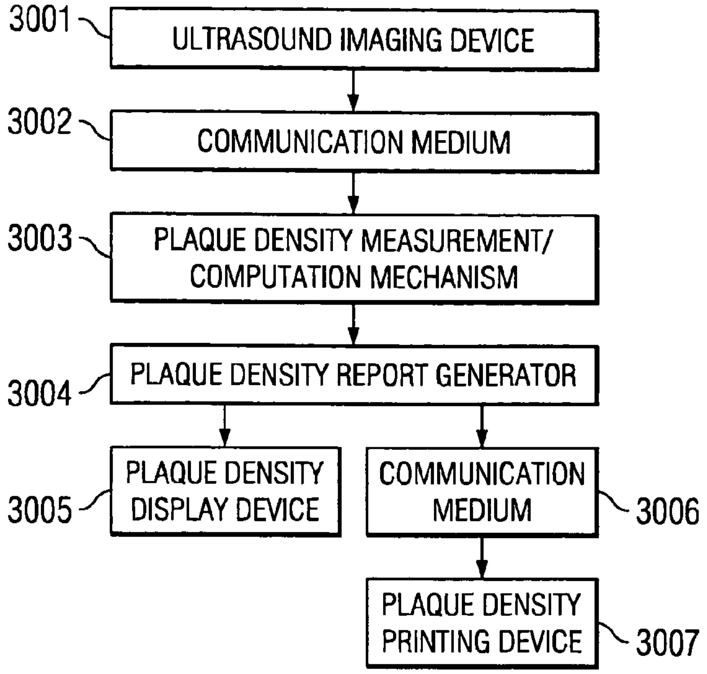
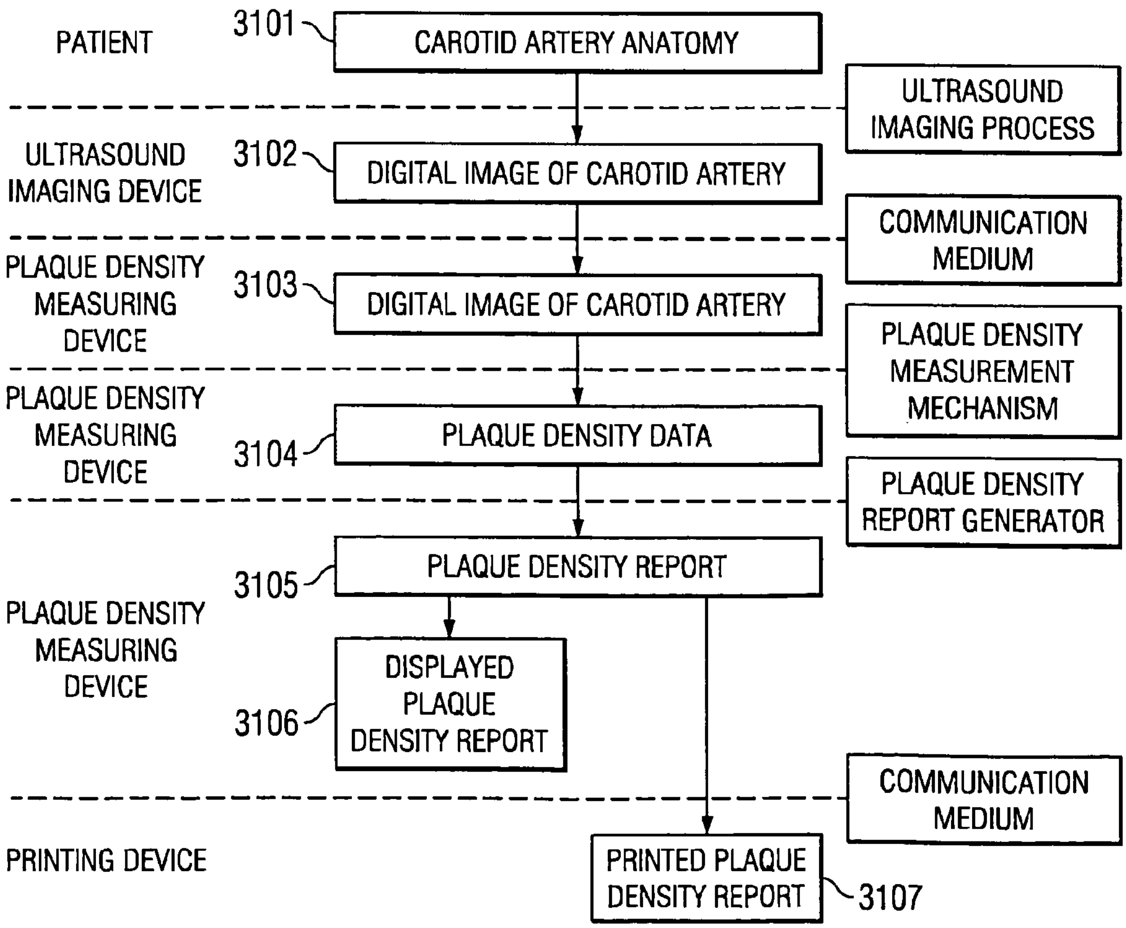

3001
ULTRASOUND IMAGING DEVICE
3002
COMMUNICATION MEDIUM
3003
PLAQUE DENSITY MEASUREMENT/ COMPUTATION MECHANISM
3004
PLAQUE DENSITY REPORT GENERATOR
3005
PLAQUE DENSITY DISPLAY DEVICE
COMMUNICATION MEDIUM
3006
PLAQUE DENSITY PRINTING DEVICE
3007

FIG. 31


PATIENT
3101
CAROTID ARTERY ANATOMY
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3102
DIGITAL IMAGE OF CAROTID ARTERY
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PLAQUE DENSITY MEASURING DEVICE
3103
DIGITAL IMAGE OF CAROTID ARTERY
PLAQUE DENSITY MEASUREMENT MECHANISM
PLAQUE DENSITY MEASURING DEVICE
3104
PLAQUE DENSITY DATA
PLAQUE DENSITY REPORT GENERATOR
3105
PLAQUE DENSITY REPORT
PLAQUE DENSITY MEASURING DEVICE
3106
DISPLAYED PLAQUE DENSITY REPORT
COMMUNICATION MEDIUM
PRINTING DEVICE
PRINTED PLAQUE DENSITY REPORT
3107

ULTRASONIC BLOOD VESSEL MEASUREMENT APPARATUS AND METHOD

CROSS-REFERENCE TO RELATED APPLICATIONS

This application is a continuation-in-part of U.S. patent application Ser. No. 10/682,699 filed Oct. 9, 2003 entitled "ULTRASONIC BLOOD VESSEL MEASUREMENT APPARATUS AND METHOD," which is a continuation-in-part of U.S. patent application Ser. No. 10/407,682 filed Apr. 7, 2002 entitled "METHOD, APPARATUS, AND PRODUCT FOR ACCURATELY DETERMINING THE INTIMA-MEDIA THICKNESS OF A BLOOD VESSEL;" and claims priority through the foregoing patent applications to U.S. provisional patent applications Ser. No. 60/424,027 filed Nov. 6, 2002 entitled "METHOD AND APPARATUS FOR INTIMA-MEDIA THICKNESS MEASURING MECHANISM EMBEDDED IN ULTRASOUND IMAGING DEVICE;" Ser. No. 60/424,464 filed Nov. 8, 2002 entitled "METHOD AND APPARATUS FOR MEASURING INTIMA-MEDIA THICKNESS ACROSS MULTIPLE SIMILAR IMAGES;" Ser. No. 60/424,471 filed Nov. 8, 2002 entitled "METHOD AND APPARATUS FOR INCORPORATING INTIMA-MEDIA TAPERING EFFECTS ON INTIMA-MEDIA THICKNESS CALCULATIONS;" Ser. No. 60/424,463 filed Nov. 8, 2002 entitled "METHOD AND APPARATUS FOR USING ULTRASOUND IMAGES TO CHARACTERIZE ARTERIAL WALL TISSUE COMPOSITION;" and Ser. No. 60/424,465 filed Nov. 8, 2002 entitled "METHOD AND APPARATUS FOR REGENERATION OF INTIMA-MEDIA THICKNESS MEASUREMENTS," the disclosures of all of which are hereby incorporated herein by reference.

TECHNICAL FIELD

This invention pertains to methods and apparatus for processing digital images of vascular structures including blood vessels. More particularly, it relates to methods for interpreting ultrasonic images of the common carotid artery.

BACKGROUND OF THE INVENTION

Coronary artery disease (CAD) is a narrowing of the arteries that supply the heart with blood carrying oxygen and nutrients. CAD may cause shortness of breath, angina, or even heart attack. The narrowing of the arteries is typically due to the buildup of plaque, or, in other words, an increase in the atherosclerotic burden. The buildup of plaque may also create a risk of stroke, heart attacks, and embolisms caused by fragments of plaque detaching from the artery wall and occluding smaller blood vessels. The risk of arterial wall rupture and detachment of portions of the blood clot covering the rupture is particularly great shortly after blood clot formation when it is soft and easily fragmented at that stage.

Measurement of the atherosclerotic burden of the coronary artery itself is difficult and invasive. Moreover, assessment of risk often involves measuring both the atherosclerotic burden and its rate of progression. This assessment therefore involves multiple invasive procedures over time. Treatment of CAD also requires additional invasive procedures to measure a treatment's effectiveness.

The carotid artery, located in the neck close to the skin, has been shown to mirror the atherosclerotic burden of the coronary artery. Moreover, studies have shown that a reduction of

the atherosclerotic burden of the coronary artery will parallel a similar reduction in the carotid artery.

One noninvasive method for measuring the atherosclerotic burden is the analysis of ultrasound images of the carotid artery. High resolution, B-mode ultrasonography is one adequate method of generating such images. Ultrasound images typically provide a digital image of the various layers comprising the carotid artery wall, which may then be measured to determine or estimate the extent of atherosclerosis. Other imaging systems may likewise provide digital images of the carotid artery, such as magnetic resonance imaging (MRI) and radio frequency imaging.

The wall of the carotid artery comprises the intima, which is closest to the blood flow and which thickens, or appears to thicken, with the deposit of fatty material and plaque; the media, which lies adjacent the intima and which thickens as a result of hypertension; and the adventitia, which provides structural support for the artery wall. The channel in which blood flows is the lumen. The combined thickness of the intima and media layers, or intima-media thickness (IMT), is reflective of the condition of the artery and can accurately identify or reflect early stages of atherosclerotic disease.

An ultrasound image typically comprises an array of pixels, each with a specific value corresponding to its intensity. The intensity (brightness) of a pixel corresponds to the density of the tissue it represents, with brighter pixels representing denser tissue. Different types of tissue, each with a different density, are therefore distinguishable in an ultrasonic image. The lumen, intima, media and adventitia may be identified in an ultrasound image due to their differing densities.

An ultrasound image is typically formed by emitting sound waves toward the tissue to be measured and measuring the intensity and phase of sound waves reflected from the tissue. This method of forming images is subject to limitations and errors. For example, images may be subject to noise from imperfect sensors. Another source of error is the attenuation of sound waves that reflect off tissue located deep within the body or beneath denser tissue. Random reflections from various objects or tissue boundaries, particularly due to the non-planar ultrasonic wave, may add noise also.

The limitations of ultrasonography complicate the interpretation of ultrasound images. Other systems designed to calculate IMT thickness reject accurate portions of the image when compensating for these limitations. Some IMT measurement systems will divide an image into columns and examine each column, looking for maxima, minima, or constant portions of the image in order to locate the layers of tissue comprising the artery wall. Such systems may reject an entire column of image data in which selected portions of the wall are not readily identifiable. This method fails to take advantage of other portions of the artery wall that are recognizable in the column. Furthermore, examining columns of pixels singly fails to take advantage of accurate information in neighboring columns from which one may extrapolate, interpolate, or otherwise guide searches for information within a column of pixels.

Another limitation of prior methods is that they fail to adequately limit the range of pixels searched in a column of pixels. Noise and poor image quality can cause any search for maxima, minima, or intensity gradients to yield results that are clearly erroneous. Limiting the field of search is a form of -filtering that eliminates results that cannot possibly be accurate. Prior methods either do not limit the field searched for critical points or apply fixed constraints that are not customized, or even perhaps relevant, to the context of the image being analyzed.

What is needed is a method for measuring the IMT that compensates for limitations in ultrasonic imaging methods. It would be an advancement in the art to provide an IMT measurement method that compensates for noise and poor image quality while taking advantage of accurate information within each column of pixels. It would be a further advancement to provide a method for measuring the IMT that limited the field of search for critical points to regions where the actual tissue or tissue boundaries can possibly be located.

BRIEF SUMMARY OF THE INVENTION

In view of the foregoing, it is a primary object of embodiments of the present invention to provide a novel method and apparatus for extracting measurements, such as IMT measurements, from ultrasound images of various tissue structure, such as the carotid artery.

It is another object of embodiments of the present invention to reduce error in measurements by restricting searches for the tissue boundaries, such as the lumen/intima boundary and media/adventitia boundary, to regions likely to contain them.

It is another object of embodiments of the present invention to bound a search region using a datum, or datums, calculated beforehand based on analysis of a large portion of a measurement region in order to improve processing speed and accuracy.

It is another object of embodiments of the present invention to validate putative boundary locations using thresholds reflecting the actual make-up of the image.

It is another object of embodiments of the present invention to validate putative boundary locations based on their proximity to known features of ultrasound images of tissue structure, such as the carotid artery.

It is another object of embodiments of the present invention to compensate for sloping and tapering of the carotid artery as well as misalignment of an image frame of reference with respect to the axial orientation of the artery.

It is another object of embodiments of the present invention to compensate for low contrast and noise by extrapolating and interpolating from high contrast portions of an image into low contrast portions of the image.

