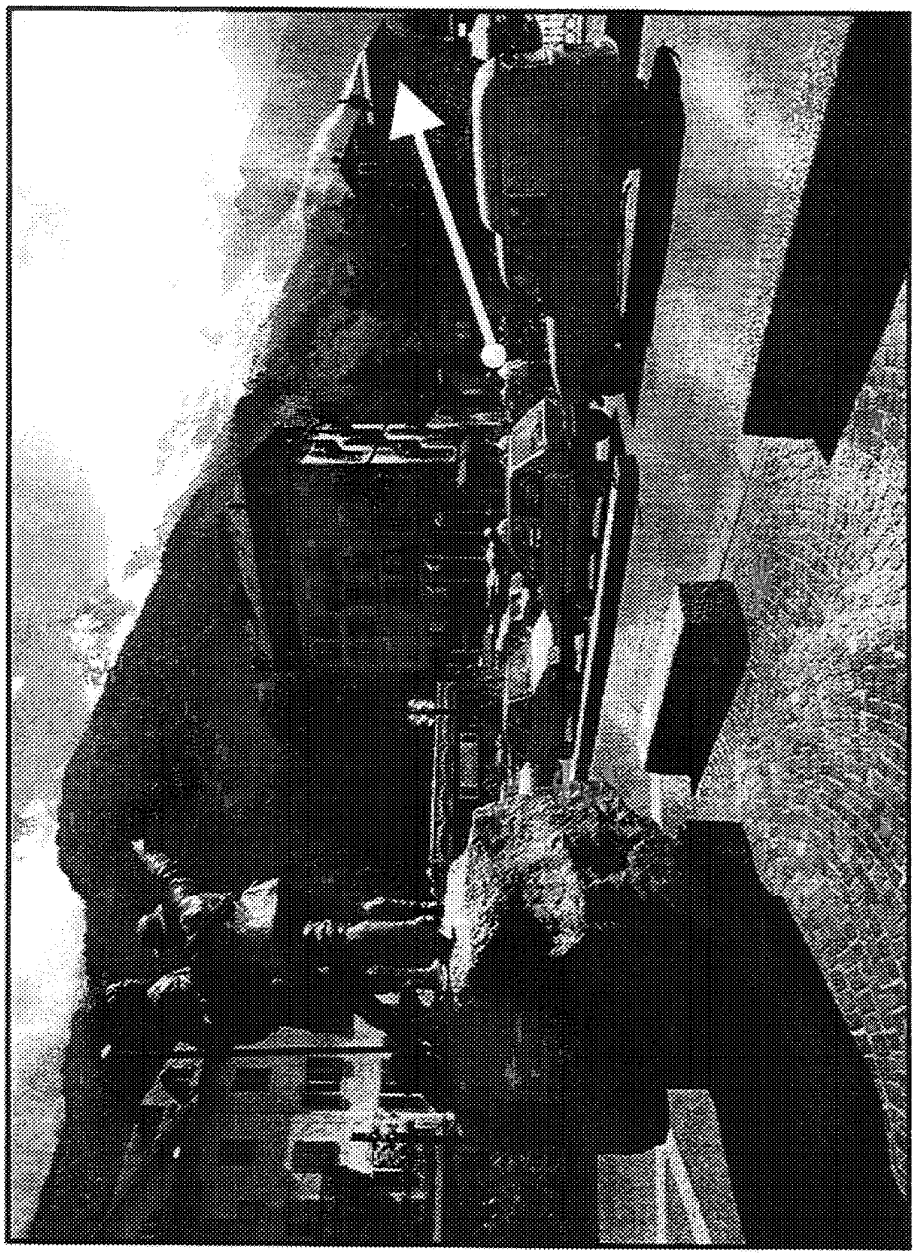

Fig. 11

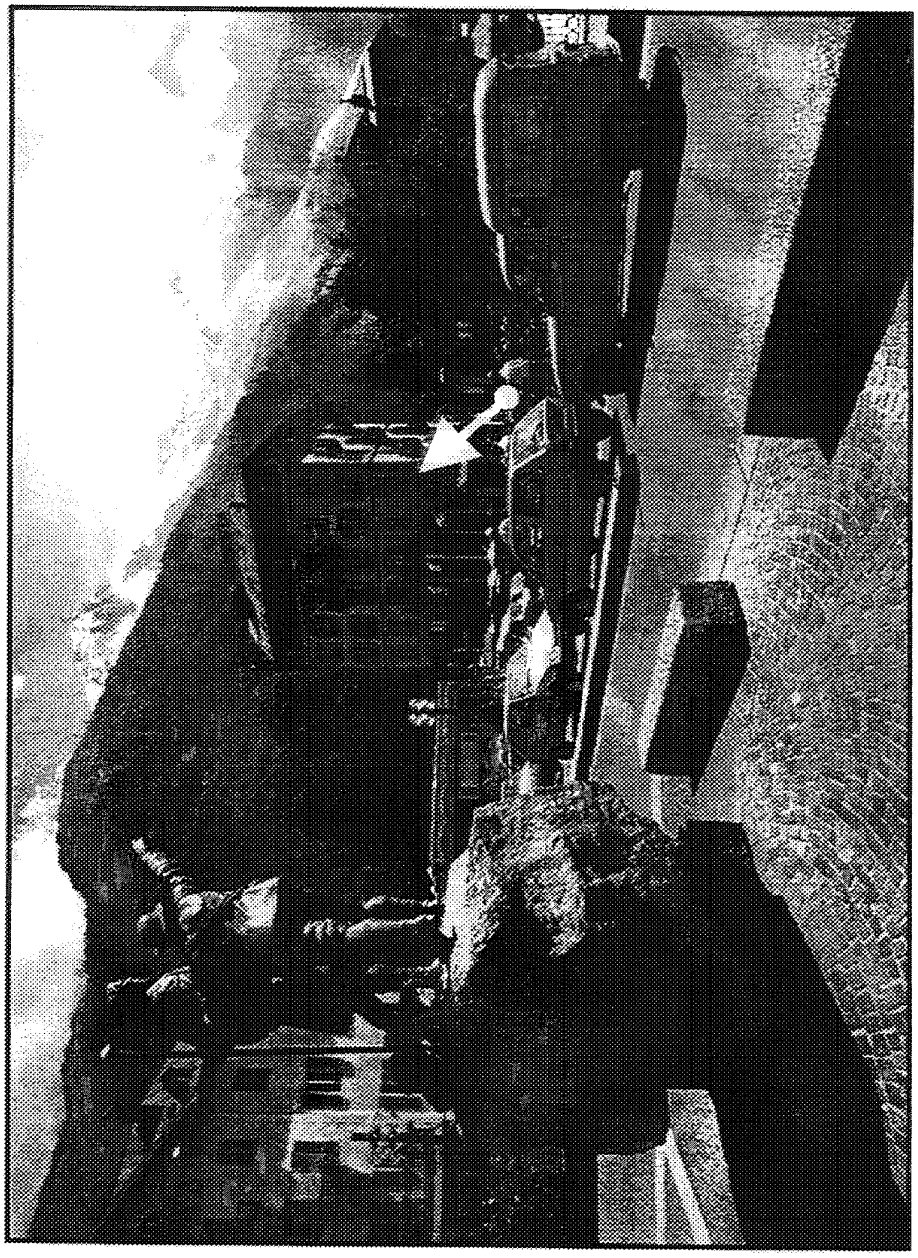

Fig. 12

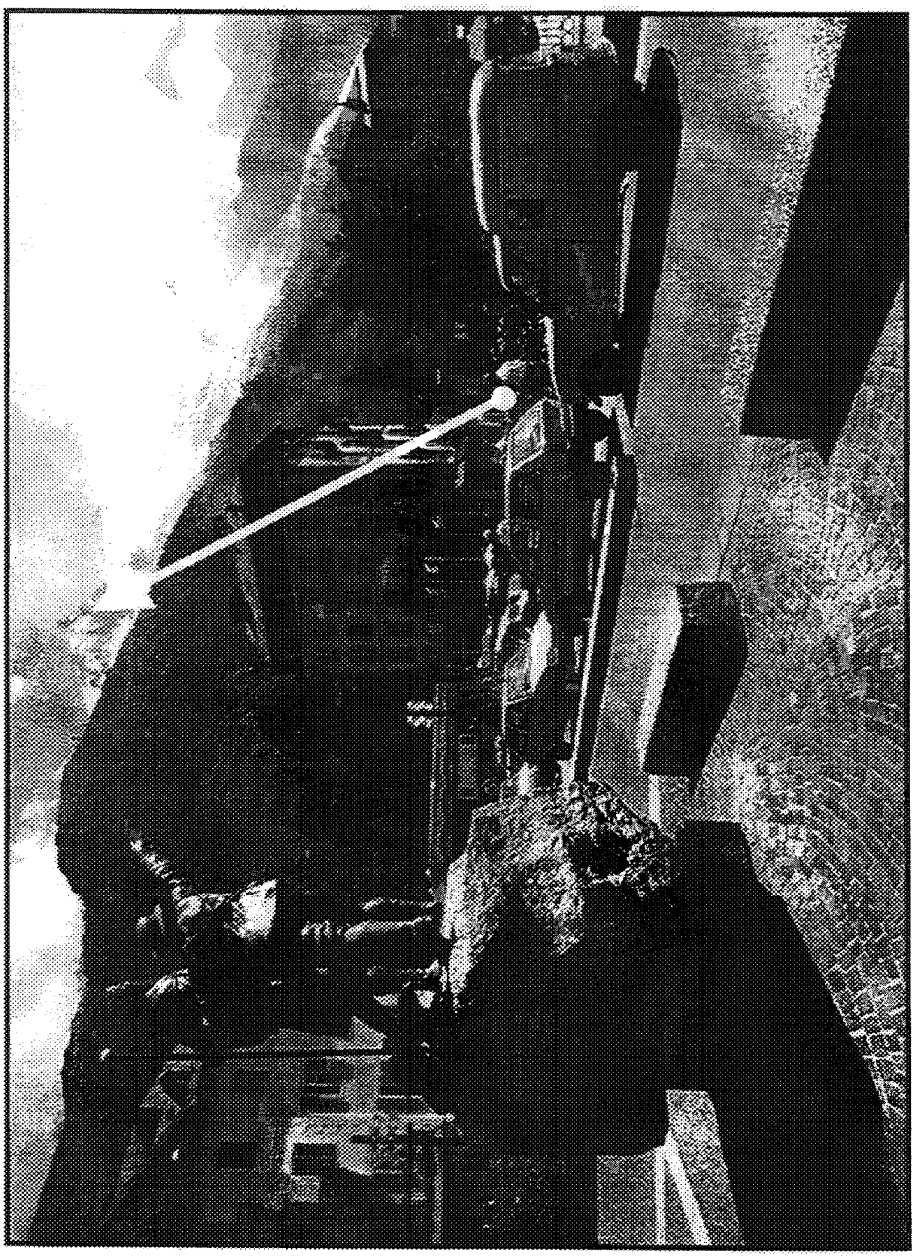

Fig. 13

Electronic Acknowledgement Receipt

EFS ID:	10582700
Application Number:	13069124
International Application Number:	
Confirmation Number:	9532
Title of Invention:	Image Capture and Identification System and Process
First Named Inventor/Applicant Name:	Wayne C. Boncyk
Customer Number:	24392
Filer:	Martin Fessenmaier/Lindsey Ripley
Filer Authorized By:	Martin Fessenmaier
Attorney Docket Number:	101044.0001US14
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Application Type:	Utility under 35 USC 111(a)

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Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Information Disclosure Statement (IDS) Form (SB08)	IDS_2.pdf	612829 225f460438fbac4244f0791535cc8ead46583029	no	8

Warnings:	
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2	Information Disclosure Statement (IDS) Form (SB08)	IDS_3.pdf	611913 15a609eb5de3320b726c5d4df926ef5fa24677cd	no	5
Warnings:					
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3	Foreign Reference	EP1012725A1.pdf	1464938 ba671d4e13f0a7397663cf19df8725a359274f29	no	81
Warnings:					
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APPLICATION NUMBER	FILING OR 371(C) DATE	FIRST NAMED APPLICANT	ATTY. DOCKET NO./TITLE
13/069,124	03/22/2011	Wayne C. Boncyk	101044.0001US14

CONFIRMATION NO. 9532

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PUBLICATION NOTICE

Title: Image Capture and Identification System and Process

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	Application Number	13069124
	Filing Date	2011-03-22
	First Named Inventor	Wayne C. Boncyk
	Art Unit	2622
	Examiner Name	to be assigned
	Attorney Docket Number	101044.0001US14

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	Art Unit	2622
	Examiner Name	to be assigned
	Attorney Docket Number	101044.0001US14

	1	98/37811	WO		1998-09-03	Electro-Optical Sciences, Inc.		☐
	2	99/44010	WO		1999-09-02	Gutkowicz-Krusin et al.		☐
	3	02/01143	WO		2002-01-03	Electro-Optical Sciences, Inc.		☐
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	Filing Date	2011-03-22
	First Named Inventor	Wayne C. Boncyk
	Art Unit	2622
	Examiner Name	to be assigned
	Attorney Docket Number	101044.0001US14

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Signature	/Nicholas J. Witchey/	Date (YYYY-MM-DD)	2011-11-04
Name/Print	Nicholas J. Witchey	Registration Number	63481

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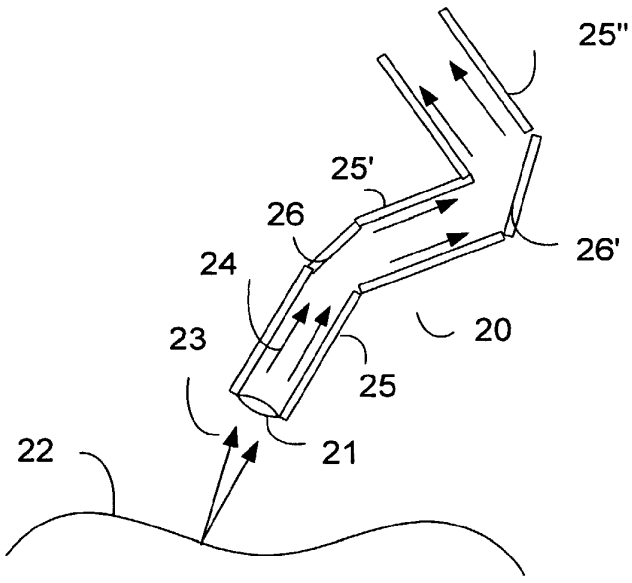

(57) Abstract: A light image is conveyed from internal biological tissue through a flexible optical system to an image receiver, where it is converted to a form which may be entered into a computer. The computer segments the image by generating a segmentation mask defining the boundary of a region of interest in at least one spectral band, estimates at least one rotationally and translationally invariant statistical measure of coefficient distributions of the multiscale wavelet maxima representations of the digital images in at least one spectral band, characterizes the condition of the tissue based on the estimated values and outputs the characterization of the condition of the tissue.

WO 02/01143 A2

MULTISPECTRAL IMAGING AND CHARACTERIZATION OF INTERNAL BIOLOGICAL TISSUE

FIELD OF THE INVENTION

The field of the invention is automatic machine vision and classification, and, in particular, the classification of biological tissue based on images of the biological tissue.

BACKGROUND OF THE INVENTION

U.S. Patent No. 6208749 B1, issued March 27, 2001, discloses systems and methods for the multispectral imaging of skin tissue enabling the automatic characterization of the condition of a region of interest of skin based on direct digital imaging of the region of interest or the digitization of color photographic slides of the region of interest, illuminated by appropriately filtered light. According to that patent, a digital image is automatically segmented in at least one spectral band. A digital processor segments the other images based on the segmentation mask. Parameters related to the texture, asymmetry, blotchiness and border irregularities are also automatically estimated. The region of interest is automatically characterized by the processor, based on the parameters. Skin lesions may be characterized as malignant or benign.

U.S. Patent No. 6,081,612, issued June 27, 2000, discloses systems and methods for characterizing the condition of a region of interest of the skin, wherein the absorption and scattering of light in different spectral bands by the region of interest is a function of the condition of the skin. The method comprises illuminating the region of interest of the skin by light in at least three spectral bands and digitally imaging the region of interest at the at least three spectral bands with the light re-emitted by the skin to generate digital images comprising digital signals whose values are a function of the condition of the skin. The digital images are provided to a processor which segments the digital images by generating a segmentation mask from a digital image in any one of the at least three spectral bands. The processor estimates at least one rotationally and translationally invariant statistical measure of coefficient distributions of the multiscale wavelet maxima representations of the digital images in each spectral band, which are functions of the

texture of the region of interest determined by the segmentation mask. The processor characterizes the condition of the skin based on the estimated values, and outputs the characterization of the condition of the skin. Preferably, the segmenting, estimating and characterizing steps are conducted without the intervention of an operator. Additional parameters include measures of the texture, asymmetry, blotchiness and border irregularity of the portion of the region of interest. The digital images may be obtained by directly imaging the region of interest with a digital camera, or digitally imaging color slides of the region of interest, through appropriately filtered light.

Not included in the above references are references to conducting light from place to place so that the image is conserved.

OBJECTS OF THE INVENTION

It is an object of the invention to illuminate and image biological tissue, principally in vivo, and to convey the image in the form of light to an image receiver for conversion to electrical signals and for automatic recognition of biological features.

SUMMARY OF THE INVENTION

A light image is conveyed from internal biological tissue through flexible optical system to an image receiver, where it is converted to a form that may be entered into a computer. The computer segments the image by generating a segmentation mask defining the boundary of a region of interest in at least one spectral band, estimates at least one rotationally and translationally invariant statistical measure of coefficient distributions of the multiscale wavelet maxima representations of the digital images in at least one spectral band, characterizes the condition of the tissue based on the estimated values, and outputs the characterization of the condition of the tissue.

Internal biological tissue encompasses tissue internal to a human or animal body, such as the stomach, the esophagus, the colon or the nasal cavities, for example.

In particular, in accordance with the present invention, a method of characterizing the condition of a region of interest of internal biological tissue, wherein the absorption and scattering of light in different spectral bands by the region of interest is a function of

the condition of the tissue, is disclosed. The method comprises inserting a flexible optical system into a body, proximate the region of interest. A portion of the tissue is illuminated including the region of interest by light in at least one spectral band. The image is conveyed through the flexible optical system to an image receiver. A portion of the tissue including the region of interest is digitally imaged at the at least one spectral band with the light re-emitted by the portion of the tissue. Digital images are generated comprising digital signals whose values are a function of the condition of the region of interest of the tissue. The digital images are provided to a processor. The processor segments the digital images by generating a segmentation mask defining the boundary of the region of interest from a digital image in any one of the at least one spectral bands, preferably without the intervention of an operator. The processor also estimates at least one rotationally and translationally invariant statistical measure of coefficient distributions of the multiscale wavelet maxima representations of the digital images in each spectral band and characterizes the condition of the tissue based on the estimated values, preferably without the intervention of an operator. The processor then outputs the characterization of the condition of the tissue.

The at least one statistical measure may be calculated separately within a border region or an interior region of the digital image. The border region is such that it encompasses the envelope of circles of fixed radius centered on the boundary of the segmentation mask. The inside region comprises all points of the image that are within the segmentation mask boundary but not included in the border region.

The computing step may comprise estimating at an individual level at least one value which is a statistical measure of texture of the portion of the region of interest within the border region and interior region. The statistical measure is chosen from the group consisting of:

the number of wavelet maxima per unit area;

the ratio of the mean coefficient magnitude to the absolute deviation of the coefficient magnitudes from the mean value;

the ratio of the mean coefficient magnitude to the standard deviation of the coefficient magnitude; and

the skewness of the coefficient magnitude, normalized to the cube of the standard deviation.

The estimating step may comprise estimating either the degree of change of a statistic of the wavelet coefficient distribution with increment of wavelet level, or the degree of deviation of such change from linearity.

The estimating step may also comprise estimating the average rate of change, with respect to level, of the number of wavelet maxima per unit area.

The estimated texture values may be compared to a threshold derived from statistical analysis of a multiscale wavelet transformation of the digital image, to characterize the condition of the tissue.

In accordance with another embodiment of the invention, a system for characterizing the condition of a region of interest of internal biological tissue is disclosed, comprising a source of light for illuminating the region of interest in at least one spectral band. A flexible optical system is provided for conveying the image of the region of interest to an image receiver. An image receiver is provided for acquiring digital images of the region of interest based on the light re-emitted from the illuminated region of interest at each of the spectral bands. The digital image comprises digital signals whose values are a function of the condition of the region of interest. Memory is provided for storing the digital images provided by the image receiver. A digital processor is provided, programmed to perform the steps of:

segmenting the digital images stored in memory by generating a segmentation mask from a digital image in any one of the at least one spectral band;

estimating at least one rotationally and translationally invariant statistical measure of coefficient distributions for the multiscale wavelet maxima representations of the digital images in each spectral band, which are functions of the texture of the region of interest determined by the segmentation mask;

characterizing the condition of the tissue based on the estimated values; and

outputting the characterization of the region of interest.

The flexible optical system may be an endoscope, a fiber optic bundle or an articulated arm.

BRIEF DESCRIPTION OF THE DRAWINGS

Fig. 1 is a sketch of the system of the invention; and

Fig. 2 is a sketch of an articulated arm of a system of the invention.

DETAILED DESCRIPTION OF THE INVENTION

Fig 1 shows a sketch of the system of the invention. A patient 10 has a flexible endoscope 11 inserted into a natural or surgically provided orifice of the body. As is very well known in the art of endoscopy, light is provided for illuminating the tissue inside the body, and the light reflected from the tissue and scattered from under the surface of the tissue falls on the end 12 of the endoscope. The first end of the endoscope 12 generally has a lens (not shown) which images the tissue on to the end of a coherent fiber bundle (not shown). The light imaged on to the fiber bundle is carried to the other end of the endoscope 13, where it may be projected on to a film or an electronic image receiver 14 such as are found in video or digital cameras. The light for illuminating the tissue may be provided through the endoscope.

The output of the image receiver is carried to a processor or computer 15 where the computer segments the image by generating a segmentation mask defining the boundary of a region of interest in at least one spectral band, estimates at least one rotationally and translationally invariant statistical measure of coefficient distributions of the multiscale wavelet maxima representations of the digital images in at least one spectral band, characterizes the condition of the tissue based on the estimated values, and outputs the characterization of the condition of the tissue. The computer processes are described in great detail in U.S. Patent No. 6,208,749, B1, issued March 27, 2001, U.S. Patent No. 6,081,612, issued June 27, 2000, International Publication No. WO99/44010, published 2 September 1999; and International Publication No. WO98/37811, published 3 September 1998, which are incorporated by reference herein, in their entireties.

Fig. 2 shows a sketch of an articulated arm 20 for conveying the images. The articulated arm is especially useful when the illuminating light is of a wavelength which is not transmitted well by the glass used in typical endoscopes. A lens 21 is placed so that the tissue to be imaged 22 is removed from the lens 21 by the focal distance l of the lens

22. Light 23 diverging from the tissue 22 is converted to a parallel beam 24 which propagates through a tube 25. The parallel light beam 24 may be reflected from mirrors 25 and 25' mechanically set to direct the beam 24 through other tubes 24' flexibly connected to tube 24. Tubes 24, 24', and 24" rotate on their axis to change the plane of propagation of the light beam 24. When the light beam 24 exits the articulated arm, it may be focused on an image receiver (not shown) to capture an image of the tissue 22.

Obviously, many modifications and variations of the present invention are possible in light of the above teachings. It is therefore to be understood that, within the scope of the appended claims, the invention may be practiced otherwise than as specifically described.

We claim:

1. A method of characterizing the condition of a region of interest of internal biological tissue, wherein the absorption and scattering of light in different spectral bands by the region of interest is a function of the condition of the tissue, the method comprising:

inserting a flexible optical system into a body, proximate the region of interest;

illuminating a portion of the tissue including the region of interest by light in at least one spectral band;

conveying an image of the region of interest through the flexible optical system to an image receiver;

digitally imaging a portion of the tissue including the region of interest at the at least one spectral band with the light re-emitted by the portion of the tissue to generate digital images comprising digital signals whose values are a function of the condition of the region of interest of the tissue; and

providing the digital images to a processor, wherein the processor:

segments the digital images by generating a segmentation mask defining the boundary of the region of interest from a digital image in any one of the at least one spectral band;

estimates at least one rotationally and translationally invariant statistical measure of coefficient distributions of the multiscale wavelet maxima representations of the digital images in each spectral band;

characterizes the condition of the tissue based on the estimated values; and

outputs the characterization of the condition of the tissue.

2. The method of claim 1, wherein the at least one statistical measure is calculated separately within either of a border region and an interior region of the digital image, wherein:

the border region encompasses the envelope of circles of fixed radius centered on the boundary of the segmentation mask; and

the inside region comprises all points of the image that are within the segmentation mask boundary but not included in the border region.

3. The method of claim 2, wherein the computing step comprises estimating at an individual level at least one value which is a statistical measure of texture of the portion of the region of interest within the border region and interior region, chosen from the group consisting of:

the number of wavelet maxima per unit area;

the ratio of the mean coefficient magnitude to the absolute deviation of the coefficient magnitudes from the mean value;

the ratio of the mean coefficient magnitude to the standard deviation of the coefficient magnitude; and

the skewness of the coefficient magnitude, normalized to the cube of the standard deviation.

4. The method of claim 1, further comprising estimating either of the degree of change of a statistic of the wavelet coefficient distribution with increment of wavelet level, and the degree of deviation of such change from linearity.

5. The method of claim 2, further comprising estimating the average rate of change, with respect to level, of the number of wavelet maxima per unit area.

6. The method of claim 1, further comprising comparing the estimated texture values to the threshold derived from statistical analysis of a multiscale wavelet transformation of the digital image.

7. The method of claim 1, wherein the estimating and characterizing steps are conducted without the intervention of an operator.

8. The method of claim 1, wherein the segmenting step is conducted without the intervention of an operator.

9. The method of claim 1, comprising conveying the image through an endoscope.

10. The method of claim 1, comprising conveying the image through a fiber optic bundle.

11. The method of claim 1, comprising conveying the image through an articulated arm.

12. A system for characterizing the condition of a region of interest of internal biological tissue, comprising:

a source of light for illuminating the region of interest in at least one spectral band;

a flexible optical system for insertion into a body and for conveying the image of the region of interest to an image receiver;

an image receiver for acquiring digital images of the region of interest based on the light re-emitted from the illuminated region of interest at each of the spectral bands, the digital image comprising digital signals whose values are a function of the condition of the region of interest;

memory for storing the digital images provided by the image receiver;

a digital processor programmed to perform the steps of:

segmenting the digital images stored in memory by generating a segmentation mask from a digital image in any one of the at least one spectral band;

estimating at least one rotationally and translationally invariant statistical measure of coefficient distributions for the multiscale wavelet maxima representations of the digital images in each spectral band, which are functions of the texture of the region of interest determined by the segmentation mask;

characterizing the condition of the tissue based on the estimated values; and

outputting the characterization of the region of interest.

13. The system of claim 12, where the flexible optical system is an endoscope.

14. The system of claim 12, where the flexible optical system is a fiber optic bundle.

15. The system of claim 12, where the flexible optical system is an articulated arm.

1/1

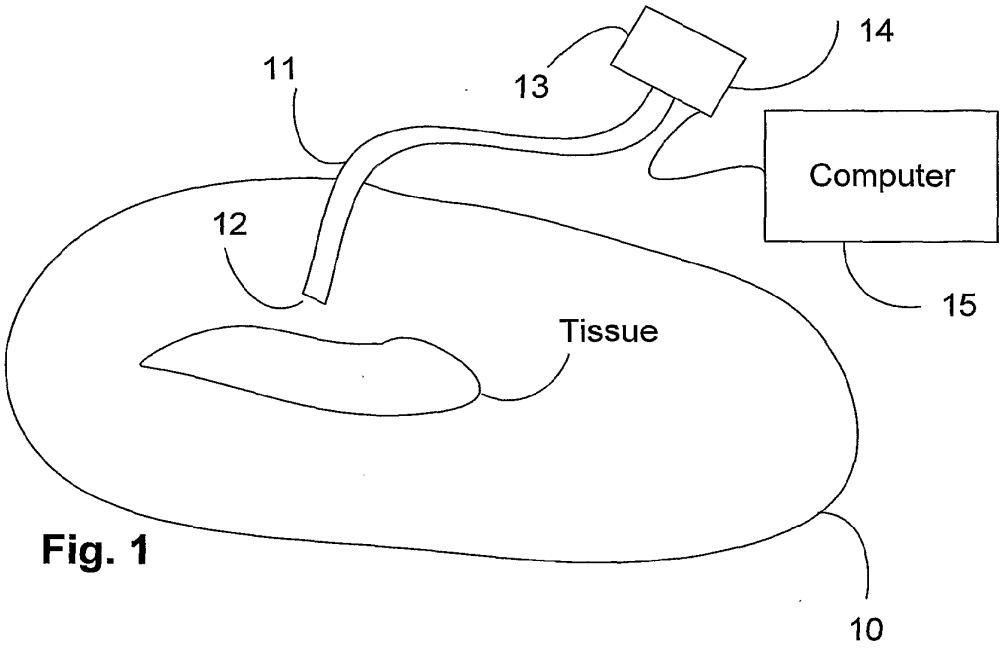

Fig. 1

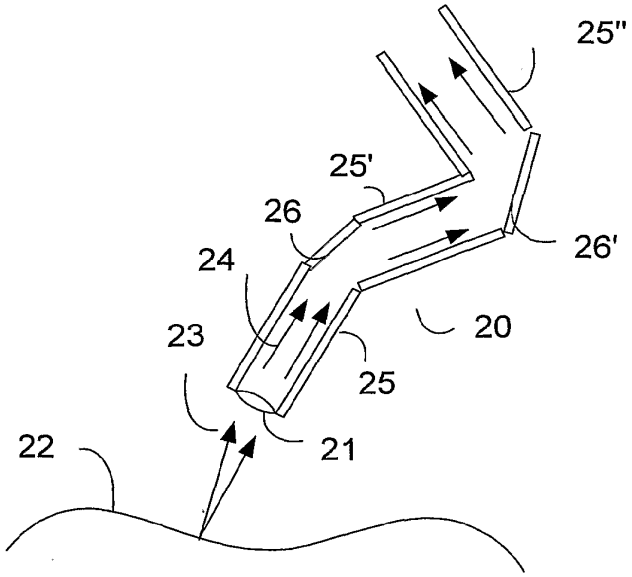

Fig. 2

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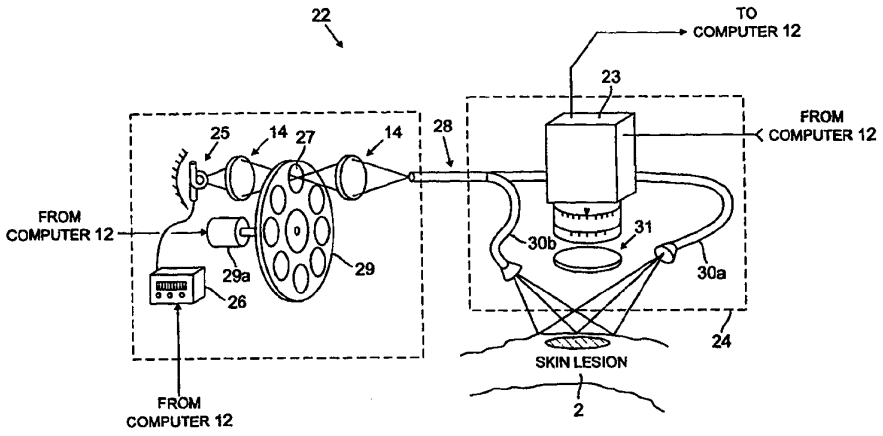

(57) Abstract

Systems and methods for the multispectral imaging of skin tissue enables automatic characterization of the condition of a region of interest of the skin (2), based on direct digital imaging of the region of interest or the digitization of color photographic slides of the region of interest, illuminated by appropriately filtered light. Preferably, a digital image at a low spectral band is automatically segmented and that segmented mask is used to segment the other images by a digital processor (12c). Parameters related to the texture, assymetry, blotchiness and border irregularities are also automatically estimated. The region of interest is automatically characterized by the digital processor, based on those parameters. The region of interest may include a skin lesion, in which case the present invention enables the characterization of the lesion as malignant or benign.

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SYSTEMS AND METHODS FOR THE MULTISPECTRAL IMAGING AND CHARACTERIZATION OF SKIN TISSUE

This application claims the benefit of U.S. Provisional Application Nos. 60/039,218 and 60/039,407, both of which were filed on February 28, 1997, and are incorporated by reference, herein.

FIELD OF THE INVENTION

This invention relates to methods and systems for the computer controlled analysis of digital images of skin tissue at a plurality of wavelengths, which may include those outside of the red-green-blue bands. The methods and systems further include the automatic characterization of the condition of the skin tissue, based on automatically computed values of parameters which are functions of characteristics of the skin tissue, based on the digital images. Skin lesions can be analyzed for determining whether the lesion is a melanoma, for example. Systems for digitally imaging and analyzing skin tissue are disclosed, as well.

BACKGROUND OF THE INVENTION

Melanoma is a usually fatal skin cancer, unless it is detected and surgically removed in its earliest stages. Early detection of malignant melanoma is difficult because early melanomas, those having a Breslow thickness less than 1 mm, share many diagnostic features with benign lesions, such as dysplastic nevi or atypical melanocytic nevi.

To aid in the analysis of lesions, conventional photography, referred to as "clinical imaging", has been used to image the lesion for further study. The effectiveness of clinical imaging can be compromised, however, by specular reflection by the skin. Polarizers have been used for polarized imaging, which minimizes specular reflection.

Dermoscopy is another technique for examining skin, in which specular reflection is minimized. Dermoscopy also assists in clinically differentiating melanoma from its benign simulants by enabling the observation of features of pigmented melanocytic lesions that are not discernible by the naked eye. In dermoscopy, the skin is made more transparent to light by providing an oil layer over the skin, in front of the optical system. A glass plate is placed over the oil layer. The oil has an index of refraction between the index of refraction of the

horny layer of the skin and the glass plate. Standard magnifying optics may be used to enlarge the structures rendered visible on and under the surface of the skin by the oil layer. The region of interest can then be examined visually. Slides of the region of interest can be made, as well, for future study.

Despite their similarities, most malignant melanomas differ in certain of their characteristics from other melanocytic lesions. A major advance in characterizing skin lesions based on certain of the observable differences between malignant and other lesions is the "ABCD" rule, where A=asymmetry, B=border irregularity, C=color variability, and D=diameter greater than 6 mm. A corresponding ABCD rule, where "D" refers to dermoscopic structures, such as brown globules, black dots or pigment networks within the lesion, is applied to dermoscopic images. Because the clinical and dermoscopic applications of these rules are subjective, they are not very reliable.

