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(54) **MAMMOGRAPHY APPARATUS**

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A61B 6/00 (2006.01)
G06T 7/11 (2017.01)
(Continued)

(52) **U.S. Cl.**
CPC ***A61B 6/502*** (2013.01); ***A61B 6/0414*** (2013.01); ***A61B 6/0435*** (2013.01); ***A61B 6/481*** (2013.01);
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(58) **Field of Classification Search**
CPC A61B 6/0414; A61B 6/0435; A61B 6/12; A61B 6/481; A61B 6/502; A61B 6/5205;
(Continued)

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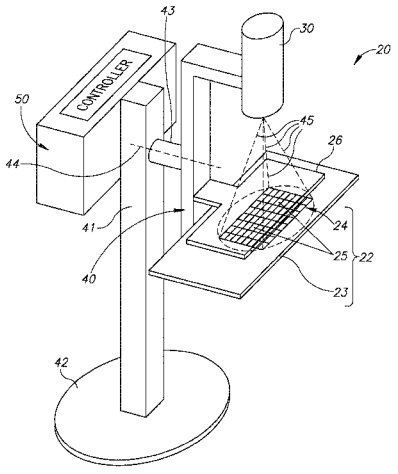
(57) **ABSTRACT**

A method of diagnosing breast cancer, the method comprising: acquiring a contrast enhanced region of interest (CE-ROI) comprised in an X-ray image of a patient's breast, the X-ray image comprising X-ray pixels that indicate intensity of X-rays that passed through the breast to generate the image; generating a texture feature vector (TF) having components based on the indications of intensity provided by a plurality of X-ray pixels in the CE-ROI; and using a classifier to classify the texture feature vector TF to determine whether the CE-ROI is malignant.

16 Claims, 8 Drawing Sheets



(51) **Int. Cl.**

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G06K 9/46	(2006.01)
A61B 6/04	(2006.01)
G06T 7/00	(2017.01)
G06T 7/44	(2017.01)
G06K 9/50	(2006.01)
G06K 9/48	(2006.01)
A61B 6/12	(2006.01)

(52) **U.S. Cl.**

CPC ***A61B 6/5205*** (2013.01); ***G06K 9/4642*** (2013.01); ***G06K 9/48*** (2013.01); ***G06K 9/50*** (2013.01); ***G06T 7/0012*** (2013.01); ***G06T 7/11*** (2017.01); ***G06T 7/13*** (2017.01); ***G06T 7/44*** (2017.01); *A61B 6/12* (2013.01); *G06K 2209/05* (2013.01); *G06T 2207/10116* (2013.01); *G06T 2207/20081* (2013.01); *G06T 2207/30068* (2013.01)

(58) **Field of Classification Search**

CPC G06K 9/4642; G06K 9/48; G06K 9/50; G06T 2207/10116; G06T 2207/20081; G06T 2207/30068; G06T 7/0012; G06T 7/11; G06T 7/13; G06T 7/44

See application file for complete search history.

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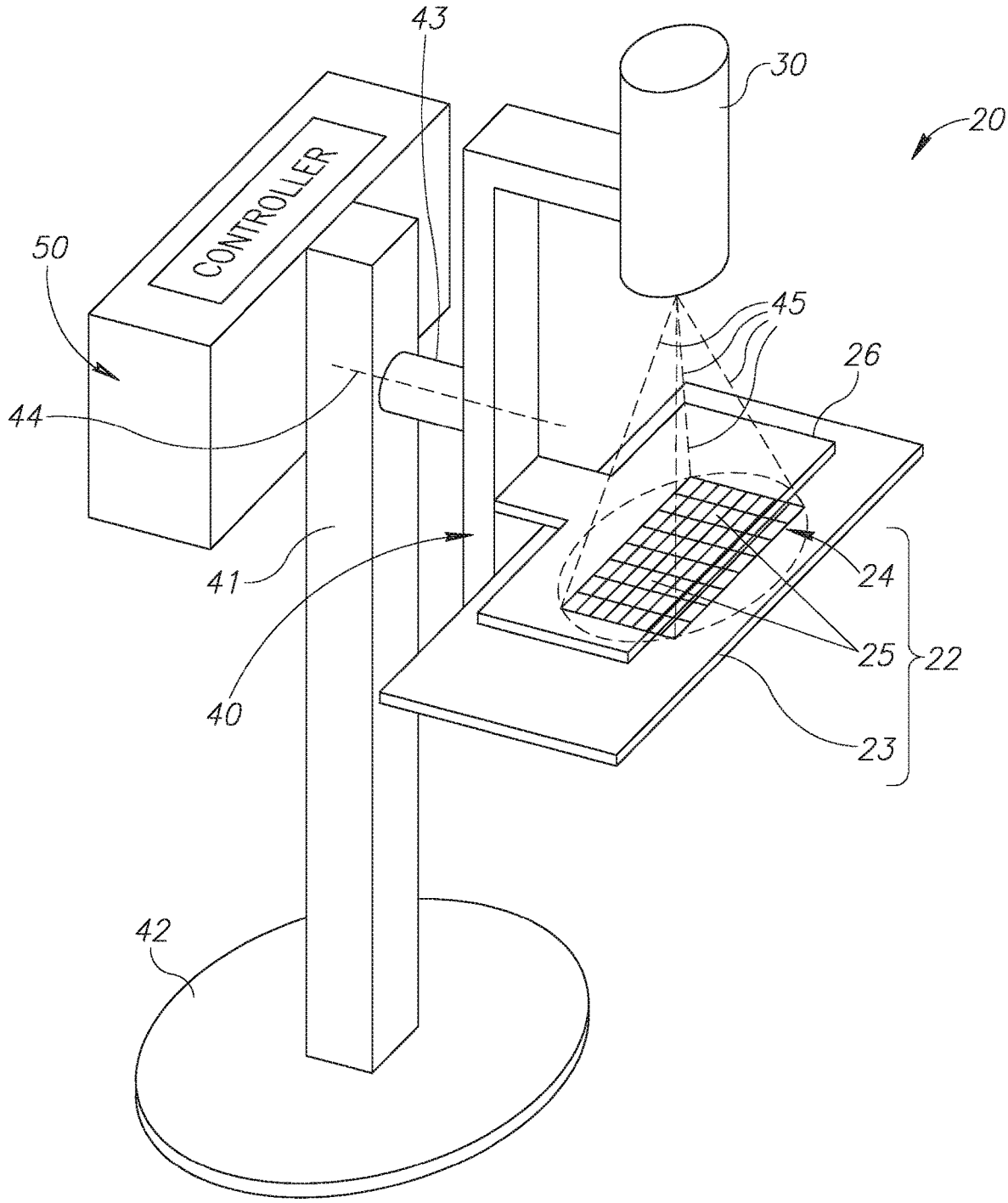

FIG.1A

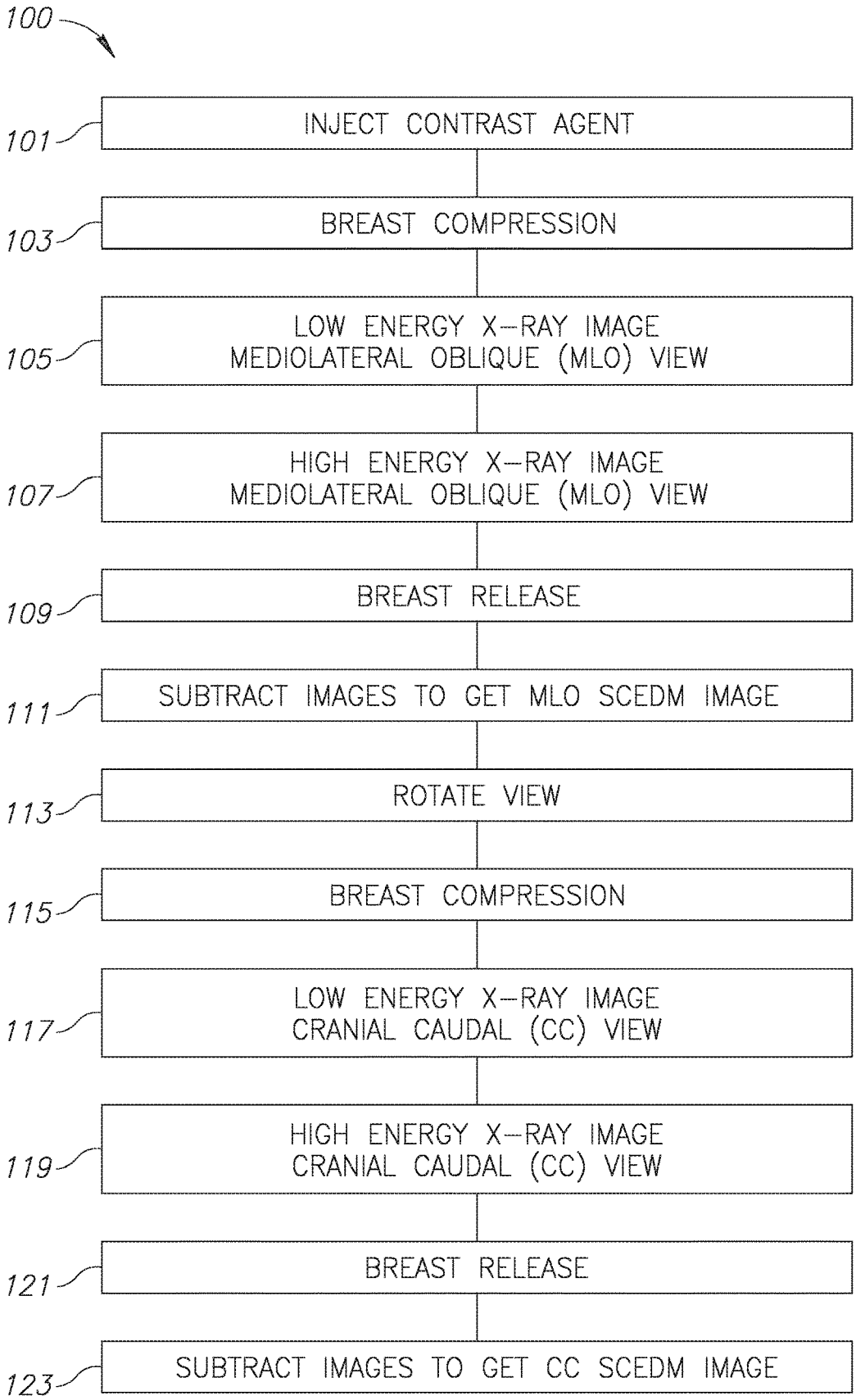
100
101
INJECT CONTRAST AGENT
103
BREAST COMPRESSION
105
LOW ENERGY X-RAY IMAGE
MEDIOLATERAL OBLIQUE (MLO) VIEW
107
HIGH ENERGY X-RAY IMAGE
MEDIOLATERAL OBLIQUE (MLO) VIEW
109
BREAST RELEASE
111
SUBTRACT IMAGES TO GET MLO SCEDM IMAGE
113
ROTATE VIEW
115
BREAST COMPRESSION
117
LOW ENERGY X-RAY IMAGE
CRANIAL CAUDAL (CC) VIEW
119
HIGH ENERGY X-RAY IMAGE
CRANIAL CAUDAL (CC) VIEW
121
BREAST RELEASE
123
SUBTRACT IMAGES TO GET CC SCEDM IMAGE