It is another object of embodiments of the present invention to determine tissue density information, such as plaque density information, using ultrasound imagery.

Consistent with the foregoing objects, and in accordance with the invention as embodied and broadly described herein, an apparatus is disclosed in one embodiment of the present invention as including a computer programmed to run an image processing application and to receive ultrasound images of tissue structure, such as images of the common carotid artery.

An image processing application may carry out a process for measuring the intima-media thickness (IMT) providing better measurements, less requirement for user skill, and a higher reproducibility. As a practical matter, intensity varies with the constitution of particular tissues. However, maximum difference in intensity is not typically sufficient to locate the boundaries of anatomical features. Accordingly, it has been found that in applying various techniques of curve fitting analysis and signal processing, structural boundaries may be clearly defined, even in the face of comparatively "noisy" data.

In certain embodiments of a method and apparatus in accordance with the invention, an ultrasonic imaging device or other imaging devices, such as a magnetic resonance imaging system (MRI), a computed tomography scan (CT-Scan), a radio frequency image, or other mechanism may be used to create a digital image. Typically, the digital image contains various pixels, each pixel representing a picture element of a specific location in the image. Each pixel is recorded with a degree of intensity. Typical intensity ranges run through values between zero and 255. In alternative embodiments, pixels may have color and intensity.

In certain embodiments, an image is first calibrated for dimensions. That is, to determine an IMT value, for example, the dimensions of the image are preferably calibrated against a reference measurement. Accordingly, the scale on an image may be applied to show two dimensional measurements across the image.

In certain embodiments, an ultrasonic image is made with a patient lying on the back with the image taken in a horizontal direction. Accordingly, the longitudinal direction of the image is typically horizontal, and coincides with approximately the axial direction of the carotid artery. A vertical direction in the image corresponds to the approximate direction across the carotid artery.

In certain embodiments of methods and apparatus in accordance with the invention, a measurement region may be selected by a user, or by an automated algorithm. A user familiar with the appearance of a computerized image from an ultrasound system may quickly select a measurement region. For example, the horizontal center of an image may be selected near the media/adventitia boundary of the blood vessel in question.

Less dense materials tend to appear darker in ultrasound images, having absorbed the ultrasonic signal from a transmitter, and thus provide less of a return reflection to a sensor. Accordingly, a user may comparatively quickly identify high intensity regions representing the more dense and reflective material in the region of the adventitia and the darker, low density or absorptive region in the area of the lumen.

In general, a method or characterizing plaque buildup in a blood vessel may include a measurement of an apparent intima-media thickness. In one embodiment, the method may include providing an image. An image is typically oriented with a longitudinal direction extending horizontally relative to a viewer and a transverse direction extending vertically relative to a viewer. This orientation corresponds to an image taken of a carotid artery in the neck of the user lying on an examination table. Thus, the carotid artery is substantially horizontally oriented. The axial direction is the direction of blood flow in a blood vessel, and the lateral direction is substantially orthogonal thereto. The image is typically comprised of pixels. Each pixel has a corresponding intensity associated with the intensity of the sound waves reflected from that location of the subject represented by a selected region of the image created by the received waves at the wave receiver.

In selected embodiments of an apparatus and method in accordance with the invention, a series of longitudinal positions along the image may be selected and the brightest pixel occurring in a search in the lateral direction is identified for each longitudinal position. The brightest pixel at any longitudinal position is that pixel, located in a lateral traverse of pixels in the image, at which the image has the highest level of intensity. The brightest pixels maybe curve fit by a curve slaving a domain along the longitudinal direction, typically comprising the longitudinal locations or positions, and having a range corresponding to the lateral locations of each of the brightest pixels. A curve fit of these brightest pixels provides a curve constituting an adventitia datum.

The adventitia datum is useful, although it is not necessarily the center, nor a boundary, of the adventitia. Nevertheless, a polynomial, exponential, or any other suitable mathematical function may be used to fit the lateral locations of pixels. The curve fit may also be accomplished by a piecewise fitting of the brightest pixel positions distributed along the longitudinal direction. Other curve fits may be made over the same domain using some other criterion for selecting the pixels in the range of the curve. In some embodiments, a first, second, or third order polynomial may be selected to piecewise curve fit the adventitia datum along segments of the longitudinal extent of the image. Other functions may be used for piecewise or other curve fits of pixels meeting selected criteria over the domain of interest.

In certain embodiments, a lumen datum may be located by one of several methods. In one embodiment, the lumen datum is found by translating the adventitia datum to a location in the lumen at which substantially every pixel along the curve shape has an intensity less than some threshold value. The threshold value may be a lowest intensity of the image. Alternatively, a threshold value may be something above the lowest intensity of pixels in the image, but nevertheless corresponding to the general regional intensity or a bounding limit thereof found within or near the lumen. The lowest intensity of the image may be extracted from a histogram of pixel intensities within a measurement region. In some embodiments, the threshold is set as the intensity of the lowest intensity pixel in the measurement region plus 10 percent of the difference in intensities between the highest and lowest intensities found in the measurement region. In still other embodiments, an operator may simply specify a threshold.

In another embodiment, the lumen datum may be identified by locating the pixel having a lowest intensity proximate some threshold value or below some threshold value. This may be further limited to a circumstance where the next several pixels transversely are likewise of such low intensity in a lateral (vertical, transverse) direction away from the adventitia. By whichever means it is found, a lumen datum comprises a curve fit of pixels representing a set of pixels corresponding to some substantially minimal intensity according to a bounding condition.

In certain embodiments, a media datum may be defined or located by fitting yet another curve to the lateral position of media dark pixels distributed in a longitudinal direction, substantially between the lumen datum and the adventitia datum. Media dark pixels have been found to evidence a local minimal intensity in a sequential search of pixels in a lateral direction, between the lumen datum and the adventitia datum. That is, image intensity tends to increase initially with distance from the lumen, then it tends to decrease to a local minimum within the media, then it tends to increase again as one moves from the media toward the adventitia.

As a practical matter, threshold values of intensity or distance may be provided to limit ranges of interest for any search or other operation using image data. For example, it has been found that a threshold value of ten percent of the difference, between the maximum intensity in a measurement region and the minimum intensity. Lidded to the minimum intensity is a good minimum threshold value for assuring that media dark pixels found are not actually located too close to the lumen. Similarly, a threshold may be set below the maximum intensity within the measurement region, in order to assure that minima arc ignored that may still be within the region of non-interest near the adventitia when searching for the location of media dark pixels. In some instances. 25 percent of the difference between maximum and minimum intensities added to the minimum intensity is a good increment for creating a threshold value.

In some circumstances, a pixel located within or at half the distance between (from) the adventitia datum and (to) the lumen datum may be used as the location of a media dark pixel, such as a circumstance where no adequate local minimum is found. That is, if the actual intensities are monotonically decreasing from the adventitia toward the lumen, then no local minimum may exist short of the lumen. In such a circumstance, limiting the media datum points considered to those closer to the adventitia than to the halfway point between the lumen datum and the adventitia datum has been shown to be an effective filter.

In general, the media datum is curve fit to the line of media dark pixels. However, it has also been found effective to establish a temporary curve fit of media dark pixels and move all media dark pixels lying between the temporary curve fit and the adventitia datum directly over (laterally) to the temporary curve fit. By contrast, those media dark pixels that may lie toward the lumen from the temporary curve fit are allowed to maintain their actual values. One physical justification for this filtering concept is the fact that the boundary of the adventitia is not nearly so subject to variation as the noise of data appears to show. Accordingly, and particularly since the actual media/adventitia boundary is of great importance, weighting the media datum to be fit to no points between the temporary curve fit and the adventitia datum, has been shown to be an effective filter.

In certain embodiments, the lumen/intima boundary may be determined by locating the largest local intensity gradient, that is, locating the maximum rate of change in intensity with respect to movement or position in the lateral direction in a traverse from the lumen datum toward the media datum. This point of local steepest ascent in such a lateral traverse has been found to accurately represent the lumen/intima boundary. A spike removing operation may be applied to a lumen/intima boundary to remove aberrant spikes in the boundary. The resulting boundary may also be curve fit to reduce error. In some embodiments the a spike removing operation is performed before any curve fit to improve the accuracy of the resulting curve.

Similarly, the media/adventitia boundary has been found to be accurately represented by those points or pixels representing the point of steepest ascent in intensity or most rapid change in intensity with respect to a lateral position, in a traverse from the media datum toward the adventitia datum. Clearly, the distance between the lumen/intima boundary and the media/adventitia boundary represents the intima-media thickness. A spike removing operation may be applied to a media/adventitia boundary to remove aberrant spikes in the boundary. The resulting boundary may also be curve fit to reduce error. In some embodiments the a spike removing operation is performed before any curve fit to improve the accuracy of the resulting curve.

In one embodiment of the present invention, a software technique is used to automatically locate one or more aspects of a tissue structure, such as plaques in the carotid artery wall. For example, software techniques may process an image, such as an ultrasound image, of a known tissue structure, such as the carotid artery, and identify specific anatomical regions thereof. Using information with respect to the identified anatomical regions, software techniques may characterize an aspect of the tissue structure using knowledge with respect to the densities and locations of various features of the tissue structure and/or the aspect being characterized. For example, plaque in a carotid artery may be characterized by knowing typical densities and sizes of plaques and where these plaques reside in relation to the anatomy of the carotid artery.

In another embodiment, the operator of the software specifies a point inside the region of interest within the tissue structure, e.g., carotid artery wall, and a software technique is employed to determine the physical extent of an aspect thereof, such as plaque therein.

In another embodiment, the operator of the software specifies a path or region around an aspect of a tissue structure, and a software technique is employed to search inward from this region until the outer boundary of the tissue structure aspect is determined.

In another embodiment, once an aspect of a tissue structure, such as plaque, is located, either automatically, semiautomatically or manually, a software algorithm is used to determine the density characteristics of the tissue structure aspect. These can include average density, peak density, density extent (maximum density minus minimum density), total area of plaque, area of densest region, density histogram, density standard deviation or variance and, but not limited to density centroid.

In another embodiment, once a tissue structure aspect density is determined, the density values can be normalized to remove any dependency on the instrument gain setting when the imaging device, e.g., ultrasound device, captured the tissue structure image. This can be accomplished by normalizing the density values obtained by both 1) The minimum average intensity of the image (which typically corresponds to the lumen of the carotid artery when the image is of the carotid artery), and/or 2) The maximum average intensity of the image (which typically corresponds to the adventitia of the far wall of the carotid artery when the image is of the carotid artery).

In another embodiment, the normalized or un-normalized tissue structure aspect information can be used to construct a database of tissue structure aspect density information as well as events (stroke, heart attack, etc.) for the corresponding patients the density information was collected from to construct a risk stratification database.

In another embodiment, once the density of an aspect of a tissue structure is determined and after the optional normalization process to remove ultrasound instrument gain settings, the density information can then be recorded for use in comparison with tissue structure aspect densities collected over a broad population, which can then be used for risk stratification.

In another embodiment, tissue structure aspect densities can be tracked over time for a patient to determine density velocity as well as aspect formation velocity.

In another embodiment, the tissue structure aspect location can be determined manually or automatically from known landmarks and recorded for future reference. This location information could also be correlated with a tissue structure aspect database to determine the severity of this tissue structure aspect location.

The foregoing has outlined rather broadly the features and technical advantages of the present invention in order that the detailed description of the invention that follows may be better understood. Additional features and advantages of the invention will be described hereinafter which form the subject of the claims of the invention. It should be appreciated by those skilled in the art that the conception and specific embodiment disclosed may be readily utilized as a basis for modifying or designing other structures for carrying out the same purposes of the present invention. It should also be realized by those skilled in the art that such equivalent constructions do not depart from the spirit and scope of the invention as set forth in the appended claims. The novel features which are believed to be characteristic of the invention, both as to its organization and method of operation, together with further objects and advantages will be better understood from the following description when considered in connection with the accompanying figures. It is to be expressly understood, however, that each of the figures is provided for the purpose of illustration and description only and is not intended as a definition of the limits of the present invention.