When skin is illuminated by light, the light can be re-emitted by reflection, scattering or fluorescence. It is known in the art that the re-emission of light absorbed at different wavelengths by a region of interest of skin can provide different information. For example, as the wavelength of the light increases, its depth of penetration into the skin or other tissue also increases. Chromophores at different depths in the tissue therefore absorb and re-emit light at various wavelengths. Melanin and hemoglobin are examples of such chromophores. In addition, since the unaided eye cannot perceive light outside of the visible region or low-contrast structure in visible-light images, information which may be useful in diagnosing a lesion may not be directly observable. Digital acquisition and processing of dermoscopic images may, therefore, improve diagnostic reliability by employing more of the information residing in such images that is not directly observable. There have therefore been attempts to use objective, computer-based, image analysis algorithms that can discern meaningful differences between benign and malignant melanocytic lesions with sufficient accuracy.

Computer processing of images requires that the image be in digital form. A digital image is an array of digital signals whose values are a function of certain characteristics of the subject of the image. When imaging skin lesions, the

digital images comprise digital signals whose values are a function of the re-emission characteristics of the skin and lesion, at the spectral bands of the light illuminating the skin. The array of numbers is obtained by spatial sampling and quantizing the intensity of images obtained with film or directly by electronic cameras. Practical limitations on the number of picture elements or pixels per unit area of image determine the achievable spatial resolution of the digital image. The digital image typically needs to be segmented to separate the digital signals which are a function of the skin lesion from the digital signals which are a function of the surrounding skin.

Computer aided analysis has also been used to classify skin lesions using quantitative values indicative of particular characteristics of lesions, referred to as parameters. Based on histopathological diagnosis of lesions, algorithms have been developed which use linear or non-linear classifiers to combine parameters provided by the operator of an imaging device or a physician or computed by a processor, to yield a value which can be used to classify the lesion. Because some of the steps in the computer-aided analysis of which we are aware to date depend on subjective judgments of an individual, such analysis may provide highly variable results.

The images heretofore available have been obtained with commercially available red-green-blue color imaging apparatus. Color photographic transparencies of skin lesions have been digitized and skin lesions have been directly imaged with "three-chip" digitizing cameras. Such cameras employ broad-band filter bandpasses that are ultimately based on the wavelength response of the human visual system and have large regions of overlap.

Electronic images may also be obtained in narrower, non-overlapping filter bandpasses, which may reveal additional, wavelength-dependent differences between the images of melanomas and of benign lesions. However, such devices have had poor resolution and/or poor signal-to-noise characteristics which prevent the acquisition of digital images of melanocytic skin lesions of sufficient quality for effective application of machine vision techniques for lesion diagnosis. Existing imaging systems and processes also tend to suffer from an inability to provide the required repeatability of the values of extracted lesion parameters, due

in part to a lack of standardization with respect to spatially varying artifacts. The parameters, therefore, lack invariance to lighting and image exposure conditions, for example. Obtaining high signal-to-noise ratios in images recorded in narrow filter bandpasses, when exposure times are sufficiently short that the skin is effectively "frozen" during the exposure sequence, has also been difficult. In addition, since the optimum wavelengths for automatic characterization may not be the optimum wavelengths for visual observation, it may be difficult to reconstruct high-fidelity color images from the digital images for visual interpretation by a clinician.

The assessment of wounds and burns through the appearance of color images present similar challenges. Existing technology for the imaging of skin *in vivo* for these purposes is also inadequate. Practical solutions to the problems of employing multispectral digital imaging of skin for the analysis of lesions, wounds, or other conditions have not been found.

SUMMARY OF THE INVENTION

The methods and systems of the present invention provide for the acquisition of digital images of skin at a plurality of spectral bands to automatically characterize the condition of the tissue based on the digital images. Spectral wavelength bands within and outside of the visible band may be used. In accordance with the present invention, a pigmented skin lesion can be characterized as malignant or benign, for example. The digital images comprise a plurality of digital signals whose values are functions of the condition of the tissue. The digital images acquired are subjected to objective and quantitative analysis by a digital processor to detect and identify abnormalities. The analysis includes image segmentation, parameter estimation and characterization of the skin. The estimation and characterization steps are automatic. The segmentation step may be automatic, as well. Subjective judgments are therefore minimized or eliminated.

It has been found that generating the segmentation mask from a digital image acquired with light in a spectral band which does not penetrate deeply into the skin, such as a spectral band with a center less than about 500 nanometers,

provides superior results. After segmentation, estimated values which are functions of characteristics of the lesion, such as its texture, asymmetry, blotchiness, and border irregularities, are computed and used to automatically characterize the condition of the skin. Digital signals corresponding to hair or blob-like structures are preferably removed during segmentation.

In accordance with the present invention, a method for characterizing the condition of a region of interest of the skin, wherein the absorption and scattering of light in different spectral bands by the region of interest is a function of the condition of the skin, is disclosed. The method comprises illuminating the region of interest of the skin by light in at least three spectral bands and digitally imaging the region of interest at the at least three spectral bands with the light re-emitted by the skin to generate digital images comprising digital signals whose values are a function of the condition of the skin. The digital images are provided to a processor which segments the digital images by generating a segmentation mask from a digital image in any one of the at least three spectral bands, computes at least one estimated value for each digital image at each spectral band which is a function of a characteristic of the region of interest within the segmentation mask, characterizes the condition of the skin based on the estimated values, and outputs the characterization of the condition of the skin. Preferably, the segmenting, estimating and characterizing steps are conducted without the intervention of an operator. Useful parameters include measures of the texture, asymmetry, blotchiness and border irregularity of the portion of the region of interest.

The digital images may be obtained by directly imaging the region of interest with a digital camera, or digitally imaging color slides of the region of interest, through appropriately filtered light.

The characterizing step may include comparing a weighted combination of the parameter values against a threshold value. The weight coefficients for each parameter value and the threshold value may be selected based on a training set of images of lesions or other skin conditions, whose condition has been determined, preferably through histological examination by a

plurality of doctors. Preferably, specificity is maximized under the constraint of 100% sensitivity to melanoma.

In accordance with another aspect of the invention, a system for characterizing the condition of a region of interest of skin includes means for illuminating the region of interest with light in at least three spectral bands and a camera for acquiring digital images of the region of interest based on the light re-emitted from the illuminated region of interest at each of the spectral bands, the digital image comprises digital signals whose values are a function of the condition of the region of interest. A digital processor segments the digital images by generating a segmentation mask from a digital image in any one of the at least three spectral bands and computes at least one estimated value for each digital image at each spectral band which is a function of the texture of the portion of the region of interest within the segmentation mask. The processor characterizes the lesion based on the estimated value or values. The other parameters discussed above may be used, as well.

The camera may be a single-chip or multiple-chip charge-coupled device which detects light in a plurality of spectral bands between the near ultraviolet to near infrared. The filter means may be a plurality of interference filters mounted on a wheel for stepping any filter into a position intercepting the light from the light source. Preferably, at least one of the spectral bands has a center which lies between about 400 and 500 nanometers, at least one of the spectral bands has a center which lies between about 500 and 600 nanometers, and at least one other spectral band has a center which lies between about 750 and 1000 nanometers.

DESCRIPTION OF THE FIGURES

Fig. 1(a) is a schematic illustration of a method and system of imaging a region of interest of skin in accordance with the present invention;

Fig. 1(b) is a schematic illustration of a plurality of narrow spectral bandwidths which may be used to illuminate the skin in the embodiment of Fig. 1(a);

Fig. 1(c) is a schematic illustration of alternative methods and systems for digitizing and analyzing color photographic slides of a region of interest of skin;

Fig. 2 is a schematic illustration of preferred illumination and imaging portions of a computer controlled imaging system for direct imaging of a lesion;

Fig. 3(a) is a flow chart of a calibration procedure for use with the present invention;

Fig. 3(b) is a flow chart of a method of processing images for classifying lesions as malignant or benign, in accordance with the present invention;

Figs. 4(a) and 4(b) are histograms of a malignant melanoma and of an atypical melanocytic nevus, respectively, showing two peaks in each histogram;

Figs. 5(a) and 5(b) are histograms of another malignant melanoma and another atypical melanocytic nevus, respectively, showing three or more peaks in each histogram;

Figs. 6(a) and 6(d) are digital images in the blue spectral band of another malignant melanoma and another atypical melanocytic nevus, respectively;

Figs. 6(b) and 6(e) are digital images of the images of Figs. 6(a) and 6(d) respectively, after thresholding;

Figs 6(c) and 6(f) are digital images of the images of Figs. 6(a) and 6(d), respectively, after iterative thresholding;

Figs. 7(a) and 7(d) are digital images in the blue spectral band of another malignant melanoma and another atypical melanocytic nevus;

Figs. 7(b) and 7(e) are digital images of Figs. 7(a) and 7(d), respectively, resulting from iterative processing and showing dark blobs outside the lesion area;

Figs. 7(c) and 7(f) are digital image masks of Figs. 7(b) and 7(d), respectively, resulting from image cleaning;

Figs. 8(a) and 8(e) are digital images in the blue spectral band of another malignant melanoma and another atypical melanocytic nevus, respectively, showing hair;

Figs. 8(b) and 8(f) are reverse intensity contrast images of the lesions of Figs. 8(a) and 8(e), respectively;

Figs. 8(c) and 8(g) are digital images resulting from an averaging process applied to the images of Figs. 8(a) and 8(b), to remove hair;

Figs. 8(d) and 8(h) are binary lesion masks resulting from the segmentation of the images of Figs. 8(c) and 8(g), respectively;

Fig. 9 is a spatial filter used to remove hair;

Figs. 10(a) - 10(c) are segmented digital images in the blue, green and red spectral bands, of the malignant melanoma whose histogram is shown in Fig. 5(a);

Figs. 10(d) - 10(f) are segmented digital images in the blue, green and red spectral bands, of an atypical melanocytic nevus whose histogram is shown in Fig. 5(b);

Fig. 11 is a chart of lesion parameters and their associated diagnostic accuracy, sensitivity and specificity when used individually;

Fig. 12 is a plot of linear classifier values versus lesion identification number, for 41 malignant melanomas and 104 atypical melanocytic nevi;

Fig. 13 is a plot of linear classifier values versus lesion identification number for 24 superficial spreading melanomas and 16 melanomas *in-situ; and*

Fig. 14 is a plot of lesion parameter versus Breslow thickness for 24 superficial spreading melanomas.

DESCRIPTION OF THE INVENTION

Fig. 1(a) is a schematic illustration of a method and system 1 in accordance with the present invention, by which images of the skin 2 are acquired by a camera nearly simultaneously at a plurality of spectral bands, λ_i, i=1,2,...M, that are preferably effectively non-overlapping, as shown schematically in FIG. 1(b). The skin is illuminated by a source of white light 3, which is filtered by narrow passband filters 4. The filtered light is preferably conveyed to the skin 2 through a fiberoptic illuminator 5. The light re-emitted by the illuminated skin is imaged by a low-noise, high-resolution monochrome camera 6, which is preferably

an electronic charge-coupled ("CCD") camera. Digital images output by the camera 6 are provided to a computer 12 for processing.

The computer 12 includes a digital interface 12a, a memory 12b and a digital processor 12c. A display 19 is preferably provided as well. The computer 12 includes an input to a digital interface 12a for receiving the digital images. A memory 12b stores the digital images, and the software controlling operation of the imaging system, the image processing, and the classification and characterization of the lesion. The digital processor 12c, under control of the software, performs the calculations. The computer 12 has an output connected to a display 19, which can display the processed images and the results of the classification and characterization procedures for each image. The computer 12 also preferably has outputs connected to the source of light 3 and the camera 6, for controlling their illumination level and exposure times, respectively, as described below.

The image processing, classification or characterization and other programs can be implemented on a personal computer, using a programming language, such as FORTRAN or C. The memory 12b which stores the software can be any convenient media readable by the computer 12, such as the hard drive of the computer, read only memory, random access memory with a battery backup, electrically programmed ROM, electrically erasable ROM, floppy disc, or CD ROM. Other suitable media may be used, as well.

When the filter bandpasses have minimal overlap, as in FIG. 1(b), each monochromatic image will contain spectrally independent information. Such spectral separation is believed to be useful for differential diagnosis of skin lesions that contain varying amounts of melanin, and of hemoglobin in different oxidation states, for example. Spectral separation is also believed to be useful in distinguishing granulation of tissue and other structural details of wounds in various stages of healing. One or more of the wavelength bands may lie outside the visible region, such as in the near infrared and/or the near ultraviolet, as long as the wavelength is within the response range of the combined optical system including the electronic camera 6.

In accordance with another aspect of the invention, the digital images of skin lesions can be derived from color slides of the lesions obtained by clinical imaging, dermoscopy, or polarization imaging. Fig. 1(c) is a schematic illustration of alternative approaches to the acquisition and digitization of images of skin lesions from color slides. A photo camera 13 produces 35-mm color slides of a region of the skin 14. The camera 13 can be a Dermaphot ® camera from Heine, Optotechnik Gmbh & Co. AG, Germany, for example. The slides are typically stored in an archive 15. The slides are subsequently reimaged by a monochrome camera 16, which may be a CCD camera, that photographs each slide as it is illuminated by white light that has passed through a sequence of bandpass filters 17 to create a color filtered version of the image. The slides can be illuminated at broad or narrow blue (B), green (G) and red (R) wavelength bands, respectively. The broad wavelength bands may overlap somewhat. In one example, the blue wavelength band was about 400 nm $\pm$ 30 nm, the green wavelength band was about 550 nm $\pm$ 30 nm, and the red wavelength band was about 700 nm $\pm$ 30 nm.

Each of the filtered representations is recorded by the monochrome camera 16, which provides the resulting digital images 18 to an input of the computer 12. If an electronic camera such as a CCD camera is not used, the slide images could be digitized by any available commercial digitizer including three channels, one for red, one for green and one for blue, as long as the pixel size in the lesion plane after digitization is less than about 60 micrometers ("μm").

An appropriate CCD camera 16 is available from Electrim, Inc., Princeton, N.J. The camera 16 has a photographic macro-lens, wherein f#/2.8 and f=100 mm. Preferably, the spatial resolution of the CCD camera 16 provides pixels having a size about 10-30 μm in the lesion plane. The CCD camera 16 from Electrim, Inc., has 753 X 488 pixels. The spatial resolution with such a camera is approximately 21 x 24 μm at the lesion plane. Digital images of lesions obtained with this imaging system were used to classify lesions as malignant or benign, and to characterize lesions as invasive or non-invasive, as described further, below. The Electrim, Inc., CCD camera 16 has rectangular pixels. A CCD camera with square pixels would simplify the calculating procedures.

Alternatively, a 3-chip CCD camera 20, indicated in phantom in Fig. 1c, may be used to reimage the slides of the region of interest. The CCD camera 20 provides digitized images for subsequent analysis by the computer 12. Broad bandpass filters, which are part of the CCD camera 20, produce a representation of the lesion as a set of three narrowband images. The filters are typically in accordance with CIE Standard Observer, wherein the bandwidths are broad.

Fig. 2 is a schematic illustration of the illumination and imaging portions of a preferred computer controlled imaging system 22 in accordance with the present invention, for imaging a region of interest of skin including a lesion. The electronic camera 23 may be a 10-bit monochromatic electronic CCD camera 23, such as the Xillix Model 1400, available from Xillix Technologies Corp., Canada. The Xillix camera is equipped with wide band, low distortion foreoptics, such as the XJP 1.9/0501, available from Jos. Schneider Werke, Germany. The lower distortion fore optics and the camera minimize chromatic aberrations of the optical system over the "multispectral" sequence of exposures, enabling registration of images with sub-pixel accuracy, over the entire field of view. To ensure repeatability of imaging conditions and minimize required intervention by the operator, it is preferred that the system be operated at a preset f/stop. For cameras such as the Xillix Model 1400, exposure times are preferably controlled by the computer 12 through an electromechanical shutter that can operate reliably between minimum and maximum exposure times t_{min} and t_{max}.

The imaging system provides low-noise, high-resolution digital images at high data transfer rates, with low distortion imaging over the entire range of wavelengths covered by the collection of filters. The Xillix camera, discussed above, has a resolution at the skin surface of about 20 microns per pixel. The CCD camera 23 is preferably contained in a hand-held unit, represented schematically as box 24. The illuminator source 25 is a tungsten-halogen lamp whose intensity is controlled by a light-stabilized power supply 26 whose setting is automatically adjusted by the computer 12. A 150 watt lamp, such as the Phillips EJA, available from Phillips Electronics North America Corporation, N.Y., may be used, for example. The output of the lamp 25 is white light. A narrowband filter 27 is provided between the source and an optical fiber 28. A plurality of narrowband

filters, each one corresponding to a different spectral wavelength band, are mounted on a filter wheel 29. Preferred filter bandwidths are listed in Table 1, below. The filter wheel 29, which is driven by a stepping motor 29a, advances each filter to its proper position between the lamp 25 and the optical fiber 28, and holds each filter in position for a sufficient period of time. The computer 12 controls the motor 29a. More or fewer filters may be used. Appropriate lenses 14 are provided between the lamp 25 and the filter 27, and between the filter 27 and the optical fibers 28, as well. One or more fiber illuminators are provided for conveying the light from the source to the lesion. Two such illuminators 30a, 30b are shown in Fig. 2 for simplicity. Although the fiber illuminator illustrated is a bifurcated pair, a ring illuminator which provides more nearly uniform illumination at the skin surface, is preferred. An angle of illumination of about 20° is also preferred. A Fostec Model A0603 ring illuminator, available from Fostec, Inc., N.Y., may be used, for example.

The hand-held portion of the system 24 of Fig. 2, which includes the camera 23, may be mounted on a cantilevered arm (not shown) that can be locked into position.

The digital signals making up each of the digital images output from the camera 23 are provided to the computer 12. The computer 12 conducts image processing procedures on the digital images to calibrate the images, and to objectively segment, estimate parameters, and classify the lesions based on the estimated parameters. Operator judgment is not required at any point in the process.

Control is maintained by the computer 12 over source intensity, filter position, and such camera settings as shutter timing, through the digital interface 12a. Key control parameters are empirically chosen on the basis of feedback from histograms of trial images. The intensity of the lamp 25 may be maintained at a stable value, commensurate with the 10-bit dynamic range of the camera 26, by monitoring a secondary light source, connected electrically in series with the primary light source 25. The light output from the secondary source is monitored by a light sensor that is optically isolated from light reflections associated with the primary source. Such reflections may be caused by the filters that are located on

the filter wheel, or from the housing of the primary light source. This method provides optical feedback which is sensitive to changes in light intensity caused by changes in lamp lead resistance, for example, while it is insensitive to the variable amounts of light reflected from the filters, for example. By means of a closed control loop, the optical feedback from the secondary source is used to maintain long-term constant light output from the primary source.

The apparatus of Fig. 2 can be used for either clinical imaging of the skin, wherein the skin is imaged directly, dermoscopic imaging, wherein a layer of oil is provided over the skin and a layer of glass placed over the oil layer, or polarized imaging, where a polarizer 31 is added to minimize specular reflection as shown in Fig. 2. In dermoscopic imaging, the index-matching oil sufficiently reduces the specular reflection to avoid the need for a polarizer.

Instead of being positioned between the light source 25 and the optical fiber 28, the narrow bandpass filters 27 may be placed between the skin and the CCD camera 23 to filter the light reflected, scattered and radiated from the skin 2.

The front end of the system preferably consists of a flat glass plate (not shown) for being placed over the skin. Light pressure is applied through the glass, onto the skin, throughout the imaging process. This helps to stabilize the region of interest against unwanted motion which could blur an image or which could lead to spatial misregistration between images obtained in different filter bandpasses.

The preferred filters 27 for lesion imaging with a tungsten-halogen white light source 25 have the center wavelengths λ_i and bandwidths (FWHM) listed in Table 1, for i=l,2,...,M, M=l0, wherein the bands are labeled by j=i-l = 0,l,...M-l. Such filters are available, for example, from Intor, Inc., Tucson, AZ. In each band, the exposure time is preferably selected to avoid saturation of the detector elements of the CCD camera 23, as well as to maximize the linear dynamic range over which the image data are recorded. These exposure times should be constrained to be within limits t_{min} and t_{max} which are related to the electromechanical design of the shutter, optical throughput of the camera 23, and avoidance of image blur associated with motion during the exposure sequence. Suitable values of t_{min} and t_{max} could be 10 ms and 550 ms, respectively, for

example. The choice of center wavelength and FWHM for the filter channels, as well as the corresponding exposure times, should preferably also take into account the following considerations:

(a) The center wavelength and FWHM for at least two channels should be chosen so that characteristic absorption lines can be differentiated, such as those associated with melanin and hemoglobin;

(b) For a given set of center wavelengths, there are upper limits on the associated bandwidths if spectral independence of data in different channels is to be maintained, as illustrated in FIG. 1(a);

(c) Bandpasses should be chosen in the red, green and blue portions of the spectrum which enable "true-color" reconstruction of skin images that are suitable for visualization by clinicians;

(d) The need for high signal-to-noise ratio in each image sets practical lower limits on the product of exposure time and filter bandwidth, especially at short wavelengths, where detector response falls off and lesion reflectance is low; and

(e) The total time taken to acquire the images in all filter bands is preferably less than about three minutes, to minimize patient discomfort and possible motion.

Based on considerations (d) and (e) above, and also taking into account the varying spectral reflectances of skin of different colors, the exposure times in each filter channel are preferably adjustable, with settings based on the dynamic range achieved on an empirical basis, with trial images. In this manner, both dynamic range and signal-to-noise ratio can be maximized for each filter channel. The preferred method is to choose t_{expi} by iteration, based on intensity histograms of images of the skin obtained with trial exposures at each wavelength band. The histograms are analyzed to determine the number of pixels at the saturation intensity level, $I_{sat} = 2^b-1$ (1023 for b=l0 bits). The exposure time is decreased if the number of saturated pixels exceeds a predetermined amount, such as 0.01% of the total. Conversely, to maintain high signal-to-noise ratio, the exposure time is increased if a predetermined percentile in the histogram, 99.9%,

for example, is reached at less than a preset threshold, such as 99.5% of I_{sat}. The iteration process typically converges after two or three trials.

The preferred exposure times at each wavelength for imaging skin of different colors to classify melanomas are listed in Table 1, for the embodiment of Fig. 2 with 10 filters. It has been found that for the blue channel centered at 450 nm, the optimal exposure time for dark skin is 273 ms, which is more than double the optimal 107 ms exposure time for light skin. On the other hand, in the near infrared channel centered at 780 nm, the exposure times listed are much shorter, between 24 and 35 ms, and vary relatively little with skin type. The optimal exposure time for dark skin in the deep blue channel at 430 nm is at t_{max} = 550 ms, due to the low skin reflectance and relatively low optical throughput of the system at this short wavelength. Even with an exposure time this long, therefore, the image is less than fully exposed. Greater throughput at this wavelength could be achieved, at the expense of poorer response in the infrared.

In Table 1, the FWHM at 450 nm, is 100 nm, which is much broader than for other wavelengths. It has been found that where images are desired for visual analysis as well as computer processing, the broad wavelength band at 450 nm more closely matches the blue response of the human eye and is therefore preferred. In addition, the broad wavelength band provides data at a higher signal-to-noise ratio.

Table 1 appears below:

Optimal Exposure Times (msec) vs. Skin Color

Filter Number (j=i-l)	Center Wavelength (nm)	Filter FWHM (nm)	Very Light Skin	Medium Skin	Tan Skin	Dark Skin
0	430	60	405.2	436.5	484.4	550.0
9	450	100	106.8	124.9	156.1	273.3
1	500	40	56.4	62.9	88.7	130.7
2	550	10	44.2	50.4	71.3	92.9
3	600	10	19.1	24.0	29.6	39.2
8	650	10	74.5	92.3	104.9	132.0
4	700	10	71.6	86.0	98.0	114.4

5	780	30	25.8	29.1	34.9	23.6
6	880	50	34.1	38.6	44.8	46.1
7	950	60	161.1	187.6	205.8	212.0

Tables similar to Table 1 can be readily constructed based on experimental results for other applications, where other spectral bands may be better suited. For example, in the analysis of wound healing, the ability to distinguish oxygenated from deoxygenated blood would be desirable. In addition, the wavelengths and exposure times in Table 1 reflect a balance between the best results for subsequent analysis of the images by a computer, and the best results for visual observation of the images. If visual observation is not necessary, other wavelength bands and exposure times may be used.

FIG. 3(a) describes how the systems and methods of the present invention provide for calibration of the recorded images. The calibration procedure permits 10-bit image data to be recorded over a large linear dynamic range in each spectral band, independent of skin type. The recorded images can also be standardized for diffuse spectral reflectance. Consistent measures of reflectance ratios in different spectral bands can therefore be obtained, despite variations in illumination pattern with wavelength, changes in the position of the illuminator, or aging of the lamp, for example.

First, the effects of dark current and "fixed pattern noise" are removed in Step 1. N images are recorded by the camera without illumination. Preferably 8 such dark images are recorded. The average of these N dark images, I_D is calculated and stored in the computer 12.

Second, spatial inhomogeneities in the illumination and in the response associated with each CCD pixel are removed in Step 2. A sequence of N' images of an illuminated flat, diffuse reflectance standard, such as a white Spectralon® target (R>99%) recorded. As above, N' is preferably 8. The N' images are recorded at each wavelength band. To average over local inhomogeneities in the reflectance standard, the target is moved continuously during the integration time and between exposures. A small motor, such as a reciprocating motor, may be used. The integration time and/or lamp intensity are adjusted by the computer 12 at each wavelength band until negligibly few of the

pixels are at or just below an intensity level corresponding to saturation. These N' "flat-field" images are averaged to reduce the effect of spatial non-uniformities in the reflectance standard, as well as to improve the detection signal-to-noise ratio. The resulting averages are stored in the computer as I_{wi}, where i=1,2,...M.

Next, monochromatic "raw data" images of the skin, I_{si}, are captured by the camera and digitally acquired by the computer 12 within each filter passband, i=l,2,...M. If dermoscopic imaging is used, where a thin layer of mineral oil is spread between the skin and a cover glass is fixed in position in front of the camera, each image of the skin preferably contains an image of a narrow strip of oil-free, diffusely reflecting gray material, held in place on the inside surface of the cover glass, and located along one edge of the field of view. The material may be cut out of a Kodak "18% gray" card. Dermoscopic imaging is preferred for melanocytic lesions. The alternative clinical imaging mode is preferred for the imaging of wounds and burns because contact with the wound or burn by a cover glass is not desired. Although FIG. 2 indicates a lesion present on the skin 2, it will be readily understood that the same method will apply when a wound or burn is present, instead. In the clinical imaging mode, it is preferable to reduce specular reflections by employing the polarizer 31, as indicated in FIG. 2.

In either the dermoscopic or clinical imaging techniques, a fourth step is preferably provided, in which the raw data is compensated for dark current and fixed pattern noise and then normalized to the flat-field images. The dark-field compensation is performed by subtracting the stored average dark image I_D both from the flat-field image I_{wi} and from the raw data image I_{si}. The ratio of the results of these subtractions is then taken. This standardizes the dark-corrected raw data to the flat-field image, compensating for spatially varying illumination and pixel-to-pixel response variations. After the ratio is taken, the result is standardized to the maximum level, 2^b-1 which equals 1023 where b = 10 in a 10-bit data representation. The normalization process thus converts the image of the skin and the gray strip into a standardized diffuse reflectance map, with the result preserving a large linear recording dynamic range. In FIG. 3(a), the dark-field corrected and flat-field-normalized images, also referred to as "flat-field-calibrated" images, are denoted as I_{si}. In any image, standardization to maximum level can be

reinterpreted directly in terms of equivalent diffuse reflectance on the basis of the average gray level over the image of the gray strip, $\langle I_{gray\ strip} \rangle_i$ and the measured average diffuse reflectance of the gray strip, which is approximately 0.2 and varies in a known and repeatable manner with wavelength.

Preferably, the average image intensity in the gray-strip region is also used to calculate weighting factors for combining three or more monochromatic images to provide "true-color" visualizations of lesion images on the computer 12 and display 19. This is preferably accomplished in Step 5, where the user selects the spectral bands to be used in the color visualization. Step 5 can take place prior to the imaging session. Four bands are currently preferred for such visualization. Filter bands j=3 and 8, in a 3:2 ratio, for the red (R) channel, filter band j=2 for the green (G) channel, and filter band j=9 for the blue (B) channel, in Table 1. As indicated in Step 6 of FIG. 3(a), the relative weights applied to the R:G:B channels are preferably inversely proportional to $\langle I_{gray\ strip} \rangle_i$ the average intensity over the portion occupied by the gray strip area in each image. This procedure tends to reconstruct the hues and saturations in the original scene to within accuracy limits associated with response nonlinearities of the display 19. To minimize the effects of such nonlinearities with display monitors such as the Sony Model GDM-175E1 Multiscan monitor, for example, the viewer may prefer to adjust the maximum brightness in the image to correspond to the maximum image intensity level of the monitor. A linear transformation step, which can be readily accomplished by commercial software such as Adobe Photoshop, may be used. If the digital images are derived from photographic slides, as in the embodiment of Fig. 1(c), steps 5 and 6 are not necessary.

As indicated by dashed lines in FIG. 3(a), either the normalized monochromatic images resulting from Step 4 or the color visualization provided from Step 6 can be displayed on the display 19. Any or all of the monochromatic raw images could be displayed as well.

Fig. 3(b) is a flow chart of a preferred method of processing images according to the present invention for characterizing the condition of a region of interest of the skin of a subject which includes a skin lesion. A skin lesion is selected in Step 50. Digital images of the lesions illuminated by light filtered at the

desired wavelengths of λ_1 -λ_4..., are digitally recorded in Steps 52, 54, 56 and 57..., as described above. Each of these digital images is processed separately. In Step 58, the image taken at the lowest spectral band is used to create a mask for segmentation. A blue spectral band is preferred. At Steps 60, 62, 64, 65..., each of the images of the lesion that correspond to different wavelengths are segmented by means of the segmentation mask obtained at Step 58. Lesion parameters are computed from each of the segmented images, in Step 66. Lesion parameters found to be useful for classifying and characterizing the lesion and statistical methods for computing the estimated values of the parameters, are discussed further, below. The estimated values of the parameters are provided to a linear classifier in Step 68. The linear classifier employs a linearly weighted sum of the individual parameters to derive a value used to classify the lesion as malignant or benign. A non-linear classifier such as a Gaussian quadratic classifier or an artificial neural-net classifier, each employing a suitable defined merit function, may be used as well. In either case, the numerical value produced by the classifier is subjected to a threshold test at Step 100, such that if the test is passed, the lesion is suspected to be malignant melanoma. If the test is failed, the lesion is declared not to be melanoma. The lesion could also be characterized as invasive or non-invasive with a different classifier.

I. SEGMENTATION

The segmentation algorithms will now be described. The function of the segmentation algorithms is to discriminate between the lesion and normal skin in the field-of-view of the imaging device. This is a complex function since not only is the lesion appearance highly variable but so is the appearance of healthy skin due, for example, to the presence of blotches, hair, wrinkles, etc. The automatic algorithm described here is based on the images in the blue spectral band, from about 400 nanometers (nm) to 500 nm. This spectral band was selected because melanin absorption increases rapidly as the wavelength decreases. While the use of ultraviolet radiation could be advantageous, since ultraviolet radiation is carcinogenic, only low doses can be used.

Segmentation in blue consists of several automatic steps:

Location of major peaks in the histogram

First, the histogram of intensity levels in the whole image is determined. Then, given a sliding window with the range of $(2I_r + 1)$ intensity levels, the number of peaks N_p in the histogram over that range is determined. If $N_p < 2$, the range is decreased by two levels and if $N_p > 3$, the range is increased by two levels and the process is repeated until $N_p = 2$ or 3. For most of the images in the data base used in this study, there are two major peaks in the histogram. Examples of such histograms are shown in Fig. 4(a) for a malignant melanoma and in Fig. 4(b) for an atypical melanocytic nevus. The lesions correspond to the lower intensity peak, since it is darker than the surrounding skin due to strong absorption by melanin at 400 nm. However, some lesions are quite inhomogeneous, and the automatic procedure described can find 3 major peaks, as illustrated in Figs. 5(a) and 5(b).

Location of the intensity threshold

If two major peaks are found in the intensity histogram, then the threshold value I_{th} is selected to be at the histogram minimum between these two peaks, as indicated in Figs. 4(a) and 4(b). In the case of three peaks, it has been found that, if the middle peak is closer to the lowest intensity peak, the threshold value is at the minimum between the middle and the highest intensity peak. If the middle peak is closer to the highest intensity peak, then the threshold value is at the minimum between the middle and the lowest intensity peak, as shown in Figs. 5(a) and 5(b).

Iterative thresholding of the image

The next step in image segmentation is iterative thresholding of the images. Given the intensity threshold value, image thresholding has been typically accomplished as follows. The intensity $I(x, y)$ of a pixel at location (x, y) is set to zero if it exceeds I_{th}, i.e.,

$$I_L(x,y) = \begin{cases} I(x,y), & \text{if } I(x,y) < I_{th}; \\ 0, & \text{otherwise.} \end{cases} \quad (1)$$

Figs. 6(a) and 6(d) are examples of digital images of malignant melanoma and atypical melanocytic nevus in the blue spectral band, respectively. Figs. 6(b) and 6(e) are images resulting from the direct thresholding as in Eq. (1). As shown in Figs. 6(b) and 6(e), "holes" can appear within the lesion. Therefore, an iterative approach is preferably used. First, the intensity of pixels at the image edges is set to zero. Then as each iteration proceeds, the intensity $I(x,y)$ of a pixel at location (x,y) is set to zero if it exceeds I_{th} and at least one of its nearest neighbors has zero intensity, i.e.,

$$I_L(x,y) = \begin{cases} 0, & \text{if } I(x,y) \geq I_{th} \text{ and } N_{nn} = 0\ ; \\ I(x,y), & \text{otherwise,} \end{cases} \tag{2}$$

where

$$N_{nn} = \min[I(x-1,y), I(x+1,y), I(x,y-1), I(x,y+1),]. \tag{3}$$

This procedure is iterated until there are no pixels with $I(x,y) \geq I_{th}$ and a nearest neighbor with zero intensity. Typically, only a few iterations are required to complete this step. The resulting images are shown in Figs. 6(c) and 6(f).

Figs. 7(a) and 7(d) are other examples of digital images of malignant melanoma and atypical melanocytic nevus, respectively. Figs. 7(b) and 7(e) are images resulting from the iterative thresholding described above. Various dark blobs are seen in the images outside of the lesion area. These are removed in the following step.

Image cleaning

Some of the blobs in the thresholded images arise naturally due either to dark spots on the normal skin or to hair as in Fig. 7(b). Others are artifacts such as the film edge at the top of the nevus image in Fig. 7(e), or dark bands at the image edges from the slide mounts. These bands are removed by automatically testing for their presence and then setting the intensity of appropriate pixels to zero. The remaining blobs could also be removed by determining the overall number and size, i.e., number of pixels, of connected blobs, and then setting to zero the intensity of pixels belonging to the small ones. However, since the size of some lesions exceeds 100,000 pixels, this would be computationally very intensive. Therefore, in practice, this step is preferably carried out as follows. First, perimeter pixels for all blobs in the image are located. The number of such pixels is typically less than 10,000. Then, each of these perimeter pixels is assigned to a unique blob and its size, the number of perimeter pixels in the blob, is determined. The intensities of pixels belonging to blobs of size less than 30% of the maximum size for that image are set to zero. This process is iterated until all the small blobs are removed. Typically less than 10 iterations are needed. The intensity of all the nonzero pixels is then set to 1. The resulting binary lesion mask has the following property:

$$I_B(x,y) = \begin{cases} 1, & \text{if pixel at } (x,y) \text{ belongs to lesion ;} \\ 0, & \text{otherwise.} \end{cases} \tag{4}$$

Figs. 7c) and 7(f) illustrate the resulting lesion masks.