FIG.1B

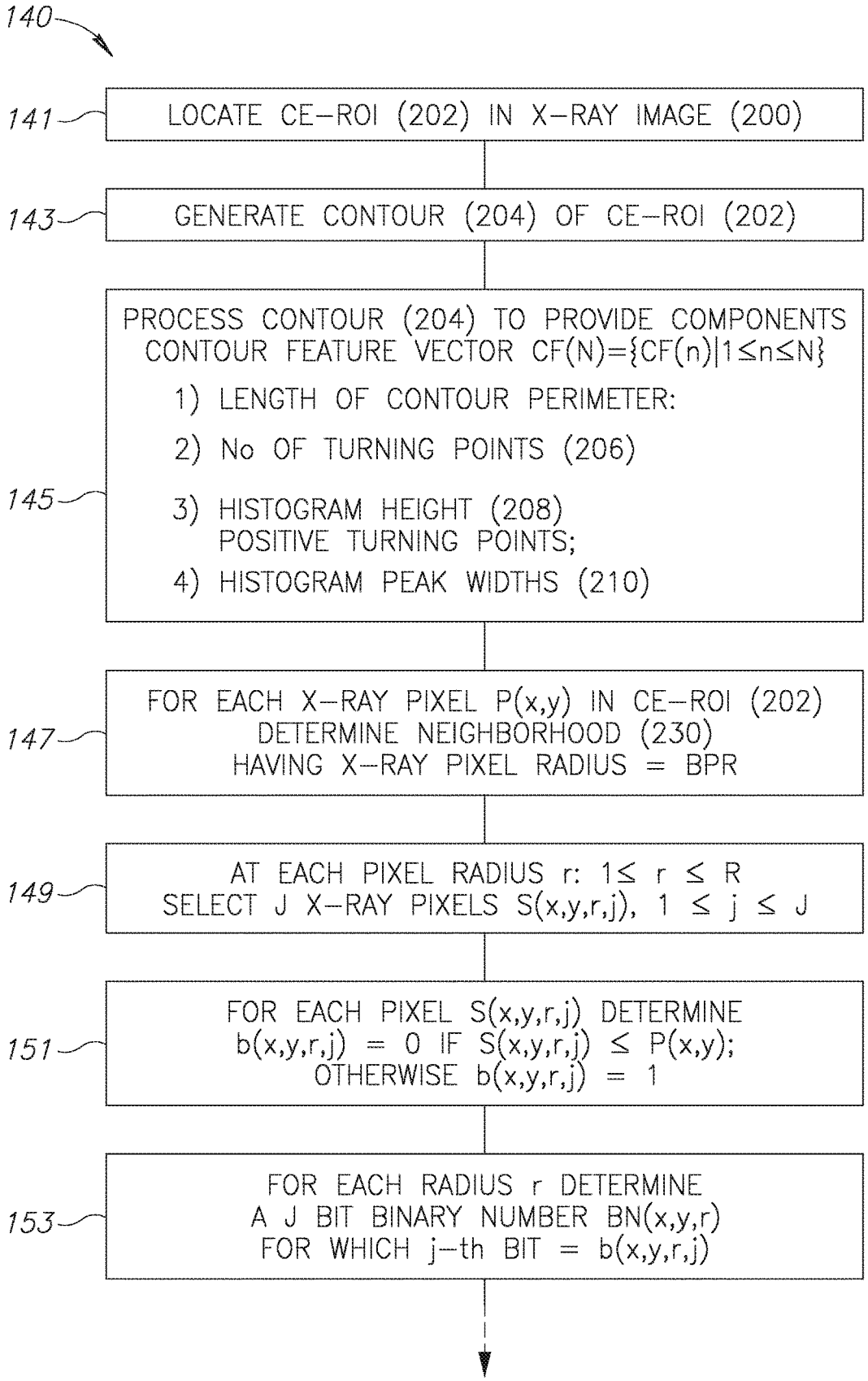
140
141
LOCATE CE-ROI (202) IN X-RAY IMAGE (200)
143
GENERATE CONTOUR (204) OF CE-ROI (202)
145
PROCESS CONTOUR (204) TO PROVIDE COMPONENTS
CONTOUR FEATURE VECTOR CF(N)={CF(n)|1≤n≤N}
1) LENGTH OF CONTOUR PERIMETER:
2) No OF TURNING POINTS (206)
3) HISTOGRAM HEIGHT (208)
POSITIVE TURNING POINTS;
4) HISTOGRAM PEAK WIDTHS (210)
147
FOR EACH X-RAY PIXEL P(x,y) IN CE-ROI (202)
DETERMINE NEIGHBORHOOD (230)
HAVING X-RAY PIXEL RADIUS = BPR
149
AT EACH PIXEL RADIUS r: 1≤ r ≤ R
SELECT J X-RAY PIXELS S(x,y,r,j), 1 ≤ j ≤ J
151
FOR EACH PIXEL S(x,y,r,j) DETERMINE
b(x,y,r,j) = 0 IF S(x,y,r,j) ≤ P(x,y);
OTHERWISE b(x,y,r,j) = 1
153
FOR EACH RADIUS r DETERMINE
A J BIT BINARY NUMBER BN(x,y,r)
FOR WHICH j-th BIT = b(x,y,r,j)

FIG.2A

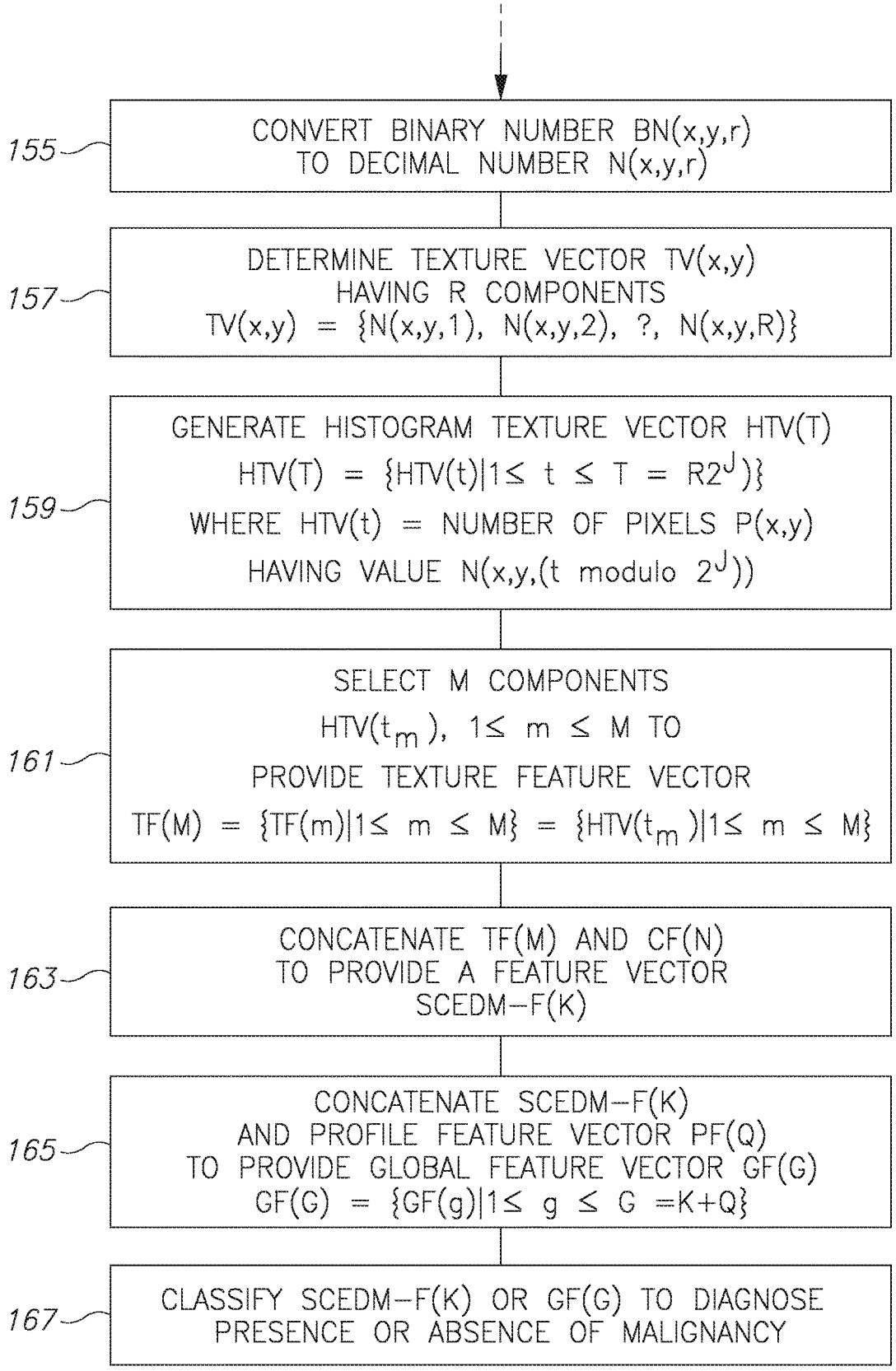
155
CONVERT BINARY NUMBER BN(x,y,r) TO DECIMAL NUMBER N(x,y,r)
157
DETERMINE TEXTURE VECTOR TV(x,y) HAVING R COMPONENTS
TV(x,y) = {N(x,y,1), N(x,y,2), ?, N(x,y,R)}
159
GENERATE HISTOGRAM TEXTURE VECTOR HTV(T)
HTV(T) = {HTV(t)|1≤ t ≤ T = R2^J)}
WHERE HTV(t) = NUMBER OF PIXELS P(x,y)
HAVING VALUE N(x,y,(t modulo 2^J))
161
SELECT M COMPONENTS
HTV(t_m), 1≤ m ≤ M TO
PROVIDE TEXTURE FEATURE VECTOR
TF(M) = {TF(m)|1≤ m ≤ M} = {HTV(t_m)|1≤ m ≤ M}
163
CONCATENATE TF(M) AND CF(N) TO PROVIDE A FEATURE VECTOR SCEDM-F(K)
165
CONCATENATE SCEDM-F(K) AND PROFILE FEATURE VECTOR PF(Q) TO PROVIDE GLOBAL FEATURE VECTOR GF(G)
GF(G) = {GF(g)|1≤ g ≤ G =K+Q}
167
CLASSIFY SCEDM-F(K) OR GF(G) TO DIAGNOSE PRESENCE OR ABSENCE OF MALIGNANCY