BRIEF DESCRIPTION OF THE DRAWINGS

For a more complete understanding of the present invention, reference is now made to the following descriptions taken in conjunction with the accompanying drawing, in which:

The foregoing and other objects and features of the present invention will become more fully apparent from the following description, taken in conjunction with the accompanying drawings. Understanding that these drawings depict only typical embodiments of the invention and are, therefore, not to be considered limiting of its scope, the invention may be seen in additional specificity and detail in the accompanying drawings where:

FIG. **1** is a schematic diagram of a general purpose computer suitable for use in accordance with the present invention;

FIG. **2** is a schematic representation of a system suitable for creating and analyzing ultrasonic images of a carotid artery;

FIG. **3** is an example of an ultrasonic image of the common carotid artery;

FIG. **4** is a simplified representation of certain features of an ultrasonic image of the common carotid artery;

FIG. **5** is a schematic block diagram of a computing system and data structures suitable for analyzing ultrasonic images, in accordance with the invention;

FIG. **6** is a process flow diagram of a process suitable for locating certain features in an ultrasonic image of an artery, in accordance with the invention;

FIG. **7** is a schematic block diagram of data structures suitable for implementing a preparing module in accordance with the invention;

FIG. **8** is a schematic representation of a measurement region and a sampling region superimposed on an ultrasound image of the wall of an artery, in accordance with the invention;

FIG. **9** is a process flow diagram of an adapting process in accordance with the invention;

FIG. **10** is a histogram of the intensity of pixels within a sampling region with the location of thresholds marked in accordance with the invention;

FIG. **11** is a graph of pixel intensities versus their locations for a column of pixels, in accordance with the invention;

FIG. **12** is a simplified representation of a portion of an ultrasound image of the carotid artery having lumen, media, and adventitia datums superimposed thereon, in accordance with the invention;

FIG. **13** is a process flow diagram of an adventitia locating process, in accordance with the invention;

FIG. **14** is a series of graphs representing pixel intensity versus location for columns of pixels with lines representing a process used to compensate for noise and poor contrast, in accordance with the invention;

FIG. **15** is a process flow diagram of a lumen locating process. in accordance with the invention;

FIG. **16** is a process flow diagram of a process for compensating for low contrast, in accordance with the invention;

FIG. **17** is a process flow diagram of an alternative lumen locating process, in accordance with the invention:

FIG. **18** is a simplified representation of an ultrasonic image of the common carotid artery with lines representing he process of adapting an adventitia datum to find a rumen cialum. in, accordance with the invention;

FIG. **19** is a process flow diagram of a media datum locating process, in accordance with the invention;

FIG. **20** is a flow chart representing a process for locating a media dark pixel in a column of pixels, in accordance with the invention;

FIG. **21** is a process flow diagram representing an alternative media datum locating process, in accordance with the invention;

FIG. **22** is a graphical representation of the process of adjusting minima locations in order to find a media datum;

FIG. **23** is a process flow diagram of a lumen/intima boundary locating process, in accordance with the invention;

FIG. **24** is a process flow diagram of a media/adventitia boundary locating process, in accordance with the invention;

FIG. **25** is a schematic block diagram of data structures suitable for implementing a calculating module in accordance with the invention;

FIG. **26** is a process flow diagram of a taper compensating process in accordance with the invention;

FIG. **27** is a Graph representing the IMT measurements taken along a measurement region;

FIG. **28** is a graph illustrating the portions of an IMT measurement used to calculate a normalization factor. in accordance with the invention;

FIG. **29** is a graph illustrating the normalization of IMT thicknesses along a portion of, the carotid artery, in accordance with the invention;

FIG. **30** shows a block diagram a system used to measure density information with respect to a tissue structure aspect according to an embodiment of the present invention; and

FIG. **31** shows a flow diagram illustrating measuring density information with respect to a tissue structure aspect according to an embodiment of the present invention.

DETAILED DESCRIPTION OF THE INVENTION

It will be readily understood that the components of the present invention, as generally, described and illustrated in the Figures herein, could be arranged and designed in a wide variety of different configurations. Thus, the following more detailed description of the embodiments of the system and method of the present invention, as represented in FIGS. **1-29**, is not intended to limit the scope of the invention, as claimed, but is merely representative of certain presently preferred embodiments in accordance with the invention. These embodiments will be best understood by reference to the drawings, wherein like parts are designated by like numerals throughout.

Those of ordinary skill in the art will, of course, appreciate that various modifications to the details illustrated in FIGS. **1-29** may easily be made without departing from the essential characteristics of the invention. Thus, the following description is intended only by way of example, and simply illustrates certain presently preferred embodiments consistent with the invention as claimed herein.

Referring now to FIG. **1**, an apparatus **10** may include a node **11** (client **11**, computer **11**.) containing a processor **12** or CPU **12**. The CPU **12** may be operably connected to a memory device **14**. A memory device **14** may include one or more devices such as a hard drive **16** or non-volatile storage device **16**, a read-only memory **18** (ROM) and a random-access (and usually volatile) memory **20** (RAM).

The apparatus **10** may include an input device **22** for receiving inputs from a user or another device. Similarly, an output device **24** may be provided within the node **11**, or accessible within the apparatus **10**. A network card **26** (interface card) or port **28** may be provided for connecting to outside devices, such as the network **30**.

Internally, a bus **32** (system bus **32**) may operably interconnect the processor **12**, memory devices **14**, input devices **22**, output devices **24**, network card **26** and port **28**. The bus **32** may be thought of as a data carrier. As such, the bus **32** may be embodied in numerous configurations. Wire, fiber optic line, wireless electromagnetic communications by visible light, infrared, and radio frequencies may likewise be implemented as appropriate for the bus **32** and the network **30**.

Input devices **22** may include one or more physical embodiments. For example, a keyboard **34** may be used for interaction with the user, as may a mouse **36**. A touch screen **38**, a telephone **39**, or simply a telephone line **39**, may be used for communication with other devices. with a user, or the like.

Similarly, a scanner **40** may be used to receive graphical inputs which may or may not be translated to other character formats. A hard drive **41** or other memory device **14** may be used as an input device whether resident within the node **11** or some other node **52** (e.g., **52***a*, **52***b*, etc.) on the network **30**. or from another network **50**.

Output devices **24** may likewise include one or more physical hardware units. For example, in general, the port **28** may be used to accept inputs and send outputs from the node **11**. Nevertheless, a monitor **42** may provide outputs to a user for feedback during a process, or for assisting two-way communication between the processor **12** and a user. A printer **44** or a hard drive **-46** may be used for outputting information as output devices **24**.

In general, a network **30** to which a node **11** connects may, in turn, be connected through a router **48** to another network **50**. In general, two nodes **11**, **52** may be on a network **30**, adjoining networks **30**, **50**, or may be separated by multiple routers **48** and multiple networks **50** as individual nodes **11**, **52** on an internetwork. The individual nodes **52** may have various communication capabilities.

In certain embodiments, a minimum of logical capability may be available in any node **52**. Note that any of the individual nodes **52**, regardless of trailing reference letters, may be referred to, as may all together, as a node **52** or nodes **52**.

A network **30** may include one or more servers **54**. Servers may be used to manage, store, communicate, transfer, access, update, and the like, any number of files for a network **30**. Typically, a server **54** may be accessed by all nodes **11**, **52** on a network **30**. Nevertheless, other special functions, including communications, applications, and the like may be implemented by an individual server **54** or multiple servers **54**.

In general, a node **11** may need to communicate over a network **30** with a server **54**, a router **48**, or nodes **52**. Similarly, a node **11** may need to communicate over another network (**50**) in an internetwork connection (e.g. Internet) with some remote node **52**. Likewise, individual components of the apparatus **10** may need to communicate data with one another. A communication link may exist, in general, between any pair of devices or components.

By the expression "nodes" **52** is meant anyone or all of the nodes **48**, **52**, **54**, **56**, **58**, **60**, **62**, **11**. Thus, any one of the nodes **52** may include any or all of the component parts illustrated in the node **11**.

To support distributed processing, or access, a directory services node **60** may provide directory services as known in the art. Accordingly, a directory services node **60** may host software and data structures required for providing directory services to the nodes **52** in the network **30** and may do so for other nodes **52** in other networks **50**.

The directory services node **60** may typically be a server **54** in a network. However, it may be installed in any node **52**. To support directory services, a directory services node **52** may typically include a network card **26** for connecting to the network **30**, a processor **12** for processing software commands in the directory services executables, a memory device **20** for operational memory as well as a non-volatile storage device **16** such as a hard drive **16**. Typically, an input device **22** and an output device **24** are provided for user interaction with the directory services node **60**.

Referring to FIG. **1** in one embodiment, a node **11** may be embodied as any digital computer **11**, such as a desktop computer **11**. The node **11** may communicate with an ultrasound system **62** having a transducer **64**, or "sound head" **64**, for emitting sound waves toward tissue to be imaged and sensing sound waves reflected from the tissue. The ultrasound system **62** then interprets the reflected sound waves to form an image of the tissue. The image may then be transmitted to the node **11** for display on a monitor **42** and/or for analysis. The transducer **64** may be positioned proximate the carotid artery **65** located in the neck of a patient **66** in order to produce an ultrasonic image of the common carotid artery (hereinafter "the carotid artery"). Of course, other imaging methods such as magnetic resonance imaging (MRI) or the like may be used to generate an image of a carotid artery **65**.

A server **54** may be connected to the node **11** via a network **30**. The server **54** may store the results of analysis and/or archive other data relevant to the measurement of the carotid artery and the diagnosis of medical conditions.

FIG. **3** is an example of an ultrasonic image of a carotid artery produced by an ultrasound system **62**. The shades of gray indicate reflectivity, and typically density, of the tissue, with white areas representing the densest and most reflective tissue and black areas the least dense or least reflective tissue. The image output by the ultrasound system may also include markings such as calibration marks **72***a*-**72***e* or a time stamp **72***f*.

Referring to FIG. **4**, an ultrasonic image of the carotid artery comprises an array of pixels each associated with a numerical value representing the intensity (e.g. black, white, gray shade, etc.) of that pixel. Accordingly, a horizontal direction **74** may be defined as extending along the rows or pixels in the image and a lateral direction **76** may be defined as extending along the columns of pixels. In some embodiments of the invention, the lateral direction **76** may be substantially perpendicular to the direction of blood flow in the carotid artery. The horizontal direction **74** may be substantially parallel to the direction of blood flow.

An ultrasonic image of the carotid artery typically reveals various essential features of the artery, such as the lumen **78**, representing the cavity portion of the artery wherein the blood flows, as well as the intima **80**, the media **82**, and the adventitia **84**, all of which form the wall of the artery. The thickness of the intima **80** and the media **82** (intima-media thickness or IMT) may be measured to diagnose a patient's risk of arterial sclerosis such as coronary artery disease.

The image typically shows the near wall **86** and the far wall **88** of the artery. The near wall **86** being closest to the skin. The far wall **88** typically provides a clearer image inasmuch as the Intima **80** and media **82** are less dense than the adventitia **84** and therefore interfere less with the sound waves reflected from the adventitia **84**. To image the near wall **86**, the sound waves reflected from the intima **80** and media **82** must pass through the denser adventitia **84**, which interferes measurably with the sound waves.

As the common carotid artery extends toward the head it eventually bifurcates into the internal and external carotid arteries. Just before the bifurcation, the common carotid artery has a dilation point **90**. The IMT **92** of the approximately 10 mm segment **94** below this dilation point **90** (the portion of the common carotid artery distal from the heart) is typically greater than the IMT **96** of the segment **98** extending between 10 mm and 20 mm away from the dilation point **90** (the portion of the common carotid artery proximate the heart). This is the case 88% of the time in the younger population (average age 25), with the IMT **92** of the segment **94** being 14% thicker than the IMT **96** of the segment **98**. On the other hand, 12% of the time the IMT **92** may be the same as the IMT **96**, or thinner. Among the older population (average age 55), the IMT **92** is 8% greater than the IMT **96** in 69% of the population. However. in 31% of the older population, the IMT **92** is the same as or smaller than the IMT **96**.

This tapering of the IMT as one moves away from the bifurcation may introduce uncertainty into the interpretation of an IMT measurement, inasmuch as variation in IMT measurements may simply be due to shifting the point at which a measurement was taken.

Furthermore, the walls **86**, **88** may be at an angle **100** relative to the horizontal direction **74**. Therefore. IMT measurements that analyze lateral columns of pixels may vary due to the orientation of the carotid artery in the image rather than actual variation in thickness.

Referring to FIG. **5**, a memory device **14** coupled to a processor **12** may contain an image processing application **110** having executable and operational data structures suitable for measuring, among other things, the IMT of the carotid artery. The image processing application may include a calibration module **112**, an image referencing module **114**, a preparing module **116**, a locating module **118**, a calculating module **120**, an image quality module **122**, and a reporting module **124**.

The calibration module **112** may correlate the distances measured on the image to real world distances. The calibration module **112** typically takes as inputs the pixel coordinates of two points in an image as well as the actual distance between the points. The calibration module then uses these known values to convert other distances measured in the image to their true values.

The calibration module **112** may extract the pixel coordinates from the image by looking for the calibration marks **72***a*-**72***e*. The true distance between the marks **72***a*-**72***d* may be known such that no user intervention is needed to provide it, or the calibration module may prompt a user to input the distance or extract the value from a file or the like. Alternatively mark **72***e* may indicate this distance between the calibration points **72***a*-**72***d* in some embodiments, such information as the model of ultrasound machine **62** zoom mode, or the like may be displayed, and the calibration module **112** may store calibration factors and the like mapped to the various ultrasound machines **62** and their various zoom modes.

The calibration module may then calibrate an image based on known calibration factors for a particular ultrasound machine **62** in a particular zoom mode. The calibration module **112** may also search for "landmarks," such as physical features, patterns, or structures, in an image and perform the calibration based on a known distance between the landmarks or a known size of a landmark.

The image referencing module **114**, preparing module **116**, locating module **118**, and calculating module **120** typically interpret the image and extract IMT measurements and the like. The operation of these modules will be described in greater detail below.

The image quality module **122** may operate on the image, or a selected region of interest within an image, to remove noise and otherwise improve the image. For example, the image quality module **122** may apply a low pass filter to remove noise from the image or use an edge detection or embossing filter to highlight edges. In a typical ultrasound image of the carotid artery, the layers of tissue extend parallel to the horizontal direction **74**. Accordingly, a lateral filter may be applied in a substantially horizontal direction **74** , or a direction parallel to the boundary between the layers of tissue, to reduce noise in a biased direction, to prevent loss of edge data that may indicate the boundary between different lavers of tissue.

The image quality module **122** may also notify a user when an image is too noisy to be useful. For example, the image quality module may display on a monitor **42** a gauge, such as a dial indicator, numerical value, color coded indicator, or the like, indicating the quality of the image. In some embodiments, the image quality module **122** may evaluate the quality of an image by first locating the portion of the image representing the lumen **78**. Because the lumen **78** is filled with blood of substantially constant density, a high quality image of the lumen would be of substantially constant pixel intensity. Accordingly, the image quality module **122** may calculate and display the standard deviation of pixel intensities within the lumen as an indicator of the noisiness of an image. The smaller the standard deviation of the pixel intensities the higher the quality of the image.