In the images illustrated in Figs. 7(a) and 7(d), dark hairs were either absent or were not adjacent to the lesion. However, there are many images with prominent dark hair overlapping lesions. Segmentation of such images is described in the following section.

Segmentation of images in presence of hair

Figs. 8(a) and 8(e) are examples of lesion images with hair. Since the segmentation algorithm described in the previous section would leave some of these dark hairs connected to the lesion, images with hair require special preprocessing to allow for hair removal from the normal skin. Since hair is a problem because of its high contrast with respect to the normal skin in the blue, a spatial filter was designed to locate hairs. This filter, shown in Fig. 9, is magnification dependent. It is applied to every pixel of the original image and the result is thresholded at the 5% of maximum value in the whole filtered image. The filtered images are shown in Figs. 8(b) and 8(f) in reverse intensity contrast, wherein bright features are dark. Hairs are clearly located in the filtered images. It should be noted that the lesion interior is almost entirely blank, indicating poor contrast between hair and lesion.

Hairs are removed by an averaging process. For every non-zero pixel at (x, y) in the filtered image one finds the locations of 4 nearest pixels (x_l, y), (x_u, y), (x, y_l), (x, y_u) (where $x_l < x < x_u$ and $y_l < y < y_u$) with zero intensity. Then the intensity of every pixel in the original image that has non-zero intensity in the filtered image is replaced as follows:

$$I_n(x,y) = \frac{1}{12}\sum_{k=1}^{3}[I(x_u + k, y) + I(x_l - k, y) + I(x, y_u + k) + I(x, y_l - k)]. \qquad (5)$$

The images averaged in this way are shown in Figs. 8(c) and 8(g). It is seen that the contrast between hairs and normal skin is considerably reduced in these images. After this preprocessing, the segmentation algorithm described in the previous section is applied to the averaged image. The final binary lesion masks are shown in Figs. 8(d) and 8(h).

The preprocessing step described above may be used for all lesion images, regardless of the presence of hair, enabling fully automated lesion segmentation. However, since this requires more computation and causes some border blurring, the need for preprocessing due to the presence of dark hair is preferably indicated interactively by an operator, and images preprocessed only when necessary.

Segmentation of images in other spectral bands

Since melanin absorption is strongest in the shortest-wavelength band, the lesion area, which appears as a dark region in the image, appears largest in the blue spectral band. Since longer wavelength radiation penetrates deeper into skin, if the thickness

of the melanin-containing layer compensates for the weak absorption, that part of the lesion will appear dark even in the red spectral band. For thick melanomas, with Breslow thickness greater than 1 mm, one expects dark lesions even in the infrared bands. This was observed, for example, by Marchesini *et al.*, Photochemistry & Photobiology, "In vivo spectrophotometric evaluation of neoplastic and non-neoplastic skin pigmented lesions. III. CCD camera-based reflectance imaging," Vol. 62, 1995, pp. 151-154. However, for early malignant melanomas, with Breslow thickness less than 1 mm, great variability of images in the red spectral band has been found. There may be so little contrast between the lesion and the normal skin that direct segmentation is not possible. Therefore, segmentation of lesion images in all spectral bands with wavelength λ uses the binary lesion mask of Eq. (4), obtained in the shortest-wavelength band, here blue, i.e.,

$$I_L(x,y;\lambda) \equiv I(x,y;\lambda) \times I_B(x,y). \tag{6}$$

Figs. 10(a) - 10(f) are a series of images of the lesions, with their corresponding histograms shown in Figs. 5(a) and 5(b), segmented in the blue, green, and red spectral bands, as indicated. The automatically determined lesion borders are superimposed on the original lesion images. The area of dark regions is largest in the blue.

II. LESION PARAMETER ESTIMATION

Objective and automatic lesion classification requires quantitative algorithms for lesion parameter estimation from their segmented images. Such parameters should be dimensionless, independent of lesion location and orientation in the image, and of the overall image brightness. It is convenient to separate the parameters used here into four broad classes: asymmetry, blotchiness, border, and texture. Parameters with the highest diagnostic accuracy for malignant melanoma are listed in Fig. 11, together with the values of diagnostic accuracy, sensitivity, and specificity, for a training set of images of 41 malignant melanomas and 104 atypical melanocytic nevi obtained with the imaging system described above, with respect to Fig. 1(a) wherein the monochrome camera 16 was used to digitize slides. The subscript r, g, or b refers to the red, green, or blue spectral band in which the parameter is evaluated. If additional spectral bands are used, then each of the parameters could be computed at the additional spectral bands, as well.

Specific algorithms for these parameters are described below. For simplicity it is assumed that the image pixels are square but the algorithms described below may be implemented for rectangular pixels as well.

Lesion Asymmetry

Asymmetry parameter

The lesion asymmetry parameter is based on moments of the intensity distribution. First, the lesion orientation angle θ is used to locate the principal axes, which are just the symmetry axes for symmetric lesions. The angle θ is computed from

$$\tan 2\theta = \frac{2 < (x - x_c)(y - y_c) >}{< (x - x_c)^2 > - < (y - y_c)^2 >}, \tag{7}$$

where the lesion intensity centroid is at

$$x_c = < x > \quad \text{and} \quad y_c = < y > . \tag{8}$$

The angular brackets in Eqs. (7) and (8) denote an intensity moment, which for any function $f(x, y)$ of position in the image can be computed as follows:

$$< f(x,y) > \equiv \frac{\sum_x \sum_y f(x,y) I_L(x,y)}{\sum_x \sum_y I_L(x,y)}, \tag{9}$$

where $I_L(x, y)$ is the segmented lesion image. In order to compare properties of different lesions, the parameters used are independent of the orientation of the lesion in the image. Therefore, the lesion asymmetry is determined with respect to the principal axes. The measure of asymmetry described here requires rotation of the image by an angle θ so that principal axes are parallel to the image axes. In this principal-axis coordinate system the following asymmetry factors are defined:

$$A_x = \frac{\sum_n \sum_y |I_L(x_c + n, y) - I_L(x_c - n, y)|}{\sum_x \sum_y I_L(x,y)}, \tag{10a}$$

$$A_y = \frac{\sum_x \sum_n |I_L(x, y_c + n) - I_L(x, y_c - n)|}{\sum_x \sum_y I_L(x,y)}. \tag{10b}$$

The asymmetry parameter,

$$A = A_x + A_y, \tag{11}$$

is a measure of asymmetry in the geometric shape of a lesion as well as in the distribution of lesion pigmentation. Asymmetry parameters tend to be larger for malignant melanomas than for atypical melanocytic nevi.

Binary asymmetry parameter

If the intensity distribution I_L in Eqs. (10a) and (10b) is replaced by the binary intensity distribution of Eq. (4), then the corresponding asymmetry parameter A_{bin} is

the fraction of the lesion pixels which do not have a counterpart on the other side of the principal axis. Thus, when based on the binary intensity distribution, parameter A_{bin} is a measure of the asymmetry of the geometric shape of the lesion.

Lesion Blotchiness

Visually, many early malignant melanomas appear blotchy. In multispectral images there may be darker and lighter regions or blotches of rather homogeneous intensity. In color images, in contrast, there may be regions of different colors. Therefore, it is of interest to quantify such blotchiness in order to differentiate malignant from benign lesions.

Blotchiness Parameter Based on Spatial Intensity Distribution

The lesion is divided into N_t "topographic" regions. If I_{max} and I_{min} are the maximum and minimum intensities in the lesion in some spectral band, respectively, then a pixel at (x, y) belongs to the nth region if

$$I_{min} + (n-1)\frac{I_{max} - I_{min}}{N_t} \leq I_L(x,y) < I_{min} + n\frac{I_{max} - I_{min}}{N_t}. \quad (12)$$

For nth topographic region defined in Eq. (12), a distribution of distances of pixels in that region from the intensity centroid of the binary lesion mask

$$d_n(x,y) = \sqrt{(x_n - x_c)^2 + (y_n - y_c)^2} \quad (13)$$

is obtained and its mean value $< d_n >$ and variance $\mathrm{Var}(d_n)$ are computed. The measure of lesion blotchiness based on spatial intensity distribution is

$$Bl = \frac{\sum_{n=1}^{N_t} \sqrt{\mathrm{Var}(d_n)}}{\sum_{n=1}^{N_t} < d_n >}. \quad (14)$$

This parameter can be evaluated in every spectral band.

Blotchiness Parameter Based on Centroids

The lesion is again divided into N_t "topographic" regions as defined in Eq. (12). An intensity centroid $(x_c(n), y_c(n))$, defined in Eqs. (8) and (9), is then computed for each such region separately. The blotchiness parameter based on the centroid is defined as

$$C = (X_{max} - X_{min})(Y_{max} - Y_{min})/A_l \quad (15)$$

where, for example, X_{max} is the maximum value of $x_c(n)$, and A_l is the lesion area in pixels. This blotchiness parameter is also determined in each spectral band separately.

Blotchiness Parameter Based on Spatial Color Distribution

The "color" in this analysis is not related to the visual perception of color. It is a quantitative descriptor of the relative intensities in red, blue, and green channels in a particular pixel.

All the other lesion parameters described here involve analysis of images in each spectral band separately. Therefore, absolute calibration of image intensities was not necessary. However, in order to describe the color distribution, normalization of intensities in red, green, and blue spectral bands is needed, so that intensities in the three channels are equal for white. In the spherical color coordinate system,

$$R(x,y) = \frac{I_R(x,y)}{I_R(x,y) + I_B(x,y) + I_G(x,y)},$$

$$G(x,y) = \frac{I_G(x,y)}{I_R(x,y) + I_B(x,y) + I_G(x,y)}, \tag{16}$$

where the subscripts R, G, B refer to red, green, and blue spectral bands, are chosen as the independent variables. The lesion is then divided into color regions as follows. First $R(x,y)$ and $G(x,y)$ are divided into N_R and N_G topographic regions. A color region is defined as a particular combination of two topographic regions. The total number of color regions is

$$N_C = N_R \times N_G \ . \tag{17}$$

The blotchiness parameter based on color is defined in analogy with Eq. (14):

$$Cl = \frac{\sum_{n=1}^{N_C} \sqrt{\mathrm{Var}(d_n)}}{\sum_{n=1}^{N_C} < d_n >} . \tag{18}$$

Lesion Border

Border Irregularity Parameter

Border irregularity is a well-known feature of malignant melanomas. It is typically defined as the ratio of the measured lesion perimeter to the perimeter of a circle with the same area as the lesion. Since perimeter is difficult to estimate reliably, a statistical descriptor of border irregularity is used here. In addition, many lesions are elongated and an ellipse is a better approximation for such lesions with regular borders than a circle.

Using the binary lesion mask of Eq. (4), the lesion intensity centroid from Eq. (8), orientation angle from Eq. (7), area, and the aspect ratio defined as

$$AR = \frac{\sqrt{< x' - x_c >^2}}{\sqrt{< y' - y_c >^2}}, \tag{19}$$

where primes refer to the coordinate system defined by the lesion principal axes, are determined. These values are then used to construct an ellipse that is the best regular approximation to the lesion border. For each lesion border pixel at (x_b, y_b), its angle with respect to the horizontal axis:

$$\phi = \tan^{-1}\frac{(x_b - x_c)}{(y_b - y_c)}, \tag{20}$$

and the location of the ellipse border for the same angle $(x_e(\phi), y_e(\phi))$ are determined. The distribution of distances between the ellipse border and lesion border:

$$d_{eb}(x_b, y_b) = d_b(x_b, y_b) - d_e(\phi), \tag{21}$$

where

$$d_b(x_b, y_b) = \sqrt{(x_b - x_c)^2 + (y_b - y_c)^2} \tag{22}$$

and

$$d_e(\phi) = \sqrt{x_e^2 + y_e^2}, \tag{23}$$

is obtained and the border irregularity parameter is defined as

$$B = \frac{\sqrt{\mathrm{Var}(d_{eb})}}{< d_b >}. \tag{24}$$

Border Gradient Parameter

Another parameter that quantitatively characterizes lesion border is the measure of intensity gradients across the lesion borders over the length scale defined by n_g, in units of pixels. For each lesion border pixel at (x_b, y_b) one determines whether pixels at $(x_b \pm n_g, y_b \pm n_g)$ are at the border. If they are not, then the gradient is defined as

$$G(x_b, y_b) = \frac{1}{2}[|I(x + n_g, y) - I(x - n_g, y)| + |I(x, y + n_g) - I(x, y - n_g)|]; \tag{25a}$$

otherwise, if pixels at $(x \pm n_g, y)$ are not on the border,

$$G(x_b, y_b) = |I(x + n_g, y) - I(x - n_g, y)|, \tag{25b}$$

or, if pixels at $(x, y \pm n_g)$ are not on the border,

$$G(x_b, y_b) = |I(x, y + n_g) - I(x, y - n_g)|. \tag{25c}$$

The border gradient parameter is defined as

$$G = \frac{\sqrt{\mathrm{Var}(G)}}{< G >}. \tag{26}$$

Lesion Texture

The description of lesion texture is particularly vulnerable to subjective judgement. The quantitative evaluation of lesion texture parameters is possible only using computer-based image analysis. While many such parameters are possible, those found to be helpful in discriminating between malignant melanomas and atypical melanocytic nevi are described below.

Texture Parameters Based on Local Intensity Variations

Texture parameters are defined over a length scale n_t in units of pixels. For example, consider a pixel located at (x, y) in the lesion. Let I_l and I_u be the minimum and the maximum intensities in an image in the $2n_t + 1 \times 2n_t + 1$ window around this pixel, i.e., in the range $[x - n_t, x + n_t]$ and $[y - n_t, y + n_t]$. Consider a variable

$$C_1(x, y) = \frac{I_u - I_l}{I_l}. \tag{27}$$

The first two texture parameters are defined as:

$$T1 = \frac{\sqrt{\mathrm{Var}(C_1)}}{< C_1 >} \tag{28}$$

and

$$T2 = \sqrt{\mathrm{Var}(C_1)} \tag{29}$$

Another texture parameter uses the following variable:

$$\begin{aligned} C_3(x, y) = {} & 4w(0,0) + w(-n_t, 0) + w(n_t, 0) + w(0, -n_t) + w(0, n_t) \\ & - 2[w(-n_t, -n_t) + w(-n_t, n_t) + w(n_t, -n_t) + w(n_t, n_t)] \end{aligned}, \tag{30}$$

where

$$w(i, j) = I(x + i, y + j)/I(x, y). \tag{31}$$

If the value of C_3 is negative, it is set to zero and the corresponding texture parameter is

$$T3 = \frac{\sqrt{\mathrm{Var}(C_3)}}{< C_3 >}. \tag{32}$$

Another variable that leads to a texture parameter useful for classification of melanocytic lesions is:

$$\begin{aligned} C_4(x, y) = {} & 8w(0,0) - w(-n_t, 0) - w(n_t, 0) - w(0, -n_t) - w(0, n_t) \\ & - w(-n_t, -n_t) - w(-n_t, n_t) - w(n_t, -n_t) - w(n_t, n_t) \end{aligned} \tag{33}$$

Again, if the value of the variable is negative it is set to zero and the corresponding texture parameter is

$$T4 = \frac{\sqrt{\mathrm{Var}(C_4)}}{< C_4 >}. \tag{34}$$

Texture Parameters Based on Pigmented Network

Texture parameters have also been developed by considering the properties of a pigmented network. These texture parameters are measures of variability in the area of the dermal papillae and in the aspect ratio (length/width) of the rete ridges.

Since dermal papillae appear as the brighter part of the network, one seeks all the local maxima over a $2n_t + 1 \times 2n_t + 1$ window. Starting from such a maximum at (x_m, y_m), one finds local one-dimensional minima in eight directions (2 vertical, 2 horizontal, and 4 diagonal) and locates the vertices of an octagonal region one pixel closer to the maximum intensity pixel than the minimum pixel. Such octagonal regions approximate the areas of dermal papillae A_{dp} which are computed from the known location of vertices; the corresponding texture parameter is

$$T5 = \frac{\sqrt{\mathrm{Var}(A_{dp})}}{< A_{dp} >}. \tag{35}$$

Some of the areas determined by this algorithm are due to bubbles visible in some of these dermoscopic images. However, since there are typically on the order of hundreds of areas, and on the order of tens of bubbles, the statistical parameters should not be significantly biased by this artifact.

The aspect ratio of rete ridges is determined in a similar fashion, although one starts with local minima since rete ridges appear dark in the images. The vertices of an octagonal region are determined in this case from one-dimensional maxima in the eight directions. The maximum and minimum extents of this region are then determined and the aspect ratio R is computed. This texture parameter then is

$$T6 = \frac{\sqrt{\mathrm{Var}(R)}}{< R >}. \tag{36}$$

III. LESION CLASSIFICATION

Selection of lesion parameters for classification was done by determining the maximum diagnostic accuracy for malignant melanoma for each parameter computed in every spectral band available for the training set of images. As mentioned above, diagnostic accuracy, sensitivity to malignant melanoma and specificity for the selected twenty two parameters are shown in Fig. 11. These parameters were then used as input to the linear classifier. Nonlinear classifiers may be used as well.

For each lesion k the linear classifier is

$$L(k) = \sum_{n=1}^{22} w_n X_n(k), \tag{37}$$

where $X_n(k)$ are the parameters for the kth lesion and weights w_n are to be determined so that a specified function $F(L)$ attains maximum value. The following functions $F(L)$ were used: 1) specificity under constraint of 100% sensitivity to malignant melanoma for the training set which included 41 malignant melanomas and 104 atypical melanocytic nevi; (2) classification accuracy for the 24 invasive and 16 noninvasive malignant melanomas of the training set; and 3) correlation with the Breslow thickness for the 24 invasive malignant melanomas.

Given any training set of lesion images and corresponding set of lesion image parameters, the weights that maximize $F(L)$ are found as follows. First, an initial range and resolution Δ for w_n are selected. For each allowed set of values of w_n, the values $L(k)$ are computed for each lesion. The value $F(L)$ is determined based on the input from histopathological evaluation of the lesion based on a biopsy, such as the diagnosis of the lesion as benign or malignant, and the Breslow thickness for a malignant melanoma. The range of w_n's is adjusted until the maximum value of $F(L)$ is inside the range. Then the resolution Δ is reduced by a factor of two, and the process is repeated until Δ reaches specified minimum value Δ_{min}. This procedure determines the weights w_n only up to a multiplicative constant. It is noted that the classifiers resulting from a particular training set are applicable only to images with a specific spatial and spectral resolution, and that lesion images obtained with a different imaging system may require the development of different classifiers, by the procedures described above.

Since detection of melanoma in its early stage significantly improves prognosis, there is a need for reliable methods of early detection. Clinical evaluation of melanocytic lesions is, however, a problem since reliable differentiation between early malignant melanoma with Breslow thickness less than 1 mm and atypical melanocytic nevus is difficult even for experienced dermatologists. In order to detect as many early melanomas as possible, weights in the linear classifier are preferably chosen to maximize specificity under the constraint of 100% sensitivity to malignant melanoma for the training set. For each set of weights, one finds the threshold value L_{th} of the linear classifier such that a kth lesion

is classified as suspicious of malignancy if $L(k) > L_{th}$, and as benign otherwise. The resulting classifier for the training set is

$$\begin{aligned} L_1 = {} & 0.025\,A_{bin} + 0.090\,A_b + 0.069\,A_g + 0.160\,A_r + 0.128\,C_b \\ & + 0.095\,Cl + 0.038\,B + 0.107\,T1_g + 0.064\,T2_g + 0.018\,T2_r \\ & + 0.111\,T3_b + 0.167\,T3_g + 0.268\,T5_b \end{aligned} \tag{38}$$

where the weights are normalized so that the threshold value equals one. This classifier with sensitivity to malignant melanoma of 100% and specificity of 85% is shown in Fig. 12. Statistical significance of the specificity and sensitivity was assessed by considering the binomial probabilities for the value of L_1 to exceed the threshold for the 41 malignant melanomas and 104 atypical melanocytic nevi of the training set separately. At the 95% confidence level, one finds that sensitivity is not less than 93% while specificity is not less than 79%. Since there are several melanomas very close to the threshold value, a practical classifier may use a threshold value that is less than one. It has been found that this set of 145 images is sufficient to yield statistically significant results. A greater number of images may be used, as well.

Some of the noninvasive melanomas, called melanomas in-situ, are confined to epidermis and are 100% curable by surgery. The invasive melanomas, i.e., superficial spreading melanomas in our data base, require more extensive surgery. Therefore, it is of clinical interest to differentiate between invasive and noninvasive melanomas and a linear classifier was trained to perform this task. This classifier, with weights chosen to maximize the overall classification accuracy for the 24 superficial spreading melanomas and 16 melanomas in-situ of the training set is

$$\begin{aligned} L_2 = {} & -1.00\,A_b - 0.14\,Bl_g - 2.47\,Bl_r - 0.4\,C_b - 0.98\,Cl \\ & - 1.17\,T2_r + 0.53\,T4_b + 1.98\,T5_b + 1.58\,T6_b - 0.73 \end{aligned} \tag{39}$$

where a constant was subtracted from the classifier values to obtain the threshold value of zero. This classifier, with overall classification accuracy of 92.5%, is shown in Fig. 13.

Since prognosis for invasive melanomas correlates strongly with the Breslow thickness, a linear function of lesion parameters Q was trained to maximize the Pearson correlation coefficient between Q and the Breslow thickness for a set 24 superficial spreading melanomas. This function is

$$\begin{aligned} Q = {} & 0.955\,A_g - 1.391\,A_r + 2.791\,Bl_b - 1.320\,Bl_g + 0.146\,C_b \\ & + 0.267\,C_r - 0.506\,B + 0.202\,T1_g + 1.476\,T2_r - 0.485 \end{aligned} \tag{40}$$

and is shown in Fig. 14. Even though there are only 24 superficial spreading melanomas in the data base, the high correlation of 0.77 is statistically very significant since $p = 9 \times 10^{-6}$.

The classifiers of Eqs. (38)–(40) are applicable to the imaging system described above, with respect to Fig. 1(a) wherein the monochrome camera 16 was used to digitize slides.

For other imaging systems, having different spatial and spectral resolution, different classifiers may need to be developed, based on a sufficient data base of lesion images obtained with that imaging system, in accordance with the procedures described above.

The segmentation, parameter estimation and classification programs described in Sections I-III, above, can be implemented on any personal computer, using a programming language, such as FORTRAN or C. The program can be stored on any convenient media readable by a computer, such as read only memory, ("ROM"), random access memory with a battery backup, electrically programmed ROM (EPROM), electrically erasable ROM (EEPROM), floppy disc, CD ROM, or a hard disc. Other suitable media may be used, as well.

While the procedures of Sections I-III were described with respect to digital images obtained by imaging color photographic slides of skin lesions with a monochrome CCD camera 16 in accordance with the system of Fig. 1c, these procedures are readily adaptable to the analysis of digital images of skin lesions acquired directly from the region of interest of the skin with a monochrome CCD camera 6 of Fig. 1a and Fig. 2.

In the process described in Sections I-III, above, segmentation was conducted in the blue wavelength band. The segmented mask in blue was then applied to images in the red and green wavelength bands. Where images at additional wavelengths are provided, segmentation is preferably conducted of the image at the shortest available spectral band where the contrast between the lesion and normal skin tends to be highest because of strong absorption by melanin. The segmented mask is then applied to the images in the remaining spectral bands. These steps are shown in Fig. 3b.

In addition, where parameters are described in terms of red, green and blue wavelength bands in Section I-III, parameters can be derived at each of the other wavelengths used in the systems and methods above, in accordance with the procedures described in Section I-III. The additional parameters can be readily used to develop a classifier, also by the processes described in Section I-III.

In addition, where parameters are described in terms of red, green and blue wavelength bands in Section I-III, parameters can be derived at each of the wavelengths used in the systems and methods above, in accordance with the procedures described in Section I-III. The additional parameters can be readily used to develop a classifier, also by the processes described in Section I-III.

The references cited above are incorporated by reference herein.

While preferred systems and methods for practicing the present invention have been described above, it is understood that departures may be made from the systems and methods, without departing from the scope of the present invention, which is defined by the following claims.

We claim:

1. A method of characterizing a skin lesion wherein the absorption and scattering of light in different spectral bands by the skin lesion is a function of the condition of the skin, the method comprising:

illuminating a portion of the skin including the region of interest by light in at least three spectral bands, one of which is a blue spectral band;

digitally imaging a portion of the skin including the region of interest at the at least three spectral bands with the light re-emitted by the portion of the skin to generate digital images comprising digital signals whose values are a function of the condition of the region of interest of the skin; and

providing the digital images to a processor, wherein the processor:

segments the digital image by generating a segmentation mask defining the boundary of the region of interest from a digital image in the blue spectral band, without operator intervention;

automatically computes at least one estimated value for each digital image at each spectral band which is a function of a characteristic of the portion of the region of interest determined by the segmentation mask, without operator intervention;

characterizes the condition of the skin as malignant or benign based on the estimated values, without operator intervention; and

outputs the characterization of the condition of the skin.

2. The method of claim 1, further comprising estimating at least one value which is a function of the texture of the region of interest.

3. The method of claim 2, wherein the computing step comprises estimating values which are statistical measures of local intensity variation in the digital images in each spectral band, which are a function of the texture of the region of interest.

4. The method of claim 2, wherein the computing step comprises estimating values based on the ratio of standard deviation of the areas of dermal papillae to their mean within the segmentation mask.

5. The method of claim 2, wherein the computing step comprises estimating values of the average and standard deviation of the thickness of rete ridges within the segmentation masks.

6. The method of claim 1, further comprising estimating at least one value which is a function of the asymmetry of the region of interest in each spectral band, for two principal axes of the segmented image by:

locating the principal axes by computing an orientation angle;

computing the intensity centroid;

rotating the digital image such that the principal axes are parallel to the image axes; and

estimating the asymmetry values for each principal axis based on the intensity centroid; and

summing the estimated asymmetry value for the two principal axes.

7. The method of claim 1, further comprising estimating at least one value which is a function of the blotchiness of the region of interest.

8. The method of claim 1, further comprising estimating at least one value which is a function of the irregularity of the border of the region of interest by estimating a value which is a statistical measure of the deviation of the border of the segmentation mask from the border of an ellipse of the same area, aspect ratio, and orientation as the segmentation mask.

9. The method of claim 1, further comprising estimating a value which is a function of the gradient at the border of the region of interest by estimating a statistical measure of the gradient values of the intensity of the digital images across the border of the segmented images, at each spectral band.

10. The method of claim 1, further comprising characterizing the type of lesion as invasive or non-invasive.

11. The method of claim 1, wherein the segmenting step comprises generating the segmentation mask from a digital image by:

removing digital signals from the digital image which correspond to hair structures;

deriving a threshold from a multimodal histogram of intensity levels;

iteratively applying the threshold to the digital signals of the digital image; and

removing digital signals which correspond to small blob-like regions from the masked image.

12. The method of claim 1, wherein the digital imaging step further comprises digitally imaging the region of interest with a digital camera.

13. The method of claim 1, further comprising:

photographing the region of interest with a color camera to form color photographic slides; and

illuminating the color photographic slides with light in each spectral band;

wherein the digital imaging step comprises digitally imaging the illuminated color photographic slides of the region of interest with a digital camera.

14. A method of characterizing the condition of a region of interest of skin, wherein the absorption and scattering of light in different spectral bands by the region of interest is a function of the condition of the skin, the method comprising:

illuminating a portion of the skin including the region of interest by light in at least three spectral bands;

digitally imaging the portion of the skin including the region of interest at the at least three spectral bands with the light re-emitted by the portion of the skin to generate digital images comprising digital signals whose values are a function of the condition of the region of interest of the skin; and

providing the digital images to a processor, wherein the processor:

segments the digital images by generating a segmentation mask defining the boundary of the region of interest from a digital image in any one of the at least three spectral bands;

computes at least one estimated value for each digital image at each spectral band which is a function of a characteristic of the region of interest determined by the segmentation mask;

characterizes the condition of the region of interest of the skin based on the estimated values; and

outputs the characterization of the condition of the region of interest of the skin.

15. The method of claim 14, wherein the estimating and characterizing steps are conducted without the intervention of an operator.

16. The method of claim 14, wherein the segmenting step is conducted without the intervention of an operator.

17. The method of claim 14, wherein the illuminating step further comprises illuminating the region of interest with light in at least one spectral band which penetrates to the papillary dermis and is re-emitted therefrom.

18. The method of claim 17, wherein the digital imaging step further comprises digitally imaging the region of interest with a digital camera.

19. The method of claim 17, wherein the illuminating step further comprises illuminating the region of interest with light in a near infrared spectral band.

20. The method of claim 14, further comprising suppressing specular reflections prior to the digital imaging step.

21. The method of claim 20, wherein the processor converts the digital signals of each of the digital images into values corrected for non-uniformities of illumination and of response prior to the segmenting step.

22. The method of claim 14, further comprising:

photographing the region of interest with a color camera to form color photographic slides; and

illuminating the color photographic slides with light in each spectral band;

wherein the digital imaging step comprises digitally imaging the illuminated color photographic slides of the region of interest with a digital camera.

23. The method of claim 14, wherein the segmenting step further comprises applying the segmentation mask to the digital images in the other spectral bands.

24. The method of claim 14, wherein the segmenting step comprises generating the mask at the shortest available wavelength.

25. The method of claim 14, wherein the illuminating step comprises illuminating the region of interest by light in at least one spectral band whose center is between about 400 to about 500 nanometers, and the segmenting step comprises generating the mask from a digital image at the spectral band between about 400 to about 500 nanometers.

26. The method of claim 16, wherein the segmenting step comprises generating the segmentation mask from a digital image by:

removing digital signals from the digital image which correspond to hair structures;

deriving a threshold from a multimodal histogram of intensity levels;

iteratively applying the threshold to the digital signals of the digital image; and

removing digital signals which correspond to small blob-like regions from the masked image.

27. The method of claim 16, wherein the segmenting step comprises generating the segmentation mask by comparing estimated values which are a function of textures within the digital images with a threshold.

28. The method of claim 27, further comprising generating the segmentation mask by comparing the estimated texture values to a threshold derived through statistical analysis of each digital image.

29. The method of claim 14, wherein the computing step comprises estimating at least one value which is a function of the texture of the region of interest determined by the segmentation mask.

30. The method of claim 29, wherein the computing step further comprises estimating values which are a function of the texture of the region of interest determined by the segmentation mask separately in each spectral band, based on the same segmentation mask.

31. The method of claim 29, wherein the computing step comprises estimating values which are statistical measures of local intensity variation in the digital images in each spectral band which are a function of texture.

32. The method of claim 14, wherein the computing step further comprises estimating a value which is a function of the asymmetry of the segmented image in each spectral band, for two principal axes of the segmented image.

33. The method of claim 32, wherein the computing step further comprises:

locating the principal axes by computing an orientation angle;

computing the intensity centroid;

rotating the digital image such that the principal axes are parallel to the image axes;

estimating asymmetry values for each principal axis based on the intensity centroid; and

summing the estimated asymmetry values for the two principal axes.

34. The method of claim 33, wherein the computing step further comprises computing the intensity moment with a binary intensity distribution.

35. The method of claim 14, wherein the computing step further comprises estimating at least one value which is a function of the blotchiness of the segmented digital image, the estimated blotchiness value being defined through statistical properties of the spatial distribution of topographic regions of the digital images at each spectral band.

36. The method of claim 35, wherein the computing step further comprises determining the centroids of topographic regions of the segmented digital image at each spectral band.

37. The method of claim 14, wherein the computing step comprises estimating a value which is a statistical measure of the deviation of the border of the region of interest from the border of an ellipse of the same area, aspect ratio, and orientation as the segmentation mask.

38. The method of claim 14, wherein the computing step comprises estimating a statistical measure of the gradient values of the intensity of the digital images across the border of the segmented images, at each spectral band.

39. The method of claim 14, wherein the computing step comprises estimating values based on the ratio of standard deviation of the areas of dermal papillae to their mean within the segmentation mask.

40. The method of claim 14, wherein the computing step comprises estimating values of the average and standard deviation of the thickness of rete ridges within the segmentation mask.

41. The method of claim 14, wherein the characterizing step comprises comparing a weighted combination of parameter values against a threshold value.

42. The method of claim 41, wherein the condition of the region of interest to be characterized is the presence of a melanoma and weight coefficients for each parameter value and the threshold value are selected to maximize specificity, under the constraint of 100% sensitivity to melanoma, on a representative set of training images

43. The method of claim 14, further comprising calibrating each pixel location in the digital image in each spectral band with respect to stored images of a white target material having known diffuse reflectance, each of the stored images being an average of a plurality of images acquired at each spectral band, while the material undergoes continual in-plane motion.

44. A system for characterizing the condition of a region of interest of skin, comprising:

a source of illumination of light in at least three spectral bands;

a camera for acquiring digital images of the region of interest based on the light re-emitted from the illuminated region of interest at each of the spectral bands, the digital image comprising digital signals whose values are a function of the condition of the region of interest;

memory for storing the digital images provided by the camera;

a digital processor programmed to perform the steps of:

segmenting the digital images stored in memory by generating a segmentation mask from a digital image in any one of the at least three spectral bands;

estimating at least one value for each digital image at each spectral band which is a function of the texture of the portion of the region of interest determined by the segmentation mask;

characterizing the condition of the skin based on the estimated values; and

outputting the characterization of the region of interest.

45. The system of claim 44, further comprising means for suppressing specular reflections from the region of interest.

46. The system of claim 44, further comprising means for calibrating each digital image to provide correction for non-uniformities of illumination and response.

47. The system of claim 44, wherein the digital processor is coupled to the source of illumination and to the camera for controlling the intensity of illumination and exposure times, respectively.

48. The system of claim 44, wherein the processor applies the segmentation mask derived from the digital images at one spectral band to the digital images at the other spectral bands.

49. The system of the claim 44, wherein the processor estimates values separately from digital images at each spectral band based on the segmentation mask.

50. The system of claim 48, wherein the processor compares a weighted combination of estimated values against a threshold value.

51. The system of claim 44, wherein the camera records monochromatic images and the illumination means comprises:

a tungsten halogen light source with feedback to stabilize the intensity in each wavelength band;

means for sequentially filtering the light; and

an optical fiber ring illuminator to distribute the filtered light.

52. The system of claim 44, further comprising a feedback loop for stabilizing the intensity of the light source by the processor.

53. The system of claim 44, wherein the filter means comprises a plurality of interference filters mounted on a wheel for stepping any filter into a position intercepting the light from the light source.

54. The system of claim 44, wherein at least one of the spectral bands has a center which is between about 400 to about 500 nanometers, and at least one other band centered elsewhere in the visible region.

55. The system of claim 54, wherein the set of interference filters includes a filter whose center lies in at least one spectral band in the near infrared range whose center lies between about 750 and 1000 nanometers.