FIG.2A (cont. 1)

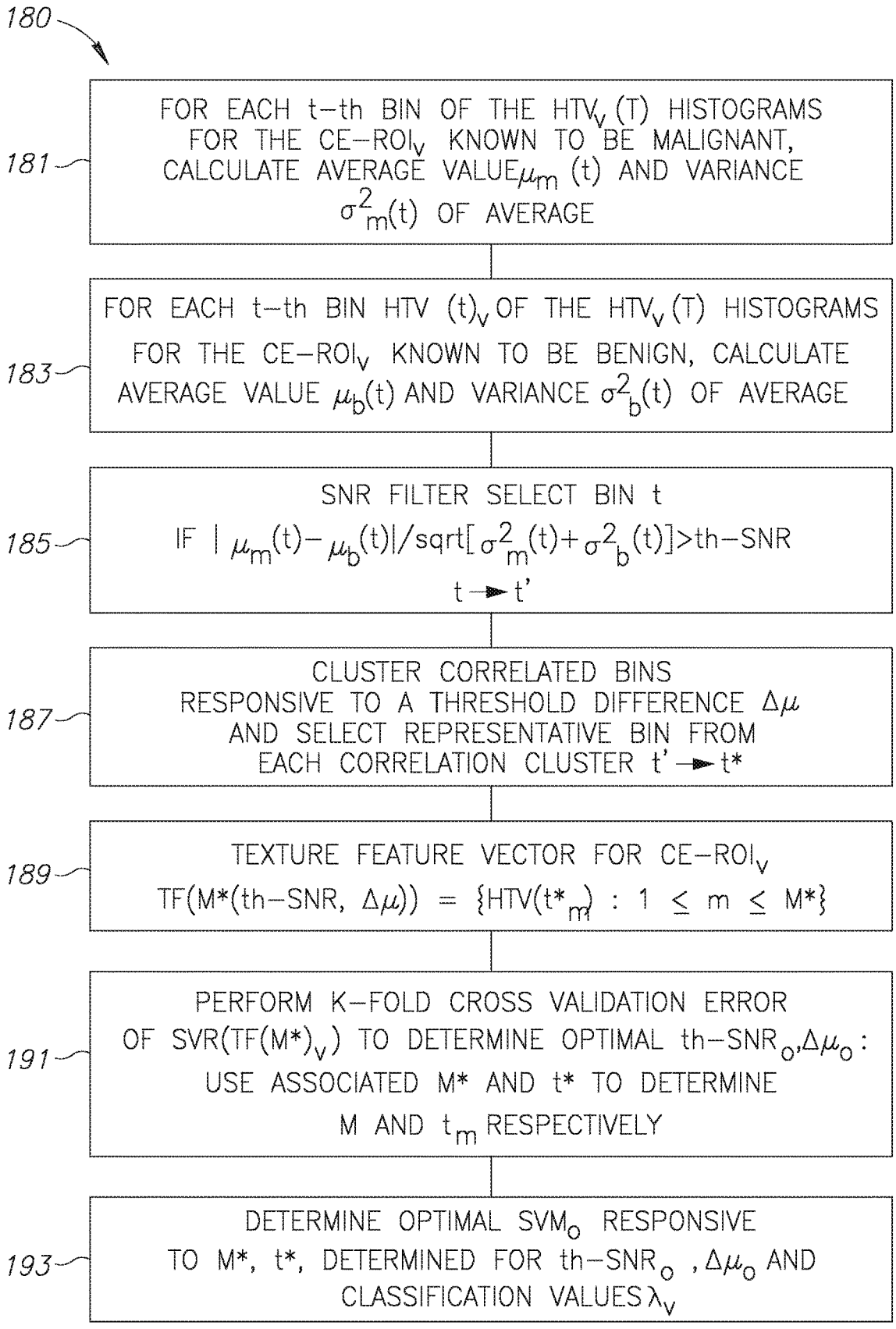
180
181
FOR EACH t−th BIN OF THE $HTV_V(T)$ HISTOGRAMS FOR THE $CE-ROI_V$ KNOWN TO BE MALIGNANT, CALCULATE AVERAGE VALUE $\mu_m(t)$ AND VARIANCE $\sigma^2_m(t)$ OF AVERAGE
183
FOR EACH t−th BIN $HTV(t)_V$ OF THE $HTV_V(T)$ HISTOGRAMS FOR THE $CE-ROI_V$ KNOWN TO BE BENIGN, CALCULATE AVERAGE VALUE $\mu_b(t)$ AND VARIANCE $\sigma^2_b(t)$ OF AVERAGE
185
SNR FILTER SELECT BIN t
IF $|\mu_m(t)-\mu_b(t)|/\mathrm{sqrt}[\sigma^2_m(t)+\sigma^2_b(t)]>th-SNR$
$t \rightarrow t'$
187
CLUSTER CORRELATED BINS RESPONSIVE TO A THRESHOLD DIFFERENCE $\Delta\mu$ AND SELECT REPRESENTATIVE BIN FROM EACH CORRELATION CLUSTER $t' \rightarrow t^*$
189
TEXTURE FEATURE VECTOR FOR $CE-ROI_V$
$TF(M^*(th-SNR, \Delta\mu)) = \{HTV(t^*_m) : 1 \leq m \leq M^*\}$
191
PERFORM K−FOLD CROSS VALIDATION ERROR OF $SVR(TF(M^*)_V)$ TO DETERMINE OPTIMAL $th-SNR_o, \Delta\mu_o$: USE ASSOCIATED M* AND t* TO DETERMINE M AND t_m RESPECTIVELY
193
DETERMINE OPTIMAL SVM_o RESPONSIVE TO M*, t*, DETERMINED FOR $th-SNR_o$, $\Delta\mu_o$ AND CLASSIFICATION VALUES λ_V