The image quality module **122** may locate the lumen **78** in the same manner as the locating module **118** as discussed below. After finding the lumen/intima boundary at both the near wall **86** and the far wall **88**, the image quality module **122** may examine the region between the two boundaries to calculate the standard deviation of lumen pixel intensities. Alternatively, the image quality module **122** may evaluate a region of predetermined dimensions with one edge lying near the lumen/intima boundary.

Another criterion that the image quality module **122** may use to evaluate quality is a histogram of pixel intensities in a measurement region or, in other words, a portion of the image where the IMT is measured. Alternatively, a larger area including the area surrounding the measurement region may be used to compute the histogram. The form of the histogram will typically vary in accordance with the quality of the image. The image quality module **122** may store an image of a histogram generated from a high quality image and display it on an output device **24** along with the histogram of the image being analyzed.

Operators may then be trained to identify a "good" histogram in order to determine whether measurements taken from a particular image are reliable. The image quality module may likewise store and display images of medium quality and poor quality histograms to aid an operator. Alternatively, the image quality module **122** automatically compare a histogram to stored images high, medium, and/or low quality histograms and rate their similarity. This may be accomplished by pattern-matching techniques or the like.

The reporting module **124** may format the results of calculations and send them to an output device **24**, such as a monitor **42**, printer **44**, hard drive **46**, or the like. The image processing application **110** may also store results in, or retrieve information from, a database **126** having a database engine **128** for storing, organizing, and retrieving archived data. The database **126**, as with any module comprising the invention, may be physically located on the same node **11** or may be located on a server **54**, or other node **52***a*-**52***d*, and may communicate with a node **11** via a network **30**. The database engine **128** may be that of any suitable databasing application known in the art.

The database **126** may store various records **129**. The records **129** may include patient records **130**. Patient records **130** may store such information as a patient's age, weight, risk factors, cardiovascular diseases, prior IMT measurements, and other relevant medical information. The diagnostic data **131** may provide data to support a statistical analysis of a patient's risk of developing a cardiovascular disease. For example, diagnostic data **131** may include the results of studies, or the like, linking IMT measurements and/or other risk factors with a patient's likelihood of developing coronary artery disease.

Measurement records **132** may include information concerning the measurement process itself. For example, measurement records **132** may include a reference to an ultrasound image analyzed or the image itself. Measurement records **132** may also include any inputs to the measurement process, the name of the operator who performed the measurement, the algorithm used to analyze the image, values of various parameters employed, the date the measurement was made, ultrasound machine data, values of sources of error, and the like.

The IMT database **133** may archive IMT measurements for use in the interpretation of later ultrasound images. The IMT database **133** may include records **134** of prior measurements, each including an index IMT **135**. The index IMT **135** maybe an IMT value used to characterize the record **134**. For example. IMT measurements along a portion of the carotid artery may be stored based on the IMT at a standardized point on an individual carotid artery. Accordingly, the index IMT **135** may be the IMT at the standardized point. Alternatively, the average of all IMT measurements along the portion measured may be used as the index IMT **135**. IMT measurements **136** may include IMT measurements made at various points along the length of the carotid artery. The IMT measurements **136** may be of one ultrasound image, or an average of measurements from multiple ultrasound images. In some embodiments an IMT measurement **36** may be a polynomial curve fit of IMT measurements taken along a portion of an artery.

The memory device **14** may also contain other applications **137** as well as an operating system **138**. The operating system **138** may include executable (e.g. programming) and operational (e.g. information) data structures for controlling the various components comprising the node **11**. Furthermore, it will be understood that the architecture illustrated in FIGS. **2** and **5** is merely exemplary, and various other architectures are possible without departing from the essential nature of the invention. For example, a node **11** may simply be an ultrasound system **62** having at least a memory device **14** and a processor **12**. Accordingly, the image processing application **110** and/or the database **126** may be embedded in the ultrasound system **62**. An ultrasound **62** may also include a monitor **42**, or other graphical display such as an LCD or LED, for presenting ultrasound images and the results of calculations.

Referring to FIG. **6**, the process of locating essential features of the carotid artery may include the illustrated steps. It will be understood that the inclusion of steps and the ordering of steps is merely illustrative and that other combinations and orderings of steps are possible without departing from the essential nature of the invention.

The process may include an image calibration step **140** to perform the operations described above in conjunction with the calibration module **112**. The preparing step **142** may identify the region of the image representing a portion of the near wall **86** or far wall **88** to be analyzed. The referencing step **143** may calculate thresholds, or other reference values, based on the image for use in later calculations.

The locating process **144** may identify the various layers of tissue forming the artery walls **86**, **88**. It may also locate the boundaries between the layers of tissue. Accordingly, the locating process may include an adventitia datum locating step **146**, which identifies the location of the adventitia **84** and establishes a corresponding datum. The lumen datum locating step **148** may establish a datum curve within the lumen. The media datum locating step **150** may identify the portion of the artery wail corresponding to the media and establish a corresponding datum. The lumen/intima boundary locating step **152** may search between the lumen datum and the media datum for the lumen/intima boundary. The media/adventitia boundary locating step **154** may search between the media datum and the adventitia datum for the media/adventitia boundary.

Referring to FIG. **7**, modules are executables, programmed to run on a processor **12**, and may be stored in a memory device **14**. The preparing step **142** may be carried out by the preparing module **116**, which may comprise an input module **160**, an automation module **162**, a reconstruction module **164**, and an adapting module **166**.

Referring to FIG. **8**, the input module **160** may permit a user to select a point **170** in an image, which will serve as the center of a measurement region **172**. The IMT of columns of pixels within the measurement region may be measured and all columns averaged together, or otherwise combined, to yield a final IMT measurement and other information. Alternatively, the IMT can be curve fit longitudinally. Accordingly, the height **174** of the measurement region **172** may be chosen such that it includes at least portions of the lumen **78**, the intima **80**, the media **82**, and the adventitia **84**.

The input module **160** may enable a user to specify a width **176** of the measurement region **172**. Alternatively, the input module **160** may simply use a predetermined value. For example, one adequate value is 5 mm, which is also approximately the diameter of the carotid artery in most cases. Whether found automatically, bounded automatically or by a user, or specified by a user, the width **176** may also be selected based on the image quality. Where the image is noisy or has poor contrast, a larger width **176** may be used to average out errors. In embodiments where the width **176** is chosen automatically, the input module **160** may choose the width based on an indicator of image quality calculated by the image quality module **122**. Likewise, an operator may be trained to manually adjust the width **176** based on indicators of image quality output by the image quality module **122**. In some embodiments, the input module may incrementally increase or decrease the width **176** in response to a user input such as a mouse click or keystroke.

The input module **160** may also determine which wall **86**, **88** to measure by determining which wall **86**, **88** is laterally nearest the point **170**. This may be accomplished by finding the highly recognizable adventitia **84** in each wall **86**, **88** and comparing their proximity to the point **170**. Alternatively, the input module **160** may choose the wall **86**, **88** having the highest (or highest average, highest mean, etc.) intensity in the adventitia **84**, and which therefore has a greater likelihood of having desirable high contrast.

The point **170** may also serve as the center of a sampling region **178**. The pixels bounded by the sampling region **178** are used to generate a histogram of pixel intensities that is used by other modules to determine certain threshold values and to evaluate the quality of the image. The height **180** is typically chosen to include a portion of both the lumen **78** and adventitia **84** inasmuch as these represent the lowest and highest intensity regions, respectively, of the image and will be relevant to analysis of the histogram. The width **182** may be chosen to provide an adequate sampling of pixel intensities. In some embodiments, the width **182** is simply the same as the width **176** of the measurement region **172**. Adequate values for the height **180** have been shown to be from one-half to about one-fourth of the width **176** of the measurement region **172**.

The automating or automation module **162** may automatically specify the location of a measurement region **172** and/or a sampling region **178**. The automation module **162** may accomplish this by a variety of means. For example, the automation module may simply horizontally center the region **172** at the center of the image. The lateral center of the region **172** may be set to the location of the brightest pixels in the lateral column of pixels at the center of the image. These brightest pixels would correspond to the adventitia **84** of the wall having the highest, and therefore the best, contrast. Alternatively, the automation module **162** may located the lumen **78** by searching a central column of pixels for a large number of contiguous pixels whose intensity, or average intensity, is below a specific threshold corresponding to the intensity of pixels in the lumen. One side of this group of pixels may then be chosen as the center of the measurement region **172** inasmuch as the sides will have a high probability of being proximate the lumen/intima boundary. The automating module **162** may also adjust the size and location of the measurement region **172** and sampling region **178** to exclude marks **72*a*-72*f*** that may be found in an image. The automating module **162** may also adjust a user selected measurement region **172** and sampling region **178** to avoid such marks **72*a*-72*f***.

Referring again to FIG. **7**, the reconstruction module **164** may store relevant user inputs, such as the location of the point **170** or any user specified dimensions for the regions **172**, **178** in the database **126**. The reconstruction module **164** may also store a signature uniquely identifying the image measured, or may store the image itself. The reconstruction module **164** may also store other inputs such as the algorithm used to locate the layers of tissue or the method used to eliminate noise.

The reconstruction module **164** may store this information in any accessible storage location, such as in the database **126** as measurement data **132** or the hard drive **46** of the node **11**. The reconstruction module **164** may then retrieve this information and use it to recreate an IMT measurement and its process of construction. The reconstruction module **164** may also allow a user to adjust the inputs prior to recreating a prior measurement. Therefore, one can readily study the effect a change of an individual input has on the measurement results.

The ability to retrieve inputs and to recreate an IMT measurement may be useful for training operators to use the image processing application **110**. This ability enables an expert to review the measurement parameters specified by an operator and provide feedback. The inputs specified by an operator can also be stored over a period of time and used to identify trends or changes in an operator's specification of measurement parameters and ultimately allow for validation and verification of an operator's proficiency.

The adapting module **166** may adapt inputs and the results of analysis to subsequent images in order to reduce computation time. This is especially useful for tracking IMT values in a video clip of ultrasound images which comprises a series of images wherein the image before and the image after any given image will be similar to it. Given the similarity of the images, needed inputs and the results of analysis will typically not vary greatly between consecutive images.

For example, the adapting module **166** may adapt a user selected region **172**, **178** to successive images. The results of other computations discussed below may also be stored by the adapting module **166** and reused. For example, the angle **100** and the location of adventitia, media, and lumen datums, provide rough but still usefully accurate estimates of the location of the boundaries between layers of tissue. The adapting module **166** may also use reference values, or thresholds, generated from the analysis of the histogram of a previous sampling region **178** for the measurement of a subsequent image.

Referring to FIG. **9**, the adapting module **166** may also adapt inputs, datums, and other results of calculations to accommodate change in the image. For example, the adapting module **166** may shift the location of the region **172** in accordance to shifting of the carotid artery between successive images due to movement of the artery itself or movement of the transducer **64**. That is, the module **166** may re-register the image to realign object in the successive images of the same region.

Adapting the location of the regions **172**, **178** may provide a variety of benefits, such as reducing the time spent manually selecting or automatically calculating a region **172**, **178**. The reduction in computation time may promote the ability to track the location of the layers of tissue in the carotid artery in real time. By reducing the time spent computing the regions **172**, **178** the image processing application **110** can measure video images at higher frame rates without dropping or missing frames.

Accordingly, the adapting module **166** may carry out an adapting process **186** automatically or with a degree of human assistance or intervention. An analyzing step **188** is typically carried out by other modules. However, it is the first step in the adapting process **186**. Analyzing **188** a first image may include calculating reference values for use in later calculations, in identifying lumen, adventitia. and lumen datums in the image or both. Analyzing **188** may also include locating the boundaries between layers of tissue.

Once a first image has been analyzed, applying **190** analysis results to a second image may include using one or more of the same lumen, adventitia, or media datum located in a first image in the analysis of the second image. Applying **190** results from a first image to a second may simply include using results without modification in the same manner as the results were used in the first image. For example, a datum calculated for a first image may be used without modification in a second. Alternatively, applying **190** may involve using the results as a rough estimate (guess) that is subsequently refined and modified during the measurement process.

For example, the adventitia **84** typically appears in ultrasound images as the brightest portion of the carotid artery. Accordingly, locating the adventitia may involve finding a maximum intensity (brightness) region. Once the adventitia **84** is located in a first image, searches for the adventitia in a second image may be limited to a small region about the location of the adventitia in the first image. Thus, the field of search for the adventitia **84** in the second image is reduced by assuming that the adventitia **84** in the second image is in approximately the same position as the adventitia **84** in the first image. Registration may be based on aligning the adventitia **84** in two images, automatically or with human assistance.

Applying **192** inputs to a second image may include using inputs provided either manually or automatically for the analysis of a first image in comparison with or directly for use with a second image. The inputs to the analysis of a first image may also be the result of a calculation by the adapting module **166** as described below for the adapting step **194**. Thus, for example, the point **170** selected by a user for a first image may be used in a second image. Likewise, any user-selected, or automatically determined, height **174**, **180** or width **176**, **182** for a measurement region **172** or sampling region **178** may be used to analyze a new, or compare a second image.

Adapting **194** inputs to a second image may include determining how a second image differs from a first image. One method for making this determination may be to locate the adventitia **84** and note the location and/or orientation of recognizable irregularities in both the first and second images. By comparing the location, orientation, or both of one or more points on the adventitia, which may be represented by the adventitia datum, the adapting module **166** may calculate how the carotid artery has rotated or translated within the image. One such point may occur where the carotid artery transitions from straight to flared at the dilation point **90**. Any translation and/or rotation may then be applied to the point **170** selected by a user to specify the measurement region **172** and the sampling region **178**. The rotation and/or translation may also be applied to any automatically determined position of the regions **172**, **178**.