56. The system of claim 49, wherein the camera is a single-chip, charge-coupled device and the control means comprises a digital computer including means for determining exposure times for the camera which maximize the signal-to-noise ratio in the image at each spectral band.

57. The system of claim 44, wherein:

the source of illumination provides broad-band ("white") light; and

the camera comprises multiple charge-coupled devices which detect light in a plurality of spectral bands between the near ultraviolet to near infrared.

58. The system of claim 44, wherein the processor estimates values which are statistical measures of local intensity variation in the digital images in each spectral band, which are a function of the texture of the region of interest.

59. The system of claim 44, wherein the processor estimates values based on the ratio of standard deviation of the areas of dermal papillae to their mean within the segmentation mask.

60. The system of claim 44, wherein the processor estimates values of the average and standard deviation of the thickness of rete ridges within the segmentation masks.

61. The system of claim 44, wherein the processor estimates at least one value which is a function of the asymmetry of the region of interest in each spectral band, for two principal axes of the segmented image by:

locating the principal axes by computing an orientation angle;

computing the intensity centroid;

rotating the digital image such that the principal axes are parallel to the image axes; and

estimating asymmetry values for each principal axis based on the intensity centroid; and

summing the estimated asymmetry values for the two principal axes.

62. The system of claim 44, wherein the processor further estimates at least one value which is a function of the blotchiness of the region of interest.

63. The system of claim 44, wherein the processor further estimates at least one value which is a function of the irregularity of the border of the region of interest by estimating a value which is a statistical measure of the deviation of the border of the segmentation mask from the border of an ellipse of the same area, aspect ratio, and orientation as the segmentation mask.

64. The system of claim 44, wherein the processor further estimates a value which is a function of the gradient at the border of the region of interest by estimating a statistical measure of the gradient values of the intensity of the digital images across the border of the segmented images, at each spectral band.

65. The system of claim 44, wherein the processor characterizes the type of lesion as invasive or non-invasive.

66. The system of claim 44, wherein the processor generates the segmentation mask from a digital image by:

removing digital signals from the digital image which correspond to hair structures;

deriving a threshold from a multimodal histogram of intensity levels;

iteratively applying the threshold to the digital signals of the digital image; and

removing digital signals which correspond to small blob-like regions from the masked image.

67. A system for characterizing the condition of a region of interest of skin, comprising:

a source of illumination of light in at least three spectral bands;

a camera for acquiring digital images of the region of interest based on the light re-emitted from the illuminated region of interest at each of the spectral bands, the digital image comprising digital signals whose values are a function of the condition of the region of interest;

a memory for storing the digital images;

a digital processor including:

digital processing means for segmenting the digital images stored in memory and computing estimated values of parameters which are a function of the segmented images;

digital processing means for automatically characterizing the condition of the tissue based on the estimated values; and

means for outputting the characterization of the region of interest.

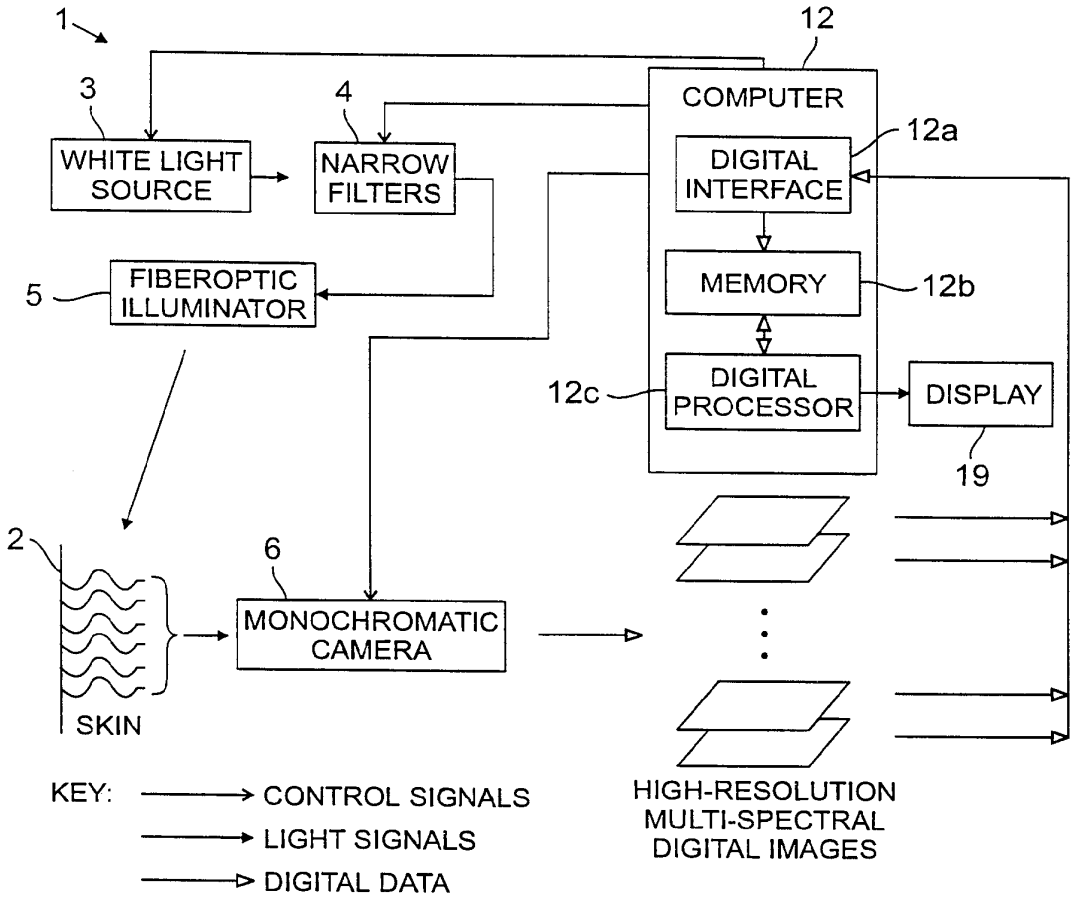
1
12
3
4
COMPUTER
WHITE LIGHT SOURCE
NARROW FILTERS
12a
DIGITAL INTERFACE
5
FIBEROPTIC ILLUMINATOR
MEMORY
12b
12c
DIGITAL PROCESSOR
DISPLAY
19
2
6
MONOCHROMATIC CAMERA
SKIN
KEY:
CONTROL SIGNALS
LIGHT SIGNALS
DIGITAL DATA
HIGH-RESOLUTION MULTI-SPECTRAL DIGITAL IMAGES

FIG. 1a

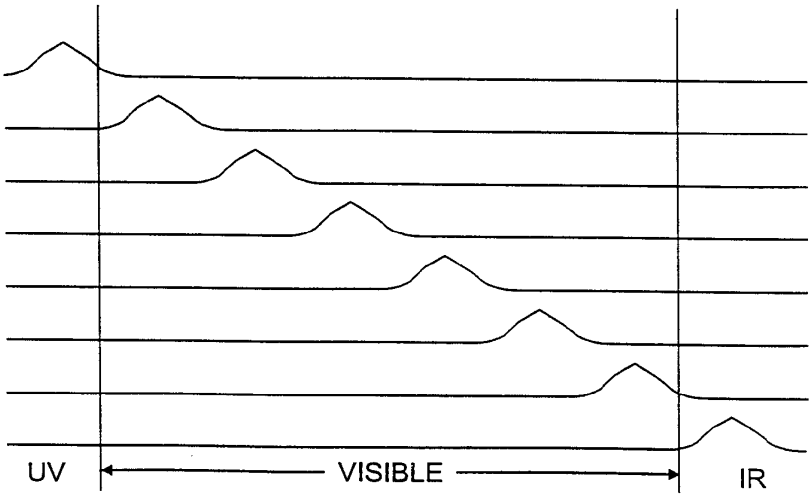
UV
VISIBLE
IR

FIG. 1b

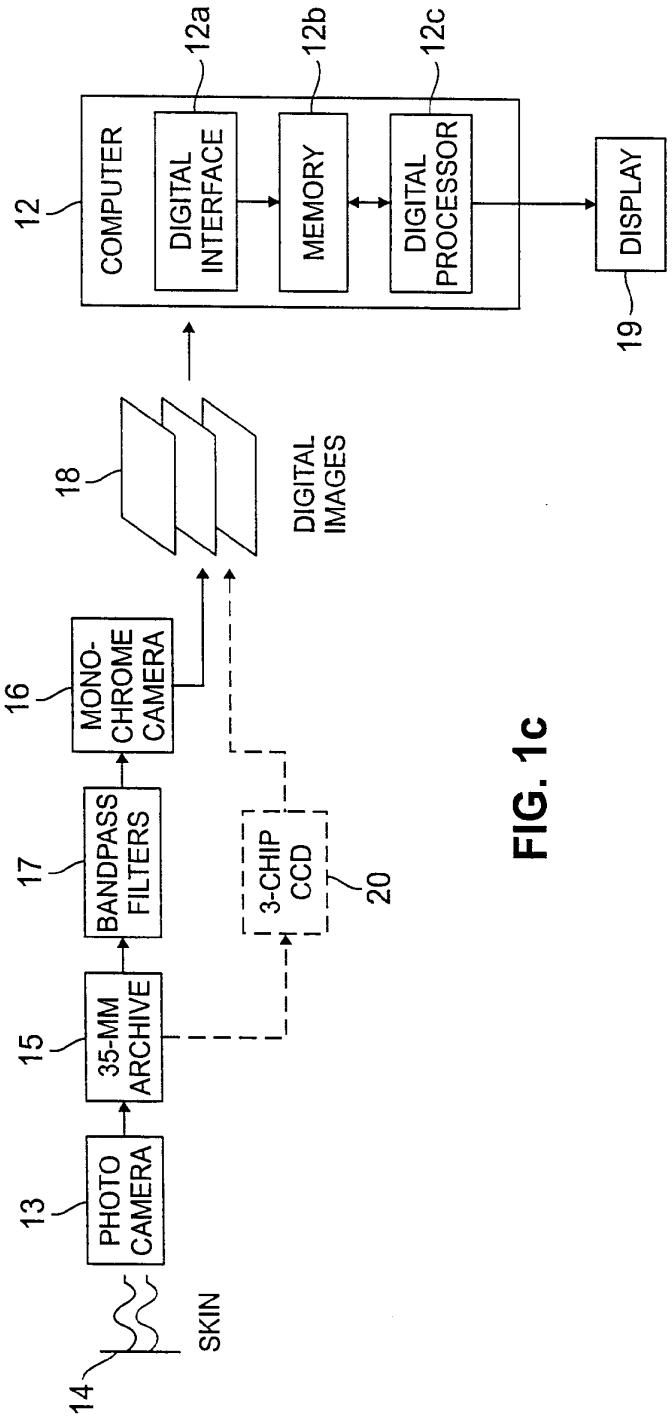
12
COMPUTER
12a
DIGITAL INTERFACE
12b
MEMORY
12c
DIGITAL PROCESSOR
DISPLAY
19
18
DIGITAL IMAGES
16
MONO-CHROME CAMERA
17
BANDPASS FILTERS
3-CHIP CCD
20
15
35-MM ARCHIVE
13
PHOTO CAMERA
SKIN
14

FIG. 1c

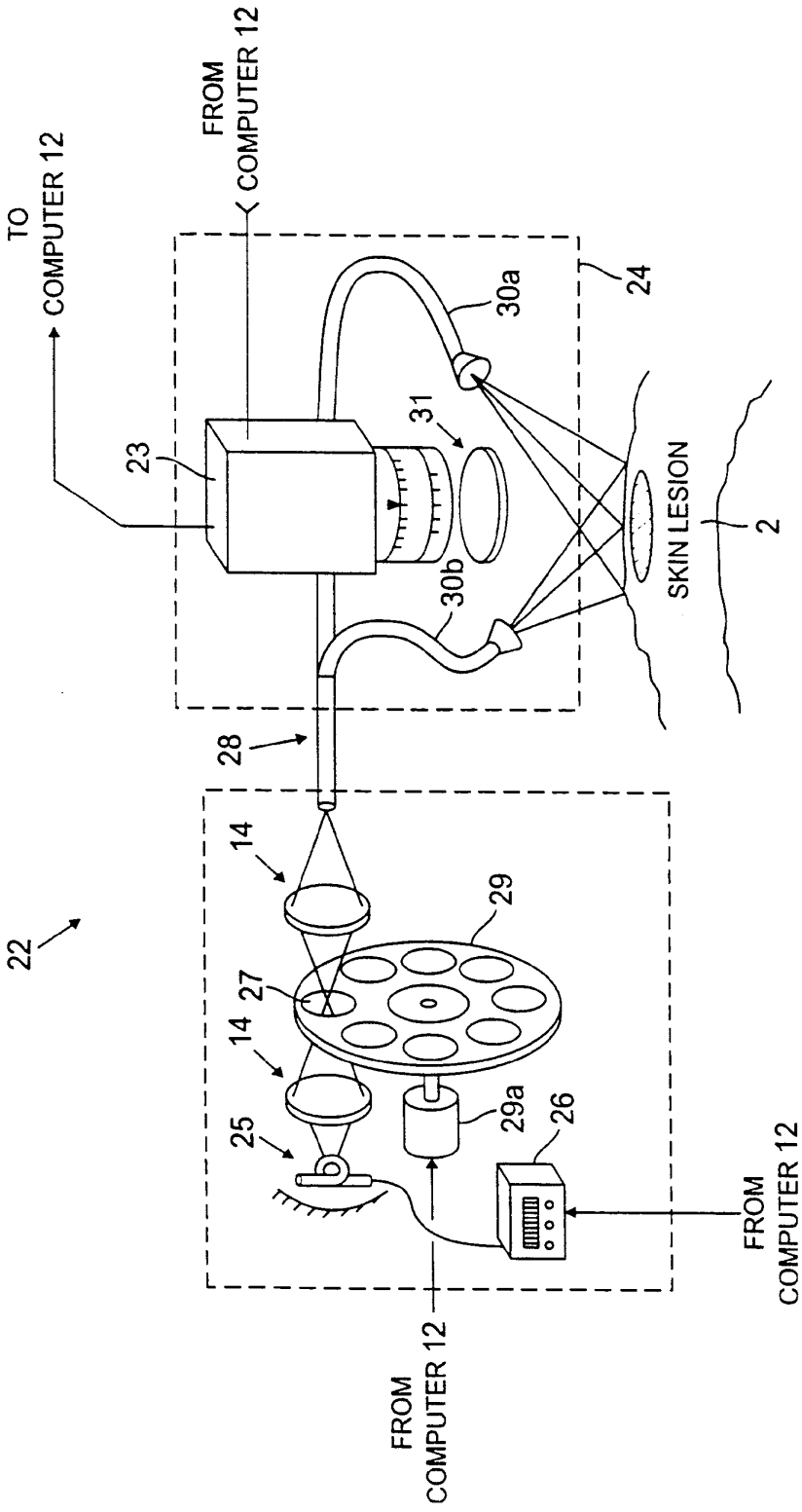
TO COMPUTER 12
FROM COMPUTER 12
24
30a
31
23
SKIN LESION
2
30b
28
14
29
22
27
14
29a
26
25
FROM COMPUTER 12
FROM COMPUTER 12

FIG. 2

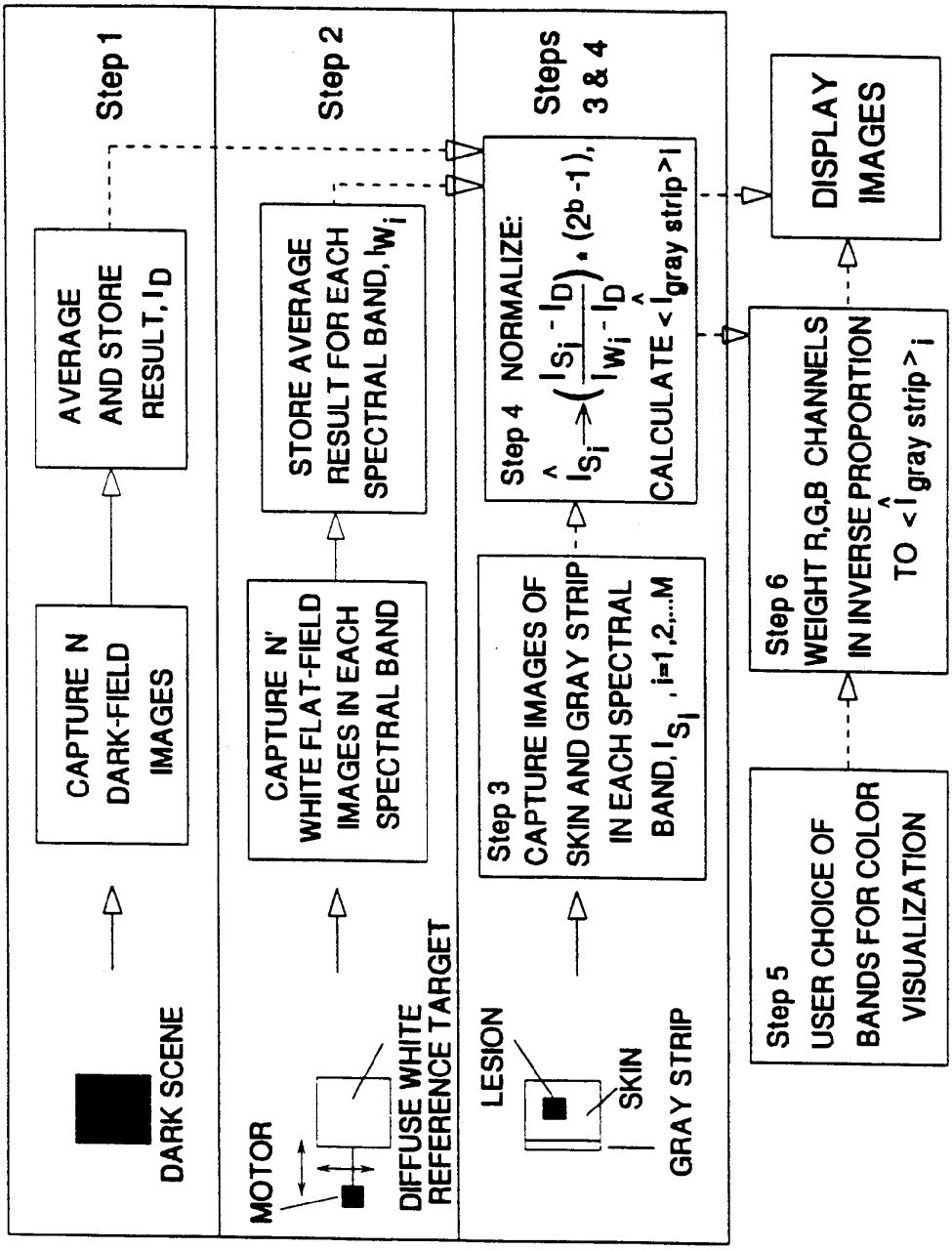
Step 1
Step 2
Steps 3 & 4
AVERAGE AND STORE RESULT, I_D
CAPTURE N DARK-FIELD IMAGES
DARK SCENE
STORE AVERAGE RESULT FOR EACH SPECTRAL BAND, ^hW_j
CAPTURE N' WHITE FLAT-FIELD IMAGES IN EACH SPECTRAL BAND
MOTOR
DIFFUSE WHITE REFERENCE TARGET
Step 3 CAPTURE IMAGES OF SKIN AND GRAY STRIP IN EACH SPECTRAL BAND, I_{S_j}, i=1,2,...M
LESION
SKIN
GRAY STRIP
Step 4 NORMALIZE: $\hat{I}_{S_j} \rightarrow \left(\frac{I_{S_j} - I_D}{I_{W_j} - I_D}\right) * (2^b - 1)$, CALCULATE $\hat{I}_{gray\ strip}$
DISPLAY IMAGES
Step 6 WEIGHT R,G,B CHANNELS IN INVERSE PROPORTION TO $\hat{I}_{gray\ strip}$
Step 5 USER CHOICE OF BANDS FOR COLOR VISUALIZATION

FIG. 3a

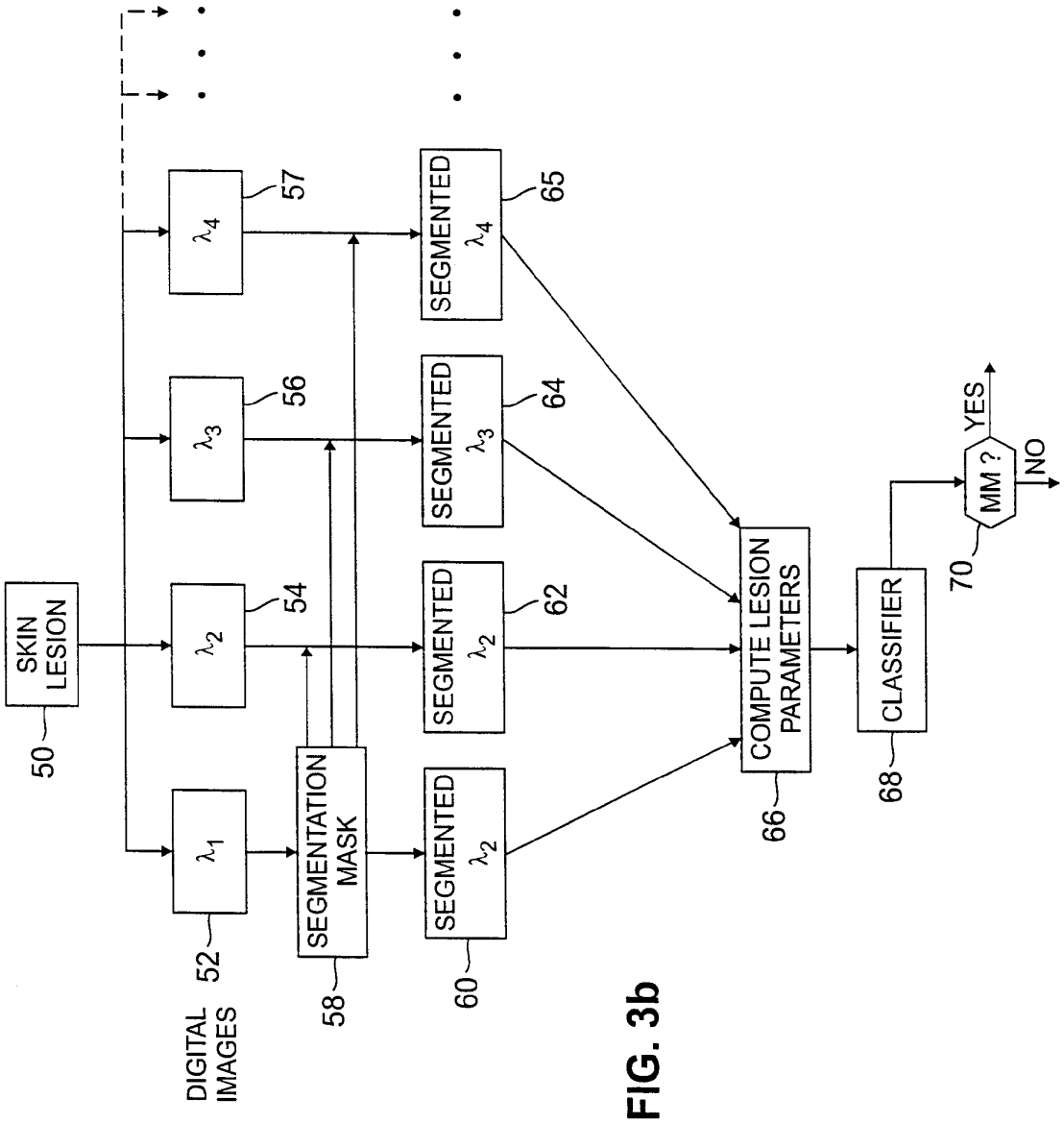
SKIN LESION
50
DIGITAL IMAGES
52
54
56
57
58
60
62
64
65
66
68
70
SEGMENTATION MASK
SEGMENTED
COMPUTE LESION PARAMETERS
CLASSIFIER
MM ?
YES
NO

FIG. 3b

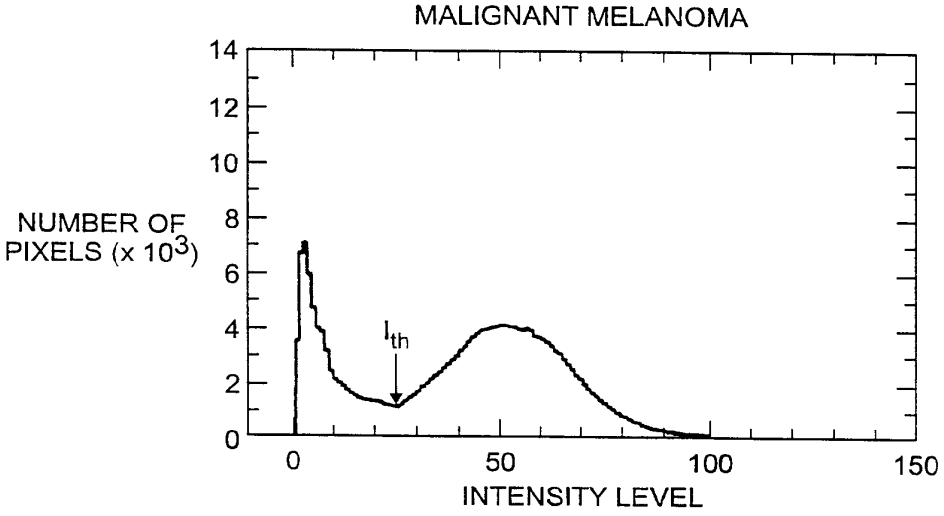
MALIGNANT MELANOMA
NUMBER OF PIXELS (x 10^3)
14
12
10
8
6
4
2
0
I_{th}
0
50
100
150
INTENSITY LEVEL

FIG. 4a

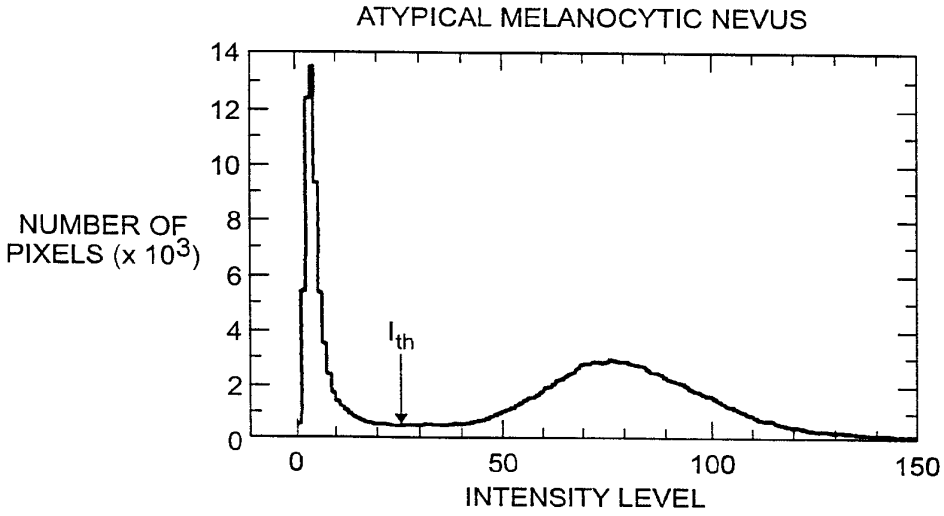
ATYPICAL MELANOCYTIC NEVUS
NUMBER OF PIXELS (x 10^3)
14
12
10
8
6
4
2
0
I_{th}
0
50
100
150
INTENSITY LEVEL

FIG. 4b

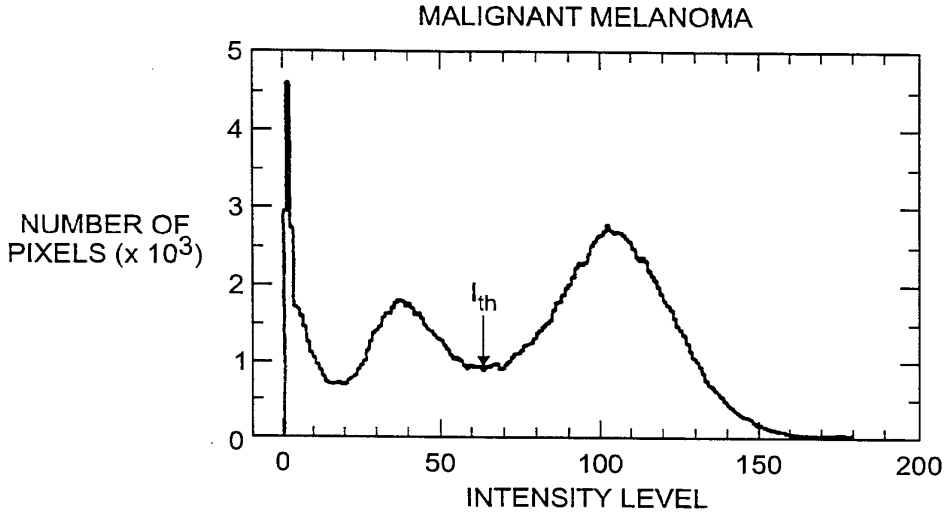

FIG. 5a

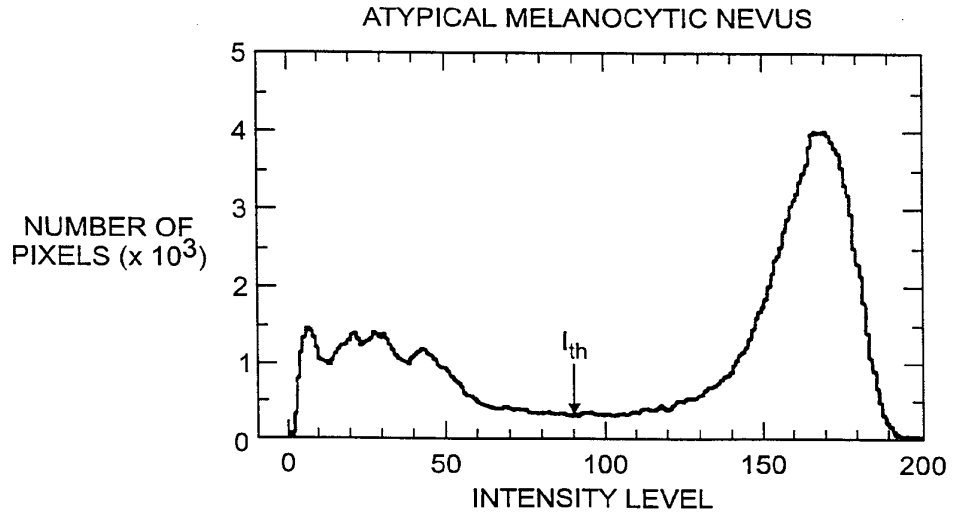

FIG. 5b

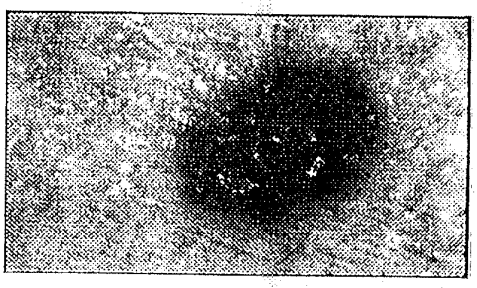

FIG. 6(a)

FIG. 6(d)

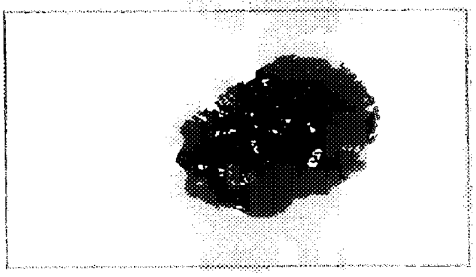

FIG. 6(b)

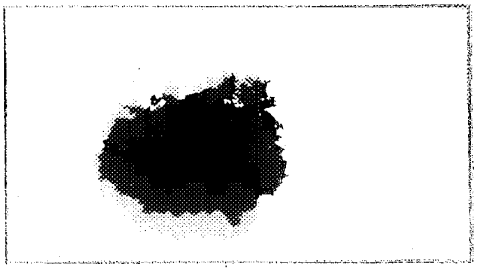

FIG. 6(e)

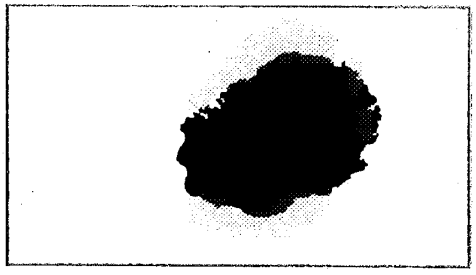

FIG. 6(c)

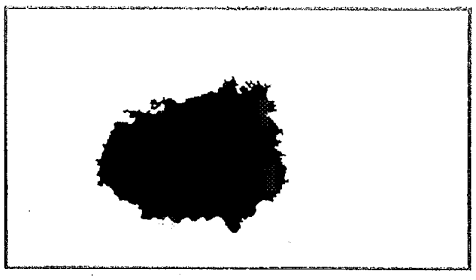

FIG. 6(f)

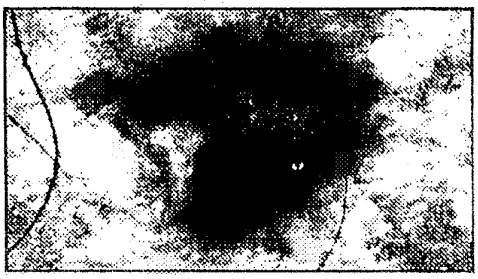

FIG. 7(a)

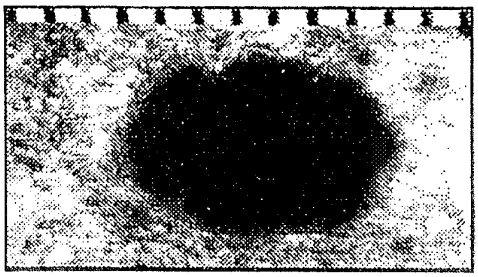

FIG. 7(d)

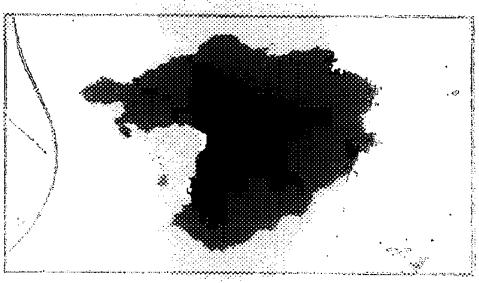

FIG. 7(b)

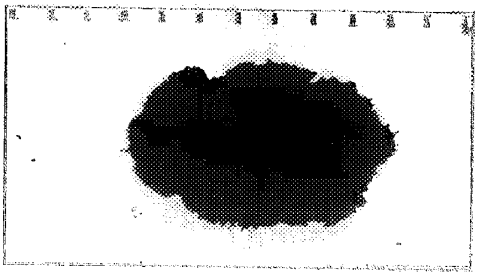

FIG. 7(e)

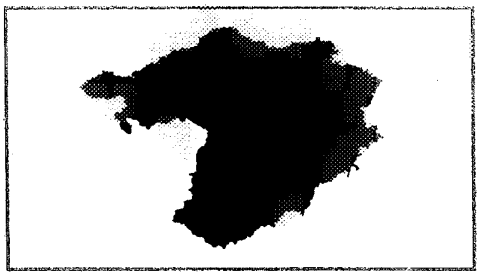

FIG. 7(c)