FIG.2B

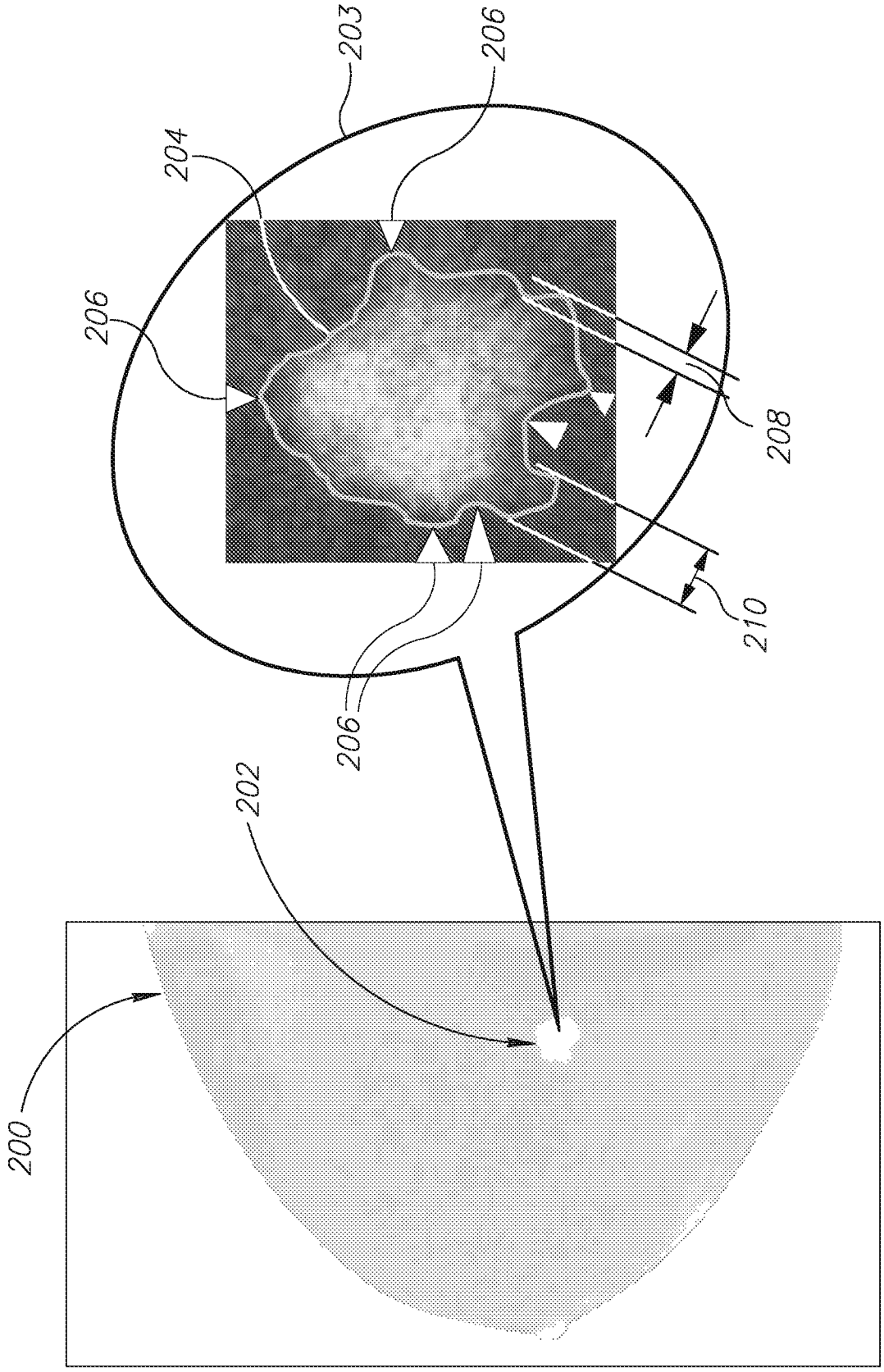

FIG.3

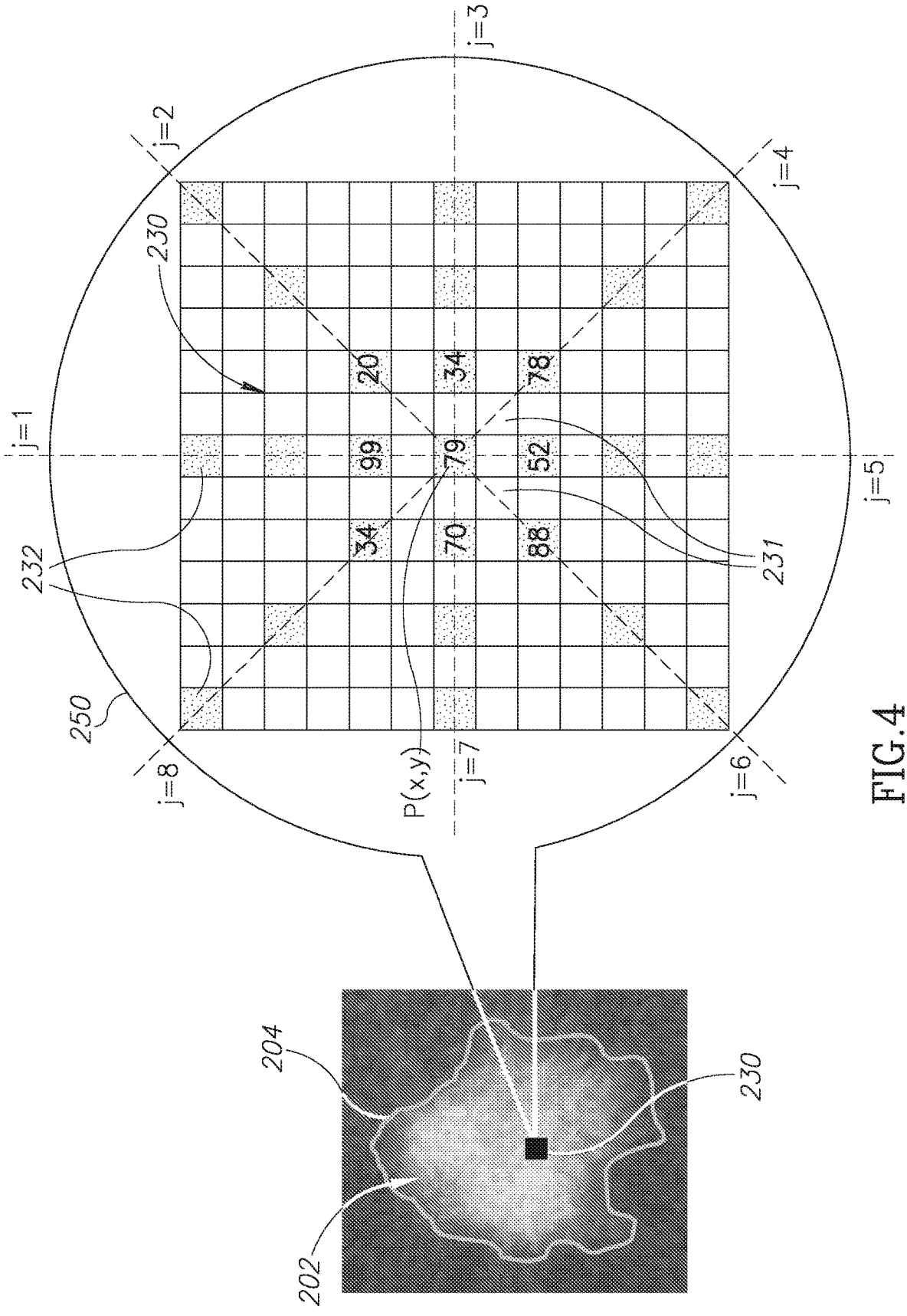
j=1
j=2
j=3
j=4
j=5
j=6
j=7
j=8
230
232
231
250
P(x,y)
20
34
78
99
79
52
34
70
88
204
202
230

FIG. 4

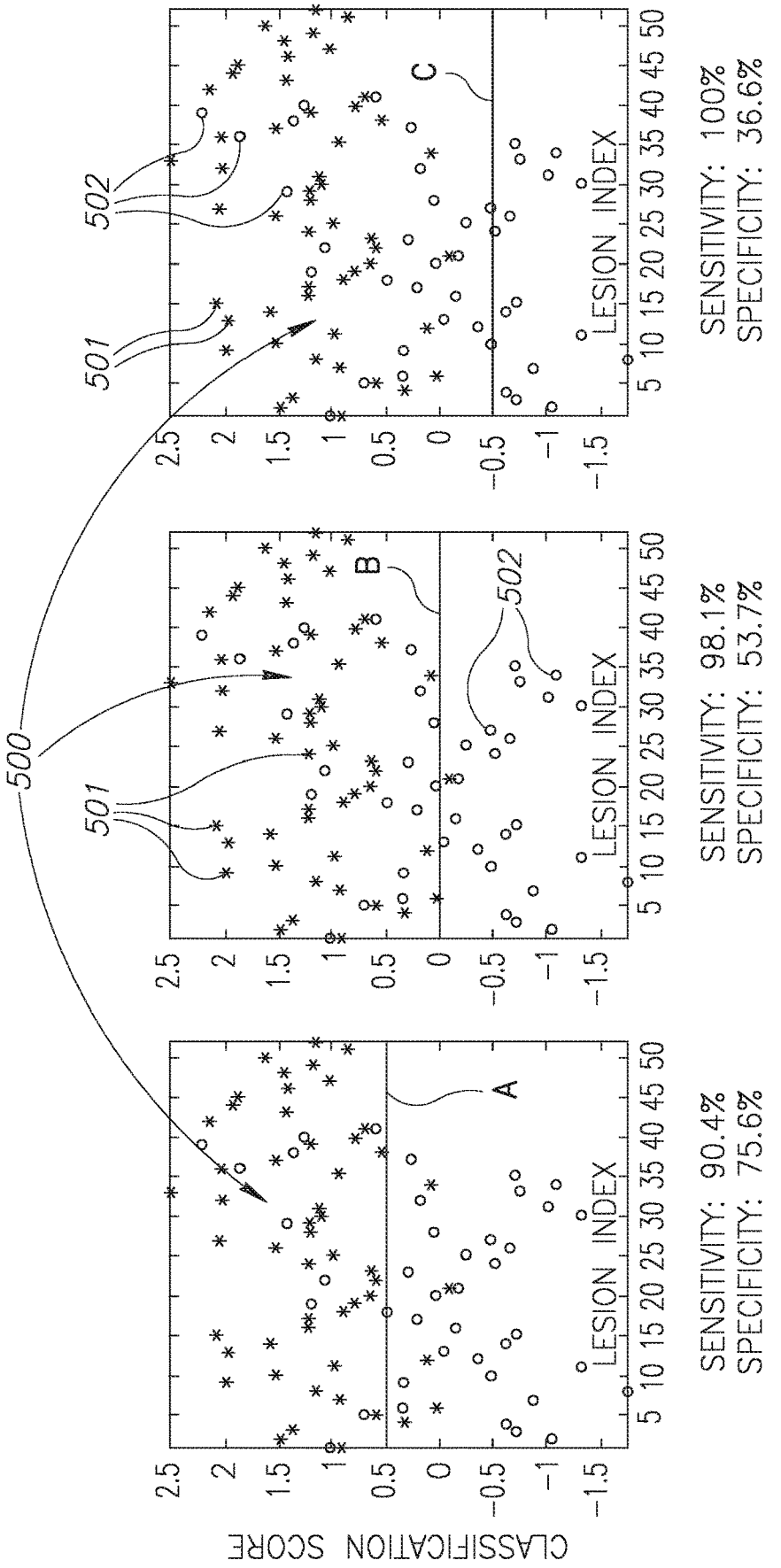
500
501
502
A
B
C
CLASSIFICATION SCORE
LESION INDEX
SENSITIVITY: 90.4%
SPECIFICITY: 75.6%
SENSITIVITY: 98.1%
SPECIFICITY: 53.7%
SENSITIVITY: 100%
SPECIFICITY: 36.6%

FIG.5

MAMMOGRAPHY APPARATUS

RELATED APPLICATIONS

The present application is a US National Phase of PCT Application No. PCT/IB2016/054707 filed on Aug. 4, 2016, which claims the benefit under 35 U.S.C. 119(e) of U.S. Provisional Application 62/201,774 filed on Aug. 6, 2015 and U.S. Provisional Application 62/260,549 filed on Nov. 29, 2015 the disclosures of which are incorporated herein by reference.

TECHNICAL FIELD

Embodiments of the disclosure relate to apparatus and methods for diagnosing breast cancer.

BACKGROUND

X-ray imaging of the human breast to detect malignancies has been clinically available since about 1970. As might very well be expected, since then, over the period of almost half a century the technology has undergone a number of changes and refinements. Initially, X-ray images were captured on film. Today X-ray breast images are directly captured by arrays of small X-ray detectors which convert intensity of X-rays incident on the detectors to electrical signals. The electrical signals are digitized to provide digital representations of the images that are stored in computers for later diagnoses.