Referring to FIG. **10**, while referring generally to FIGS. **6-9**, the image referencing step **143** may calculate values characterizing a particular image for later use during analysis of the image. For example, the image referencing module **114** may generate a histogram **200** of pixel intensities within the sampling region **178**. The image referencing module may also calculate adventitia, media, and lumen thresholds based on the histogram **200** in order to facilitate the location of regions of the image corresponding to the lumen **78**, media **82** and adventitia **84**.

For example, the lumen threshold **202** may be chosen to be at a suitable (e.g. the 10th) percentile of pixel intensities. Of course other values may be chosen depending on the characteristics of the image. Alternatively, the lumen threshold **202** may be chosen based on the absolute range of pixel intensities present in the sampling region **78**. In some embodiments, the lumen threshold **202** may be calculated based on the minimum intensity **204** and maximum intensity **206** apparent in the histogram **200**. For example, the lumen threshold **202** may be calculated as a suitable fraction of the maximum difference in pixel intensity. The following formula has been found effective:

$$\text{lumen threshold} = \text{minimum intensity} + (\text{fraction}) \times (\text{maximum intensity} - \text{minimum intensity})$$

A fraction of from 0.05 to 0.25 can work and a value of from about 0.1 to about 0.2 has been successfully used routinely.

The adventitia threshold **208** may be hard coded to be at a fixed (e.g. the 90th) percentile of pixels ranked by intensity. The actual percentile chosen may be any suitable number of values depending on the quality of the image and the actual intensity of pixels in the adventitia portion of the image. Alternatively, the adventitia threshold **208** may equal the maximum intensity **206**. This choice is possible inasmuch as the adventitia often appears in ultrasound image as the brightest band of pixels. In some embodiments, the adventitia threshold **208** may also be chosen to be below the highest intensity by a fixed fraction of the maximum difference in intensities. The top 5-25 percent, or other percentage, of the range of pixel intensities may be used, and the top 10 percent has routinely served as a suitable threshold.

A media threshold **210** may be calculated based on the minimum intensity **204** and maximum intensity **206**. For example, the media threshold may be calculated according to the formula:

$$\text{media threshold} = \text{minimum intensity} + 0.25 \times (\text{minimum intensity} + \text{maximum intensity}).$$

this is effectively the 25th percent of the total range of intensities.

Of course, other values for the media threshold **210** are possible depending on the quality of the image and the actual intensity- of pixels in the portion of the image corresponding to the media **82**. In some embodiments, the media threshold **210** may be equal to the adventitia threshold **208**. In some embodiments, the media threshold **210** may be the intensity corresponding to a local minimum on the histogram **200** located between the lumen threshold **202** and the adventitia threshold **208**.

The image referencing module **114** may also receive and process inputs to enable a user to manually specify the thresholds **202**, **208**, **210**. For example, the image referencing module **114** may enable a user to manually select a region of pixels in the lumen **78**. The average or the maximum intensity of the pixels in this region is then used as the lumen threshold **202**. A user may determine adequate values for the adventitia threshold **208** and the media threshold **210** in a like manner relying on maximum, minimum, or average intensity, as appropriate.

In some embodiments, the image referencing module **114** may display the histogram **200** and permit a user to select a threshold based on an informed opinion of what portion of the histogram pixels correspond to the lumen, media, or adventitia. The image referencing module **114** may also simultaneously display the histogram **200** and the ultrasonic image of the carotid artery, highlighting the pixels that fall below, or above, a particular threshold **202 208**. **210**. The image referencing module **114** may then permit an operator to vary the lumen threshold **202** and observe how the area of highlighted pixels changes.

Referring to FIG. **11**, having determined threshold values **202**, **208**, **210** the locating module **118** may then analyze lateral columns of pixels to locate the lumen **78**, intima **80**, media **82**, adventitia **84**, the lumen/intima boundary, the media adventitia boundary, or any combination, including all. The locating module **118** may analyze lines of pixels oriented horizontally or at another angle, depending on the orientation of the carotid artery within an image. The locating module **118** will typically analyze a line of pixels that extends substantially perpendicular to the boundaries between the layers of tissue.

The graph **218** is an example of a graph of the intensity of pixels versus their location within a column of pixels, with the horizontal axis **220** representing location and the vertical axis **222** representing pixel intensity. Beginning at the left of the graph **218**, some significant portions of the graph **218** are: the lumen portion **224**, which may be that portion below the lumen threshold **202**; the lumen/intima boundary **226**, which may correspond to the highest intensity gradient between the lumen portion **224** and the intima maximum **228**; the intima maximum **228**, a local maximum corresponding to the intima; the media portion **230**, which may correspond to the portion of the graph below the media threshold **210**; the media dark pixel **231** typically providing a local minimum within the media portion **230**; the media/adventitia boundary **234** located at or near the highest intensity gradient between the media dark pixel **231** and the adventitia maximum **236**; and the adventitia maximum **236**, which is typically the highest intensity pixel in the measurement region **172**. It should be understood that the graph **218** is representative of an idealized or typical image, but that noise and poor contrast may cause graphs of pixel columns to appear different.

Referring to FIG. **12**, the locating process **144** may include locating datums to reduce the field of search for the boundaries between layers of tissue. In one embodiment the locating module may identify a lumen datum **240** and media datum **242** that have a high probability of bounding the lumen/intima boundary **244**. The media datum **242** and adventitia datum **246** may be chosen such that they have a high probability of bounding the media/adventitia boundary **248**. In some embodiments, the locating process **144** may not locate a media datum **242**, but rather search between the lumen datum **240** and the adventitia datum **246** for the lumen/intima boundary **244** and the media adventitia boundary **248**.

The locating process **144** may allow an operator to manually specify one, or all of, the datums **240**, **242**, **246**, or boundaries **244**, **248**. Any method for manually specifying a line may be used to specify a boundary **244**, **248**, or datum **240**, **242**. **246**. For example, an operator may trace a boundary **244**, **248** or a datum **240**, **242**, **246** on a graphical display of an ultrasound image using an input device **22**, such as a mouse **36**. A user may establish a boundary **244**. **248** or datum **240**, **242**, **246** by clicking at a series of points which are then automatically connected to form a curve. Alternatively, an operator may establish the end points of a line and subsequently establish control points to define the curvature and points of deflection of the line (i.e. a Bezier curve). In still other embodiments, an edge of a measurement region **172** may serve as a lumen datum **240** or adventitia datum **246**. Referring to FIG. **13**, the adventitia datum locating process **146** may include locating **252** an initial adventitia pixel. The initial adventitia pixel may be found in the column of pixels centered on a user selected point **170**. Other suitable approaches may include searching the column of pixels at the extreme left or right of the measurement region or selecting the column at the center of a region selected through an automatic process. The adventitia **84** is typically the brightest portion of the image, so the absolute maximum intensity pixel may be searched for as indicating the location of the adventitia **84**.

Alternatively, the initial adventitia locating step **252** may comprise prompting a user to manually select an initial adventitia pixel. Yet another alternative approach is to search for a minimum number of contiguous pixels each with an intensity above the adventitia threshold **208** and mark (e.g. label, identify, designate) one of them as the adventitia pixel. This pixel will be used to fit the adventitia datum **246**.

The adventitia locating process **146** may also include locating **254** adjacent adventitia pixels. Proceeding column by column, beginning with the columns of pixels next to the initial adventitia pixel, the locating module **118** may search for adjacent adventitia pixels in the remainder of the measurement region **172**. The adjacent adventitia pixels may be located in a similar manner to that of the initial adventitia pixel. In certain embodiments, the adventitia pixels may be found in a variety of sequences other than moving from one column to a contiguous column. Sampling, periodic locations, global maximum, left to right, right to left, and the like may all provide starting points, subject to the clarity and accuracy of the image.

Referring to FIG. **14**, while continuing to refer to FIG. **13**, the adventitia locating process **146** may compensate for noise and poor contrast by including a constraining step **256** and an extrapolating step **258**. The constraining step **256** may limit the field of search for an adventitia pixel to a small region centered or otherwise registered with respect to the lateral location of the adventitia pixel in an adjacent column.

For example, contiguous columns of pixels may yield a series of graphs **260***a*-**260***e*. Graph **260***a* may represent the first column analyzed. Accordingly, the maximum **262***a* is found and marked as the adventitia pixel, inasmuch as it has the maximum value of intensity. The constraining step **256** may limit searches for a maximum **262***b* in graph **260***b* to a region **264** centered on or otherwise registered with respect to the location of the maximum **262***a*. Maxima falling outside this range may then be dismissed as having a high probability of being the result of noise. That is, a blood vessel is smooth. The adventitia does not wander radically. Rejected maxima may then be excluded from any curve fit of an adventitia datum **246**.

The extrapolating step **258** may involve identifying a line **266** having a slope **268** passing through at least two of the maxima **262***a*-**262***e*. Searches for other maxima may then be limited to a region **270** limited with respect to the line **266**. Thus, in the illustrated graphs, the maxima **262***c* in graph **260***c* is not within the region **270** and may therefore be ignored. In some instances, the extrapolating step may involve ignoring multiple graphs **260***a*-**260***e* whose maxima **262***a*-**262***e* do not fall within a region **264**, **270**.

As illustrated, a graph **260***d* may have a maximum **262***d* outside the region **270** as well, whereas the graph **260***e* has a maxima **262***e* within the region **270**. The number of columns that can be ignored in this manner may be adjustable by a user or automatically calculated based on the quality of the image. Where the image is of poor quality the extrapolating step **258** may be made more aggressive, looking farther ahead for an adequate (suitable, clear) column of pixels. In some embodiments, the maxima **262***a*-**262***e* used to establish the line **266** may be limited to those that are in columns having good high contrast.

Referring again to FIG. **13**, a curve fitting step **272** may establish an adventitia datum **246**, a curve fit to the adventitia pixels located in the columns of pixels. A curve fit is typically performed to smooth the adventitia **84** and compensate for noise that does not truly represent the adventitia **84**. In one embodiment, the curve fitting step **272** may involve breaking the measurement region into smaller segments (pieces) and curve fitting each one, piecewise. A function, such as a second order polynomial, a sinusoid or other trigonometric function, an exponential function or the like may be selected to be fit to each segment. The segments may be sized such that the path of adventitia pixels is likely to be continuous, be monotonic, have a single degree of curvature (e.g. no 'S' shapes within a segment) or have continuity of a derivative. A segment width of 0.5 to 2 mm has been found to provide a fair balance of adequate accuracy, function continuity, and speed of calculation.

Other embodiments are also possible. For example, wider segments may be used with a third order polynomial interpolation to accommodate a greater likelihood of inflection points (an 'S' shape) or derivative continuity in the adventitia pixel path. However, a third order polynomial interpolation imposes greater computational complexity and time. Another alternative is to use very narrow segments with a linear interpolation. This provides simple calculations, functional continuity, but no first derivative continuity.

In some embodiments, the segments curve fitted may overlap one another. This may provide the advantage of each curve fitted segment having a substantially matching slope with abutting segments at the point of abutment. However, this approach may introduce computational complexity by requiring the analysis of many pixels twice. However, it provides for comparatively simpler computations for each segment.

Referring to FIG. **15**, the lumen datum locating process **148** may identify the portion of an image corresponding to the lumen **78** and establish a lumen datum **240**. The lumen datum locating process **148** may include locating **280** a low intensity region. This step may include finding, in a column of pixels, a specific number of contiguous pixels below the lumen threshold **202**. The search for a band of low intensity pixels typically begins at the adventitia **84** and proceeds toward the center of the lumen **78**. A region four pixels wide has been found to be adequate. Alternatively, step **280** may include searching for a contiguous group of pixels whose average intensity is below the lumen threshold **2022**.

Having located a low intensity region, the next step may be a validating step **282**. In some instances, dark areas within the intima/media region may be large enough to have four pixels below the lumen threshold **202**. Accordingly, a low intensity region may be validated to ensure that it is indeed within the lumen **78**. One method of validation is to ensure that the low intensity region is adjacent a large intensity gradient, which is typically the lumen/intima boundary **226**. The proximity to the intensity gradient required to validate a low intensity region may vary.

For example, validation may optionally require that the low intensity region be immediately next to the large intensity gradient. Alternatively, validation may only require that the low intensity region be within a specified number of pixels (e.g. distance) from the high intensity gradient. Where a low intensity region has a high probability of being invalid, the lumen datum locating process **148** may be repeated, beginning at the location of the invalid low intensity region found during the first iteration and moving away from the adventitia **84**.

The lumen datum locating process **148** may also include a compensating step **284**. In some cases, it may be difficult to verify that a low intensity region is proximate the lumen/intima boundary **224**, because limitations in the ultrasound imaging process may fail to capture intensity gradients, but rather leave regions of the image with poor contrast. Accordingly, a compensating step **284** may include methods to compensate for this lack of contrast by extrapolating, interpolating, or both, the boundaries into areas of poor contrast. Validating **282** may therefore include verifying a low intensity region's proximity to an interpolated or extrapolated boundary.

A curve fitting step **286** may incorporate the found low intensity regions into the lumen datum **240**. In some embodiments, a path comprising the first pixel found in the low intensity region of each column is curve fitted to establish the lumen datum **240**. In embodiments that use an average value of intensity to locate the lumen, a centrally (dimensionally) located pixel in a group of pixels averaged may be used to curve fit the lumen datum **240**. The curve fitting step **286** may curve fit the pixel path in the manner discussed above in conjunction with the adventitia datum locating process **146**.

FIG. **16** illustrates one method for implementing an optional low contrast compensating step **284**, which includes an identifying step **288**, a constraining step **290**, a bridging step **292**, and a verifying step **294**. An identifying step **288** may identify portions of the measurement region **172** that appear to be of high quality. Identifying **288** may include identifying a horizontal region at least three to five pixel columns wide, with each column having comparatively high contrast. A larger or smaller horizontal region may be chosen based on the nature and quality of the image, in some embodiments, the degree of contrast may be determined by looking for the largest, or sufficiently large, intensity gradient in a column. The value of the gradient sufficient to qualify a column of pixels as "high contrast" may be hard coded, user selected, automatically selected, a combination thereof, or all of the above, based on the characteristics of the image. In some embodiments, the intensity gradient required may be a certain percentage of the maximum intensity gradient found in the sampling region **178**.