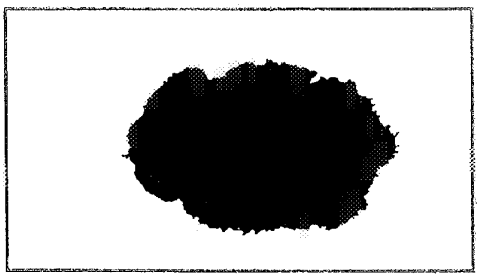

FIG. 7(f)

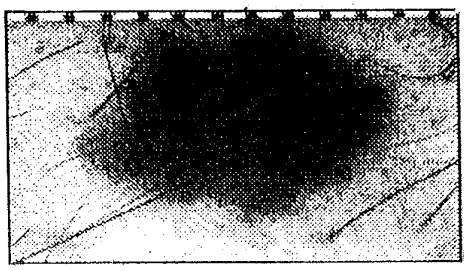

FIG. 8(a)

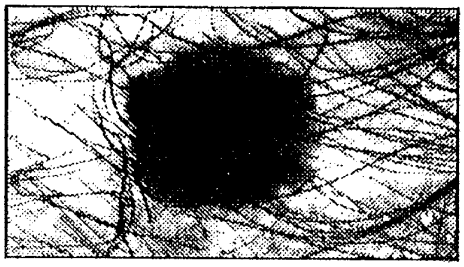

FIG. 8(e)

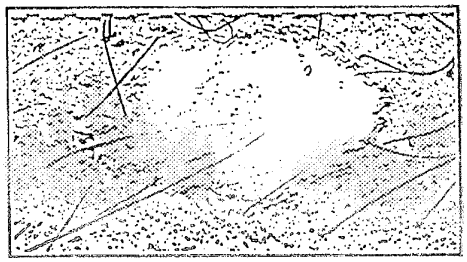

FIG. 8(b)

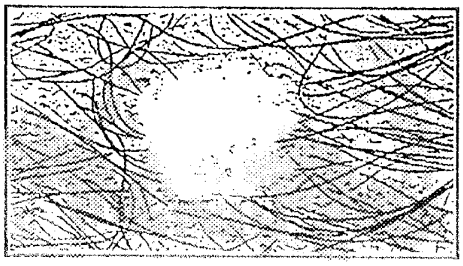

FIG. 8(f)

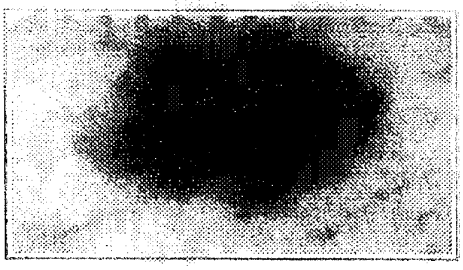

FIG. 8(c)

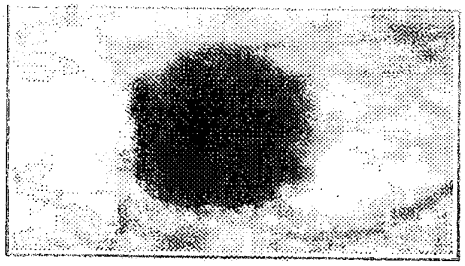

FIG. 8(g)

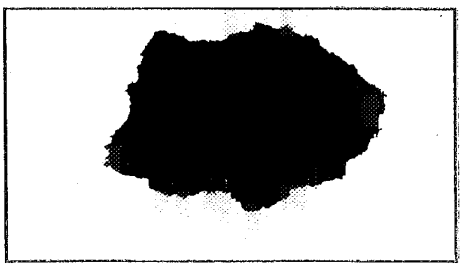

FIG. 8(d)

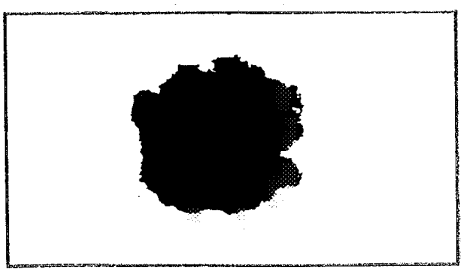

FIG. 8(h)

	I - 3	I - 2	I - 1	I	I + 1	I + 2	I + 3
J - 5	0	1	0	0	0	1	0
J - 4	0	1	1	0	1	1	0
J - 3	0	0	2	3	2	0	0
J - 2	1	0	0	1	0	0	1
J - 1	1	0	-3	-5	-3	0	1
J	1	1	-5	-8	-5	1	1
J + 1	1	0	-3	-5	-3	0	1
J + 2	1	0	0	1	0	0	1
J + 3	0	0	2	3	2	0	0
J + 4	0	1	1	0	1	1	0
J + 5	0	1	0	0	0	1	0

FIG. 9

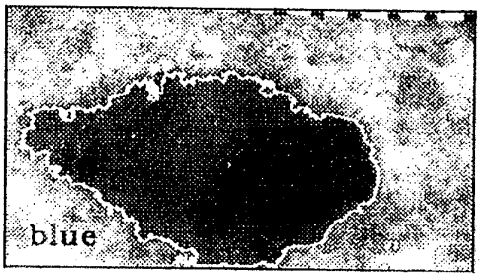

FIG. 10(a)

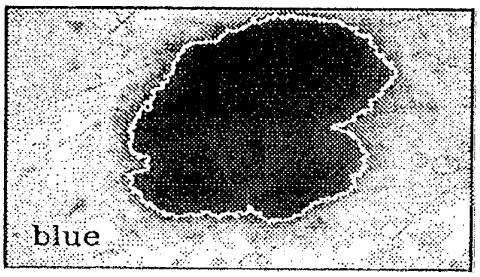

FIG. 10(d)

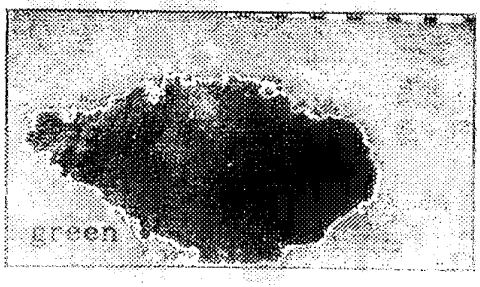

FIG. 10(b)

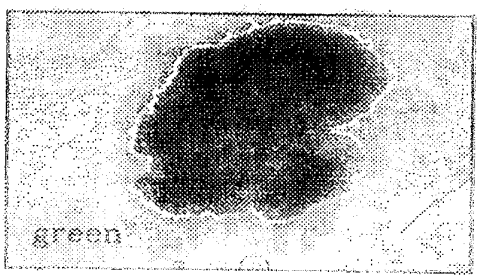

FIG. 10(e)

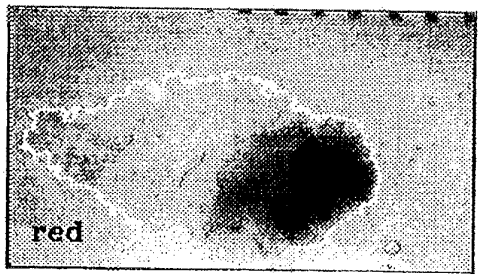

FIG. 10(c)

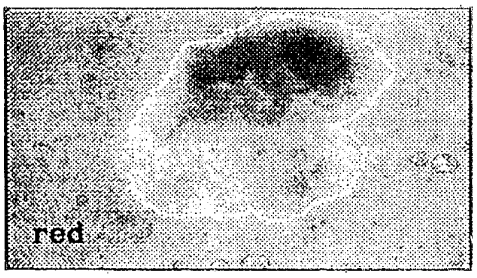

FIG. 10(f)

PARAMETER		DIAGNOSTIC ACCURACY (%)	SENSITIVITY (%)	SPECIFICITY (%)
ASYMMETRY:	A_{bin}	52	71	86
	A_b	48	68	84
	A_g	50	73	82
	A_r	62	78	89
BLOTCHINESS:	Bl_b	45	56	90
	Bl_g	40	68	72
	Bl_r	42	68	75
	C_b	37	80	55
	C_r	38	80	57
	Cl	44	78	70
BORDER:	B	44	66	81
	G_b	36	76	56
TEXTURE:	$T1_b$	38	88	49
	$T1_g$	49	61	90
	$T2_g$	41	66	76
	$T2_r$	43	73	72
	$T3_b$	39	80	59
	$T3_g$	38	63	74
	$T4_b$	38	68	69
	$T4_g$	39	56	83
	$T5_b$	36	76	58
	$T6_b$	38	90	46

FIG. 11

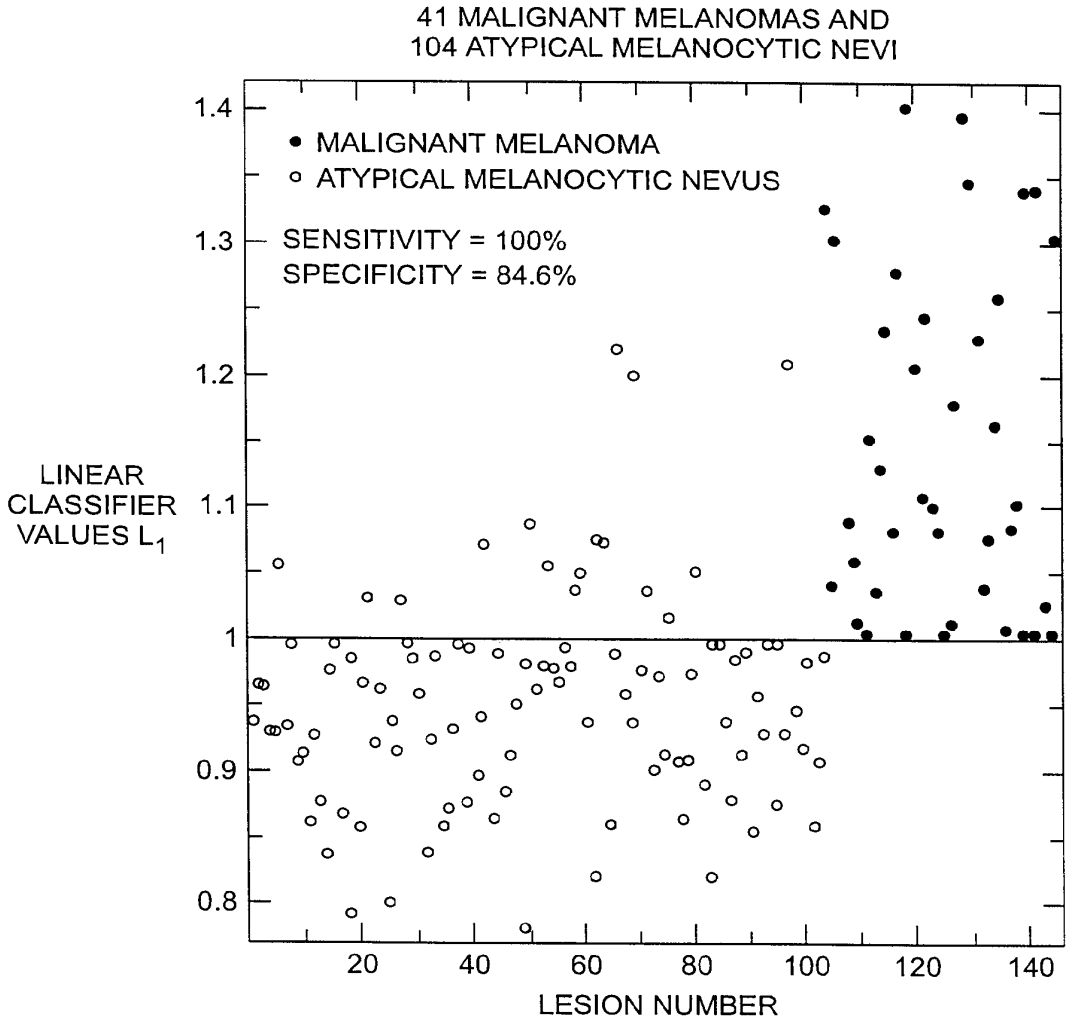
41 MALIGNANT MELANOMAS AND
104 ATYPICAL MELANOCYTIC NEVI
MALIGNANT MELANOMA
ATYPICAL MELANOCYTIC NEVUS
SENSITIVITY = 100%
SPECIFICITY = 84.6%
LINEAR CLASSIFIER VALUES L_1
1.4
1.3
1.2
1.1
1
0.9
0.8
20
40
60
80
100
120
140
LESION NUMBER

FIG. 12

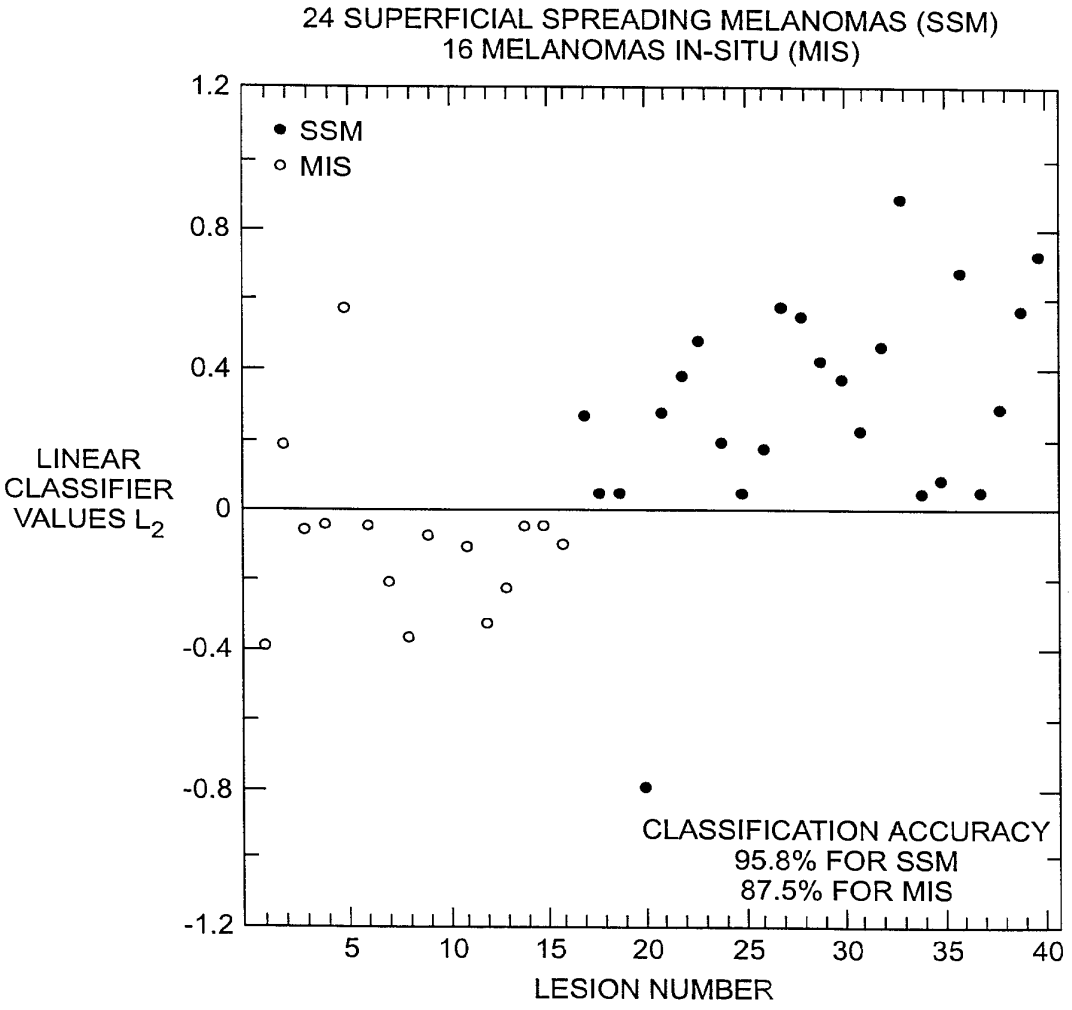
24 SUPERFICIAL SPREADING MELANOMAS (SSM)
16 MELANOMAS IN-SITU (MIS)
SSM
MIS
LINEAR CLASSIFIER VALUES L_2
1.2
0.8
0.4
0
-0.4
-0.8
-1.2
5
10
15
20
25
30
35
40
LESION NUMBER
CLASSIFICATION ACCURACY
95.8% FOR SSM
87.5% FOR MIS

FIG. 13

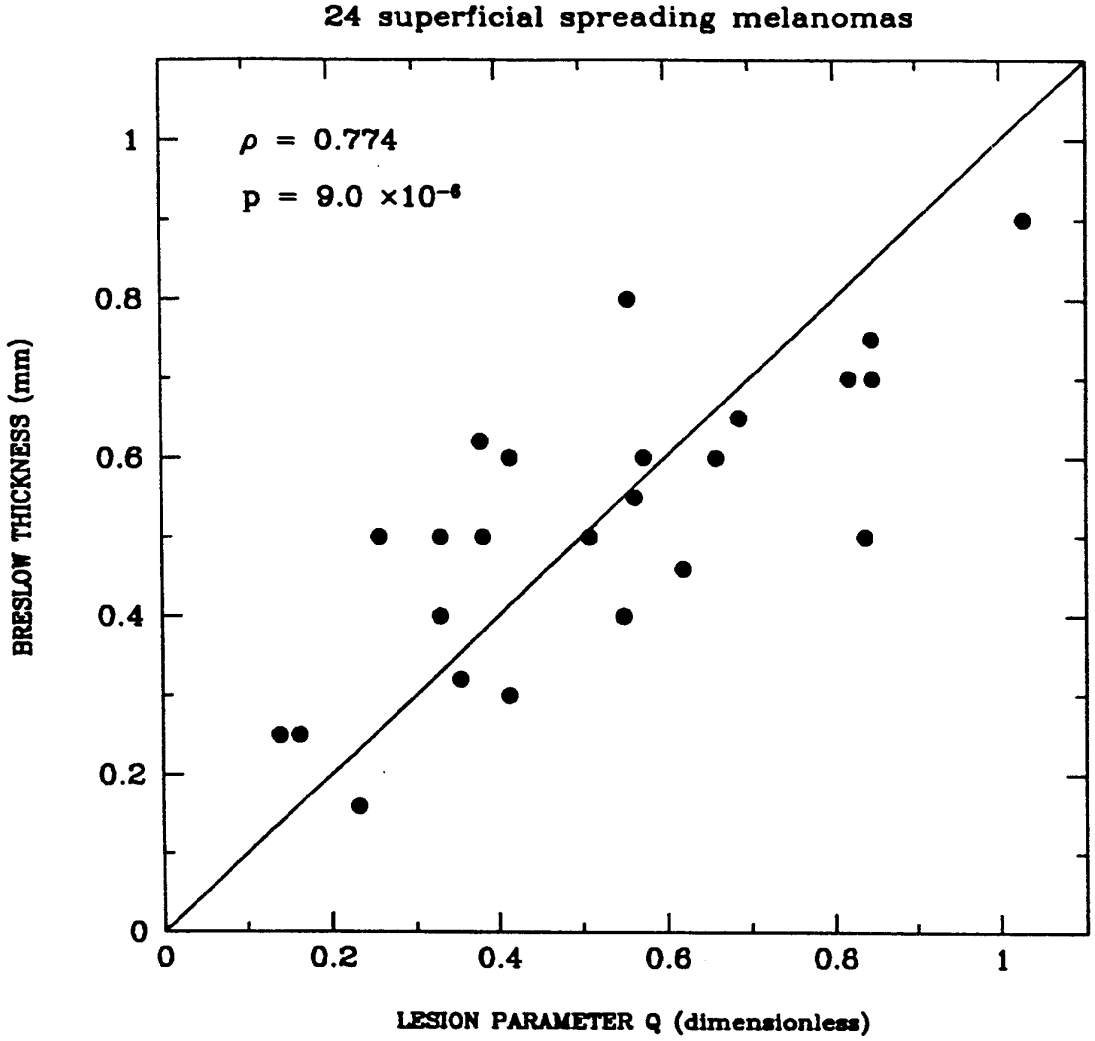
24 superficial spreading melanomas
ρ = 0.774
p = 9.0 ×10⁻⁶
BRESLOW THICKNESS (mm)
LESION PARAMETER Q (dimensionless)
0
0.2
0.4
0.6
0.8
1

Fig. 14

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US98/03826

A. CLASSIFICATION OF SUBJECT MATTER

IPC(6) :A61B 06/08
US CL :600/476; 382/128; 348/77

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 600/476, 473; 382/128, 133; 348/, 4577

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

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

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X --- Y	US 5,515,449 A (TSURUOKA ET AL.) 07 MAY 1996, SEE ABSTRACT, FIGURES 1-26 AND CLAIMS 1-6.	1, 12, 14-16, 20, 23, 24, 67 --- 44, 45, 47, 48
X ---E Y	US 5,749,830 A (KANEKO ET AL.) 12 MAY 1998, SEE ABSTRACT, FIGURES 1-71, COLUMN 1 LINES 43-62, COLUMN 8 LINES 61, COLUMN 9 LINES 6-32, COLUMN 11 LINES 13-30, COLUMN 17 LINES 9-41, COLUMN 26 LINE 55 - COLUMN 27 LINE 30, COLUMN 32 LINES 33-56, COLUMN 52 LINES 26-35, COLUMN 57 LINES 27-33, COLUMN 63 LINES 3-7 AND CLAIMS 1-6.	1-3, 12, 14-16, 20-25, 27-31, 41, 44-50, 53-56, 58, 67 --- 18

[X] Further documents are listed in the continuation of Box C. [ ] See patent family annex.

*	Special categories of cited documents:	"T"	later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
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C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X ---P Y	US 5,701,902 A (VARI et al.) 30 December 1997, see abstract, figures 1-17, column 2 lines 25-67, column 4 lines 15-28, column 5 lines 5-12, column 7 lines 25-44, column 8 lines 21-34 and claims 1-15.	1-4, 14-17, 19, 25, 44, 54, 55, 67 --------- 18
X --- Y	US 4,768,513 A (SUZUKI) 06 September 1988, see abstract, figures 1-15, column 1 lines 7-42, column 2 lines 34-47, column 5 lines 22-30, column 7 lines 32-50, column 8 lines 16-46, column 9 lines 25-56, column 10 lines 35-43 and claims 1-16.	1, 12-16, 22, 67 --------- 44
A	US 4,556,057 A (HIRUMA et al.) 03 December 1985, see abstract, figures 1-3 and claims 1-7	1-67
A	US 5,528,703 A (LEE) 18 June 1996, see abstract, figures 1-11 and claims 1-4.	1-67
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A	US 5,241,468 A (KENET) 31 August 1993, see abstract and claims 1-13.	1-67
A	US 4,957,114 A (ZENG et al.) 18 September 1990, see abstract, figures 1-4 and claims 1-7.	1-67
A, P	US 5,699,798 A (HOCHMAN et al.) 23 December 1997, see abstract, figures 1-11 and claims 1-45.	1-67

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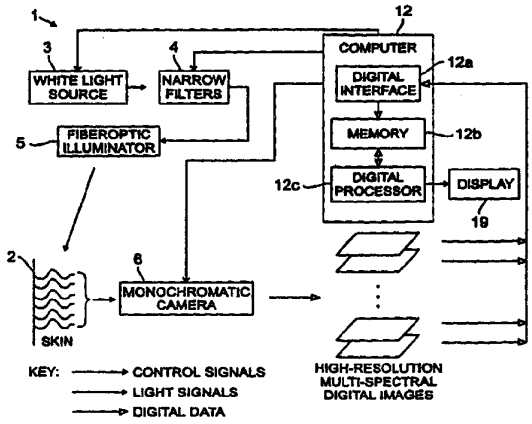

(57) Abstract

Systems and methods for the multispectral imaging of skin tissue enables automatic characterization of the condition of a region of interest of the skin, based on direct digital imaging of the region of interest (Figures 1a and 2) or the digitization of color photographic slides of the region of interest, illuminated by appropriately filtered light. Preferably, a digital image at a low spectral band is automatically segmented and that segmented mask is used to segment the other images by a digital processor (Figure 3b). Parameters are estimated through wavelet maxima representation. Parameters related to the texture, asymmetry, blotchines and border irregularities are also automatically estimated (Figure 11). The region of interest is automatically characterized by the digital processor, based on those parameters. The region of interest may include a skin lesion, in which case the present invention enables the characterization of the lesion as malignant or benign (Figures 4a and 4b). The region of interest may also include wounds or burns.

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SYSTEMS AND METHODS FOR THE MULTISPECTRAL IMAGING AND CHARACTERIZATION OF SKIN TISSUE

FIELD OF THE INVENTION

This invention relates to methods and systems for the computer controlled analysis of digital images of skin tissue at a plurality of wavelengths, which may include those outside of the red-green-blue bands. The methods and systems further include the automatic characterization of the condition of the skin tissue, based on automatically computed values of parameters which are functions of characteristics of the skin tissue, derived the digital images. Skin lesions can be analyzed for determining whether the lesion is a melanoma, for example. Systems for digitally imaging and analyzing skin tissue are disclosed, as well.

BACKGROUND OF THE INVENTION

Melanoma is a usually fatal skin cancer, unless it is detected and surgically removed in its earliest stages. Early detection of malignant melanoma is difficult because early melanomas, those having a Breslow thickness less than 1 mm, share many diagnostic features with benign lesions, such as dysplastic nevi or atypical melanocytic nevi.

To aid in the analysis of lesions, conventional photography, referred to as "clinical imaging", has been used to image the lesion for further study. The effectiveness of clinical imaging can be compromised, however, by specular reflection by the skin. Polarizers have been used for polarized imaging, which minimizes specular reflection.

Dermoscopy is another technique for examining skin, in which specular reflection is minimized. Dermoscopy also assists in clinically differentiating melanoma from its benign stimulants by enabling the observation of features of pigmented melanocytic lesions that are not discernible by the naked eye. In dermoscopy, the skin is made more transparent to light by providing an oil layer over the skin, in front of the optical system. A glass plate is placed over the oil layer. The oil has an index of refraction between the index of refraction of the horny layer of the

skin and the glass plate. Standard magnifying optics may be used to enlarge the structures rendered visible on and under the surface of the skin by the oil layer. The region of interest can then be examined visually. Slides of the region of interest can be made, as well, for future study.

Despite their similarities, most malignant melanomas differ in certain of their characteristics from other melanocytic lesions. A major advance in characterizing skin lesions based on certain of the observable differences between malignant and other lesions is the "ABCD" rule, where A=asymmetry, B=border irregularity, C=color variability, and D=diameter greater than 6 mm. A corresponding ABCD rule, where "D" refers to dermoscopic structures, such as brown globules, black dots or pigment networks within the lesion, is applied to dermoscopic images. Because the clinical and dermoscopic applications of these rules are subjective, they are not very reliable.

When skin is illuminated by light, the light can be re-emitted by reflection, scattering or fluorescence. It is known in the art that re-emission of light absorbed at different wavelengths by the region of interest can provide different information. For example, as the wavelength of the light increases, its depth of penetration into the skin also increases. Chromophores at different depths in the tissue therefore absorb and re-emit light at various wavelengths. Melanin and hemoglobin are examples of such chromophores.

Since the unaided eye cannot perceive light outside of the visible region or low-contrast structure in visible-light images, information which may be useful in diagnosing a lesion may not be directly observable. Digital acquisition and processing of dermoscopic images may, therefore, improve diagnostic reliability by employing more of the information residing in such images that is not directly observable. There have therefore been attempts to use objective, computer-based, image analysis algorithms that can discern meaningful differences between benign and malignant melanocytic lesions with sufficient accuracy.

Computer processing of images requires that the image be in digital form. A digital image is an array of digital signals whose values are a function of certain characteristics of the subject of the image. When imaging skin lesions, the digital images comprise digital signals whose values are a function of the re-emission

characteristics of the skin and lesion, at different spectral bands of the light. The array is obtained by spatial sampling and quantizing the intensity of images obtained with film or directly by electronic cameras. Practical limitations on the number of picture elements or pixels per unit area of image determine the achievable spatial resolution of the digital image. The digital image typically needs to be segmented to separate the digital signals which are a function of the skin lesion from the digital signals which are a function of the surrounding skin.

Computer aided analysis has also been used to classify skin lesions using quantitative values indicative of particular characteristics of lesions, referred to as parameters. Based on histopathological diagnosis of lesions, algorithms have been developed which use linear or non-linear classifiers to combine parameters provided by the operator of an imaging device or a physician or computed by a processor, to yield a value which can be used to classify the lesion. Because some of the steps in the computer-aided analysis of which we are aware depend on subjective judgments of an individual, such analysis may provide highly variable results.

The images heretofore available have been obtained with commercially available red-green-blue color imaging apparatus. Color photographic transparencies of skin lesions have been digitized and skin lesions have been directly imaged with "three-chip" digitizing cameras. Such cameras employ broad-band filter bandpasses that are ultimately based on the wavelength response of the human visual system and have large regions of overlap.

Electronic images may also be obtained in narrower, non-overlapping filter bandpasses, which may reveal additional, wavelength-dependent differences between the images of melanomas and of benign lesions. However, such devices have had poor resolution and/or poor signal-to-noise characteristics which prevent the acquisition of digital images of melanocytic skin lesions of sufficient quality for effective application of machine vision techniques for lesion diagnosis.

Existing imaging systems and processes also tend to suffer from an inability to provide the required repeatability of the value of extracted lesion parameters, due in part to a lack of standardization with respect to spatially varying artifacts, so that the parameters, therefore, lack invariance to lighting and image exposure conditions, for example. Obtaining high signal-to-noise ratios in images

recorded in narrow filter bandpasses, when exposure times are sufficiently short that the skin is effectively "frozen" during the exposure sequence, has also been difficult. In addition, since the optimum wavelengths for automatic characterization may not be the optimum wavelengths for visual observation, it may be difficult to reconstruct high-fidelity color images from the digital images for visual interpretation by a clinician.

The assessment of wounds and burns through the appearance of color images present similar challenges. Existing technology for the imaging of skin *in vivo* for these purposes is also inadequate. Practical solutions to the problems of employing multispectral digital imaging of skin for the analysis of lesions, wounds, or other conditions, have not been found.

SUMMARY OF THE INVENTION

The methods and systems of the present invention provide for the acquisition of digital images of skin at a plurality of spectral bands to automatically characterize the condition of the tissue based on the digital images. Spectral wavelength bands within and outside of the visible band may be used. In accordance with the present invention, a pigmented skin lesion can be characterized as malignant or benign, for example. Wounds or burns can also be characterized with respect to their rate of healing. The digital images comprise a plurality of digital signals whose values are functions of the condition of the tissue. The digital images acquired are subjected to objective and quantitative analysis by a digital processor to detect and identify abnormalities. The analysis includes image segmentation, parameter estimation and characterization of the skin. The estimation and characterization steps are automatic. The segmentation step may be automatic, as well. Subjective judgments are therefore minimized or eliminated.

It has further been found that generating the segmentation mask from a digital image acquired with light in a spectral band which does not penetrate deeply into the skin, such as a spectral band with a center less than about 500 nanometers, provides superior results. After segmentation, estimated values which are functions of characteristics of the lesion, such as its texture, asymmetry, blotchiness, and border irregularities, are computed and used to automatically characterize the condition of the

skin. Clinically significant dimensional parameters such as diameter may also be evaluated. Digital signals corresponding to hair or blob-like structures are preferably removed during segmentation. Some or all of the values may be estimated through wavelet maxima representations, as well.

In accordance with the present invention, a method for characterizing the condition of a region of interest of the skin, wherein the absorption and scattering of light in different spectral bands by the region of interest is a function of the condition of the skin, is disclosed. The method comprises illuminating the region of interest of the skin by light in at least three spectral bands and digitally imaging the region of interest at the at least three spectral bands with the light re-emitted by the skin to generate digital images comprising digital signals whose values are a function of the condition of the skin. The digital images are provided to a processor which segments the digital images by generating a segmentation mask from a digital image in any one of the at least three spectral bands. The processor estimates at least one rotationally and translationally invariant statistical measure of coefficient distributions of the multiscale wavelet maxim representations of the digital images in each spectral band, which are functions of the texture of the region of interest determined by the segmentation mask. The processor characterizes the condition of the skin based on the estimated values, and outputs the characterization of the condition of the skin. Preferably, the segmenting, estimating and characterizing steps are conducted without the intervention of an operator.

Additional parameters include measures of the texture, asymmetry, blotchiness and border irregularity of the portion of the region of interest.

The digital images may be obtained by directly imaging the region of interest with a digital camera, or digitally imaging color slides of the region of interest, through appropriately filtered light.

The characterizing step may include comparing a weighted combination of the parameter values against a threshold value. The weight coefficients for each parameter value and the threshold value may be selected based on a training set of images of lesions or other skin conditions, whose condition has been determined, preferably through histological examination by a plurality of doctors.

Preferably, for skin lesions, specificity is maximized under the constraint of 100% sensitivity to melanoma.

In accordance with another aspect of the invention, a system for characterizing the condition of a region of interest of skin includes means for illuminating the region of interest with light in at least three spectral bands and a camera for acquiring digital images of the region of interest based on the light re-emitted from the illuminated region of interest at each of the spectral bands. The digital image comprises digital signals whose values are a function of the condition of the region of interest. A digital processor segments the digital images by generating a segmentation mask from a digital image in any one of the at least three spectral bands. The processor estimates at least one rotationally and translationally invariant statistical measure of coefficient distributions of the multiscale wavelet maxim representations of the digital images in each spectral band, which are functions of the texture of the region of interest determined by the segmentation mask. The processor characterizes the skin condition based on the estimated value or values. The other parameters discussed above may be used, as well.

The camera may be a single-chip or multiple-chip charge-coupled device which detects light in a plurality of spectral bands between the near ultraviolet to near infrared. The filter means may be a plurality of interference filters mounted on a wheel for stepping any filter into a position intercepting the light from the light source. Preferably, at least one of the spectral bands has a center which lies between about 350 and 500 nanometers, at least one of the spectral bands has a center which lies between about 500-600 nanometers, and at least one other spectral band has a center which lies between about 750-1000 nanometers.