A relatively recent change in X-ray breast imaging technology that was made practical by digital X-ray imaging is referred to as spectral contrast enhanced digital mammography (SCEDM). In SCEDM a patient is injected with a contrast agent that is preferably taken up by cancerous lesions in the patient's breast. The breast is exposed to X-rays at two different energies, typically a relatively low X-ray energy at which the contrast agent is a relatively poor absorber of X-rays and a relatively high X-ray energy at which the contrast agent is a relatively good absorber of X-rays. The exposures to the high and low energy X-rays provide high and low energy X-ray digital images respectively of the breast. The images are digitally subtracted to provide a "subtracted image" in which concentrations of the contrast agent in the breast, and thereby malignant lesions in the breast, generally have enhanced contrast and visibility. In particular, for dense breast tissues, known to be relatively opaque in classical mammography, normal breast tissue becomes substantially transparent in the subtracted image, enhancing contrast of lesions that in conventional non-subtracted X-ray images may be difficult to discern. Typically, the contrast agent used to acquire the high and low X-ray images is an iodine based contrast agent, and the low energy X-rays have an energy below the k-edge of iodine and the high energy X-rays have an energy above the k-edge of iodine.

Although SCEDM has the potential to improve sensitivity of mammography, in practice, a relatively large number of biopsies is performed on lesions detected in SCEDM images that turn out to be benign. More than 60% of the biopsies triggered by a lesion detected in SCEDM are actually performed on benign lesions. The relatively large number of biopsies that turn out to be unnecessary imposes a relatively high financial cost and psychological burden on patients and society.

SUMMARY

An aspect of an embodiment of the disclosure relates to providing apparatus for diagnosing presence of breast malignancies in a patient's breast, the apparatus comprising an X-ray imager configured to acquire an SCEDM image of the breast and a processor configured to process the image to provide a determination of the presence of malignancies. In an embodiment, the processor processes the SCEDM image to generate an image feature vector for a contrast enhanced region of interest (CE-ROI) in the SCEDM that is a function of morphology and/or texture of the CE-ROI. The processor uses the CE-ROI feature vector, to provide a determination as to whether or not the CE-ROI comprises a malignancy. A determination may comprise an estimate of a probability that a CE-ROI comprises a malignancy. The processor may also use a context feature vector, hereinafter also referred to as a "profile feature vector", based on a personal profile of the patient, to provide the determination as to whether or not the CE-ROI comprises a malignancy. In an embodiment, the processor operates on the CE-ROI feature vector and/or the profile feature vector in accordance with a classifier to determine whether or not the CE-ROI comprises a malignancy. Optionally, the classifier comprises a support vector machine (SVM) or a neural network.

Experiments carried out on SCEDM images acquired from actual patients and for which biopsies were performed indicate that apparatus, in accordance with an embodiment of the disclosure, hereinafter also referred to as an X-ray Breast Imager (XBI) may provide sensitivity to detecting breast malignancies that ranges from about 90% to 100% with associated specificities that range respectively from about 70% to about 37%. For an embodiment for which sensitivity is equal to about 98.1% associated specificity was equal to about 53.7%. It is noted that human inspection of SCEDM images to detect breast malignancies typically provide sensitivity of about 90%-95% and associated specificity of about 55%-65%.

This Summary is provided to introduce a selection of concepts in a simplified form that are further described below in the Detailed Description. This Summary is not intended to identify key features or essential features of the claimed subject matter, nor is it intended to be used to limit the scope of the claimed subject matter.

BRIEF DESCRIPTION OF FIGURES

Non-limiting examples of embodiments of the disclosure are described below with reference to figures attached hereto that are listed following this paragraph. Identical features that appear in more than one figure are generally labeled with a same label in all the figures in which they appear. A label labeling an icon representing a given feature of an embodiment of the disclosure in a figure may be used to reference the given feature. Dimensions of features shown in the figures are chosen for convenience and clarity of presentation and are not necessarily shown to scale.

FIG. **1**A schematically shows an X-Ray breast imager (XBI) for acquiring SCEDM images of a breast, in accordance with an embodiment of the disclosure;

FIG. **1**B shows a flow diagram in accordance with which the XBI schematically shown in FIG. **1**A acquires SCEDM images, in accordance with an embodiment of the disclosure;

FIG. **2**A shows a flow diagram of a procedure by which a XBI processes an SCEDM image of a breast to generate and use a feature vector to determine whether the image indicates presence of malignancy in the breast, in accordance with an embodiment of the disclosure;

FIG. **2**B shows a flow diagram of a procedure by which a XBI may configure a texture feature vector for use with the

procedure illustrated in FIG. **2**A in diagnosing malignancy, in accordance with an embodiment of the disclosure;

FIG. **3** schematically shows an SCEDM image of a breast comprising a contrast enhanced region of interest (CE-ROI) having a contour processed in accordance with the procedure flow diagram show in FIG. **2** to provide a contour feature vector "CF" for diagnosing malignancy, in accordance with an embodiment of the disclosure;

FIG. **4** schematically shows pixels that image the CE-ROI in the X-ray breast image shown in FIG. **3** and are processed in accordance with the procedure flow diagram show in FIG. **2** to provide a texture feature vector "TF" for diagnosing malignancy, in accordance with an embodiment of the disclosure; and

FIG. **5** shows a distribution of classification scores generated responsive to texture feature vector TFs determined for CE-ROIs in SCEDM X-ray images acquired for patients for which biopsies were preformed, and different threshold values for determining whether the scores indicate malignancy, in accordance with an embodiment of the disclosure.

DETAILED DESCRIPTION

In the discussion, unless otherwise stated, adjectives such as "substantially" and "about" modifying a condition or relationship characteristic of a feature or features of an embodiment of the disclosure, are understood to mean that the condition or characteristic is defined to within tolerances that are acceptable for operation of the embodiment for an application for which the embodiment is intended. Wherever a general term in the disclosure is illustrated by reference to an example instance or a list of example instances, the instance or instances referred to, are by way of non-limiting example instances of the general term, and the general term is not intended to be limited to the specific example instance or instances referred to. Unless otherwise indicated, the word "or" in the description and claims is considered to be the inclusive "or" rather than the exclusive or, and indicates at least one of, or any combination of more than one of items it conjoins.

FIG. **1**A schematically shows an X-Ray breast imager (XBI) **20** for acquiring SCEDM images of a breast, in accordance with an embodiment of the disclosure. XBI **20** optionally comprises a controller **50**, an X-ray source **30** configured to generate a beam of X-rays for acquiring SCEDM images of a breast, and a breast holder **22** for holding and positioning a breast in the X-ray beam provided by the X-ray source. X-rays generated by X-ray source **30** are schematically indicated by dashed lines **45**. Embodiments of controller **50** may comprise any electronic and/or optical, memory, processing, and/or control circuitry advantageous for providing controller functionalities. By way of example, controller **50** may, comprise any one or any combination of more than one of, a microprocessor, an application specific circuit (ASIC), field programmable array (FPGA) and/or system on a chip (SOC). The controller may comprise any one or any combination of more than one of a flash memory, random access memory (RAM), read only memory (ROM), and/or erasable programmable read-only memory (EPROM). And whereas controller **50** is shown in FIG. **1**A as a single localized entity, the controller may be configured as a distributed entity or at least in part a cloud based entity.

Breast holder **22** comprises a breast support plate **23** and a breast compressor plate **26** for compressing a breast positioned on support plate **23** in preparation for exposure to X-rays **45** to acquire an X-ray image of the breast. Breast support plate **23**, comprises a digital X-ray camera **24** having an array of X-ray sensors **25**, each sensor **25** operable to generate electronic signals responsive to intensity of X-rays **45** that pass through the breast held in breast holder **22**. Compressor plate **26** is made from a material such as a suitable plastic that is substantially transparent to X-rays **45**. X-ray source **30** and breast holder **22** are optionally mounted to a support beam **40** attached to a column support **41** by a shaft **43**. Column support **41** is attached to a base **42** for floor mounting XBI **20**.

Support beam **40** and shaft **43** may be configured to slide up and down along column support **41** to adjust height of breast holder **22** to a patient's height, and to enable the support beam to rotate about an axis of rotation, indicated by a dashed line **44**, of shaft **43** so that X-Ray images of the breast, may be acquired from various angles. By way of example, support beam **40** is schematically shown in FIG. **1**A oriented vertically parallel to column support **41** so that XBI **20** may acquire a Cranial-Caudal (CC) X-ray image of a breast. Rotation of support beam **40** away from the vertical enables XBI **20** to acquire a mediolateral-oblique (MLO) image views of the breast.

FIG. **1**B shows a flow diagram **100** illustrating a procedure by which XBI **20** may operate to acquire SCEDM images of a breast (not shown). Initially, in block **101**, a contrast agent, which is preferentially taken up in regions of increased vascularity, such as in growing tumors, is injected into a patient (not shown) in preparation for imaging a breast (not shown) of the patient. Optionally, in a block **103** the patient's breast is positioned between breast support plate **23** and breast compressor plate **26** and compressed, to even out the thickness of the breast tissue and avoid folding of the breast tissue which can obscure internal features of the breast, in preparation for acquiring, optionally, MLO X-ray images of the breast. For acquiring the MLO X-ray image support beam **40** shown in FIG. **1**A is substantially perpendicular to column support **41** and parallel to the floor. In a block **105** controller **50** controls X-ray source **30** and digital X-ray camera **24** to expose the breast to low energy X-rays and acquire a low energy MLO X-ray image of the breast. In a block **107** the controller controls X-ray source **30** and X-ray camera **24** to expose the breast to high energy X-rays and acquire a high energy MLO X-ray image of the breast. The breast may then be released in a block **109** and controller **50** (FIG. **1**A) may in a block **111** process the high and low energy X-ray images to provide a MLO SCEDM image by subtracting the low energy X-ray image from the high energy X-ray image. In a block **113** controller **50** may rotate support beam **40** of XBI **20** (FIG. **1**A) so that it is parallel to support beam **41**, as shown in FIG. **1**A, to orient X-ray source **30** and breast holder **22** for X-ray imaging of the breast at a CC view. In a block **115** the breast is optionally again positioned between the breast support plate **23** and breast compressor plate **26**, and the latter is moved towards breast support plate **23** to compress the breast and even out breast tissue. A series of two X-ray exposures are made of the breast to acquire a "low energy CC X-ray image", optionally in a block **117** and a "high energy CC X-ray image" optionally in a block **119**. The breast may then be released in a block **121** and in a block **123** controller **50** processes the low and high CC X-ray images to generate a CC SCEDM image.