Identifying **288** may also include verifying that the large intensity gradients in each column of a horizontal region occur at approximately the same position within the column, deviating from one another by no more than a predetermined number of pixels. Thus, for example, if in one column of pixels a high intensity gradient is located at the 7th pixel, identifying **288** may include verifying that a high intensity gradient in the adjacent column occurs somewhere between the 70th and 80th pixel. Columns whose high intensity gradient is not located within this region may be excluded from the horizontal region of high intensity pixels for purposes of evaluating the quality of the image and extrapolating and interpolating gradient or boundary locations. In some embodiments, only regions of a specific width having contiguous columns with high intensity gradients occurring at approximately the same lateral position are treated as high contrast regions.

A constraining step **290** may attempt to identify the location of the lumen/intima boundary **226**, or, more generally, any boundary or feature, in the absence of high contrast. One manner of accomplishing this is to constrain the area of search. Constraining **290** may therefore search for the largest gradient in a low contrast region between two high contrast regions by restricting its search to a region centered on a line drawn from the large intensity gradient n one of the high contrast regions to the urge intensity gradient in the second.

Constraining **290** may also include using a different value to define the boundary. Whereas, in a high contrast region a comparatively large value may be used to identify, limit, or specify which gradients represent boundaries, constraining **290** may include determining the maximum intensity gradient in a comparatively lower contrast region and using some percentage of this smaller value to define which gradients are sufficiently large to represent a boundary. Likewise, constraining **290** may comprise looking for the steepest gradient above some minimum value within a constrained region.

A bridging step **292** may include interpolating the location of a boundary or other intensity gradient in a low contrast region based on the location of the boundary or gradient in comparatively higher contrast regions on either side. Optionally, in some embodiments, the location of a boundary or gradient may be extrapolated based on the location of a high contrast region to one side of a low contrast region.

A verifying step **294** may verify that the high contrast regions are adequate to justify interpolation and extrapolation into the comparatively lower contrast regions. A verifying step **294** may include comparing the number of columns in these "high" contrast regions to the number of columns in the "low" contrast regions. Where more pixel columns are in low contrast regions than are in high contrast regions, extrapolation and interpolation may not improve accuracy.

Referring to FIG. **17**, in an alternative embodiment, the lumen datum locating process **148** includes a translating step **300** and a translation verifying step **302**. Referring to FIG. **18**, the translating step **300** may include translating the adventitia datum **246** toward the center of the lumen **78**. The translation verifying step **302** may average the intensities of all the pixels lying on the translated path. Where the average value, mean value, or some number of total pixels correspond to an intensity that is less than the lumen threshold **202**, or some other minimum value, the translation verifying step **302** may include establishing the translated adventitia datum **246** as the lumen datum **240**. Alternatively, the translation verifying step **302** may include marking the translated adventitia datum **246** as the lumen datum **240** only where the intensity of all pixels lying on the translated datum **246** are below the lumen threshold **202**, or some other minimum value. Alternatively, the translated adventitia datum **246** may simply serve as a starting point for another curve fit process, or serve as the center, edge, or other registering point, for a region constraining a search for a lumen datum **240**, for example the method of FIG. **15** could be used to search for a lumen datum **240** within a constrained search region.

Referring to FIG. **19**, the media datum locating process **150** may include a locating step **308** and a curve fitting step **310**. A locating step **308** may identify a media dark pixel path that is subsequently adapted to yield a media datum **242**. The curve fitting step **310** may curve fit a media dark pixel path to yield a media datum **242** in a like manner as other curve fitting steps already discussed in accordance with the invention. In some embodiments, the media datum locating process **150** may be eliminated and the lumen datum **240** may be used everywhere the media datum **242** is used to limit fields of search. In still other embodiments, a lumen datum **240** may be eliminated and the adventitia **84** alone may constrain searches for the boundaries between layers of tissue. For example, searches for the media/adventitia boundary may simply begin at the adventitia datum **246** and move toward the lumen **78**.

Referring to FIG. **20**, the locating process **312** illustrates one method for locating **308** the media dark pixel path. The process **312** may be carried out on the columns of pixels in the measurement region **172**. The process **312** may begin by examining a pixel lying on, or near, the adventitia datum **246**. After determining **314** the intensity of a pixel, the process **312** may determine **316** whether the pixel is a local minimum. If so, the process **312** may determine **318** if the pixel intensity is less than the media threshold **210**. If so, the pixel is marked **320** or designated **320** as a media dark pixel, and the process **312** is carried out on another column of pixels.

If a pixel is not a local minimum, the process **312** may determine **322** whether the pixel is located less than a predetermined distance from the adventitia **84**. An adequate value for this distance may be about one half to two thirds of the distance from the adventitia **84** to the lumen **78**. The adventitia datum **246** and the lumen datum **240** may be used to specify the location of the adventitia **84** and the lumen **78** for determining the distance therebetween. If the pixel is less than the specified distance from the adventitia **84**, then the process **312** moves **323** to the next pixel in the column, in some embodiments moving away from the adventitia **84**, and the process **312** is repeated. If the pixel is spaced apart from the lumen **78** by the specified distance, then it is marked **324** as a media dark pixel and the process **312** is carried out for any remaining columns of pixels.

If a minimum value of intensity is not less than the media threshold **210**, the process **312** may determine **326** whether the distance from the pixel to the adventitia **84** is greater than or equal to the same predetermined value as in step **322**. If greater than or equal to that valve, the corresponding pixel is marked **328** as a media dark pixel and the process **312** is carried out on any remaining columns. If less, then the process **312** moves **329** to the next pixel in the column, typically moving toward the adventitia **84**, and the process **312** is repeated.

FIG. **21** illustrates another embodiment of a media datum locating process **150**. A minimum locating step **330** may look for local minima of intensity in each column of pixels, between the adventitia **84** and the lumen **78**. In some embodiments, the minimum locating step **330** may search for a local minimum between the adventitia datum **246** and the lumen datum **240**. The minimum locating step **330** may search for minima beginning at the adventitia datum **246** and moving toward the lumen datum **240**. In columns of pixels having poor contrast, the minimum locating step **330** may include extrapolating or interpolating the probable location of a local minimum representing the media based on the location of validated minima on either side, or to one side, of a column of pixels, or columns of pixels, having poor contrast. The probable location of a local minimum determined by extrapolation or interpolation may then be used as the location of the media dark pixel in a column, rather than an actual, valid local minimum.

Once a minimum is found, a validating step **332** may verify that the minimum is likely located within the media **82**. A minimum may be validated **332** by ensuring that it is below the media threshold **210**. A minimum may also be validated **332** by ensuring that it is adjacent a high intensity gradient located between the minimum and the adventitia datum **246**, inasmuch as the comparatively dark media **82** is adjacent the comparatively brighter adventitia **84**, and these will therefore have an intensity gradient between them. The validating step **332** may include marking valid minima as media dark pixels used to establish a media datum **242**. If an inadequate minimum is found, the process **150** may be repeated beginning at the location of the inadequate minimum and moving toward the lumen **78**.

A validating, step **332** may also include inspecting the location of the minima. Validation **332** may ensure that only those minima that are within a specified distance from the adventitia **84** are marked as media dark pixels used to calculate the media datum **242**. A workable value for the specified distance may be from about one-half to about two-thirds of the distance from the adventitia **84** to the lumen **78**. In the event that no minimum falls below the media threshold **210**, is located proximate a large intensity gradient, or both, validation **332** may include marking a pixel a specified distance from the adventitia as the media dark pixel used to calculate (curve fit) the media datum **242**.

Referring to FIG. **22**, while still referring to FIG. **21**, a curve fitting step **334** may establish a temporary media datum **336** comprising a curve fit of the media dark pixels **338** located laterally in each column of pixels over the domain of the image. The curve fitting step **334** may use any of the curve fitting methods discussed above in conjunction with other datums or other suitable methods.

An adjustment step **340** may alter the locations of the media dark pixels **338** used to calculate the media datum **242**. For example, each media dark pixel **338** may be examined to see whether it is located between the temporary media datum **338** and the adventitia datum **246**. The media **82** makes no actual incursions into the adventitia **84**. Those media dark pixels between the adventitia datum **246** and the temporary media datum **338** may be moved to, or replaced by points or pixels at, the temporary media datum **336**. A curve fitting step **342** may then curve fit the media datum **242** to the modified set of media dark pixels **338**. The curve fitting step **342** may make use of any of the curve fitting methods discussed in conjunction with other datums or other suitable methods. Alternatively, the temporary media datum **338** itself may serve as the media datum **242**.

FIG. **23** illustrates the lumen/intima boundary locating process **152**. A defining step **346** may define **346** the field searched. For example, in one embodiment, the field of search is limited to the area between the lumen datum **240** and the media datum **242**. Defining **346** the field of search may include searching only the region between the lumen datum **240** and a first local maximum found when searching from the lumen datum **240** toward the media datum **242**. Some embodiments may require that the local maximum have an intensity above the media threshold **210**. In some embodiments, defining **346** the field of search may include manually or automatically adjusting the location of the lumen datum **240** and/or the media datum **242**. For example, a user may click on a graphical representation of the lumen datum **240** and translate it laterally to a different position to observe the quality of fit or correspondence. In still other embodiments, the field of search may be defined **346** as the region between the adventitia datum **246** and an edge of the measurement region **172** lying within the lumen.

In some embodiments, an operator may select a point or points approximately on the lumen/intima boundary **244**. Defining **346** the field of search may include searching only a small region centered on the operator selected points, or a line interpolated between the operator selected points. Alternatively, an operator or software may select or specify a point, or series of points, just within the lumen **78** to define one boundary of the search region.

A locating step **348** may begin at the lumen datum **240**, or other limiting boundary, such as the edge of a measurement region **172**, and search toward the media datum **242** for the largest positive intensity gradient. In embodiments where a media datum **242** is not located, the locating step **348** may search from the lumen datum **240**, or other boundary, toward the adventitia datum **246** for the largest positive intensity gradient. A validating step **350** may verify that a gradient likely represents the lumen/intima boundary **244**. In some embodiments, the locating step **348** may involve searching for the largest negative intensity gradient when moving from the adventitia datum **246**, or local maximum above the media threshold **210**, toward the lumen datum **240**, or media datum **242**. In some embodiments, validating **350** may include rejecting gradients where the pixels defining the gradient are below a specific threshold value, such as the lumen threshold **202**.

The defining step **346**, locating step **348**, and the validating step **350** may be repeated until the largest (steepest), valid intensity gradient is found. Accordingly defining **346** the field of search may include limiting the field of search to those columns of pixels that have not hitherto been examined. For example, defining **346** the field of search may include limiting the regions searched to the region between an invalid gradient and the media datum **242** or a first local maximum above the media threshold **210**.

An optional specifying step **352** may enable an operator to manually specify the location of the lumen/intima boundary **244** at one or more points. An optional compensating step **284**, as discussed above, may extrapolate or interpolate the location of the lumen/intima boundary **244** in comparatively low contrast regions based on portions of the lumen/intima boundary **244** found in a comparatively high contrast region. A compensating step **284** may also extrapolate or interpolate between operator specified points and high contrast regions.

FIG. **24** illustrates one embodiment of a media/adventitia boundary locating process **154**. A defining step **358** may define the field searched. For example, in one embodiment, the field of search is limited to the portion of a column of pixels between the media datum **242** and the adventitia datum **246**. Alternatively, the field of search may be limited to the region between the lumen datum **240** and the adventitia datum **246**. In still other embodiments, the field of search may be defined **358** as the region between the adventitia datum **246** and an edge of the measurement region **172** lying within the lumen. In some embodiments, defining **358** the field of search may also include manually or automatically translating the media datum **242**, the adventitia datum **246**, or both. In still other embodiments, the field of search may be limited to the area between the media datum **242** and a local maximum having a corresponding intensity above the adventitia threshold **208** or other minimum value.

A locating step **360** may identify the largest positive gradients within the field of search. The locating step **360** may involve examining each pixel starting at the media datum **242**, or other boundary, such as an edge of a measurement region **172** or the lumen datum **240**, and moving toward the adventitia datum **246**. The validating step **362** may verify that an intensity gradient has a high probability of being the media/adventitia boundary **248**. Validating **362** may include rejecting gradients where the pixels defining the gradient are below a certain value, such as the media threshold **210**.

Where a gradient is rejected during the validating step **362**, the defining step **358**, locating step **360**, and validating step **362** may be repeated to find and validate the next largest intensity gradient until the largest valid intensity gradient is found. The defining step **358** may therefore also include limiting the field of search to the region between the media datum **242**, or other boundary, and the location of an invalid intensity gradient. Optionally, a specifying step **364** may enable an operator to manually specify the approximate location of the media/adventitia boundary **248** at one or more points. A compensating step **284**, as discussed above, may extrapolate or interpolate the location of the media/adventitia boundary **248** in low contrast regions based on portions of the media/adventitia boundary **248** found in high contrast regions and/or operator specified points along the media/adventitia boundary **248**.

Referring to FIG. **25**, a calculating module **120** may calculate an IMT value based on the distance between the lumen/intima boundary **244** and the media/adventitia boundary **248**. In some embodiments, the calculating module **120** may calculate the distance between the lumen/intima boundary **244** and the media/adventitia boundary **248** for each column of pixels and average them together to yield a final value. The calculating module **120** may also convert a calculated IMT value to its actual, real world, value based on calibration factors calculated by the calibration module **112**.