DESCRIPTION OF THE FIGURES

Fig. 1(a) is a schematic illustration of a method and system of imaging a region of interest of skin in accordance with the present invention;

Fig. 1(b) is a schematic illustration of a plurality of narrow spectral bandwidths which may be used to illuminate the skin in the embodiment of Fig. 1(a);

Fig. 1(c) is a schematic illustration of alternative methods and systems for digitizing and analyzing color photographic slides of a region of interest of skin;

Fig. 2 is a schematic illustration of preferred illumination and imaging portions of a computer controlled imaging system for direct imaging of a lesion;

Fig. 3(a) is a flow chart of a calibration procedure for use with the present invention;

Fig. 3(b) is a flow chart of a method of processing images for classifying lesions as malignant or benign, in accordance with the present invention;

Figs. 4(a) and 4(b) are histograms of a malignant melanoma and of an atypical melanocytic nevus, respectively, showing two peaks in each histogram;

Figs. 5(a) and 5(b) are histograms of another malignant melanoma and another atypical melanocytic nevus, respectively, showing three or more peaks in each histogram;

Figs. 6(a) and 6(d) are digital images in the blue spectral band of another malignant melanoma and another atypical melanocytic nevus, respectively;

Figs. 6(b) and 6(e) are digital images of the images of Figs. 6(a) and 6(d) respectively, after thresholding;

Figs 6(c) and 6(f) are digital images of the images of Figs. 6(a) and 6(d), respectively, after iterative thresholding;

Figs. 7(a) and 7(d) are digital images in the blue spectral band of another malignant melanoma and another atypical melanocytic nevus;

Figs. 7(b) and 7(e) are digital images of Figs. 7(a) and 7(d), respectively, resulting from iterative processing and showing dark blobs outside the lesion area;

Figs. 7(c) and 7(f) are digital image masks of Figs. 7(b) and 7(d), respectively, resulting from image cleaning;

Figs. 8(a) and 8(e) are digital images in the blue spectral band of another malignant melanoma and another atypical melanocytic nevus, respectively, showing hair;

Figs. 8(b) and 8(f) are reverse intensity contrast images of the lesions of Figs. 8(a) and 8(e), respectively;

Figs. 8(c) and 8(g) are digital images resulting from an averaging process applied to the images of Figs. 8(a) and 8(b), to remove hair;

Figs. 8(d) and 8(h) are binary lesion masks resulting from the segmentation of the images of Figs. 8(c) and 8(g), respectively;

Fig. 9 is a spatial filter used to remove hair;

Figs. 10(a) - 10(c) are segmented digital images in the blue, green and red spectral bands, of the malignant melanoma whose histogram is shown in Fig. 5(a);

Figs. 10(d) - 10(f) are segmented digital images in the blue, green and red spectral bands, of an atypical melanocytic nevus whose histogram is shown in Fig. 5(b);

Fig. 11 is a chart of lesion parameters and their associated diagnostic accuracy, sensitivity and specificity when used individually;

Fig. 12 is a plot of linear classifier values versus lesion identification number, for 41 malignant melanomas and 104 atypical melanocytic nevi;

Fig. 13 is a plot of linear classifier values versus lesion identification number for 24 superficial spreading melanomas and 16 melanomas *in-situ; and*

Fig. 14 is a plot of lesion parameter versus Breslow thickness for 24 superficial spreading melanomas.

DESCRIPTION OF THE INVENTION

Fig. 1(a) is a schematic illustration of a method and system 1 in accordance with the present invention, by which images of the skin 2 are acquired by a camera nearly simultaneously at a plurality of spectral bands, λ_i, i=1,2,...M, that are preferably effectively non-overlapping, as shown schematically in FIG. 1(b). The skin is illuminated by a source of white light 3, which is filtered by narrow passband filters 4. The filtered light is preferably conveyed to the skin 2 through a fiberoptic illuminator 5. The light re-emitted by the illuminated skin through reflection, scattering or fluorescence is imaged by a low-noise, high-resolution monochrome camera 6, which is preferably an electronic charge-coupled ("CCD") camera. Digital images output by the camera 6 are provided to a computer 12 for processing.

The computer 12 includes a digital interface 12a, a memory 12b and a digital processor 12c. A display 19 is preferably provided as well. The computer 12 includes an input to a digital interface 12a for receiving the digital images. A memory 12b stores the digital images, and the software controlling operation of the imaging

system, the image processing, and the classification and characterization of the lesion. The digital processor 12c, under control of the software, performs the calculations. The computer 12 has an output connected to a display 19, which can display the processed images and the results of the classification and characterization procedures for each image. The computer 12 also preferably has outputs connected to the source of light 3 and the camera 6, for controlling their illumination level and exposure times, respectively, as described below.

The image processing, classification or characterization and other programs can be implemented on a personal computer, using a programming language, such as FORTRAN or C. The memory 12b which stores the software can be any convenient media readable by the computer 12, such as the hard drive of the computer, read only memory, random access memory with a battery backup, electrically programmed ROM, electrically erasable ROM, floppy disc, or CD ROM. Other suitable media may be used, as well.

When the filter bandpasses have minimal overlap, as in FIG. 1(b), each monochromatic image will contain spectrally independent information. Such spectral separation is believed to be useful for differential diagnosis of skin lesions that contain varying amounts of melanin, and of hemoglobin in different oxidation states, for example. Spectral separation is also believed to be useful in distinguishing granulation of tissue and other structural details of wounds in various stages of healing. One or more of the wavelength bands may lie outside the visible region, such as in the near infrared and/or the near ultraviolet, as long as the wavelength is within the response range of the combined optical system including the electronic camera 6.

In accordance with another aspect of the invention, the digital images of skin lesions can be derived from color slides of the lesions obtained by clinical imaging, dermoscopy, or polarization imaging. Fig. 1(c) is a schematic illustration of alternative approaches to the acquisition and digitization of images of skin lesions from color slides. A photo camera 13 produces 35-mm color slides of a region of the skin 14. The camera 13 can be a Dermaphot ® camera from Heine, Optotechnik Gmbh & Co. AG, Germany, for example. The slides are typically stored in an archive 15. The slides are subsequently reimaged by a monochrome camera 16, which may be a CCD camera, that photographs each slide as it is illuminated by white light that has

passed through a sequence of bandpass filters 17 to create a color filtered version of the image. The slides can be illuminated at broad or narrow blue (B), green (G) and red (R) wavelength bands, respectively. The broad wavelength bands may overlap somewhat. In one example, the blue wavelength band was about 400 nm $\pm$ 30 nm, the green wavelength band was about 550 nm $\pm$ 30 nm, and the red wavelength band was about 700 nm $\pm$ 30 nm.

Each of the filtered representations is recorded by the monochrome camera 16, which provides the resulting digital images 18 to an input of the computer 12. If an electronic camera is not used, the slide images could be digitized by any available commercial digitizer including three channels, one for red, one for green and one for blue, as long as the pixel size in the lesion plane after digitization is less than about 60 micrometers ("μm").

An appropriate CCD camera 16 is available from Electrim, Inc., Princeton, N.J. The camera 16 has a photographic macro-lens, wherein f#/2.8 and f=100 mm. Preferably, the spatial resolution of the CCD camera 16 provides pixels having a size about 10-30 μm in the lesion plane. The CCD camera 16 from Electrim, Inc., has 753 X 488 pixels. The spatial resolution with such a camera is approximately 21 x 24 μm at the lesion plane. Digital images of lesions obtained with this imaging system were used to classify lesions as malignant or benign, and to characterize lesions as invasive or non-invasive, as described further, below. The Electrim, Inc., CCD camera 16 has rectangular pixels. A CCD camera with square pixels would simplify the calculating procedures.

Alternatively, a 3-chip CCD camera 20, indicated in phantom in Fig. 1c, may be used to reimage the slides of the region of interest. The CCD camera 20 provides digitized images for subsequent analysis by the computer 12. Broad bandpass filters, which are part of the CCD camera 20, produce a representation of the lesion as a set of three narrowband images. The filters are typically in accordance with CIE Standard Observer, wherein the bandwidths are broad.

Fig. 2 is a schematic illustration of the illumination and imaging portions of a preferred computer controlled imaging system 22 in accordance with the present invention, for imaging a region of interest of skin including a lesion. The

electronic camera 23 may be a 10-bit monochromatic electronic CCD camera 23, such as the Xillix Model 1400, available from Xillix Technologies Corp., Canada. The Xillix camera is equipped with wide band, low distortion foreoptics, such as the XJP 1.9/0501, available from Jos. Schneider Werke, Germany. The lower distortion fore optics and the camera minimize chromatic aberrations of the optical system over the "multispectral" sequence of exposures, enabling registration of images with sub-pixel accuracy, over the entire field of view.

To ensure repeatability of imaging conditions and to minimize required intervention by the operator, it is preferred that the system be operated at a preset f/stop. For cameras such as the Xillix Model 1400, exposure times are preferably controlled by the computer 12 through an electromechanical shutter that can operate reliably between minimum and maximum exposure times t_{min} and t_{max}. Electronic shuttering may be more preferred for use with other cameras.

The imaging system provides low-noise, high-resolution digital images at high data transfer rates, with low distortion imaging over the entire range of wavelengths covered by the collection of filters. The Xillix camera, discussed above, has a resolution at the skin surface of about 20 microns per pixel. The CCD camera 23 is preferably contained in a hand-held unit, represented schematically as box 24. The illuminator source 25 is a tungsten-halogen lamp whose intensity is controlled by a light-stabilized power supply 26 whose setting is automatically adjusted by the computer 12. A 150 watt lamp, such as the Phillips EJA, available from Phillips Electronics North America Corporation, N.Y., may be used, for example. The output of the lamp 25 is white light. A narrowband filter 27 is provided between the source and an optical fiber 28. A plurality of narrowband filters, each one corresponding to a different spectral wavelength band, are mounted on a filter wheel 29. Preferred filter bandwidths are listed in Table 1, below. The filter wheel 29, which is driven by a stepping motor 29a, advances each filter to its proper position between the lamp 25 and the optical fiber 28, and holds each filter in position for a sufficient period of time. The computer 12 controls the motor 29a. More or fewer filters may be used. Appropriate lenses 14 are provided between the lamp 25 and the filter 27, and between the filter 27 and the optical fibers 28, as well. One or more fiber illuminators 30a, 30b are provided for conveying the light from the source to the lesion. Two such

illuminators 30a, 30b are shown in Fig. 2 for simplicity. Although the fiber illuminator is illustrated as a bifurcated pair, a ring illuminator which provides more nearly uniform illumination at the skin surface, is preferred. An angle of illumination of about 20° is also preferred. A Fostec Model A0603 ring illuminator available from Fostec, Inc., N.Y., may be used, for example.

The hand-held portion of the system 24 of Fig. 2, which includes the camera 23, may be mounted on a cantilevered arm (not shown) that can be locked into position.

The digital signals making up each of the digital images output from the camera 23 are provided to the computer 12. The computer 12 conducts image processing procedures on the digital images to calibrate the images, and to objectively segment, estimate parameters, and classify the lesions based on the estimated parameters. Operator judgment is not required at any point in the process.

Control is maintained by the computer 12 over source intensity, filter position, and such camera settings as shutter timing, through the digital interface 12a. Key control parameters are empirically chosen on the basis of feedback from histograms of trial images. The intensity of the lamp 25 may be maintained at a stable value, commensurate with the 10-bit dynamic range of the camera 26, by monitoring a secondary light source, connected electrically in series with the primary light source 25. The light output from the secondary source may be monitored by a light sensor that is optically isolated from light reflections associated with the primary source. Such reflections may be caused by the filters that are located on the filter wheel, or from the housing of the primary light source. This method provides optical feedback which is sensitive to changes in light intensity caused by changes in lamp lead resistance, for example, while it is insensitive to the variable amounts of light reflected from the filters, for example. By means of a closed control loop, the optical feedback from the secondary source may be used to maintain constant light output from the primary source. In addition, the lamp intensity may be further stabilized by monitoring light reflected from a material of stable reflectance, such as Kodak "18% gray" card. If the intensity of the light detected by the camera deviates from a predetermined desired value, the intensity of the output of the lamp can be adjusted. The power, voltage or current supplied to the lamp 25, may also be monitored.

The apparatus of Fig. 2 can be used for either clinical imaging of the skin, wherein the skin is imaged directly, dermoscopic imaging, wherein a layer of oil is provided over the skin and a layer of glass placed over the oil layer, or polarized imaging, where a polarizer 31 is added to minimize specular reflection as shown in Fig. 2. In dermoscopic imaging, the index-matching oil sufficiently reduces the specular reflection to avoid the need for a polarizer. When imaging wounds or burns, an additional polarizer 31a may be placed between the source of light 25 and the filter wheel 29, to be used in conjunction with the polarizer 31, to reject copolarized components of the light re-emitted from the region of interest, thereby reducing specular reflections, as is known in the art.

Instead of being positioned between the light source 25 and the optical fiber 28, the narrow bandpass filters 27 may be placed between the skin and the CCD camera 23 to filter the light reflected and scattered from the skin 2. Light re-emitted by the skin through fluorescence would also be filtered. In addition, instead of the filters 27, a monochromator, a plurality of lasers, each emitting at a single wavelength, multiline lasers, tunable lasers or light emitting diodes could also be used as the illumination source or sources, as is known in the art.

The front end of the system preferably consists of a flat glass plate (not shown) for being placed over the skin. Light pressure is applied through the glass, onto the skin, throughout the imaging process. This helps to stabilize the region of interest against unwanted motion which could blur an image or which could lead to spatial misregistration between images obtained in different filter bandpasses.

Preferably, the spectral bands span the range between the near ultraviolet to the near infrared. At least one spectral band preferably has a center which lies between about 350-500 nanometers, more preferably between about 400-450 nanometers, at least one of the bands preferably has a center which lies between about 500-600 nanometers, and at least one other spectral band preferably has a center which lies between about 750-1000 nanometers. The near infrared, between about 750-1000 nanometers, has been found to be useful in detecting invasive melanomas, because of its greater depth of penetration than the other spectral bands.

The preferred filters 27 for lesion imaging with a tungsten-halogen white light source 25 have the center wavelengths λ_i and bandwidths (FWHM) listed in Table 1, for i=l,2,...,M, M=l0, wherein the bands are labeled by j=i-l = 0,l,...M-l. Such filters are available, for example, from Intor, Inc., Tucson, AZ. In each band, the exposure time is preferably selected to avoid saturation of the detector elements of the CCD camera 23, as well as to maximize the linear dynamic range over which the image data are recorded. These exposure times should be constrained to be within limits t_{min} and t_{max} which are related to the electromechanical design of the shutter, optical throughput of the camera 23, and avoidance of image blur associated with motion during the exposure sequence. Suitable values of t_{min} and t_{max} could be 10 ms and 550 ms, respectively, for example. The choice of center wavelength and FWHM for the filter channels, as well as the corresponding exposure times, should preferably also take into account the following considerations:

(a) The center wavelength and FWHM for at least two channels should be chosen so that characteristic absorption lines can be differentiated, such as those associated with melanin and hemoglobin;

(b) For a given set of center wavelengths, there are upper limits on the associated bandwidths if spectral independence of data in different channels is to be maintained, as illustrated in FIG. 1(a);

(c) Bandpasses should be chosen in the red, green and blue portions of the spectrum which enable "true-color" reconstruction of skin images that are suitable for visualization by clinicians;

(d) The need for high signal-to-noise ratio in each image sets practical lower limits on the product of exposure time and filter bandwidth, especially at short wavelengths, where detector response falls off and lesion reflectance is low; and

(e) The total time taken to acquire the images in all filter bands is preferably less than about three seconds, to minimize patient discomfort and possible motion.

Based on considerations (d) and (e) above, and also taking into account the varying spectral reflectances of skin of different colors, the exposure times in each

filter channel are preferably adjustable, with settings based on the dynamic range achieved on an empirical basis, with trial images. In this manner, both dynamic range and signal-to-noise ratio can be maximized for each filter channel. The preferred method is to choose t_{expi} by iteration, based on intensity histograms of images of the skin obtained with trial exposures at each wavelength band. The histograms are analyzed to determine the number of pixels at the saturation intensity level, $I_{sat} = 2^b-1$ (1023 for b=10 bits). The exposure time is decreased if the number of saturated pixels exceeds a predetermined amount, such as 0.01% of the total. Conversely, to maintain high signal-to-noise ratio, the exposure time is increased if a predetermined percentile in the histogram, 99.9%, for example, is reached at less than a preset threshold, such as 99.5% of I_{sat}. The iteration process typically converges after two or three trials.

It may be found to be useful to minimize fluorescence by restricting bandpasses to wavelengths of 400 nanometers and above.

The preferred exposure times at each wavelength for imaging skin of different colors to classify melanomas are listed in Table 1, for the embodiment of Fig. 2 with 10 filters. It has been found that for the blue channel centered at 450 nm, the optimal exposure time for dark skin is 273 ms, which is more than double the optimal 107 ms exposure time for light skin. On the other hand, in the near infrared channel centered at 780 nm, the exposure times listed are much shorter, between 24 and 35 ms, and vary relatively little with skin type. The optimal exposure time for dark skin in the deep blue channel at 430 nm is at t_{max} = 550 ms, due to the low skin reflectance and relatively low optical throughput of the system at this short wavelength. Even with an exposure time this long, therefore, the image is less than fully exposed. Greater throughput at this wavelength could be achieved, at the expense of poorer response in the infrared.

In Table 1, the FWHM at 450 nm, is 100 nm, which is much broader than for other wavelengths. It has been found that where images are desired for visual analysis as well as computer processing, the broad wavelength band at 450 nm more closely matches the blue response of the human eye and is therefore preferred. In addition, the broad wavelength band provides data at a higher signal-to-noise ratio.

Table 1 appears below:

Optimal Exposure Times (msec) vs. Skin Color

Filter Number (j=i-l)	Center Wavelength (nm)	Filter FWHM (nm)	Very Light Skin	Medium Skin	Tan Skin	Dark Skin
0	430	60	405.2	436.5	484.4	550.0
9	450	100	106.8	124.9	156.1	273.3
1	500	40	56.4	62.9	88.7	130.7
2	550	10	44.2	50.4	71.3	92.9
3	600	10	19.1	24.0	29.6	39.2
8	650	10	74.5	92.3	104.9	132.0
4	700	10	71.6	86.0	98.0	114.4
5	780	30	25.8	29.1	34.9	23.6
6	880	50	34.1	38.6	44.8	46.1
7	950	60	161.1	187.6	205.8	212.0

Tables similar to Table 1 can be readily constructed based on experimental results for other applications, where other spectral bands may be better suited. For example, in the analysis of wound healing, where it would be desirable to distinguish oxygenated from deoxygenated blood, other spectral bands could be better suited to identify the degree of oxygenated hemoglobin. In addition, the wavelengths and exposure times in Table 1 reflect a balance between the best results for subsequent analysis of the images by a computer, and the best results for visual observation of the images. If visual observation is not necessary, other wavelength bands and exposure times may be used.

FIG. 3(a) describes how the systems and methods of the present invention provide for calibration of the recorded images. The calibration procedure permits 10-bit image data to be recorded over a large linear dynamic range in each spectral band, independent of skin type. The recorded images can also be standardized for diffuse spectral reflectance. Consistent measures of reflectance ratios in different spectral bands can therefore be obtained, despite variations in illumination pattern with wavelength, changes in the position of the illuminator, or aging of the lamp, for example.

First, the effects of dark current and "fixed pattern noise" are removed in Step 1. N images are recorded by the camera without illumination. Preferably 8 such dark images are recorded. The average of these N dark images, I_D is calculated and stored in the computer 12.

Second, spatial in homogeneities in the illumination and in the response associated with each CCD pixel are removed in Step 2. A sequence of N' images of an illuminated flat, diffuse reflectance standard, such as a white Spectralon® target (R>99%) recorded. As above, N' is preferably 8. The N' images are recorded at each wavelength band. To average over local inhomogeneities in the reflectance standard, the target is moved continuously during the integration time and between exposures. A small motor, such as a reciprocating motor, may be used. The integration time and/or lamp intensity are adjusted by the computer 12 at each wavelength band until negligibly few of the pixels are at or just below an intensity level corresponding to saturation. These N' "flat-field" images are averaged to reduce the effect of spatial non-uniformities in the reflectance standard, as well as to improve the detection signal-to-noise ratio. The resulting averages are stored in the computer as I_{wi}, where i=1,2,...M.

Next, monochromatic "raw data" images of the skin, I_{si}, are captured by the camera and digitally acquired by the computer 12 within each filter passband, i=l,2,...M. If dermoscopic imaging is used, where a thin layer of mineral oil is spread between the skin and a cover glass is fixed in position in front of the camera, each image of the skin preferably contains an image of a narrow strip of oil-free, diffusely reflecting gray material, held in place on the inside surface of the cover glass, and located along one edge of the field of view. The material may be cut out of a Kodak "18% gray" card. Dermoscopic imaging is preferred for melanocytic lesions. The alternative clinical imaging mode is preferred for the imaging of wounds and burns because contact with the wound or burn by a cover glass is not desired. Although FIG. 2 indicates a lesion present on the skin 2, it will be readily understood that the same method will apply when a wound or burn is present, instead. In the clinical imaging mode, it is preferable to reduce specular reflections by employing the polarizer 31, as indicated in FIG. 2.

In either the dermoscopic or clinical imaging techniques, a fourth step is preferably provided, in which the raw data is compensated for dark current and fixed pattern noise and then normalized to the flat-field images. The dark-field compensation is performed by subtracting the stored average dark image I_D both from the flat-field image I_{wi} and from the raw data image I_{si}. The ratio of the results of

these subtractions is then taken. This standardizes the dark-corrected raw data to the flat-field image, compensating for spatially varying illumination and pixel-to-pixel response variations. After the ratio is taken, the result is standardized to the maximum level, 2^b-1 which equals 1023 where b = 10 in a 10-bit data representation. The normalization process thus converts the image of the skin and the gray strip into a standardized diffuse reflectance map, with the result preserving a large linear recording dynamic range. In FIG. 3(a), the dark-field corrected and flat-field-normalized images, also referred to as "flat-field-calibrated" images, are denoted as I_{si}. In any image, standardization to maximum level can be reinterpreted directly in terms of equivalent diffuse reflectance on the basis of the average gray level over the image of the gray strip, $\langle I_{gray\ strip} \rangle_i$ and the measured average diffuse reflectance of the gray strip, which is approximately 0.2 and varies in a known and repeatable manner with wavelength.

Preferably, the average image intensity in the gray-strip region is also used to calculate weighting factors for combining three or more monochromatic images to provide "true-color" visualizations of lesion images on the computer 12 and display 19. This is preferably accomplished in Step 5, where the user selects the spectral bands to be used in the color visualization. Step 5 can take place prior to the imaging session. Four bands are currently preferred for such visualization. Filter bands j=3 and 8, in a 3:2 ratio, for the red (R) channel, filter band j=2 for the green (G) channel, and filter band j=9 for the blue (B) channel, in Table 1. As indicated in Step 6 of FIG. 3(a), the relative weights applied to the R:G:B channels are preferably inversely proportional to $\langle I_{gray\ strip} \rangle_i$ the average intensity over the portion occupied by the gray strip area in each image. This procedure tends to reconstruct the hues and saturations in the original scene to within accuracy limits associated with response nonlinearities of the display 19. To minimize the effects of such nonlinearities with display monitors such as the Sony Model GDM-175E1 Multiscan monitor, for example, the viewer may prefer to adjust the maximum brightness in the image to correspond to the maximum image intensity level of the monitor. A linear transformation step, which can be readily accomplished by commercial software such

as Adobe Photoshop, may be used. If the digital images are derived from photographic slides, as in the embodiment of Fig. 1(c), steps 5 and 6 are not necessary.

As indicated by dashed lines in FIG. 3(a), either the normalized monochromatic images resulting from Step 4 or the color visualization provided from Step 6 can be displayed on the display 19. Any or all of the monochromatic raw images could be displayed as well.

Fig. 3(b) is a flow chart of a preferred method of processing images according to the present invention for characterizing the condition of a region of interest of the skin of a subject which includes a skin lesion. A skin lesion is selected in Step 50. Digital images of the lesions illuminated by light filtered at the desired wavelengths of λ_1 -λ_4..., are digitally recorded in Steps 52, 54, 56 and 57..., as described above. Each of these digital images is processed separately. In Step 58, the image taken in a spectral band wherein the amount of light re-emitted by abnormal skin is less than the amount of light re-emitted by normal skin, is used to create a mask for segmentation. Preferably, the image used for segmentation is the image of the shortest available spectral band. A blue spectral band is preferred. At Steps 60, 62, 64, 65..., each of the images of the lesion that correspond to different wavelengths are segmented by means of the segmented mask obtained at Step 58. Alternatively, one or all of the images may be separately segmented. Estimated values of lesion parameters are computed from each of the segmented images, in Step 66. Lesion parameters found to be useful for classifying and characterizing the lesion and statistical methods for computing the estimated values of the parameters, are discussed further, below. The estimated values of the parameters are provided to a linear classifier in Step 68. The linear classifier employs a linearly weighted sum of the individual parameters to derive a value used to classify the lesion as malignant or benign. A non-linear classifier such as a Gaussian quadratic classifier or an artificial neural-net classifier, each employing a suitable defined merit function, may be used as well. In either case, the numerical value produced by the classifier is subjected to a threshold test at Step 100, such that if the test is passed, the lesion is suspected to be malignant melanoma. If the test is failed, the lesion is declared not to be melanoma. The lesion could also be characterized as invasive or non-invasive with a different classifier.

If automatic segmentation is not successful in step 58, i.e., a closed boundary curve is not formed at the first spectral band chosen, the next lowest spectral band is used. This process may be repeated at a predetermined sequence of spectral bands. If segmentation cannot be completed automatically, the operator may intervene to complete the segmentation, as is known in the art.

I. SEGMENTATION

The segmentation algorithms will now be described. The function of the segmentation algorithms is to discriminate between the lesion and normal skin in the field-of-view of the imaging device. This is a complex function since not only is the lesion appearance highly variable but so is the appearance of healthy skin due, for example, to the presence of blotches, hair, wrinkles, etc. The automatic algorithm described here is based on the images in the blue spectral band, from about 400 nanometers (nm) to 500 nm. This spectral band was selected because melanin absorption increases rapidly as the wavelength decreases. While the use of ultraviolet radiation could be advantageous, since ultraviolet radiation is carcinogenic, only low doses can be used.

Segmentation in blue consists of several automatic steps:

Location of major peaks in the histogram

First, the histogram of intensity levels in the whole image is determined. Then, given a sliding window with the range of $(2I_r + 1)$ intensity levels, the number of peaks Np in the histogram over that range is determined. If $Np < 2$, the range is decreased by two levels and if $Np > 3$, the range is increased by two levels and the process is repeated until $Np = 2$ or 3. For most of the images in the data base used in this study, there are two major peaks in the histogram. Examples of such histograms are shown in Fig. 4(a) for a malignant melanoma and in Fig. 4(b) for an atypical melanocytic nevus. The lesions correspond to the lower intensity peak, since it is darker than the surrounding skin due to strong absorption by melanin at 400 nm. However, some lesions are quite inhomogeneous, and the automatic procedure described can find 3 major peaks, as illustrated in Figs. 5(a) and 5(b).

Location of the intensity threshold

If two major peaks are found in the intensity histogram, then the threshold value I_{th} is selected to be at the histogram minimum between these two peaks, as indicated in Figs. 4(a) and 4(b). In the case of three peaks, it has been found that, if the middle peak is closer to the lowest intensity peak, the threshold value is at the minimum between the middle and the highest intensity peak. If the middle peak is closer to the highest intensity peak, then the threshold value is at the minimum between the middle and the lowest intensity peak, as shown in Figs. 5(a) and 5(b).

Iterative thresholding of the image

The next step in image segmentation is iterative thresholding of the images. Given the intensity threshold value, image thresholding has been typically accomplished as follows. The intensity $I(x,y)$ of a pixel at location (x,y) is set to zero if it exceeds I_{th}, i.e.,

$$I_L(x,y) = \begin{cases} I(x,y), & \text{if } I(x,y) < I_{th}; \\ 0, & \text{otherwise}. \end{cases} \quad (1)$$

Figs. 6(a) and 6(d) are examples of digital images of malignant melanoma and atypical melanocytic nevus in the blue spectral band, respectively. Figs. 6(b) and 6(e) are images resulting from the direct thresholding as in Eq. (1). As shown in Figs. 6(b) and 6(e), "holes" can appear within the lesion. Therefore, an iterative approach is preferably used. First, the intensity of pixels at the image edges is set to zero. Then as each iteration proceeds, the intensity $I(x,y)$ of a pixel at location (x,y) is set to zero if it exceeds I_{th} and at least one of its nearest neighbors has zero intensity, i.e.,

$$I_L(x,y) = \begin{cases} 0, & \text{if } I(x,y) \geq I_{th} \text{ and } N_{nn} = 0; \\ I(x,y), & \text{otherwise}, \end{cases} \quad (2)$$

where

$$N_{nn} = \min[I(x-1,y), I(x+1,y), I(x,y-1), I(x,y+1),]. \quad (3)$$

This procedure is iterated until there are no pixels with $I(x,y) > I_{th}$ and a nearest neighbor with zero intensity. Typically, only a few iterations are required to complete this step. The resulting images are shown in Figs. 6(c) and 6(f).

Figs. 7(a) and 7(d) are other examples of digital images of malignant melanoma and atypical melanocytic nevus, respectively. Figs. 7(b) and 7(e) are images resulting from the iterative thresholding described above. Various dark blobs are seen in the images outside of the lesion area. These are removed in the following step.

Image cleaning

Some of the blobs in the thresholded images arise naturally due either to dark spots on the normal skin or to hair as in Fig. 7(b). Others are artifacts such as the film edge at the top of the nevus image in Fig. 7(e), or dark bands at the image edges from the slide mounts. These bands are removed by automatically testing for their presence and then setting the intensity of appropriate pixels to zero. The remaining blobs could also be removed by determining the overall number and size, i.e., number of pixels, of connected blobs, and then setting to zero the intensity of pixels belonging to the small ones. However, since the size of some lesions exceeds 100,000 pixels, this would be computationally very intensive. Therefore, in practice, this step is preferably carried out as follows. First, perimeter pixels for all blobs in the image are located. The number of such pixels is typically less than 10,000. Then, each of these perimeter pixels is assigned to a unique blob and its size, the number of perimeter pixels in the blob, is determined. The intensities of pixels belonging to blobs of size less than 30% of the maximum size for that image are set to zero. This process is iterated until all the small blobs are removed. Typically less than 10 iterations are needed. The intensity of all the nonzero pixels is then set to 1. The resulting binary lesion mask has the following property:

$$I_B(x,y) = \begin{cases} 1, & \text{if pixel at } (x,y) \text{ belongs to lesion ;} \\ 0, & \text{otherwise.} \end{cases} \qquad (4)$$

Figs. 7c) and 7(f) illustrate the resulting lesion masks.

In the images illustrated in Figs. 7(a) and 7(d), dark hairs were either absent or were not adjacent to the lesion. However, there are many images with prominent dark hair overlapping lesions. Segmentation of such images is described in the following section.

Segmentation of images in presence of hair

Figs. 8(a) and 8(e) are examples of lesion images with hair. Since the segmentation algorithm described in the previous section would leave some of these dark hairs connected to the lesion, images with hair require special preprocessing to allow for hair removal from the normal skin. Since hair is a problem because of its high contrast with respect to the normal skin in the blue, a spatial filter was designed to locate hairs. This filter, shown in Fig. 9, is magnification dependent. It is applied to every pixel of the original image and the result is thresholded at the 5% of maximum value in the whole filtered image. The filtered images are shown in Figs. 8(b) and 8(f) in reverse intensity contrast, wherein bright features are dark. Hairs are clearly located in the filtered images. It should be noted that the lesion interior is almost entirely blank, indicating poor contrast between hair and lesion.

Hairs are removed by an averaging process. For every non-zero pixel at (x, y) in the filtered image one finds the locations of 4 nearest pixels (x_l,y), (x_u,y), (x,y_l), (x,y_u) (where $x_l < x < x_u$ *and* $y_l < y < y_u$) with zero intensity. Then the intensity of every pixel in the original image that has non-zero intensity in the filtered image is replaced as follows:

$$I_n(x,y) = \frac{1}{12}\sum_{k=1}^{3}[I(x_u + k, y) + I(x_l - k, y) + I(x, y_u + k) + I(x, y_l - k)]. \qquad (5)$$

The images averaged in this way are shown in Figs. 8(c) and 8(g). It is seen that the contrast between hairs and normal skin is considerably reduced in these images. After this preprocessing, the segmentation algorithm described in the previous section is applied to the averaged image. The final binary lesion masks are shown in Figs. 8(d) and 8(h).

The preprocessing step described above may be used for all lesion images, regardless of the presence of hair, enabling fully automated lesion segmentation. However, since this requires more computation and causes some border blurring, the need for preprocessing due to the presence of dark hair is preferably indicated interactively by an operator, and images preprocessed only when necessary.

Segmentation of images in other spectral bands

Since melanin absorption is strongest in the shortest-wavelength band, the lesion area, which appears as a dark region in the image, appears largest in the blue spectral band. Since longer wavelength radiation penetrates deeper into skin, if the thickness of the melanin-containing layer compensates for the weak absorption, that part of the lesion will appear dark even in the red spectral band. For thick melanomas, with Breslow thickness greater than 1 mm, one expects dark lesions even in the infrared bands. This was observed, for example, by Marchesini et al., Photochemistry & Photobiology, "In vivo spectrophotometric evaluation of neoplastic and non-neoplastic skin pigmented lesions. III. CCD camera-based reflectance imaging," Vol. 62, 1995, pp. 151-154. However, for early malignant melanomas, with Breslow thickness less than 1 mm, great variability of images in the red spectral band has been found. There may be so little contrast between the lesion and the normal skin that direct segmentation is not possible. Therefore, segmentation of lesion images in all spectral bands with wavelength λ uses the binary lesion mask of Eq. (4), obtained in the shortest-wavelength band, here blue, i.e.,

$$I_L(x,y;\lambda) \equiv I(x,y;\lambda) \times I_B(x,y). \qquad (6)$$

Figs. 10(a) - 10(f) are a series of images of the lesions, with their corresponding histograms shown in Figs. 5(a) and 5(b), segmented in the blue, green, and red spectral bands, as indicated. The automatically determined lesion borders are superimposed on the original lesion images. The area of dark regions is largest in the blue.

II. LESION PARAMETER ESTIMATION

Objective and automatic lesion classification requires quantitative algorithms for lesion parameter estimation from their segmented images. Such parameters should be dimensionless, independent of lesion location and orientation in the image, and of the overall image brightness. It is convenient to separate the parameters used here into four broad classes: asymmetry, blotchiness, border, and texture. Parameters with the highest diagnostic accuracy for malignant melanoma are listed in Fig. 11, together with the values of diagnostic accuracy, sensitivity, and

specificity, for a training set of images of 41 malignant melanomas and 104 atypical melanocytic nevi obtained with the imaging system described above, with respect to Fig. 1(a) wherein the monochrome camera 16 was used to digitize slides. The subscript *r*, *g*, or *b* refers to the red, green, or blue spectral band in which the parameter is evaluated. If additional spectral bands are used, then each of the parameters could be computed at the additional spectral bands, as well.

Specific algorithms for these parameters are described below. For simplicity it is assumed that the image pixels are square but the algorithms described below may be implemented for rectangular pixels as well.