It is noted that contrast agents that preferentially accumulate in malignant lesions and are used in SCEDM breast imaging are generally iodinated agents. Therefore to acquire low energy images in SCEDM imaging of breast tissue the energy of the X-rays provided by X-ray source **30** in XBI **20**

is below the k-edge of iodine. To acquire the high energy images the energy of X-rays provided by X-ray source **30** is above the k-edge of the iodine in the contrast agent.

In an embodiment of the disclosure, controller **50** (FIG. **1**A) may process an SCEDM X-ray image of a patient's breast acquired by XBI **20** to determine presence of a malignancy in accordance with a procedure illustrated by a flow diagram **140** shown in FIG. **2**. The numerical label **140** may be used to refer to the procedure illustrated by flow diagram **140** as well as to the flow diagram. FIG. **3** shows an example SCEDM X-ray image **200** acquired for a breast of a patient. SCEDM X-ray image **200** exhibits a CE-ROI **202**, shown greatly enlarged in FIG. **3** in an inset **203**, that may comprise a malignancy and may be processed by controller **50** in accordance with procedure **140**. FIG. **4** schematically shows pixels in a region of CE-ROI **202** greatly enlarged in an inset **250** to illustrate how they may be processed to provide a texture feature vector TF for use in diagnosing breast malignancy, in accordance with procedure **140**. Features shown in FIGS. **3** and **4** may be referred to where relevant in the flow diagram of FIG. **2** by their labels in FIGS. **3** and **4**.

In a block **141** of procedure **140** controller **50** may receive via a suitable user interface (not shown) to the controller, a segmentation of X-ray image **200** shown in FIG. **3** made by a medical practitioner that locates CE-ROIs, of which CE-ROI **202** is an example, in the image. Alternatively or additionally controller **50** may process the X-ray image using a suitable segmentation algorithm to locate CE-ROIs. In a block **143** a contour **204** of CE-ROI **202** may be determined. The contour may be determined automatically by controller **50** or may be manually determined and input to controller **50** by a user operating the interface to the controller.

Optionally, in a block **145**, controller **50** processes contour **204** to provide components of a contour feature vector CF(N) characterizing the contour and having components CF(n), $1 \leq n \leq N$. Components CF(n) may comprise, by way of example, a length of contour **204**, a number of turning points in the contour, entries in a histogram of heights of positive turning points, and entries in a histogram of widths of peaks in the contour.

Turning points in contour **204** are points along the contour at which a derivative as a function of a parameter measuring displacement along the contour is zero. A positive turning point is a point at which contour **204** is concave facing inwards to the area of CE-ROI **202** surrounded by the contour. A negative turning point is a point at which contour **204** is convex facing inwards to the area of CE-ROI **202**. Example turning points in contour **204** are indicated by a triangle pointer **206** and may be referred to by the numeral **206**. A height of a positive turning point **206** may be a distance between the positive turning point and an adjacent negative turning point along contour **204**. An example height of a positive turning point is indicated in FIG. **3** by a distance **208**. In accordance with an embodiment, entries in a histogram of heights of positive turning points **206** in contour **204** may be features of feature vector CF(N). A peak of contour **204** may be a segment of contour **204** between two negative turning points adjacent to and located on opposite sides of a positive turning point in the contour. Width of the may be a distance between points on the contour on opposite sides of the peak's positive turning point located at respective half heights to the peak's negative turning points. A peak width of contour **204** is indicated by a numeral **210**. Entries in a histogram of peak widths in contour **204** may be features of feature vector CF(N) in accordance with an embodiment of the disclosure.

Optionally, in a block **147**, for each X-ray pixel "P(x,y)" of X-ray image **200** located in CE-ROI **202** at row and column image coordinates (x,y) of the X-ray image, controller **50** determines a neighborhood, optionally referred to as a "texture neighborhood", of X-ray pixels in CE-ROI **202** for processing to determine a measure of texture of CE-ROI **202**. The neighborhood, also referred to as a "texture neighborhood" extends "radially" a "radial pixel distance", also referred to as a "pixel radius" (PR), equal to a bounding pixel radius, "BPR", pixels in any direction from location (x,y) of X-ray pixel P(x,y).

FIG. **4** schematically shows a texture neighborhood **230** determined for an X-ray pixel P(x,y) in CE-ROI **202**. Texture neighborhood **230** may extend to a radial pixel distance PR=BPR greater than or equal to about 25 pixels. Optionally, texture neighborhood **230** extends to a bounding pixel radius BPR of about 50 pixels or more. In an embodiment, texture neighborhood **230** extends to a bounding pixel radius BPR of at least about 75 pixels. A portion of texture neighborhood **230** that extends to a pixel radius PR of 7 pixels is schematically shown greatly enlarged in an inset **250** in the figure. X-ray pixels **231** are adjacent to pixel P(x,y) and are located at a pixel radius PR equal to 1 pixel from X-ray pixel P(x,y), while X-ray pixels **232** are located at a pixel radius PR=4 pixels from X-ray pixel P(x,y).

In a block **149**, controller **50** selects X-ray pixels at R different pixel radii PR(r), $1 \leq r \leq R$, in texture neighborhood **230** for processing to determine a measure of texture for CE-ROI **202**. Pixel radii PR(r) increase with increase in index r, and PR(R) is equal to the bounding pixel radius BPR of texture neighborhood **230**. R may be equal to at least 2. Optionally, R is equal to or greater than about 10. Optionally R is greater than 20. By way of a numerical example, in the discussion that follows BPR for texture neighborhood **230** is assumed to be 64 pixels and R equal to 4. For convenience of presentation a pixel radius PR(r) may be referred to by its index as pixel radius r.

For each pixel radius r, $1 \leq r \leq R$, controller **50** selects, optionally a same number "J", of X-ray pixels S(x,y,r,j), $1 \leq j \leq J$ for processing. Optionally, J is equal to or greater than 4. In an embodiment J is equal to or greater than 8. By way of example, in FIG. **4**, J=8, therefore eight X-ray pixels S(x,y,r,j) are selected from the X-ray pixels for each pixel radius, r=1, 2, 3, and 4. Selected pixels S(x,y,r,j) are indicated in FIG. **4** by shading and for convenience of presentation are shown for only pixel radii PR(1) and PR(2) as examples equal respectively to 2 pixels and 4 pixels. It is noted that practice of an embodiment of the disclosure is not limited to pixel radii PR(1)=2 and PR(2)=4. In an embodiment, by way of numerical example, for texture neighborhood **230** having BPR=64 and R=4 as noted above, pixel radii PR(1), PR(2), PR(3), and PR(4) in the texture neighborhood may be equal to 15, 30, 45 and 70 pixels respectively. Optionally, the selected pixels S(x,y,r,j) are symmetrically located around pixel P(x,y), along straight lines extending from pixel P(x,y). Optionally, selected pixels S(x,y,r,j) are located along lines extending from pixel P(x,y) every 45°, at angles (j−1) 45° respectively. The lines are labeled with the value of the index j of the X-ray pixels S(x,y,r,j) associated with the lines. Selected X-ray pixels having index j=1, that is pixels S(x,y,r,1), lie along a 12 o'clock direction, and angles increase with increase in j in a clockwise direction.

In a block **151** controller **50** assigns a binary number 0 or 1, to each selected X-ray pixel S(x,y,r,j), depending on

whether intensity of incident X-rays represented by a gray level of the selected X-ray pixel is respectively less than or greater than incident X-ray intensity represented by a gray level of pixel P(x,y). Let P(x,y) and S(x,y,r,j), in addition to identifying particular X-ray pixels in CE-ROI **202**, represent intensity of X-rays that gray levels of the identified pixels respectively represent. Then the calculation performed in block **151** may be represented in symbols as: IF (S(x,y,r,j)≤P(x,y), b(x,y,r,j)=0; otherwise, b(x,y,r,j)=1).

By way of example, arbitrary gray levels are shown in FIG. **4** for X-ray pixel P(x,y) and selected X-ray pixels S(x,y,1,j) that are located at pixel radius r=1 (that is PR(1)=2 pixels) from P(x,y). The arbitrary gray level for pixel P(x,y) is 79, and gray levels for selected X-ray pixels S(x,y,1,1)-S(x,y,1,8) are 99, 20, 34, 78, 52, 88, 70, 34 respectively. The selected X-ray pixels (S(x,y,1,j) are therefore assigned in block **151** corresponding binary numbers b(x,y,1,1), . . . , b(x,y,1,8) that are respectively equal to 1, 0, 0, 0, 0, 1, 0, 0.

Optionally, in a block **153** controller **50** assigns a binary number BN(x,y,r) comprising J bits for each pixel radius r in CE-ROI **202**. A j-th bit of binary number BN(x,y,r) is equal to b(x,y,r,j) and a most significant bit in the binary number is optionally b(x,y,r,1). For example, for CE-ROI **202**, BN(x,y,1) is determined from the binary numbers b(x,y,1,1)-b(x,y,1,8) discussed above, and is equal to 10000100. In a subsequent block **155**, the controller may convert each binary number BN(x,y,r) to a decimal number N(x,y,r) that may assume any of 2^J values between 0 and (2^J−1). And in a block **157**, the controller assigns an R dimensional texture vector TV(x,y) for X-ray pixel P(x,y) having R components: N(x,y,1), N(x,y,2), . . . , N(x,y,R). For CE-ROI **202** having R=4, and J=8 selected X-ray pixels S(x,y,r,j) for each pixel radius r, the decimal number N(x,y,r) may assume any of 256 values between and inclusive of 0 and 255, and TV(x,y) for X-ray pixel P(x,y) has 4 components.