In some embodiments, the calculating module **120** may remove (filter) spikes or other discontinuities of slope on the media/adventitia boundary **258**. For example, the calculating module **120** may look for spikes whose height is a specific multiple of their width. For instance, spikes having a height three (or other effective multiple) times the width of their base may be identified. The portion of the media/adventitia boundary **248** forming the spike may be replaced with an average of the location of the boundary on either side of the spike. The calculating module **120** may likewise remove spikes from the lumen/intima boundary **244**.

The calculating module **120** may also curve fit either the media/adventitia boundary **248**, the lumen/intima boundary **244**, or both. In some embodiments, the calculating module **120** will curve fit the boundaries **244**, **248** after having removed spikes from the boundaries **244**, **248**, in order that clearly erroneous data not influence the resulting curve fit.

The calculating module **120** may include a slope compensating module **370**. The slope compensating module **370** may adjust IMT measurements for the angle **100** of the carotid artery relative to the horizontal direction **74**. For example, in some embodiments, the slope compensating module **370** may multiply an IMT measurement by the cosine of the angle **100**. The angle **100** may be calculated by fitting a line to the lumen/intima boundary **244**, the media/adventitia boundary **248**, or a line of pixels at the midpoint between the lumen/intima boundary **244** and the media/adventitia boundary **248**, for each column of pixels. The angle **100** may be set equal to the angle of the line relative to the horizontal direction **74**. Alternatively, the angle **100** may be calculated using a line fit to one, or a combination, of the lumen datum **240**, the media datum **242**, and/or the adventitia datum **248**. In some embodiments, the angle **100** may be calculated based on a line connecting the leftmost and rightmost points comprising the lumen datum **240**, media datum **242**. adventitia datum **240**. lumen/intima boundary **244**. or media adventitia boundary **248**. Alternatively, an operator may select two points which the slope compensating module **370** may then use to define the angle **100**.

The calculating module **120** may also include a taper compensating module **372** for adjusting an IMT measurement to counter the effect that any taper of the IMT thickness may have on a measurement. One method for eliminating this type of variation is to measure the IMT in a region where tapering effects are not present. For example, the IMT of the segment **98** located between 10 mm and 20 mm away from the flared portion **90** typically does not taper greatly.

The taper compensating module **372** may locate the bifurcation by searching for the dilation point **90**. In one embodiment, the taper compensating module **372** fits a straight line to the substantially straight portion of the adventitia **84**. The taper compensating module **386** may then extrapolate this tine toward the bifurcation, examining the intensity of the pixels lying on the line. Where the pixels falling on the line consistently have an intensity below the lumen threshold **202**, the line is extending into the lumen **78**. The location where the line initially encounters the low intensity pixels will correspond approximately to the dilation point **90** and the approximate location of the bifurcation. Of course, a variety of methods may be used to locate the dilation point **90**.

Referring to FIGS. **26**, while still referring to FIG. **25**, the taper compensating module **372** may carry out the taper compensating process **374**. The taper compensating process **374** may comprise generating **376** an IMT database **133**. Referring to FIG. **27**, generating **390** an IMT database **133** may include measuring the IMT of the carotid artery at various subsections **378**, and recording the average IMT of each subsection along with its location. In some embodiments, the IMT of the various subsections **378** may be curve fit and a polynomial, or other mathematical description, of the curve fit recorded. The subsections **378** will typically span both segments **94**, **98**, or portions of both segments **94**, **98**, in order to include tapering effects near the dilation point **90**. The width of the subsections **378** may correlate to the degree of taper, with areas having a large degree of taper being divided into narrower subsections **378**. The IMT database **133** typically includes measurements from a large number of patients.

Studies have shown that the degree of taper depends largely on the average IMT, with an artery having a smaller average IMT having less taper than an artery having a larger average IMT. Accordingly, generating **376** the IMT database may include indexing each series of measurements taken from an ultrasound image based on the IMT at a point a standardized distance from the dilation point **90**. For example, inasmuch as a segment **98**, extending from 10 mm to 20 mm from the dilation point **90**, has a substantially constant IMT, measurements taken from an image may be indexed by the IMT at a point 15 mm away from the dilation point **90**. Alternatively, the average IMT of a region centered on, or proximate, the 15 mm point may be used.

Furthermore, the IMT measurements of multiple patients having a similar IMT at a standardized point may be averaged together and the average stored for later use, indexed by their average IMT at the standardized point. Typically, the IMT measurement for one patient of a subsection **378** located a specific distance from the dilation point **90** is averaged with the IMT of a subsection **378** at the same distance in an ultrasound image of another patient.

Referring to FIG. **28**, while still referring to FIGS. **26** and **27**, calculating **380** a normalization factor may include retrieving from the IMT database **133** the IMT measurements **136** taken from a carotid artery, or carotid arteries, having substantially the same IMT thickness as the current ultrasound image at the same point. Thus, for example, if the current ultrasound image has an IMT of 0.27 mm at a point 15 mm from the dilation point **90**, calculating **380** a normalization factor may include retrieving IMT measurements **136** for arteries having an IMT of 0.27 mm at the corresponding point. Alternatively, IMT measurements **136** may be retrieved for recorded measurements of arteries having IMT values at the standardized point that bound the IMT of the current artery at that point.

Normalization factors may be calculated **380** based on subsections **378** of stored IMT measurement **136**, or measurements **136**. For example, a subsection **378***a* may have an IMT **382** and be located at a point **384**. Subsection **378***b* may have an IMT **386** and be located at another point **388**. The point **388** may be chosen to be a standardized distance from the dilation point **90** used to normalize substantially all IMT measurements **136**. A normalization factor may be calculated for a subsection **378***a* by dividing the IMT **386** by the IMT **382**. In a like manner, the IMT **386** may be divided by the IMT for each subsection **378** to calculate **380** a normalization factor for each subsection **378**.

Referring again to FIG. **26**, applying **390** a normalization factor may include multiplying the normalization factors by the IMT of their corresponding subsections **378** in a current ultrasound image. Thus, for example, a subsection **378** centered at a distance 7 mm from the dilation point **90** in a current image will be multiplied by a normalization factor calculated at a distance 7 mm from the dilation point **90**. In this manner, as shown in FIG. **29**, the IMT at each subsection **378** in the graph **392** is converted to an approximately equivalent IMT at a standardized point **388** in graph **394**. The normalized IMT of each subsection **378** may then be averaged to yield a final value that may be reported.

Various alternative approaches to applying normalization factors are possible. For example, rather than dividing a current ultrasound image into subsections **378**, the normalization factors may be applied to the IMT of each column of pixels. An interpolation between normalization factors calculated for subsections **378** centered at locations bounding the horizontal location of a column of pixels may be used to normalized the IMT of a single column of pixels. Alternatively, normalization factors may be calculated for each column of pixels in a retrieved IMT measurement **136**. In still other embodiments, a mathematical description of a stored IMT measurement **136** is used to calculate a normalization factor at the location of each column of pixels.

Referring again to FIG. **25**, the calculating module **120** may also include a data reduction module **398** and a diagnostic module **400**. The data reduction module **398** may compile and statistically analyze IMT measurements and other data to arrive at diagnostic data **131**. The diagnostic module **400** may retrieve the diagnostic data **131** in order to relate a patient's IMT with the patient's risk of cardiovascular disease.

As can be appreciated from the foregoing, imaging devices, such as ultrasound imaging devices, computer aided tomography imaging devices, magnetic resonance imaging devices, and the like can accurately capture fine detail of anatomical features of the human body. By using an imaging device in conjunction with a measurement technique, tissue densities of aspects of tissue structures, such as "plaques" associated with arterial walls, can be determined (plaque being defined as an abnormally thickened localized area of any portion of the arterial wall).

It may, for example, be desired to determine tissue densities in the carotid artery wall. The presence of plaque of the carotid artery has been shown to be a good indicator of the presence and degree of atherosclerosis throughout the entire vascular system.

The density of aspects of a tissue structure may vary depending upon the characteristics of these tissue structure aspects. Often knowing that the tissue structure has a particular characteristic, as may be determinable from the density associated therewith, is useful in diagnosis of conditions and/or is otherwise informative. For example, plaque can be dense and significantly calcified, it can be soft and uncalcified, or it can be anywhere in between. Softer non-calcified plaques are typically the more risky types of plaques, since they are more likely to rupture/dislodge and cause blockages or blood clots. Accordingly, it is very important to be able to both determine the presence of these softer plaques and determine the density of these plaques. Although there are techniques for non-invasively determining the presence of calcified plaques other than ultrasound, e.g., CAT scans, these techniques often have a difficult time finding non-calcified plaques. Ultrasound technology can detect both dense calcified plaques as well as softer non-calcified plaques. Embodiments of the present invention utilize an image, such as that available from an ultrasound device or other suitable imaging device, to locate and characterize the density of plaques of the carotid artery and/or branches associated therewith.

Digital images, such as those provided by ultrasound devices, are often composed of rows and columns of digitally sampled values representing the tissue density at each position in the image. These sampled values are referred to as pixel values, or simply, pixels. Brighter pixel intensities correspond to denser tissue. A measurement process for measuring plaque density in the carotid artery according to an embodiment of the invention uses these pixel intensities, along with their relative position in the digital image, to determine plaque size, location, and/or density.

FIG. **30** shows a system for providing tissue structure aspect density information according to an embodiment of the present invention. In the illustrated embodiment, ultrasound imaging device **3001** captures an image including tissue structure of interest, such as an image of a carotid artery, and provides the image to plaque density measurement mechanism **3003** via communication medium **3002**. For example, plaque density measurement mechanism **3003** may comprise a general purpose computer (e.g., personal computer) system operable under control of an instruction set defining operation as described herein. Alternatively, plaque density measurement mechanism **3003** may be integral to imaging device **3001**, such as may comprise a processor operable under control of an instruction set defining operation as defined herein and/or one or more application specific integrated circuits (ASICs). Communication medium **3002** may comprise a digital or analog interface, such as may include a network link (e.g., wide area network (WAN), metropolitan area network (MAN), local area network (LAN), the public switched telephone network (PSTN), the Internet, an intranet, an extranet, a cable transmission system, and/or the like), a parallel data link (e.g., a Centronics parallel interface, an IEEE 1284 parallel interface, an IEEE 488 parallel interface, a small computer systems interconnect (SCSI) parallel interface, a peripheral component interconnect (PCI) parallel bus, and/or the like), a serial data link (e.g., RS232 serial interface, RS422 serial interface, universal serial bus (USB) interface, IEEE 1394 serial interface, and/or the like).

Plaque density measurement mechanism **3003** identifies an area of plaque in a tissue structure, e.g., carotid artery, within the ultrasound image and determines a density thereof. For example, plaque density measurement mechanism **3003** may establish datums as described above to identify an area of plaque. Additionally or alternatively, user input may be used to identify an area of plaque, a plaque boundary, a center of a plaque, etcetera. Having identified an area of plaque, plaque density measurement mechanism **3003** of a preferred embodiment determines the density of the plaque by analyzing the image intensity within the area of plaque. For example, plaque density measurement mechanism **3003** may normalize the intensity of the entire image, or some portion thereof, and then use an average or mean pixel intensity value associated with the area of plaque. Additionally or alternatively, plaque density measurement mechanism **3003** may analyze different portions of the area of plaque, e.g., different strata, areas in proximity to other tissue structures, etcetera, to determine a density associated therewith. Accordingly, several plaque densities may be determined with respect to an identified area of plaque. Plaque density measurement mechanism **3003** may additionally or alternatively determine associated information, such as a size of the plaque area, a thickness of the plaque area, a relative size (e.g., percentage) of the plaque area as compared to another aspect of the tissue structure or the tissue structure itself, a relative location of the plaque area to another aspect of the tissue structure or the tissue structure itself, and/or the like.

Plaque density measurement mechanism **3003** of the illustrated embodiment provides the aforementioned plaque density information to plaque density report generator **3004**. Plaque density report generator **3004** may comprise a general purpose computer (e.g., personal computer) system operable under control of an instruction set defining operation as described herein. Alternatively, plaque density report generator **3004** may be integral to imaging device **3001**, such as may comprise a processor operable under control of an instruction set defining operation as defined herein and/or one or more ASICs. Plaque density report generator **3004** of a preferred embodiment provides output of plaque density information in a form useful in diagnosing a condition of the tissue structure or which is otherwise useful. For example, plaque density report generator **3004** may compare plaque density value, thickness, size, location, etcetera to a database of plaque density values, thicknesses, sizes, locations, etcetera to report a relative condition of a patient. Additionally or alternatively, plaque density report generator **3004** may compare plaque density value, thickness, size, location, etcetera with historical information associated with a particular individual in order to determine a trend, such as the rate of growth of the plaque, the rate of calcification of the plaque, etcetera.

Any or all of the forgoing information generated by plaque density report generator **3004** may be reported to a user or operator in any of a number of formats and using a variety of mediums. For example, plaque density report generator **3004** may display the information in real-time or near real-real time on plaque density display device **3005**, such as may comprise a display monitor (e.g., a cathode ray tube (CRT), a liquid crystal display (LCD), a plasma display, etcetera), which may be part of ultrasound imaging device **3001** or separate therefrom. Plaque density report generator **3004** may output the information in hard-copy on plaque density printing device **3007**, such as may comprise a printer (e.g., a dot matrix printer, a laser printer, a page printer, an ink-jet printer, etcetera), which is coupled to plaque density report generator **3004** through communication medium **3006**. Communication medium **3006** may comprise any of a number of communication mediums, such as those described above with respect to communication medium **3002**. In addition to or in the alternative to plaque density report generator **3004** reporting the foregoing information to a user or operator, the information may be stored in one or more databases and/or transmitted to one or more systems by embodiments of the invention.