Lesion Asymmetry

Asymmetry parameter

The lesion asymmetry parameter is based on moments of the intensity distribution. First, the lesion orientation angle is used to locate the principal axes, which are just the symmetry axes for symmetric lesions. The angle θ is computed from

$$\tan 2\theta = \frac{2 < (x - x_c)(y - y_c) >}{< (x - x_c)^2 > - < (y - y_c)^2 >}, \quad (7)$$

where the lesion intensity centroid is at

$$x_c = < x > \ and \ \ y_c = < y >. \quad (8)$$

The angular brackets in Eqs. (7) and (8) denote an intensity moment, which for any function *f (2, y)* of position in the image can be computed as follows:

$$< f(x,y) > \equiv \frac{\sum_x \sum_y f(x,y) I_L(x,y)}{\sum_x \sum_y I_L(x,y)}, \quad (9)$$

where I_L *(x,y)* is the segmented lesion image. In order to compare properties of different lesions, the parameters used are independent of the orientation of the lesion in the image. Therefore, the lesion asymmetry is determined with respect to the principal axes. The measure of asymmetry described here requires rotation of the image by an angle θ so that principal axes are parallel to the image axes. In this principal-axis coordinate system the following asymmetry factors are defined:

$$A_x = \frac{\sum_n \sum_y |I_L(x_c + n, y) - I_L(x_c - n, y)|}{\sum_x \sum_y I_L(x, y)}, \quad (10a)$$

$$A_y = \frac{\sum_x \sum_n |I_L(x, y_c + n) - I_L(x, y_c - n)|}{\sum_x \sum_y I_L(x, y)}. \quad (10b)$$

The asymmetry parameter,

$$A = A_x + A_y, \quad (11)$$

is a measure of asymmetry in the geometric shape of a lesion as well as in the distribution of lesion pigmentation. Asymmetry parameters tend to be larger for malignant melanomas than for atypical melanocytic nevi.

Binary asymmetry parameter

If the intensity distribution I_L in Eqs. (l0a) and (l0b) is replaced by the binary intensity distribution of Eq. (4), then the corresponding asymmetry parameter A_{bin} is the fraction of the lesion pixels which do not have a counterpart on the other side of the principal axis. Thus, when based on the binary intensity distribution, parameter A_{bin} is a measure of the asymmetry of the geometric shape of the lesion.

Lesion Blotchiness

Visually, many early malignant melanomas appear blotchy. In multispectral images there may be darker and lighter regions or blotches of rather homogeneous intensity. In color images, in contrast, there may be regions of different colors. Therefore, it is of interest to quantify such blotchiness in order to differentiate malignant from benign lesions.

Blotchiness Parameter Based on Spatial Intensity Distribution

The lesion is divided into N_t "topographic" regions. If I_{max} and I_{min} are the maximum and minimum intensities in the lesion in some spectral band, respectively, then a pixel at *(x,y)* belongs to the *n*th region if

$$I_{\min} + (n-1)\frac{I_{\max} - I_{\min}}{N_I} \le I_L(x, y) < I_{\min} + n\frac{I_{\max} - I_{\min}}{N_t}. \quad (12)$$

For *n*th topographic region defined in Eq. (12), a distribution of distances of pixels in that region from the intensity centroid of the binary lesion mask

$$d_n(x,y) = \sqrt{(x_n - x_c)^2 + (y_n - y_c)^2} \tag{13}$$

is obtained and its mean value $< d_n >$ and variance $Var(d_n)$ are computed. The measure of lesion blotchiness based on spatial intensity distribution is

$$Bl = \frac{\sum_{n=1}^{N_t} \sqrt{Var(d_n)}}{\sum_{n=1}^{N_t} < d_n >}. \tag{14}$$

This parameter can be evaluated in every spectral band.

Blotchiness Parameter Based on Centroids

The lesion is again divided into N_t "topographic" regions as defined in Eq. (12). An intensity centroid $(x_c(n), y_c(n))$, defined in Eqs. (8) and (9), is then computed for each such region separately. The blotchiness parameter based on the centroid is defined as

$$C = (X_{\max} - X_{\min})(Y_{\max} - Y_{\min}) / A_l \tag{15}$$

where, for example, X_{max} is the maximum value of $x_c(n)$, and A_l is the lesion area in pixels. This blotchiness parameter is also determined in each spectral band separately.

Blotchiness Parameter Based on Spatial Color Distribution

The "color" in this analysis is not related to the visual perception of color. It is a quantitative descriptor of the relative intensities in red, blue, and green channels in a particular pixel.

All the other lesion parameters described here involve analysis of images in each spectral band separately. Therefore, absolute calibration of image intensities was not necessary. However, in order to describe the color distribution, normalization of intensities in red, green, and blue spectral bands is needed, so that intensities in the three channels are equal for white. In the spherical color coordinate system,

$$R(x,y) = \frac{I_R(x,y)}{I_R(x,y)+I_B(x,y)+I_G(x,y)},$$
$$G(x,y) = \frac{I_G(x,y)}{I_R(x,y)+I_B(x,y)+I_G(x,y)}, \quad (16)$$

where the subscripts *R, G, B* refer to red, green, and blue spectral bands, are chosen as the independent variables. The lesion is then divided into color regions as follows. First *R(x,y)* and *G(x,y)* are divided into N_R and N_G topographic regions. A color region is defined as a particular combination of two topographic regions. The total number of color regions is

$$N_C = N_R \times N_G . \quad (17)$$

The blotchiness parameter based on color is defined in analogy with Eq. (14):

$$CI = \frac{\sum_{n=1}^{N_C}\sqrt{Var(d_n)}}{\sum_{n=1}^{N_C} < d_n >} \quad (18)$$

Lesion border

Border Irregularity Parameter

Border irregularity is a well-known feature of malignant melanomas. It is typically defined as the ratio of the measured lesion perimeter to the perimeter of a circle with the same area as the lesion. Since perimeter is difficult to estimate reliably, a statistical descriptor of border irregularity is used here. In addition, many lesions are elongated and an ellipse is a better approximation for such lesions with regular borders than a circle.

Using the binary lesion mask of Eq. (4), the lesion intensity centroid from Eq. (8), orientation angle from Eq. (7), area, and the aspect ratio defined as

$$AR = \frac{\sqrt{< x' - x_c >^2}}{\sqrt{< y' - y_c >^2}}, \quad (19)$$

where primes refer to the coordinate system defined by the lesion principal axes, are determined. These values are then used to construct an ellipse that is the best regular approximation to the lesion border. For each lesion border pixel at (x_b,y_b), its angle with respect to the horizontal axis:

$$\phi = \tan^{-1}\frac{(x_b - x_c)}{(y_b - y_c)}, \tag{20}$$

and the location of the ellipse border for the same angle $(x_e(\phi), y_e(\phi))$ are determined. The distribution of distances between the ellipse border and lesion border:

$$d_{eb}(x_b, y_b) = d_b(x_b, y_b) - d_e(\phi), \tag{21}$$

where

$$d_b(x_b, y_b) = \sqrt{(x_b - x_c)^2 + (y_b - y_c)^2} \tag{22}$$

and

$$d_e(\phi) = \sqrt{x_e^2 + y_e^2}, \tag{23}$$

is obtained and the border irregularity parameter is defined as

$$B = \frac{\sqrt{Var(d_{eb})}}{< d_b >}. \tag{24}$$

Border Gradient Parameter

Another parameter that quantitatively characterizes lesion border is the measure of intensity gradients across the lesion borders over the length scale defined by n_g, in units of pixels. For each lesion border pixel at (x_b, y_b) one determines whether pixels at $(x_b \pm n_g, y_b \pm n_g)$ are at the border. If they are not, then the gradient is defined as

$$G(x_b, y_b) = \frac{1}{2}[|I(x + n_g, y) - I(x - n_g, y)| + |I(x, y + n_g) - I(x, y - n_g)|]; \tag{25a}$$

otherwise, if pixels at $(x \pm n_g, y)$ are not on the border,

$$G(x_b, y_b) = |I(x + n_g, y) - I(x - n_g, y)|, \tag{25b}$$

or, if pixels at $(x, y \pm n_g)$ are not on the border,

$$G(x_b, y_b) = |I(x, y + n_g) - I(x, y - n_g)|. \tag{25c}$$

The border gradient parameter is defined as

$$G = \frac{\sqrt{Var(G)}}{< G >} \tag{26}$$

Lesion Texture

The description of lesion texture is particularly vulnerable to subjective judgement. The quantitative evaluation of lesion texture parameters is possible only using computer-based image analysis. While many such parameters are possible, those found to be helpful in discriminating between malignant melanomas and atypical melanocytic nevi are described below.

Texture Parameters Based on Local Intensity Variations

Texture parameters are defined over a length scale n_t in units of pixels. For example, consider a pixel located at *(x,y)* in the lesion. Let I_l and I_u be the minimum and the maximum intensities in an image in the $2n_t + 1$ x $2n_t + 1$ window around this pixel, i.e., in the range $[x - n_t, x + n_t]$ *and* $[y - n_t, y + n_t]$. Consider a variable

$$C_1(x,y) = \frac{I_u - I_l}{I_l} \tag{27}$$

The first two texture parameters are defined as:

$$T1 = \frac{\sqrt{Var(C_1)}}{< C_1 >} \tag{28}$$

and

$$T2 = \sqrt{Var(C_1)} \tag{29}$$

Another texture parameter uses the following variable:

$$C_3(x,y) = 4w(0,0) + w(-n_t,0) + w(n_t,0) + w(0,-n_t) + w(0,n_t), \\ -2[w(-n_t,-n_t) + w(-n_t,n_t) + w(n_t,-n_t) + w(n_t,n_t)] \tag{30}$$

where

$$w(i,j) = I(x+i, y+j)/I(x,y). \tag{31}$$

If the value of C_3 is negative, it is set to zero and the corresponding texture parameter is

$$T3 = \frac{\sqrt{Var(C_3)}}{< C_3 >}. \tag{32}$$

Another variable that leads to a texture parameter useful for classification of melanocytic lesions is:

$$C_4(x,y) = 8w(0,0) - w(-n_t,0) - w(n_t,0) - w(0,-n_t) - w(0,n_t) - w(-n_t,-n_t) - w(-n_t,n_t) - w(n_t,-n_t) - w(n_t,n_t) \quad (33)$$

Again, if the value of the variable is negative it is set to zero and the corresponding texture parameter is

$$T4 = \frac{\sqrt{Var(C_4)}}{< C_4 >}. \quad (34)$$

Texture Parameters Based on Pigmented Network

Texture parameters have also been developed by considering the properties of a pigmented network. These texture parameters are measures of variability in the area of the dermal papillae and in the aspect ratio (length/width) of the rete ridges.

Since dermal papillae appear as the brighter part of the network, one seeks all the local maxima over a $2n_t + 1$ x $2n_t + 1$ window. Starting from such a maximum at (x_m, y_m), one finds local one-dimensional minima in eight directions (2 vertical, 2 horizontal, and 4 diagonal) and locates the vertices of an octagonal region one pixel closer to the maximum intensity pixel than the minimum pixel. Such octagonal regions approximate the areas of dermal papillae A_{dp} which are computed from the known location of vertices; the corresponding texture parameter is

$$T5 = \frac{\sqrt{Var(A_{dp})}}{< A_{dp} >}. \quad (35)$$

Some of the areas determined by this algorithm are due to bubbles visible in some of these dermoscopic images. However, since there are typically on the order of hundreds of areas, and on the order of tens of bubbles, the statistical parameters should not be significantly biased by this artifact.

The aspect ratio of rete ridges is determined in a similar fashion, although one starts with local minima since rete ridges appear dark in the images. The vertices of an octagonal region are determined in this case from one-dimensional maxima in the eight directions. The maximum and minimum extents of this region are then determined and the aspect ratio R is computed. This texture parameter then is

$$T6 = \frac{\sqrt{Var(R)}}{< R >}. \tag{36}$$

III. LESION CLASSIFICATION

Selection of lesion parameters for classification was done by determining the maximum diagnostic accuracy for malignant melanoma for each parameter computed in every spectral band available for the training set of images. As mentioned above, diagnostic accuracy, sensitivity to malignant melanoma and specificity for the selected twenty two parameters are shown in Fig. 11. These parameters were then used as input to the linear classifier. Nonlinear classifiers may be used as well.

For each lesion k the linear classifier is

$$L(k) = \sum_{n=1}^{22} w_n X_n(k), \tag{37}$$

where $X_n(k)$ are the parameters for the kth lesion and weights w_n are to be determined so that a specified function $F(L)$ attains maximum value. The following functions $F(L)$ were used: 1) specificity under constraint of 100% sensitivity to malignant melanoma for the training set which included 41 malignant melanomas and 104 atypical melanocytic nevi; (2) classification accuracy for the 24 invasive and 16 noninvasive malignant melanomas of the training set; and 3) correlation with the Breslow thickness for the 24 invasive malignant melanomas.

Given any training set of lesion images and corresponding set of lesion image parameters, the weights that maximize $F(L)$ are found as follows. First, an initial range and resolution Δ for w_n are selected. For each allowed set of values of w_n, the values $L(k)$ are computed for each lesion. The value $F(L)$ is determined based on the input from histopathological evaluation of the lesion based on a biopsy, such as the diagnosis of the lesion as benign or malignant, and the Breslow thickness for a malignant melanoma. The range of w_n's is adjusted until the maximum value of $F(L)$ is inside the range. Then the resolution Δ is reduced by a factor of two, and the process is repeated until Δ reaches specified minimum value Δ_{min}. This procedure determines the weights w_n only up to a multiplicative constant. It is noted that the classifiers resulting from a particular training set are applicable only to images with a specific spatial and

spectral resolution, and that lesion images obtained with a different imaging system may require the development of different classifiers, by the procedures described above.

Since detection of melanoma in its early stage significantly improves prognosis, there is a need for reliable methods of early detection. Clinical evaluation of melanocytic lesions is, however, a problem since reliable differentiation between early malignant melanoma with Breslow thickness less than 1 mm and atypical melanocytic nevus is difficult even for experienced dermatologists. In order to detect as many early melanomas as possible, weights in the linear classifier are preferably chosen to maximize specificity under the constraint of 100% sensitivity to malignant melanoma for the training set. For each set of weights, one finds the threshold value L_{th} of the linear classifier such that a L_{th} lesion is classified as suspicious of malignancy if $L(k) > L_{th}$, and as benign otherwise. The resulting classifier for the training set is

$$\begin{aligned} L_1 = {} & 0.025A_{bin} + 0.090A_b + 0.069A_g + 0.160A_r + 0.128C_b \\ & + 0.095Cl + 0.038B + 0.107T1_g + 0.064T2_g + 0.018T2_r \\ & + 0.111T3_b + 0.167T3_g + 0.268T5_b \end{aligned} \qquad (38)$$

where the weights are normalized so that the threshold value equals one. This classifier with sensitivity to malignant melanoma of 100% and specificity of 85% is shown in Fig. 12. Statistical significance of the specificity and sensitivity was assessed by considering the binomial probabilities for the value of L_1 to exceed the threshold for the 41 malignant melanomas and 104 atypical melanocytic nevi of the training set separately. At the 95% confidence level, one finds that sensitivity is not less than 93% while specificity is not less than 79%. Since there are several melanomas very close to the threshold value, a practical classifier may use a threshold value that is less than one. It has been found that this set of 145 images is sufficient to yield statistically significant results. A greater number of images may be used, as well.

Some of the noninvasive melanomas, called melanomas in-situ, are confined to epidermis and are 100% curable by surgery. The invasive melanomas, i.e., superficial spreading melanomas in our data base, require more extensive surgery. Therefore, it is of clinical interest to differentiate between invasive and noninvasive melanomas and a linear classifier was trained to perform this task. This classifier, with

weights chosen to maximize the overall classification accuracy for the 24 superficial spreading melanomas and 16 melanomas in-situ of the training set is

$$L_2 = -1.00A_b - 0.14Bl_g - 2.47Bl_r - 0.4C_b - 0.98Cl \\ -1.17T2_r + 0.53T4_b + 1.98T5_b + 1.58T6_b - 0.73 \quad (39)$$

where a constant was subtracted from the classifier values to obtain the threshold value of zero. This classifier, with overall classification accuracy of 92.5%, is shown in Fig. 13.

Since prognosis for invasive melanomas correlates strongly with the Breslow thickness, a linear function of lesion parameters Q was trained to maximize the Pearson correlation coefficient between Q and the Breslow thickness for a set 24 superficial spreading melanomas. This function is

$$Q = 0.955A_g - 1.391A_r + 2.791Bl_b - 1.320Bl_g + 0.146C_b \\ + 0.267C_r - 0.506B + 0.202T1_g + 1.476T2_r - 0.485 \quad (40)$$

and is shown in Fig. 14. Even though there are only 24 superficial spreading melanomas in the data base, the high correlation of 0.77 is statistically very significant since $p = 9 \times 10\text{-}^6$.

The classifiers of Eqs. (38)-(40) are applicable to the imaging system described above, with respect to Fig. 1(a) wherein the monochrome camera 16 was used to digitize slides.

For other imaging systems, having different spatial and spectral resolution, different classifiers may need to be developed, based on a sufficient data base of lesion images obtained with that imaging system, in accordance with the procedures described above.

The segmentation, parameter estimation and classification programs described in Sections I-III, above, can be implemented on any personal computer, using a programming language, such as FORTRAN or C. The program can be stored on any convenient media readable by a computer, such as read only memory, ("ROM"), random access memory with a battery backup, electrically programmed ROM (EPROM), electrically erasable ROM (EEPROM), floppy disc, CD ROM, or a hard disc. Other suitable media may be used, as well.

While the procedures of Sections I-III were described with respect to digital images obtained by imaging color photographic slides of skin lesions with a monochrome CCD camera 16 in accordance with the system of Fig. 1c, these procedures are readily adaptable to the analysis of digital images of skin lesions acquired directly from the region of interest of the skin with a digital electronic camera, such as the monochrome CCD camera 6 of Fig. 1a and Fig. 2. Preferred parameters for direct digital imaging of a region of interest of skin are described, below.

In the process described in Sections I-III, above, segmentation was conducted in the blue wavelength band. The segmented mask in blue was then applied to images in the red and green wavelength bands. Where images at additional wavelengths are provided, segmentation is preferably first attempted at the shortest available spectral band in which the amount of light re-emitted by skin is different within skin having an abnormal condition than within skin having a normal condition. The contrast between the melanocytic lesion and normal skin tends to be highest at the shortest spectral band because melanin close to the skin surface generally has the highest absorption and causes the greatest scattering. In other skin conditions, such as wounds or burns, other chromophores, such as hemoglobin, tend to produce strong absorption and scattering.

SECTION IV

ESTIMATION OF OTHER PARAMETERS

In addition to the new parameters defined in Section II, above, the values of conventional dermoscopic parameters may also be incorporated into the classifier. For example, a dimensional parameter which is a function of the length of a principal axis of the segmented image, may additionally be used. Whether or not the length of the principal axis of a skin lesion exceeds a suitable threshold, such as 6 mm, may be incorporated into the classifier.

Values for the standard deviation of reflectance and the mean reflectance may also be used. The ratio between the standard deviation and the mean has been found to be useful.

Wavelet maxima representations may also be used to compute estimated values of the texture and other parameters of a skin lesion or other skin condition, separately or in conjunction with the non-wavelet derived parameters described, above. Values of lesion parameters may be estimated by the following steps:

(1) segmenting each of the digital images in each spectral band, preferably automatically;

(2) subdividing each digital image into border and interior regions of the lesion;

(3) applying the dyadic, multiscale, continuous wavelet transformation ("CWT") to the digital image in each spectral band;

(4) producing wavelet maxima representations ("WMRs") of the CWT in the border and interior regions of each image at each spectral band; and

(5) computing estimated values for rotation-and translation-invariant statistical parameters from the WMRs, to characterize the textures of the border and inside regions, for each image.

Preferably, the segmentation mask is created in one spectral band in accordance with the procedure described in Section I, above, separating the skin lesion from the remaining skin in the region of interest. Then, that segmentation mask is used to define the lesion/skin "border region" separately, in each of the spectral bands. Any or all of the images may be segmented and subdivided independently, as well.

To define the border region, pixels assigned to the lesion (within the segmentation mask), which border on pixels assigned to normal skin (outside of the segmentation mask), are used to define centers of circular regions. For skin lesions, the center preferably has a fixed 8-pixel radius and a 17-pixel diameter. All pixels lying within such circular regions are assigned to the border of the lesion in each digital image.

All pixels in the neighborhood of each pixel of the image contribute to the CWTs centered within the border and interior regions of each digital image. Each pixel in each region serves as a center of a "mother" wavelet. Each mother wavelet is scaled to span six different "scale wavelets," which play the role of local band-pass spatial filters that can selectively zoom in on different scales in the lesion structures of

interest. See, for example, Daubechies, I, "The Wavelet transform, time-frequency localization and signal analysis.", IEEE Trans Inform Theory 36:961-1005 (1990); Aldroubi, A. et al., Wavelet in Medicine and Biology, C&C Press, NY, pp 11-15 (1996). The fine/coarse filtering that the scale wavelets provide also reduces background noise.

Wavelet maxima representations ("WMRs") are "multiscale" spatial maps that indicate the locations of local maxima of changes in image intensity and provide a quantitative measure of those changes. They are, therefore, suitable for characterizing textures at different "scales". See, for example, Mallat S, Hwang, W L. "Singularity detection and processing with wavelets., "IEEE Trans Inform Theory 38:617-643, 1992; Mallat S, Zhong S. "Wavelet maxima representation." Wavelets and Applications, Springer-Verlag, Y. Meyer (ed.), NY, pp. 207-284, (1992); Mallat S, Zhong S., "Characterization of signals from multiscale edges.", IEEE Trans Patt Anal Mach Intell 14:710-732 (1992). WMRs are used here to represent the border and the interior regions of each lesion, in each of the spectral bands separately. Differences in texture between the border and interior regions correspond to differences in activity of the wavelet maxima at coarse scale and at finer scale.

The coefficient distributions of the WMRs are used to estimate values of statistical parameters for each lesion which are translation- and rotation-invariant. These parameters summarize the image structure in each region and in each spectral band through statistical properties of the wavelet coefficient distribution at each of the spatial-scale levels.

The large number of candidates of wavelet parameters are used individually to train and then to test a classifier, as described in Section III, above. The classifier can be the linear classifier of Equation 37 above, preferably under the constraint of maximizing specificity subject to 100% sensitivity. A non-linear classifier such as a Gaussian quadratic classifier which is designed to minimize a cost function which is a linearly weighted sum of the fraction of missed melanomas, and of the total misclassification error, may also be used. One such Gaussian quadratic classifier is as defined in Fukunaga, K, *Introduction to Statistical Pattern Recognition*; Academic Press, Boston, pp 19-96, 125 (1990). In the process of selecting the best subset of these parameters for classification, the training and testing of the classifier

was based on a "leave-one-out" strategy, for selection of the training set. *Id.* at 219-221.

When using the quadratic Gaussian classifier, the parameters are modeled as elements of a p-dimensional vector, $X=(x_1, x_2, ..., x_p)$, each of which is normally distributed over the malignant (melanoma) and benign (AMN) classes, with (vector) means $M_1=(m_{1\,1}, m_{1\,2}, ..., m_{1\,p})$ and $M_2=(m_{2\,1}, m_{2\,2}, ..., m_{2\,p})$, respectively, and with covariance matrices Σ_1 and Σ_2 (which are generally different), for $p \leq 12$, for example. The quadratic Gaussian classifier that discriminates between the two classes employs normalized "distances" defined (in standard matrix notation) by:

$$(X-M_i)^T \Sigma_i^{-1}(X-M_i),$$

where Σi_{-1} is the matrix inverse to Σ_1. Mi and Σ_1, are estimated from the available data. In practice, each classifier is developed on the basis of the means and covariances estimated over a training set, and the resulting classifier is then exercised over a testing set. The performance of the classifier is analyzed by studying the sensitivity and specificity achieved as one varies the threshold function:

$$h(X)=f(X,M_1, \Sigma_1) - f(X,M_2, \Sigma_2)$$

where:

$$f(X,M_i, \Sigma_i) = \tfrac{1}{2}(X-M_i)^T\Sigma_i^{-1} (X-M_i) + \tfrac{1}{2}\ln|\Sigma_i|, \; i=1,2,$$

and M_i and Σ_i are estimators of M_i and Σ_i that are obtained from the sampled data sets.

Minimization of the following *cost* function is used to rank parameters that are candidates for use in the classifier:

Cost = α (1-Sensitivity) + (1-α)(1-GlobalError), where Sensitivity = (Number of correctly classified melanomas)/(Total melanomas), GlobalError = (Number of incorrectly classified lesions)/(Total lesions) and α is a constant, preferably between 0.4 and 0.6, and more preferably 0.45.

A limited database of images obtained by directly imaging skin lesions with the system of Fig. 1a was used to develop non-linear and linear classifiers and determine the most useful parameters. The wavelet parameters found most useful in characterizing the skin lesion based on the available database were: 1) the number of

maxima per unit area (per pixel); 2) the mean value of the WMR coefficients, 3) the root-mean-square value of the WMR coefficients, 4) the mean absolute deviation about the WMR coefficients, and 5) the skewness of the WMR coefficients. Preferably, in addition to the number of maxima per pixel, the ratio of the mean value of the WMR coefficients to their standard deviation, the ratio of the mean value to their mean absolute deviation, and the skewness normalized to the cube of the standard deviation, are used.

Two additional wavelet related parameters are referred to as a goodness of fit measure and an intercept measure. The intercept measure is a measurement of the degree of change of a statistic of the wavelet coefficient distribution with increment in wavelet level. The statistic is preferably the average rate of change of the number of wavelet maxima per unit area. One way to compute this average is to determine the level 0 intercept of the best linear fit of the number of wavelet maxima per unit area, with respect to wavelet level.

The goodness of fit measure quantifies the degree of deviation of the intercept measure from linearity. Preferably, the deviation of the number of wavelet maxima per unit area, with respect to level, is estimated.

Another parameter is the slope of the best fit linear trend of the variation in wavelet maxima per unit area, versus wavelet level. This parameter has not been found to be as useful as the other parameters described, based on the limited database of available images.

The large number of wavelet parameters per spectral band, wavelet level and region (border and interior) were evaluated in the same manner as described in Section III above, with linear and non-linear classifiers. It has been found that a combination of certain of the non-wavelet parameters discussed in Section II, above, and parameters estimated through the wavelet maxima representations, gives the best specificity at 100% sensitivity for the data available to date for a quadratic Gaussian classifier.

Table 2, below, indicates the most useful non-wavelet parameters and their center wavelength ("CWL"), the wavelet parameters ("WMR") and their CWL, and the best combination of WMR and non-wavelet parameters and their associated CWL. Each sequence adds the indicated parameter to the parameter or parameters in

the prior sequences. For example, the best single non-wavelet parameter was T1, (texture, Type 1) defined in Equation 28, above, at a wavelength of 950 nm. Better results were obtained when T5, defined in Equation 35, above, at wavelength 500 nm, was added in sequence 2. The parameters of sequences 1-12 identify the twelve best parameters found for characterizing skin lesions with the quadratic Gaussian classifier, above. The other columns of Table 2 are similarly interpreted. The definitions of the abbreviations used in the Table 2 appear below the Table.

When the 12 non-wavelet parameters of Table 2 were used alone, and the threshold in the nonlinear quadratic Guassian classifier was chosen such that all the melanomas in the database were correctly classified (100% sensitivity), the specificity of correct classification of benign lesions was 64%. When 12 WMR parameters were used alone, the specificity was 86%. When the 12 parameters of both types were used, the specificity was 90%.

TABLE 2

Sequence	Non Wavelet	CWL (nm)	WMR	CWL (nm)	Combined	CWL (nm)
1	T1	950	b, I*,	650	b, I*,	650
2	T5	500	b, L3K,	950	T3,	430
3	ASY,	450	b, 1W,	430	b, L6S	600
4	T6,	450	b, L6K,	430	b, L1K,	700
5	T5,	600	I, L6K,	430	T5,	550
6	GRD	430	b, L1K,	430	b, L3K,	650
7	CE,	950	b, L5S,	780	T3,	500
8	STR,	500	I, L3W,	550	B1,	950
9	STR,	430	I, L3A	450	STR,	550
10	T6,	500	b, L5A,	780	I, L3W,	780
11	STR,	550	I, L3A,	430	b, L6W,	650
12	SMR,	789	b, I*,	600	T2,	950

Key to Non-Wavelet Parameters

ASY = Asymmetry, Bl = Blotchiness, CE = Centroid, GRD = Gradient,
SMR = (Std Dev of Reflectance) / (Mean Reflectance),
STR = Std Dev of Reflectance, Tp = Texture, type p

Key to WMR Parameters

b = border region, I = interior region, Ln = Level n = 1,2,...,6

Statistics:

A = (mean coef. magnitude) / (mean absolute deviation)
I* = intercept measure (extrapolated over levels n=1-4)
K = skewness
S = (mean coef. magnitude) / (Std Dev of coef. magnitude)
W = number of wavelet maxima per pixel

Table 3 is a comparable table of preferred parameters with the linear classifier of Equation 37. The abbreviations for parameters not defined above, appear below Table 3.

TABLE 3

Sequence	Non Wavelet	CWL (nm)	WMR Code	CWL (nm)	Combined Codes	CWL (nm)
1	ASY,	450	I, L1K,	550	b, L4S,	880
2	BLr,	430	b, L3A,	780	I, L6A,	880
3	T5,	780	1, L5S,	780	b, L3S,	700
4	T6,	780	I, L6K,	880	I, L1K,	600
5	T2,	500	I, L1K,	950	b, L5S	650
6	T2,	550	I, L3W,	450	b, L2S,	700
7	GRD,	780	I, L5K,	450	ASY,	450
8	R1,	950	b, L1K,	780	GRD,	430
9	BL,	950	b, F*,	780	I, L2K,	600
10	T6,	430	b, L4A,	430	T5,	550
11	T5,	430	I, L2K,	600	CE,	450
12	T3,	950	b, L4S,	880	---	---

Key to Additional Non-Wavelet Parameters

BIr = Border Irregularity,
GRD = Gradient, R1 = Mean Reflectance,

Key to Additional WMR Parameters

Statistics:

F* = goodness-of-fit measure (levels n=1,2,3,4)

When the 12 non-wavelet parameters of Table 3 were used alone, and the threshold within the linear classifier was chosen such that all available melanomas are correctly classified (100% sensitivity), the specificity was 91%. With only the wavelet parameters, the specificity was 95%. With the combination of wavelet and non-wavelet parameters, the specificity was 97%. Although these results seem to

indicate that the linear classifier separates the two classes of lesions better than the nonlinear one, it should be recognized that sampling bias effects tend to be greater for a linear classifier.

When a similar analysis of the combination of non-wavelet and wavelet parameters was applied to the digitized images obtained with the system of Fig. 1(c), the linear classifier in Section III, which includes only the non wavelet parameters, was found to be superior than a linear classifier including wavelet parameters. Non-linear classifiers showed superior results with the non-wavelet parameters with the digitized images, as well.

The systems and methods of the present invention may also be used to differentiate between melanoma and different types of benign pigmented lesions. Classification is preferably accomplished through a multiple-step process. For example, if two classes of benign lesion share very different parameter values, as is the case for nevi and seborrheic keratoses, then a two-step classification may be used. Two different linear classifiers (with different weights) are trained as described in Section III, above, to have 100% sensitivity to melanoma; one to differentiate between melanoma and keratosis and the other to differentiate between melanoma and nevus. A lesion is then declared to be benign if at least one of its classifier values is below threshold and malignant if both of its classifier values are above threshold. In general, if there are N types of benign lesions, the N-step classification may be used. In this case the lesion is declared to be malignant if all N of its classifier values are above threshold and benign otherwise.

If other conditions of skin or tissue are to be characterized, the preferred spectral band for generating the mask may be the one in which the amount of light re-emitted is greater within abnormal tissue than for normal tissue. Preferably, the segmented mask is then applied to the images in the other wavelength bands, as shown in the flowchart of Fig. 3b. In addition, while the parameters are described in the terms of the red, green and blue wavelength bands in Sections I-III, parameters can be derived at any of the wavelengths actually used, in accordance with the procedures described in Sections I-III. The parameters in the additional wavelength bands can be readily used to develop an appropriate classifier, also by the processes described in Section I-III.

The condition of a region of interest of skin including wound or burns may be characterized by a quantitative measure of tissue abnormality with respect to normal skin. Classifiers may be developed based on images of wounds of different types or burns of varying degrees of severity, in an analogous manner as described above with respect to skin lesions. The condition of the region of interest could then be characterized as a percentage relative to normal skin, for example, to indicate the extent to which healing has occurred.

The references cited above are incorporated by reference, herein.

While preferred systems and methods for practicing the present invention have been described above, it is understood that departures may be made from the systems and methods, without departing from the scope of the present invention, which is defined by the following claims.

We claim:

1. A method of characterizing the condition of a region of interest of skin, wherein the absorption and scattering of light in different spectral bands by the region of interest is a function of the condition of the skin, the method comprising:

illuminating a portion of the skin including the region of interest by light in at least three spectral bands;

digitally imaging a portion of the skin including the region of interest at the at least three spectral bands with the light re-emitted by the portion of the skin to generate digital images comprising digital signals whose values are a function of the condition of the region of interest of the skin; and

providing the digital images to a processor, wherein the processor:

segments the digital images by generating a segmentation mask defining the boundary of the region of interest from a digital image in any one of the at least three spectral bands;

estimates at least one rotationally and translationally invariant statistical measure of coefficient distributions of the multiscale wavelet maxima representations of the digital images in each spectral band, which are functions of the texture of the region of interest determined by the segmentation mask;

characterizes the condition of the skin based on the estimated values; and

outputs the characterization of the condition of the skin.

2. The method of claim 1, wherein the at least one statistical measure is calculated separately within either of a border region and an interior region of the digital image, wherein:

the border region encompasses the envelope of circles of fixed radius centered on the boundary of the segmentation mask; and

the inside region comprises all points of the image that are within the segmentation mask boundary but not included in the border region.

3. The method of claim 2, wherein the computing step comprises estimating at an individual level at least one value which is a statistical measure of texture of the portion of the region of interest within the border region and interior region, chosen from the group consisting of:

the number of wavelet maxima per unit area;

the ratio of the mean coefficient magnitude to the absolute deviation of the coefficient magnitudes from the mean value;

the ratio of the mean coefficient magnitude to the standard deviation of the coefficient magnitude; and

the skewness of the coefficient magnitude, normalized to the cube of the standard deviation.

4. The method of claim 1, further comprising estimating either of the degree of change of a statistic of the wavelet coefficient distribution with increment of wavelet level, and the degree of deviation of such change from linearity.

5. The method of claim 2, further comprising estimating the average rate of change, with respect to level, of the number of wavelet maxima per unit area.

6. The method of claim 1, further comprising comparing the estimated texture values to the threshold derived from statistical analysis of a multiscale wavelet transformation of the digital image.

7. The method of claim 1, wherein the estimating and characterizing steps are conducted without the intervention of an operator.

8. The method of claim 1, wherein the segmenting step is conducted without the intervention of an operator.

9. The method of claim 1, wherein the illuminating step further comprises illuminating a region of interest including a burn.

10. The method of claim 9, wherein the characterizing step comprises characterizing the condition of the burn with respect to the condition of normal skin.

11. The method of claim 1, wherein the illuminating step further comprises illuminating a region of interest including a wound.

12. The method of claim 11, wherein the characterizing step comprises characterizing the condition of the wound with respect to the condition of normal skin.

13. The method of claim 1, further comprising:

photographing the region of interest with a color camera to form color photographic slides; and

illuminating the color photographic slides with light in each spectral band;

wherein the digital imaging step comprises digitally imaging the illuminated color photographic slides of the region of interest with a digital camera.