In a block **159**, controller **50** may generate a histogram HTV(T) of the texture vectors TV(x,y) determined for optionally all X-ray pixels P(x,y) having locations (x,y) in the area of CE-ROI **202**. HTV(T) has T=R2^J bins, and may be written as the set HTV(T)={HTV(t)|1≤t≤T=R2^J}, where HTV(t) is the value of a t-th bin of the histogram. A value HTV(t) is equal to a number of X-ray pixels P(x,y) in CE-ROI **202** having a decimal value N(x,y,(t modulo 2^J). By way of example, for R=4 and J=8 the number of bins T is equal to 1024.

In an embodiment of the disclosure, optionally in a block **161**, controller **50** selects "M" bins from the T bins of HTV(T) as components of a texture feature vector TF(M) for use in diagnosing malignancy in the breast imaged in X-ray image **200** (FIG. **3**). In a block **163** the controller optionally generates an SCEDM feature vector, "SCEDM-F(•)" for CE-ROI **202** responsive to contour feature vector CF(N) and/or texture feature vector TF(M) to diagnose malignancy in the CE-ROI. Optionally, SCEDM-F(•) is a K dimensional feature vector SCEDM-F(K), which may be referred to as a feature vector CF-TF, having dimension K=(N+M) generated by concatenating CF(N) and texture feature vector TF(M).

In a block **165**, controller **50** may concatenate SCEDM-F(K) with a Q dimensional profile feature vector PF(Q) of the patient for which X-ray image **200** was acquired to generate a
G=(K+Q) dimensional global feature vector "GF(G)" for diagnosing malignancy in CE-ROI **202**. Profile feature vector PF(Q) may comprise any one or any combination of more than one of personal data components, such as age, sex, family data, and genetic data. A global feature vector formed by concatenating PF and CF-TF may be referred to as a feature vector PF-CF-TF

In a block **167**, controller **50** processes feature vector SCEDM-F(K) or feature vector GF(G) to determine whether CE-ROI **202** comprises a malignancy. In an embodiment, processing the feature vector comprises operating on the feature vector using a classifier such as a support vector machine (SVM) or a neural network (NN) that has been trained on a set of training images CE-ROIs.

Controller **50** may determine a number M, and which of the components of the T components of histogram HTV(T) determined for CE-ROI **202** in block **161** of flow diagram **140**, are to be selected for components of texture feature vector TF(M) by processing a plurality of sample CE-ROIs for which it is known whether they are benign or malignant. FIG. **2**B shows a flow diagram of a procedure **180** illustrating a procedure by which controller **50** may determine how many, and which components of HTV(T) to select for texture feature vector TF(M), in accordance with an embodiment of the disclosure. Procedure **180** also provides an SVR machine for classifying CE-ROIs responsive to a texture feature vector TF(M) based on the number and components of HTV(T) selected by the procedure for features of TF(M).

Assume that the sample CE-ROIs are represented by $CE\text{-}ROI_V$ 1≤v≤V, and that for each $CE\text{-}ROI_V$ controller **50** has acquired a histogram $HTV_V(T)$, optionally in accordance with block **159** of procedure **140** shown in FIG. **2**A. Assume further that of the V samples $CE\text{-}ROI_V$, Vm are known to be malignant and Vb are known to be benign and that V=Vm+Vb.

In a block **181** of flow diagram **180**, controller **50** calculates an average value $\mu_m(t)=(1/Vm)\Sigma_1^{Vm}HTV_V(t)$ and a variance $\sigma^2_m(t)$ of the average, for each t-th bin of the Vm histograms determined for the $CE\text{-}ROI_V$ that are known to be malignant. In a block **183** controller **50** calculates an average value $\mu_b(t)=(1/Vb)\Sigma_1^{Vb}HTV_V(t)$ and a variance $\sigma_b(t)$ of the average, for each t-th bin of the Vb histograms determined for the $CE\text{-}ROI_V$ that are known to be benign. In a block **185**, the controller may calculate for each t-th bin of the $HTV_V(T)$ a signal to noise ratio, "SNR(t)", which may be defined by an expression $SNR(t)=|\mu_m(t)-\mu_b(t)|/sqrt[\sigma^2_m(t)+\sigma^2_b(t)]$, and if SNR(t) is greater than a threshold noise, "th-SNR", the controller selects the t-th bin as a candidate for providing a component of TF(M). Let an SNR selected bin number t be primed and represented by t' to indicate that it was selected. For example if a bin number **783** was selected it is represented by **783'**.

Optionally, in a block **187**, controller **50** clusters bins having SNR selected bin numbers t' into clusters of correlated bins responsive to a correlation threshold "th-correlation". Bins that are considered to be correlated are clustered in a same i-th correlation cluster. For each i-th correlation cluster a representative bin number t* is selected from the bin numbers t' in the correlation cluster. This correlation process determines, a selection of M* bins having bin numbers t^*_m, 1≤t*≤M*, selected to provide values $HTV_V(t^*)$ for texture feature vectors $TF(M^*)_V$ for $CE\text{-}ROI_V$ respectively. M* is a function of th-SNR and th-correlation, and may be written M*(th-SNR, th-correlation) to indicate the dependence. In a block **191** controller **50** optionally generates a texture feature vector TF(M*(th-SNR, th-correlation)) comprising a set $\{HTV(t^*_m): 1\leq m\leq M^*\}$ as components, where t^*_m represents a particular representative bin number of the M* different representative bin numbers.

In a block **191**, controller **50** may perform a K-fold cross validation error evaluation for an SVR model, $SVR(TF(M^*)_V)$ for the samples $CE\text{-}ROI_V$ and their known

presence or absence of malignancy using the texture feature vectors $TF(M^*)_V$ determined for each of a group of a different pairs of values for th-SNR and th-correlation. A pair of values th-SNR and th-correlation from the group that provides a minimum cross validation error in diagnosing malignancy in the CE-ROI_V may be determined as an optimal pair of values, th-SNR_O and th-$correlation_O$. M* and bin numbers t_m* associated with th-SNR_O and th-$correlation_O$ are used as the number M and bin numbers t_m to define texture feature vector in TF(M) in block **161** of flow diagram **140**.

In an embodiment, in a block **193**, classification values λ_V for CE-ROI_V, $1 \le v \le V$ respectively generated by the K-fold cross-validation performed for th-SNR_O and th-$correlation_O$, may be used to determine a corresponding optimal SVM_O based on all V members of the plurality of samples CE-ROI_V. In an embodiment of the disclosure SVM_O may be used to diagnose a CE-ROI of a breast X-ray image that XBI **20** acquires for a patient to classify and determine if the CE-ROI is malignant.

FIGS. **5**A-**5**C show dispersion graphs of results of using a texture feature vector TF(M) and a SVM_O determined in accordance with procedures similar to procedures **140** and **180** shown in the flow diagrams of FIGS. **2**A and **2**B to classify 93 CE-ROIs segmented by hand from X-ray images acquired for actual patients. The dispersion graphs were generated for texture feature vector, TF(M), parameters: BPR=64 pixels; R=4, PR(1), . . . , PR(4) equal to 15, 30, 45, and 70 pixels, and J=8; M=M*=3 and associated bin numbers t^*_m=30, 784, and 896 from a histogram HTV(T). Of the 93 CE-ROIs, 41 were known to be images of benign tissue and 52 were known to be images of malignant tissue.

Each of FIGS. **5**A-**5**C shows a same dispersion **500**. In the dispersion graphs, CE-ROIs known to be cancerous are represented by asterisks **501**. CE-ROIs known to be benign are represented by circles **502**. The 52 cancerous CE-ROIs are identified by ID indices 1-52 and the benign CE-ROIs are identified by ID indices 1-41. The abscissas in the dispersion graphs show the ID indices of the CE-ROIs associated with the asterisks and circles. The ordinates of the dispersion graphs show the classification scores determined for the CE-ROIs by the SVM_O. Cancerous CE-ROIs have higher classification scores than benign CE-ROIs. Dispersion graphs **5**A-**5**C have classification decision lines A-C respectively that may be used to make a decision as to whether a given classification score is to be considered to indicate that an entry in the dispersion graphs is cancerous or not. Classification scores above a given partition line A, B, or C may be considered to indicate that tissue in a CE-ROI represented by an entry in the graph, that is an asterisk or a circle, is malignant, while classification scores below the partition line may be considered to indicate that tissue in the CE-ROI is benign. Classification lines A, B, and C are located at classification scores 0.5, 0, and −0.5.

Graph **5**C shows that if the decision line, decision line C in the graph, is set so low as to provide 100% sensitivity, that is, to correctly classify all cancerous CE-ROIs as cancerous, XBI **20** will exhibit specificity of 36.6% and correctly identify 36.6% of the non-cancerous CE-ROIs as benign. Graph **5**C indicates that XBI **20** operating in accordance with an embodiment of the disclosure to implement procedures similar to that illustrated by flow diagram **140** and **180**, may be configured to provide 100% detection of cancerous lesions and potentially reduce unwanted biopsies by about 36%. Graph **5**B, with decision line B at 0, XBI **20** configured in accordance with an embodiment of the disclosure to provide 98% sensitivity will provide specificity of about 53% and potentially reduce unwanted biopsies by about half. Graph **5**A indicates that XBI **20** configured in accordance with an embodiment of the disclosure to reduce unwanted biopsies by about 75% will still correctly detect about 90% of cancerous lesions.

Whereas the above description references specific examples of features that may be used to provide components of a feature vector used to classify and distinguish malignant from benign lesions based on contrast enhanced images of the lesions, practice of an embodiment of the disclosure is not limited to the referenced features. By way of example, a feature or any combination of more than one feature listed and defined by the Breast Imaging Reporting and Data System (BIRADS) Lexicon Classification System established by the American College of Radiology may be used to provide a component of a feature vector for classifying a lesion in accordance with an embodiment of the disclosure. The BI-RADS classification system classifies lesions as mass like, three-dimensional space occupying lesion, or a non-mass like lesion and for each type of lesion a characteristic of the lesion that may be used to provide a determination as to whether the lesion should be classified as malignant or benign. Among the characteristics of a mass like lesion listed and defined in the BIRADS lexicon are by way of example, characteristics of the lesion's shape—whether it is round, oval or irregular, and characteristics of its margin—whether the margin appears smooth, irregular or spicualted. Among characteristics of a non-mass-lesion listed and defined in the BIRAD lexicon are by way of example, characteristics of its distribution—whether it is characterized by a focal area, whether is linear, ductal, segmental or diffuse. Furthermore, whereas a classifier may provide classification scores such as those shown in FIGS. **5**A-**5**C to determine whether a CE-ROI comprises a cancer, in an embodiment, the classifier may operate on a feature vector to provide BIRADS scores for use in determining whether a breast lesion is cancerous or not.