Having described an embodiment of a tissue structure aspect density information system above, reference is now made to FIG. **31** in which a flow diagram of operation of a tissue structure aspect density information system according to an embodiment is described. At step **3101** of the illustrated embodiment, a patient presents with a tissue structure to be analyzed, shown in the illustrated embodiment as a carotid artery. At step **3102** an ultrasound imaging device is used to capture a digital image of the carotid artery. Thereafter, the digital image of the carotid artery is provided to a plaque density measuring device of the present invention at step **3103**.

Within step **3103**, the plaque density measuring device operates to locate the position of an aspect of the carotid artery, or other tissue structure, of interest (plaque in the illustrated embodiment) within the ultrasound image. There are several ways this can be accomplished. One mechanism is to have the operator trace the boundary of the plaque. This is the simplest mechanism to implement since it requires no automated edge determination of the plaque. Another way to locate the plaque is to have the operator specify a point or points within the region of interest within the carotid artery wall. Then, from these points, an algorithm may search outward until the boundary of the plaque was determined. For example, one embodiment determines the plaque boundary from an identified point by looking for the largest intensity gradient in all directions from the specified point. Another way to locate the plaque is to have the operator specify a region or path around the outside of the plaque in a manner to ensure that every pixel that is part of the plaque is completely encompassed by the specified region. Then, an algorithm would search for the plaque boundary by searching inwards from this boundary, looking for the largest intensity gradient.

Once the plaque is located and its outer boundary is determined, several density characteristics can be computed by the plaque density measuring device at step **3103**. These include average density, peak density, density extent (maximum density minus minimum density), total area of plaque, area of densest region, density histogram, density standard deviation or variance and, but not limited to density centroid.

It should be appreciated that the intensity values that compose an ultrasound image are relative intensity values. Accordingly, the actual pixel intensity values can be adjusted to be more sensitive or less sensitive to changes in tissue density. Depending on image gain setting selected by the, the image intensities can vary dramatically even for the same image. In this way, it is important to normalize as much as possible for these operator affected pixel intensities by normalizing the density information gathered for a given plaque. This is accomplished by modifying each density value gathered by an adjustment factor that is dependent upon known tissue densities of landmarks that have relatively consistent density from patient to patient. One of the landmarks with a known density is the lumen. Measuring the density of the lumen is measuring the density of the blood flowing in the artery. Blood density is assumed to be relatively consistent from patient to patient. The density of the lumen gives a lower bound on the tissue densities found in the image. Another landmark that is used as an upper end of tissue density is the adventitia. This tends to be the densest tissue in the image of the carotid artery. This density is also relatively consistent from patient to patient. By normalizing plaque densities on a scale from lumen density to adventitia density, the gain factor which is controlled by the operator, and which directly affects tissue density readings, can be normalized.

One mechanism for normalizing to these two known tissue densities is simply a linear scaling and offsetting. For example, assuming that the lumen average density was 10 and the adventitia average density was 170, to normalize a plaque density which has a value of 77 one could determine the percentile density on a range from lumen density to adventitia density. This is done by the following equation:

$$\text{Normalized tissue density}=(77-10)/(170-10)=0.419=41.9\%$$

Specifying normalized tissue density as a percent from lumen density to adventitia density is just one choice. There are many other normalization reporting methods. For example, an embodiment may utilize a percentage from intima/media density to adventitia density.

By using a normalization process, such as one or more of those described above, the plaque density is specified on a range that is independent of the instrument gain setting. At step **3104** the plaque density data determined by the plaque density measuring device is provided to a plaque density report process. The plaque density report process outputs plaque density information in any of a number of formats, such as through displaying a plaque density report at step **3106** and/or printing a plaque density report at step **3107**.

The foregoing plaque density reports may provide plaque density information in a format readily understood and interpreted by a user. For example, an embodiment of the invention outputs a number from 1 to 5 indicating the severity of hardness of a given plaque, thereby characterizing the plaque. These five bins would correlate to 5 ranges of densities that correspond to risk level, such as may be determined by collecting plaque density values from a large population combined with event (heart attack, stroke, etc.) history.

In another embodiment of plaque density usage, generating a database of normalized plaque values allows risk stratification based on plaque densities, thereby characterizing the plaque. By having this database contain a large number of plaque densities from across a large and diverse population combined with occurrences of events, this database could then be used in conjunction with a plaque density measurement from an individual for screening purposes.

Although the present invention and its advantages have been described in detail, it should be understood that various changes, substitutions and alterations can be made herein without departing from the invention as defined by the appended claims. Moreover, the scope of the present application is not intended to be limited to the particular embodiments of the process, machine, manufacture, composition of matter, means, methods and steps described in the specification. As one will readily appreciate from the disclosure, processes, machines, manufacture, compositions of matter, means, methods, or steps, presently existing or later to be developed that perform substantially the same function or achieve substantially the same result as the corresponding embodiments described herein may be utilized. Accordingly, the appended claims are intended to include within their scope such processes, machines, manufacture, compositions of matter, means, methods, or steps.

What is claimed is:

1. A method for characterizing an aspect of a tissue structure present in an image, said method comprising:

analyzing said image to identify said aspect of said tissue structure;

normalizing intensity information of said image by applying an adjustment factor to said intensity information, said adjustment factor being dependent upon known densities of one or more landmarks in a subject of said image;

determining density information for said aspect using said normalized intensity information; and

characterizing said aspect using said density information.

2. The method of claim **1**, wherein said analyzing said image comprises:

analyzing an intensity gradient within said image.

3. The method of claim **1**, wherein said analyzing said image comprises:

identifying a datum using image intensity information.

4. The method of claim **1**, wherein said analyzing said image comprises:

identifying a tissue boundary using image intensity information.

5. The method of claim **1**, wherein said one or more landmarks have a relatively consistent density from image to image.

6. The method of claim **5**, wherein said one or more landmarks includes a lumen of a blood vessel.

7. The method of claim **5**, wherein said one or more landmarks includes an adventitia of a blood vessel.

8. The method of claim **1**, wherein said determining density information comprises:

determining an average intensity of said image within an area identified as said aspect to provide an average density.

9. The method of claim **1**, wherein said determining density information comprises:

determining a peak intensity of said image within an area identified as said aspect to provide a peak density.

10. The method of claim **1**, wherein said determining density information comprises:

determining a maximum intensity within and area identified as said aspect minus a minimum intensity within said area identified as said aspect to provide a density extent.

11. The method of claim **1**, wherein said determining density information comprises:

determining an intensity histogram with respect to intensities within an area identified as said aspect to provide a density histogram.

12. The method of claim **1**, wherein said determining density information comprises:

determining a standard deviation of intensities within an area identified as said aspect to provide a density variance.

13. The method of claim **1**, wherein said determining density information comprises:

determining a centroid of intensities within an area identified as said aspect to provide a density centroid.

14. The method of claim **1**. wherein said determining density information comprises:

determining a region of highest intensity within an area identified as said aspect to provide a densest region.

15. The method of claim **1**, wherein said characterizing said aspect comprises:

comparing a density value to a database of density values to determine a condition associated with said tissue structure.

16. The method of claim **1**, wherein said characterizing said aspect comprises:

comparing at least one of a thickness of said aspect, a size of said aspect, and a location of said aspect to a database to determine a relative condition of said tissue structure.

17. The method of claim **1**, wherein said characterizing said aspect comprises:

comparing a density value to a historical database of density values associated with a patient of which said tissue structure is a part of to determine a change in said patient's condition,

18. The method of claim **1**, wherein said change in said patient's condition comprises a rate of calcification of plaque.

19. The method of claim **1**, wherein said tissue structure comprises a blood vessel.

20. The method of claim **1**, wherein said tissue structure comprises a carotid artery.

21. The method of claim **1**, wherein said aspect comprises plaque.

22. The method of claim **1**, further comprising:

determining a total area of said aspect, wherein said characterizing said aspect further uses information with respect to said total area.

23. The method of claim **1**, further comprising:

determining a relative position of said aspect with respect to another aspect of said tissue structure, wherein said characterizing said aspect further uses information with respect to said relative position.

24. The method of claim **1** wherein said subject of said image comprises said tissue structure.

25. The method of claim **1** wherein at least said normalizing is performed by a processor-based computing device.

26. The method of claim **25** wherein said determining density information is performed by said processor-based computing device.

27. The method of claim **26** wherein said analyzing is performed by said processor-based computing device.

28. The method of claim **27** wherein said characterizing is performed by said processor-based computing device.

29. The method of claim **1** wherein said image is generated by one of an ultrasound system, a magnetic resonance imaging system, and a radio frequency imaging system.

30. A method for characterizing an aspect of a tissue structure present in an image, said method comprising:

analyzing said image to identify said aspect of said tissue structure;

determining density information for said aspect by applying an adjustment factor to intensity information associated with said image, said adjustment factor being dependent upon known densities of one or more landmarks in said image that have a relatively consistent density from image to image: and

characterizing said aspect using said density information, said characterizing providing information with respect to a severity of a condition associated with said aspect of said tissue structure.

31. The method of claim **30**, wherein said determining density information comprises:

determining an average intensity of said image within an area identified as said aspect to provide an average density.

32. The method of claim **30**, wherein said determining density information comprises:

determining a peak intensity of said image within an area identified as said aspect to provide a peak density.

33. The method of claim **30**, wherein said determining density information comprises:

determining a maximum intensity within and area identified as said aspect minus a minimum intensity within said area identified as said aspect to provide a density extent.

34. The method of claim **30**, wherein said determining density information comprises:

determining an intensity histogram with respect to intensities within an area identified as said aspect to provide a density histogram.

35. The method of claim **30**, wherein said determining density information comprises:

determining a standard deviation of intensities within an area identified as said aspect to provide a density variance.

36. The method of claim **30**, wherein said determining density information comprises:

determining a centroid of intensities within an area identified as said aspect to provide a density centroid.

37. The method of claim **30**, wherein said determining density information comprises:

determining a region of highest intensity within an area identified as said aspect to provide a densest region.

38. The method of claim **30**, wherein said density information comprises information with respect to a hardness of said aspect of said tissue structure.

39. The method of claim **38**, wherein said hardness is associated with calcification of said aspect of said tissue structure.

40. The method of claim **30**, wherein said characterizing said aspect comprises:

referencing a database of similar aspects of tissue structure.

41. The method of claim **30**, wherein said characterizing said aspect comprises:

referencing historical information to provide said information with respect to a severity of a condition.

42. The method of claim **30**, wherein said analyzing said image comprises:

analyzing an intensity gradient within said image.

43. The method of claim **30**, wherein said analyzing said image comprises:

identifying a datum using image intensity information.

44. The method of claim **30**, wherein said analyzing said image comprises:

identifying a tissue boundary using image intensity information.

45. The method of claim **30** wherein said adjustment factor is dependent upon known densities of said one or more landmarks in a subject of said image.

46. The method of claim **45** wherein said known densities of said one or more landmarks comprise known densities of at least one of the following landmarks present in the subject of the image: lumen of a blood vessel and adventitia of a blood vessel.

47. The method of claim **45** wherein said subject of said image comprises said tissue structure.

48. The method of claim **45** wherein said subject comprises at least a portion of a person to whom the image pertains, and wherein said subject has a relatively consistent density from person to person.

49. The method of claim **30** wherein at least one of said analyzing, determining, and characterizing is performed by a processor-based computing device.

50. The method of claim **49** wherein said image is generated by one of an ultrasound system, a magnetic resonance imaging system, and a radio frequency imaging system.

51. A system for characterizing an aspect of a tissue structure present in an image, said system comprising:

a processor-based system accepting input of a digital representation of said image, said processor-based system including circuitry operable to normalize intensity information of said digital representation of said image by applying an adjustment factor to said intensity information, said adjustment factor being dependent upon known densities of one or more landmarks in said image that have a relatively consistent density across a plurality of image subjects, said processor-based system also including circuitry operable to identify said aspect of said tissue structure within said digital representation of said image, said processor-based system also including circuitry operable to determine density information with respect to said aspect of said tissue structure using said normalized intensity information, and said processor-based system also including circuitry operable to characterize said aspect of said tissue structure as a function of said density information.

52. The system of claim **51**, further comprising:

a display outputting said density information to a user.

53. The system of claim **51**, further comprising:

a printer outputting said density information as a hard-copy report.

54. The system of claim **51**, wherein said aspect of said tissue structure comprises an area of plaque.

55. The system of claim **54**, wherein said plaque is characterized as a function of hardness.

56. The system of claim **51**, wherein said tissue structure comprises a blood vessel

57. The system of claim **51**, wherein said tissue structure comprises a carotid artery.

58. The system of claim **51**, wherein said density information indicates a hardness of said aspect of said tissue structure.

59. The system of claim **51**, wherein said characterization of said aspect of said tissue structure provides information with respect to a severity of a condition associated with said aspect of said tissue structure.

60. The system of claim **51**, wherein said characterization of said aspect of said tissue structure correspond to a risk level associated with said aspect of said tissue structure.

61. The system of claim **51**, further comprising:

a database of normalized intensity information for aspects of tissue structure associated with a plurality of individuals.

62. The system of claim **61**, wherein said database further includes event history associated with said aspects of tissue structure.

63. The system of claim **61**, wherein said normalized intensity information for aspects of tissue structure is normalized plaque values.

64. The system of claim **51** wherein said plurality of image subjects comprise a plurality of different persons.

65. The system of claim **51** wherein said known densities of said one or more landmarks comprise known densities of at least one of the following landmarks present in the image subject: lumen of a blood vessel and adventitia of a blood vessel.

66. The system of claim **51** wherein said image is generated by one of an ultrasound system, a magnetic resonance imaging system, and a radio frequency imaging system.

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摘要(译)

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