In an embodiment, a feature of a feature vector may be a time dependent feature. For example, as described with reference to FIGS. **1**A-**1**B, XBI **20** may be operated to acquire a plurality of SCEDM images. The images, by way of example, low and high energy MLO X-ray images and low and high energy CC X-ray images may be acquired at different times. During time lapses between acquisitions of the images concentration of a contrast agent introduced into a patient's body may change as a result of a rate at which the contrast agent is taken up or washed out by breast tissue that is being imaged. A rate of increase or decrease of the contrast agent in the imaged tissue may be estimated from a change in contrast of the imaged tissue exhibited in the images and used to provide a component of a feature vector for discriminating malignant from benign tissue in accordance with an embodiment.

For example, a time lapse between acquiring CC and MLO X-ray images of a breast tissue lesion may be as long as 1-2 minutes. If concentration of a contrast agent in the lesion is substantially maximum during acquisition of the CC X-ray images, the concentration may be substantially reduced by wash out at a time at which the MLO X-ray images are acquired. A difference in contrast between the CC and MLO X-ray images, and the time lapse between acquisition of the images may be used to provide an estimate of a rate at which blood flow washes out the contrast agent from the lesion and thereby a characteristic of magnitude of blood flow in and through the lesion. The rate of washout may be advantageous as a component of a feature vector in

accordance with an embodiment for distinguishing whether the lesion is malignant or benign.

The above description indicates, by way of example, that identification of a feature of an SCEDM image of a breast tissue lesion for generating or using as a component of a feature vector may be determined manually. In an embodiment a convolutional neural network (CNN) may be used to automatically identify and determine which features of an SCEDM image of a breast tissue lesion are advantageous for providing a component of a feature vector for classifying lesions as malignant or benign. Upon identifying and determining which features of an SCEDM image are advantageous for use as a component of the feature vector, the CNN may provide the feature to a classifier that processes the feature vector to determine malignancy or benignity. Optionally the CNN operates as the classifier, and processes the feature vector to determine malignancy or benignity. The CNN may undergo training to learn directly from input images to identify and determine which features of an SCEDM to provide to a classifier for classifying lesions as malignant or benign.

By way of example, a CNN may be used to determine a magnitude of a washout rate for a CE-ROI by processing SCEDM images comprising the CE-ROI acquired at different times after the CNN was trained on images of malignant breast tissue that exhibit a known rate of washout of a contrast agent. Images used to train the CNN may be SCEDM images of tissue for which information with respect to washout is known from MRI images of the tissue.

In the description and claims of the present application, each of the verbs, "comprise" "include" and "have", and conjugates thereof, are used to indicate that the object or objects of the verb are not necessarily a complete listing of components, elements or parts of the subject or subjects of the verb.

Descriptions of embodiments of the disclosure in the present application are provided by way of example and are not intended to limit the scope of the disclosure. The described embodiments comprise different features, not all of which are required in all embodiments of the disclosure. Some embodiments utilize only some of the features or possible combinations of the features. Variations of embodiments of the disclosure that are described, and embodiments of the disclosure comprising different combinations of features noted in the described embodiments, will occur to persons of the art. The scope of the disclosure is limited only by the claims.

The invention claimed is:

1. A method of diagnosing breast cancer, the method comprising:

acquiring a contrast enhanced region of interest (CE-ROI) comprised in an X-ray image of a patient's breast, the X-ray image comprising X-ray pixels that indicate intensity of X-rays that passed through the breast to generate the image;

determining a texture neighborhood for each of the plurality of X-ray pixels, the texture neighborhood for a given X-ray pixel of the plurality of X-ray pixels extending to a bounding pixel radius of BPR pixels from the given pixel;

selecting a plurality of R different pixel radii PR(r), $1 \le r \le R$, in the texture neighborhood, for which $PR(r) < PR(r+1)$ and $PR(R)=BPR$;

determining values for a number of M representative bins of a texture vector histogram HTV(T) having a bin length in number of bins T equal to a sum over r from 1 to R of $2^{(r)}$, where J(r) is a number of X-ray pixels at radius r selected for processing, and values HTV(t) $1 \le t \le T$ that are a function of texture vectors TV determined for the texture neighborhoods of a plurality of pixels in the CE-ROI

generating a texture feature vector (TF) having components based on at least a portion of the values determined for the M representative bins; and

using a classifier to classify the texture feature vector TF to determine whether the CE-ROI is malignant.

2. The method according to claim **1** wherein BPR is greater than or equal to about 25, 50, or 75.

3. The method according to claim **1** wherein R is greater than or equal to 2, 10, or 20.

4. The method according to claim **1** and comprising for each pixel radius assigning a binary number to each of the J(r) X-ray pixels at the pixel radius, wherein the assigned binary number is 1 if the indication of intensity of the X-ray pixel is greater than the indication of intensity of the given X-ray pixel and 0 otherwise and comprising for each pixel radius PR(r) generating a binary string based on the assigned binary numbers.

5. The method according to claim **4** and comprising converting the binary strings for the pixel radii PR(r), $1 \le r \le R$ to decimal numbers N(r), $1 \le r \le R$ respectively and determining a texture vector (TV) for the texture neighborhood of the given X-ray pixel comprising a set of the decimal numbers {N(1), N(2), . . . N(R)}.

6. The method according to claim **1** wherein if P(0)=0, and $P(r)=2^{(1)}+2^{J(2)}, \ldots, +2^{J(r)}$, for $1 \le r \le R$, a value HTV(t) of a t-th bin in the histogram for which $P(r) < t \le P(r+1)$ is equal to a number of the texture neighborhoods of the given X-ray pixels of the plurality of X-ray pixels for which $N(r)=(t-(P(r))$.

7. The method according to claim **1** and comprising determining components of the texture feature vector (TF) to comprise a set of at least a portion of the values determined for the M representative bins.

8. The method according to claim **1** wherein M is less than or equal to about 50, 20, or 5.

9. The method according to claim **1** wherein the X-ray image is a spectral contrast enhanced digital mammography (SCEDM) image.

10. The method according to claim **1** wherein the classifier comprises a support vector machine and/or a neural network and/or a convolutional neural network.

11. The method according to claim **1** and comprising processing the CE-ROI to determine a time dependent component of a feature vector and using the time dependent component to determine whether the CE-ROI indicates a malignancy.

12. The method according to claim **1** and comprising using a convolutional neural network (CNN) to automatically identify and determine which features of the CE-ROI to use to generate the feature vector.

13. A method of diagnosing breast cancer, the method comprising:

acquiring a contrast enhanced region of interest (CE-ROI) comprised in an X-ray image of a patient's breast, the X-ray image comprising X-ray pixels that indicate intensity of X-rays that passed through the breast to generate the image;

determining a texture neighborhood for each of the plurality of X-ray pixels, the texture neighborhood for a given X-ray pixel of the plurality of X-ray pixels extending to a bounding pixel radius of BPR pixels from the given pixel;

generating a texture feature vector (TF) having components based on the indications of intensity provided by a plurality of X-ray pixels in the CE-ROI that are located within the texture neighborhood;

determining a contour for the CE-ROI and a contour feature vector CF based on the contour and concatenating the texture feature vector TF and the contour feature vector CF to provide a feature vector CF-TF; and

using a classifier to classify CF-TF to determine whether the CE-ROI is malignant.

14. A method of diagnosing breast cancer, the method comprising:

acquiring a contrast enhanced region of interest (CE-ROI) comprised in an X-ray image of a patient's breast, the X-ray image comprising X-ray pixels that indicate intensity of X-rays that passed through the breast to generate the image;

determining a texture neighborhood for each of the plurality of X-ray pixels, the texture neighborhood for a given X-ray pixel of the plurality of X-ray pixels extending to a bounding pixel radius of BPR pixels from the given pixel;

generating a texture feature vector (TF) having components based on the indications of intensity provided by a plurality of X-ray pixels in the CE-ROI that are located within the texture neighborhood;

determining a profile feature vector (PF) based on a personal profile of a patient for which the X-ray image was acquired;

concatenating the profile feature vector PF with the texture feature vector TF to form a feature vector PF-TF; and

using a classifier to classify PF-TF to determine whether the CE-ROI indicates a malignancy.

15. The method according to claim **14** and comprising determining a contour for the CE-ROI and a contour feature vector CF based on the contour, determining a profile feature vector PF based on a personal profile of a patient for which the X-ray image was acquired, and concatenating the profile feature vector PF with the contour feature vector CF and the texture feature vector TF to form a feature vector PF-CF-TF, and using a classifier to classify PF-CF-TF to determine whether the CE-ROI indicates a malignancy.

16. Apparatus for diagnosing breast cancer, the apparatus comprising:

a source of X-rays;

a controller configured to control the X-ray source to acquire an SCEDM X-ray image of a patient's breast the SCEDM X-ray image comprising X-ray pixels that indicate intensity of X-rays that passed through the breast to generate the image; and

a controller comprising a set of instructions executable to process the SCEDM X-ray image to:

acquire a contrast enhanced region of interest (CE-ROI) in the SCEDM X-ray image;

determine a texture neighborhood for each of a plurality of X-ray pixels, in the CE-ROI the texture neighborhood for a given X-ray pixel of the plurality of X-ray pixels extending to a bounding pixel radius of BPR pixels from the given pixel;

generate a texture feature vector (TF) having components based on the indications of intensity provided by a plurality of X-ray pixels in the CE-ROI that are located within the texture neighborhood; and

use a classifier to classify the texture feature vector TF to determine whether the CE-ROI is malignant.

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