14. The method of claim 1, wherein the computing step further comprises estimating a value which is a function of the asymmetry of the segmented image in each spectral band, for two principal axis of the segmented image.

15. The method of claim 1, wherein the computing step further comprises:

locating the principal axes by computing an orientation angle;

computing the intensity centroid;

rotating the digital image such that the principal axes are parallel to the image axes;

estimating asymmetry values for each principal axis based on the intensity centroid; and

summing the estimated asymmetry values for the two principal axes.

16. The method of claim 1, wherein the computing step further comprises computing the intensity moment with a binary intensity distribution.

17. The method of claim 1, wherein the computing step further comprises estimating at least one value which is a function of the blotchiness of the segmented digital image, the estimated blotchiness value being defined through statistical properties of the spatial distribution of topographic regions of the digital images at each spectral band.

18. The method of claim 17, wherein the computing step further comprises determining the centroids of topographic regions of the segmented digital image at each spectral band.

19. The method of claim 1, wherein the computing step comprises estimating a value which is a statistical measure of the deviation of the border of the region of interest from the border of an ellipse of the same area, aspect ratio, and orientation as the segmentation mask.

20. The method of claim 1, wherein the computing step comprises estimating a statistical measure of the gradient values of the intensity of the digital images across the border of the segmented images, at each spectral band.

21. The method of claim 1, wherein the computing step comprises estimating values based on the ratio of standard deviation of the areas of dermal papillae to their mean within the segmentation mask.

22. The method of claim 1, wherein the computing step comprises estimating values of the average and standard deviation of the thickness of rete ridges within the segmentation mask.

23. The method of claim 1, wherein the characterizing step comprises distinguishing multiple times between melanoma and several types of benign lesion.

24. The method of claim 1, wherein the condition of the region of interest to be characterized is the presence of a melanoma and the processor compares a weighted combination of parameter values against a threshold value for melanoma and different types of benign lesions, multiple times.

25. The method of claim 1, wherein the segmentation mask is generated from a digital image in a spectral band in which the amount of light re-emitted by skin is less within skin having an abnormal condition than within skin having a normal condition.

26. The method of claim 1, wherein the segmenting step further comprises segmenting the digital images by generating a segmentation mask in more than one spectral band.

27. A system for characterizing the condition of a region of interest of skin, comprising:

a source of illumination of light in at least three spectral bands;

a camera for acquiring digital images of the region of interest based on the light re-emitted from the illuminated region of interest at each of the spectral bands, the digital image comprising digital signals whose values are a function of the condition of the region of interest;

memory for storing the digital images provided by the camera;

a digital processor programmed to perform the steps of:

segmenting the digital images stored in memory by generating a segmentation mask from a digital image in any one of the at least three spectral bands;

estimating at least one rotationally and translationally invariant statistical measure of coefficient distributions for the multiscale wavelet maxima representations of the digital images in each spectral band, which are functions of the texture of the region of interest determined by the segmentation mask;

characterizing the condition of the skin based on the estimated values; and

outputting the characterization of the region of interest.

28. The system of claim 27, further comprising means for suppressing specular reflections from the region of interest.

29. The system of claim 27, wherein the camera records monochromatic images and the illumination means comprises:

a tungsten halogen light source with feedback to stabilize the intensity in each wavelength band;

means for sequentially filtering the light; and

an optical fiber ring illuminator to distribute the filtered light.

30. The system of claim 29, further comprising a feedback loop for stabilizing the intensity of the light source by the processor.

31. The system of claim 30, further comprising a material of stable reflectance for being illuminated by the light source, wherein the feedback loop includes the monitoring by the processor, of the intensity of light reflected from the material by the processor and the adjustment of the intensity of the light source if the monitored intensity varies from a desired value.

32. The system of claim 31, wherein the power, voltage or current supplied to the light source is monitored.

33. The system of claim 27, wherein the source of illumination is at least one laser.

34. The system of claim 28, wherein the processor estimates the statistical measures separately within either of a border region and an interior region of the digital image, wherein:

the border region encompasses the envelope of circles of fixed radius centered on the boundary of the segmentation mask; and

the inside region comprises all points of the image that are within the segmentation mask boundary but not included in the border region.

35. The system of claim 34, wherein the processor estimates at an individual level at least one value which is a statistical measure of texture of the portion of the region of interest within the border region and interior region, chosen from the group consisting of:

the number of wavelet maxima per unit area;

the ratio of the mean coefficient magnitude to the absolute deviation of the coefficient magnitudes from the mean value;

the ratio of the mean coefficient magnitude to the standard deviation of the coefficient magnitude; and

the skewness of the coefficient magnitude, normalized to the cube of the standard deviation.

36. The system of claim 35, wherein the processor further estimates either of the degree of change of a statistic of the wavelet coefficient distribution with increment of wavelet level, and the degree of deviation of such change from linearity.

37. The system of claim 35, wherein the processor further estimates the average rate of change, with respect to level, of the number of wavelet maxima per unit area.

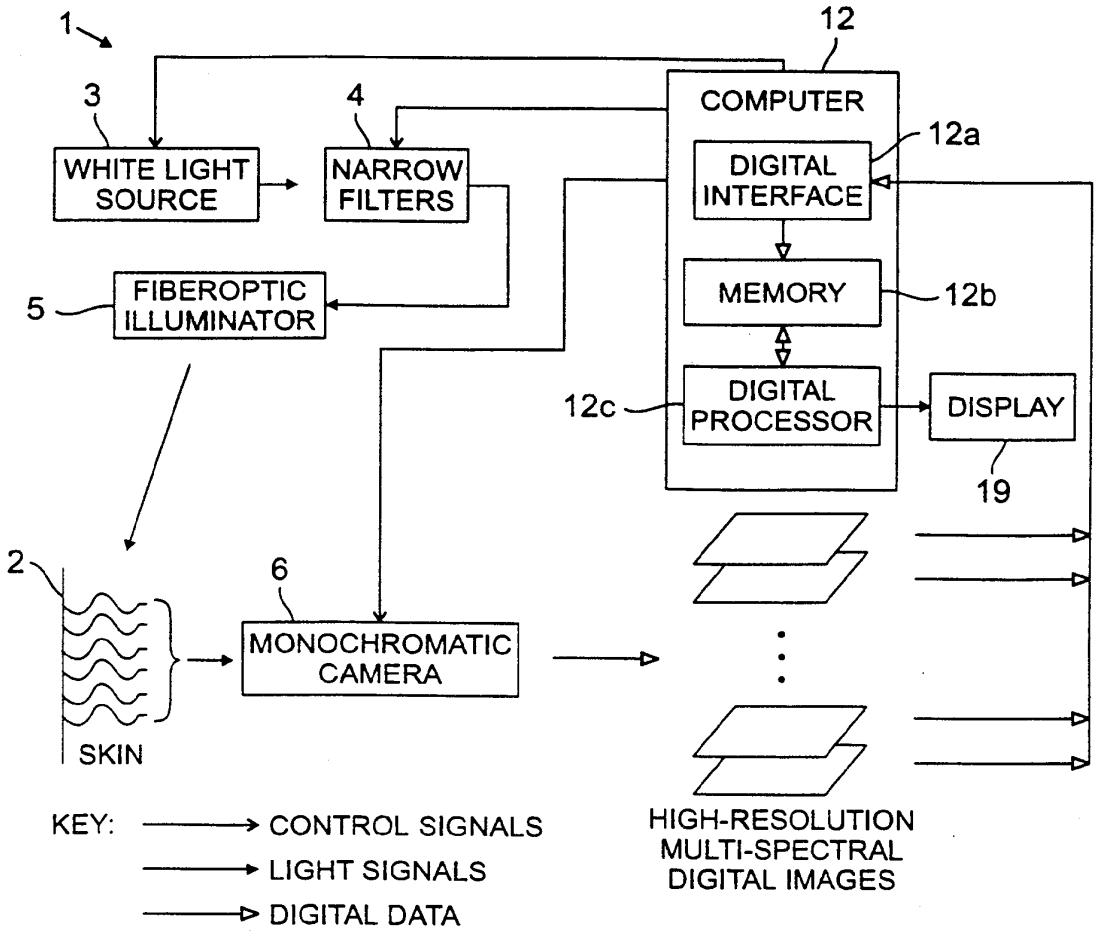
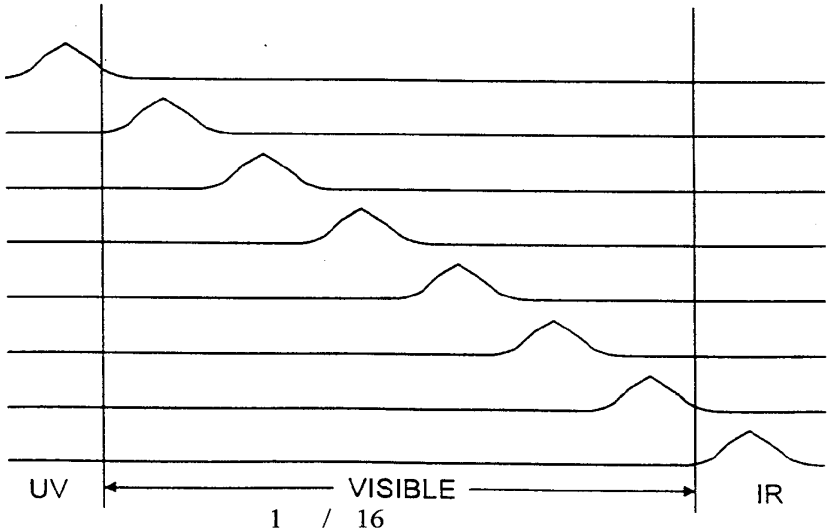

1
12
3
4
COMPUTER
12a
WHITE LIGHT SOURCE
NARROW FILTERS
DIGITAL INTERFACE
MEMORY
12b
5
FIBEROPTIC ILLUMINATOR
12c
DIGITAL PROCESSOR
DISPLAY
19
2
6
MONOCHROMATIC CAMERA
SKIN
KEY:
CONTROL SIGNALS
LIGHT SIGNALS
DIGITAL DATA
HIGH-RESOLUTION MULTI-SPECTRAL DIGITAL IMAGES

FIG. 1a

FIG. 1b


UV
VISIBLE
IR

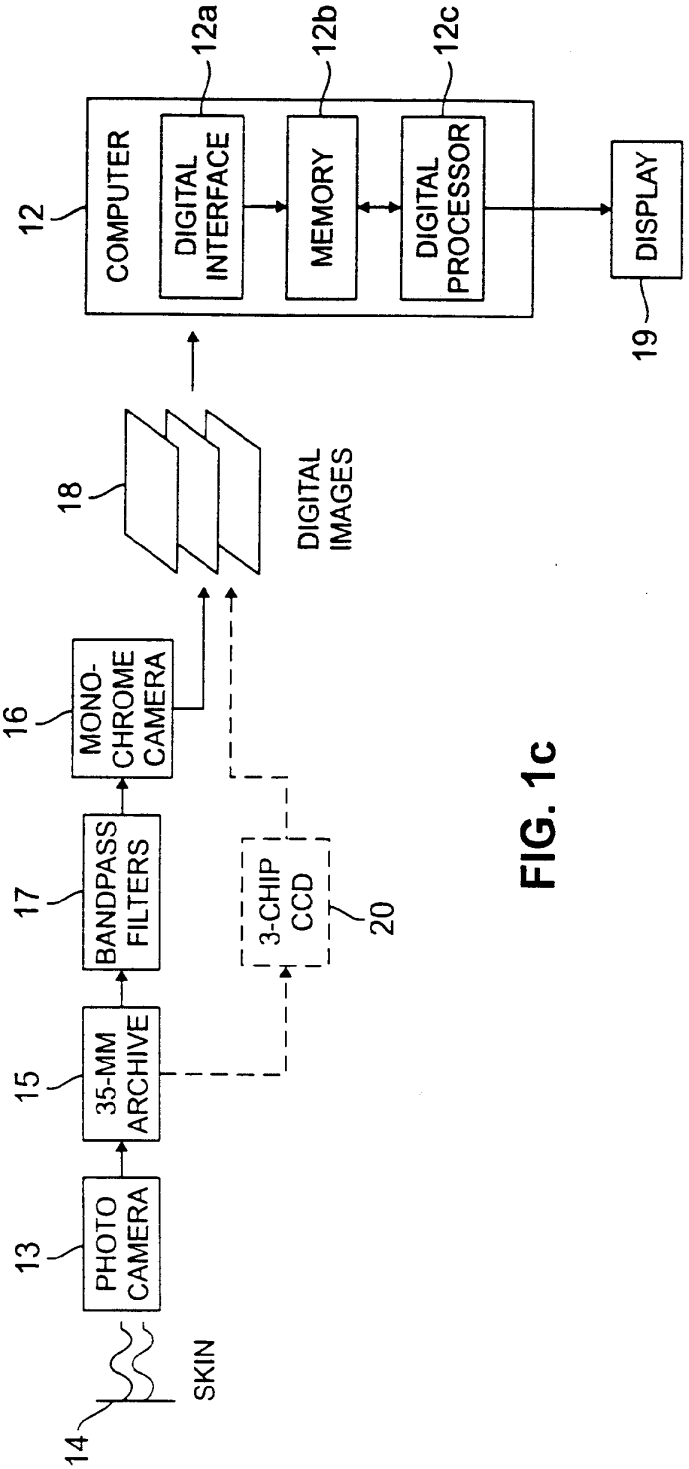

12
COMPUTER
12a
DIGITAL INTERFACE
12b
MEMORY
12c
DIGITAL PROCESSOR
DISPLAY
19
18
DIGITAL IMAGES
16
MONO-CHROME CAMERA
17
BANDPASS FILTERS
3-CHIP CCD
20
15
35-MM ARCHIVE
13
PHOTO CAMERA
SKIN
14

FIG. 1c

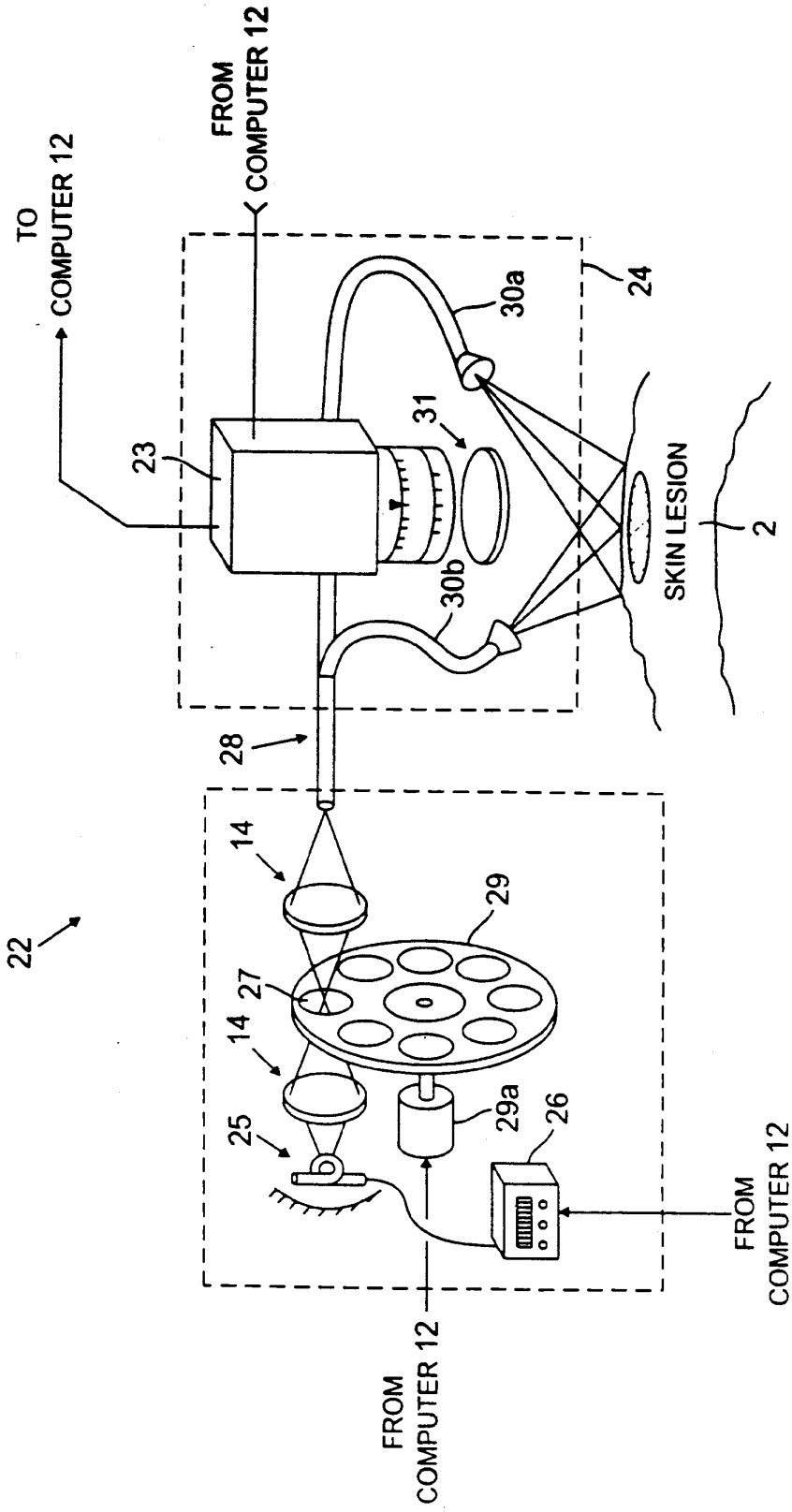

TO COMPUTER 12
FROM COMPUTER 12
24
30a
31
23
30b
SKIN LESION
2
28
22
14
29
27
14
29a
26
25
FROM COMPUTER 12
FROM COMPUTER 12

FIG. 2

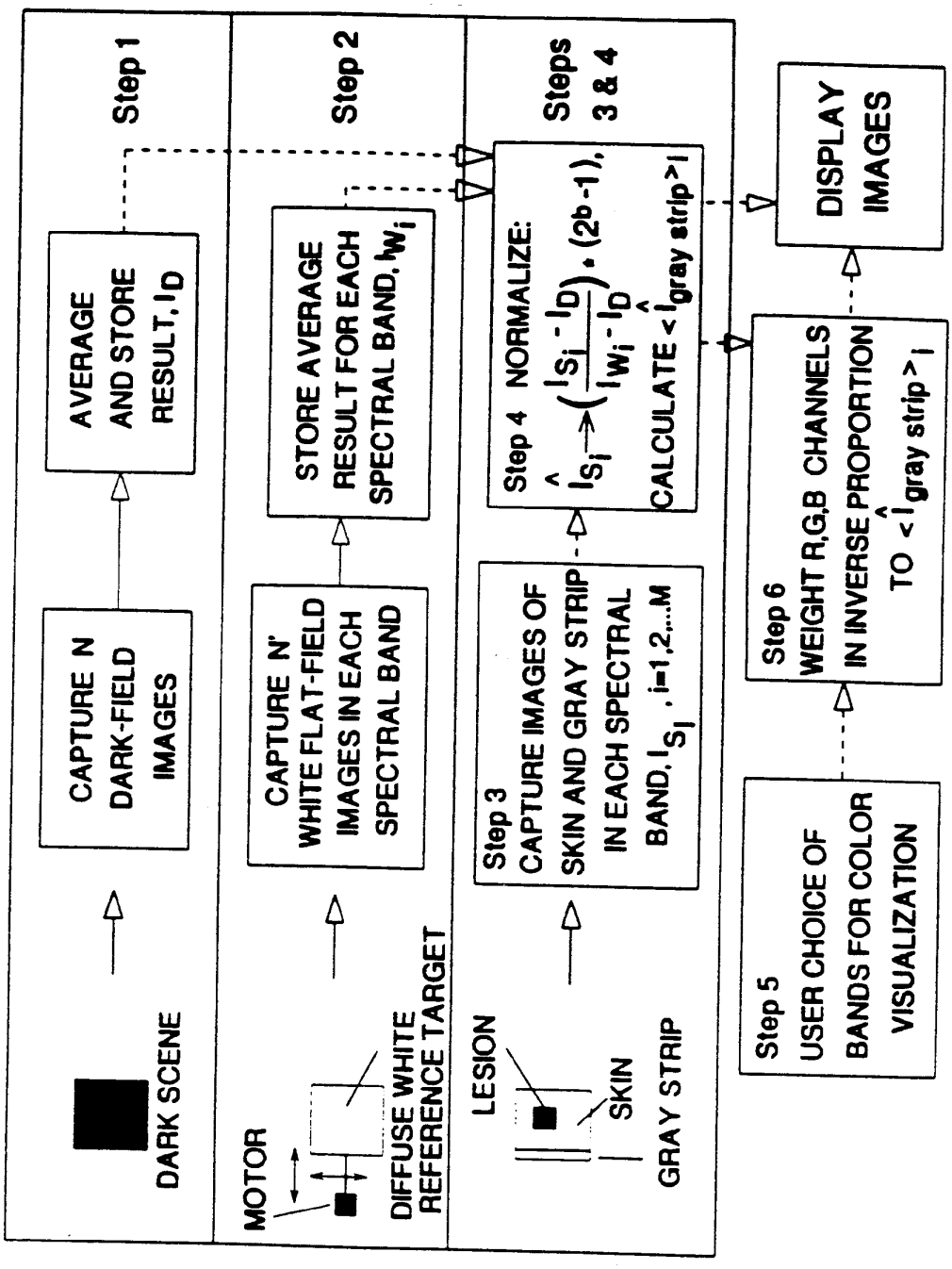

Step 1
Step 2
Steps 3 & 4
AVERAGE AND STORE RESULT, I_D
CAPTURE N DARK-FIELD IMAGES
STORE AVERAGE RESULT FOR EACH SPECTRAL BAND, I_{W_i}
CAPTURE N' WHITE FLAT-FIELD IMAGES IN EACH SPECTRAL BAND
Step 3 CAPTURE IMAGES OF SKIN AND GRAY STRIP IN EACH SPECTRAL BAND, I_{S_j}, i=1,2,...M
Step 4 NORMALIZE: $\hat{I}_{S_j} \rightarrow \left(\frac{I_{S_j} - I_D}{I_{W_i} - I_D}\right) \cdot (2^b - 1)$, CALCULATE $\hat{I}_{gray\ strip}$
DISPLAY IMAGES
Step 6 WEIGHT R,G,B CHANNELS IN INVERSE PROPORTION TO $\hat{I}_{gray\ strip}$
Step 5 USER CHOICE OF BANDS FOR COLOR VISUALIZATION
DARK SCENE
MOTOR
DIFFUSE WHITE REFERENCE TARGET
LESION
SKIN
GRAY STRIP

FIG. 3a

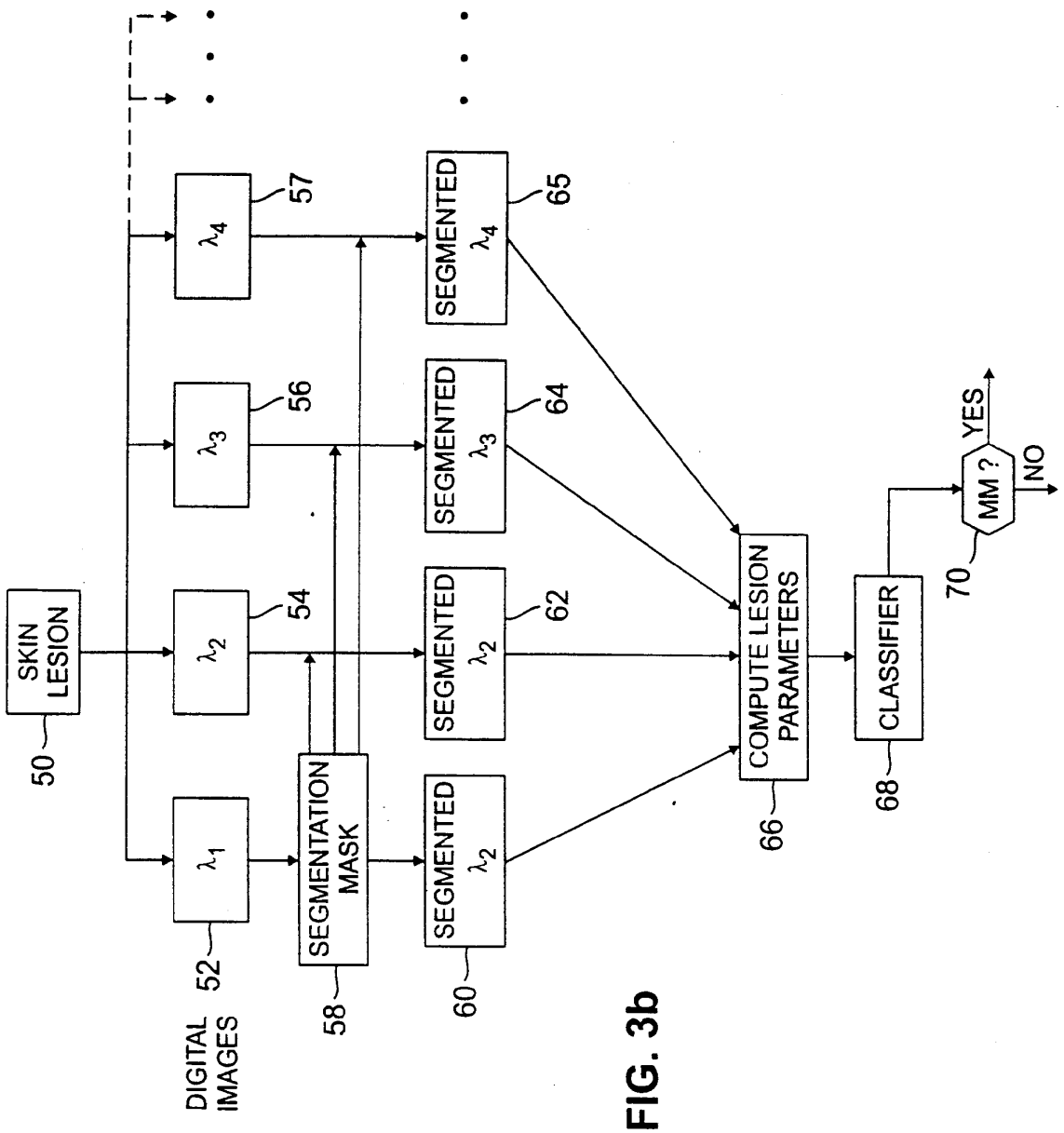

SKIN LESION
50
DIGITAL IMAGES
52
54
56
57
SEGMENTATION MASK
58
SEGMENTED
60
62
64
65
COMPUTE LESION PARAMETERS
66
CLASSIFIER
68
MM ?
70
YES
NO

FIG. 3b

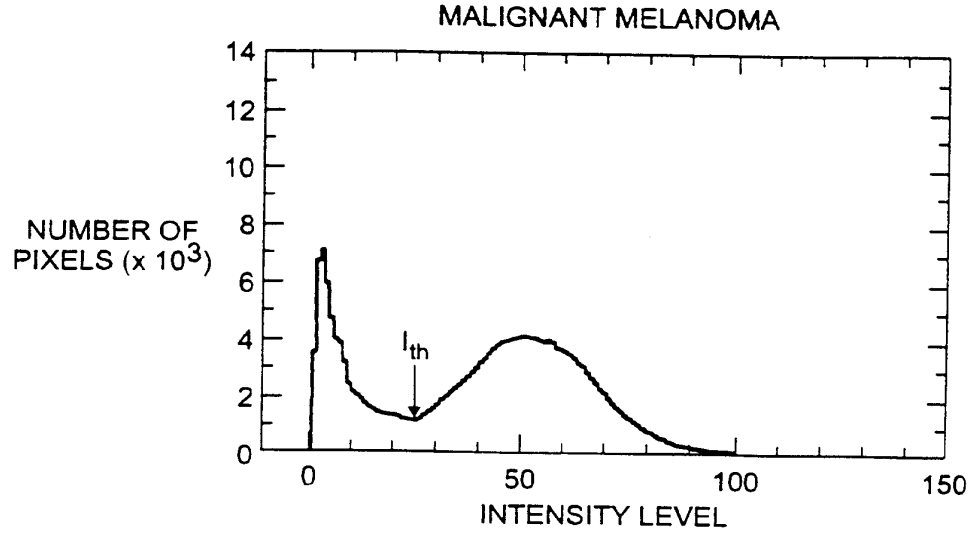

MALIGNANT MELANOMA
NUMBER OF PIXELS (x 10^3)
14
12
10
8
6
4
2
0
I_{th}
0
50
100
150
INTENSITY LEVEL

FIG. 4a

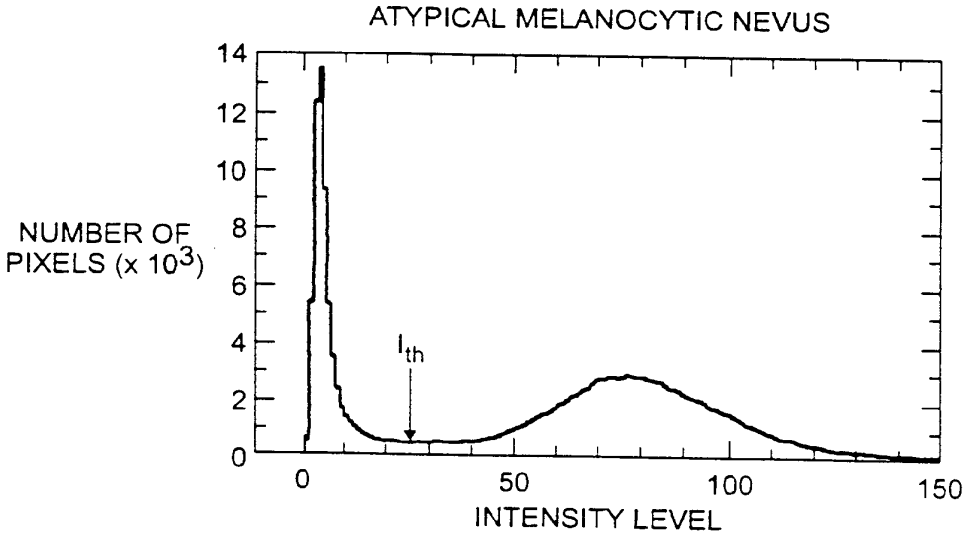

ATYPICAL MELANOCYTIC NEVUS
NUMBER OF PIXELS (x 10^3)
14
12
10
8
6
4
2
0
I_{th}
0
50
100
150
INTENSITY LEVEL

FIG. 4b

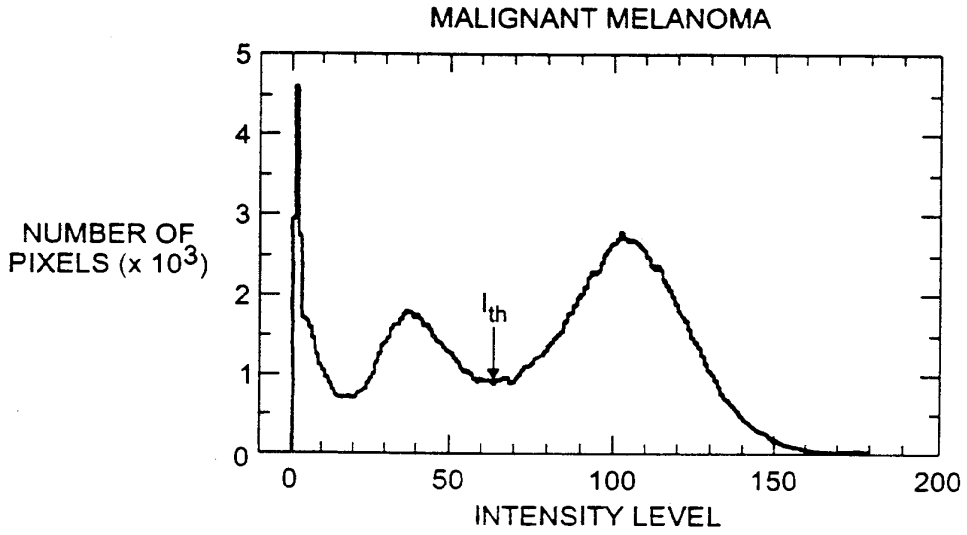

MALIGNANT MELANOMA
NUMBER OF PIXELS (x 10^3)
5
4
3
2
1
0
I_{th}
0
50
100
150
200
INTENSITY LEVEL

FIG. 5a

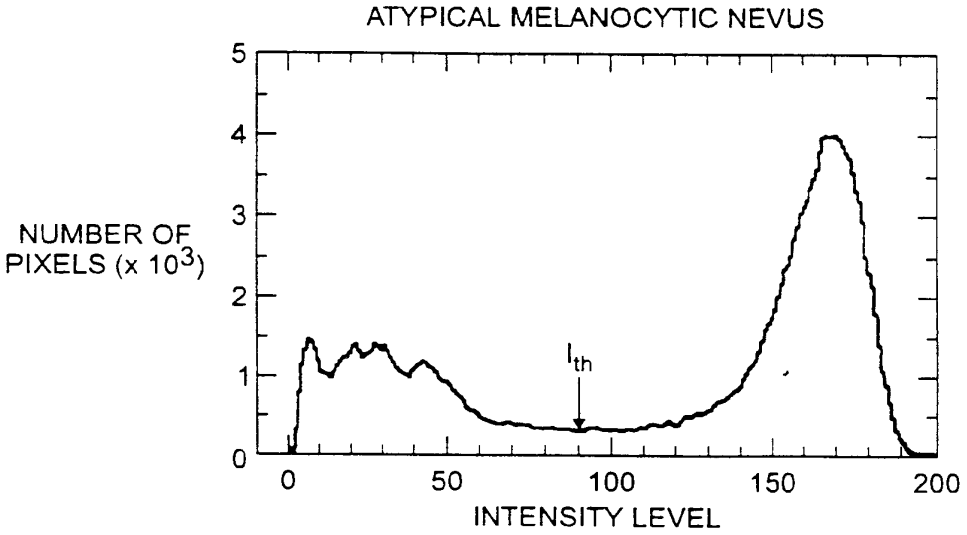

ATYPICAL MELANOCYTIC NEVUS
NUMBER OF PIXELS (x 10^3)
5
4
3
2
1
0
I_{th}
0
50
100
150
200
INTENSITY LEVEL

FIG. 5b

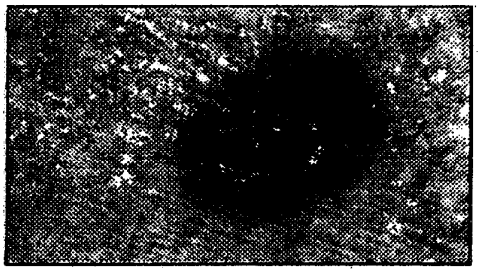


Fig. 6(a)

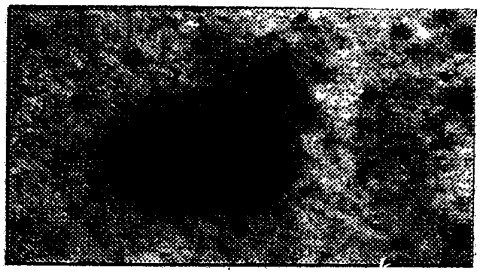


Fig. 6(d)

Fig. 6(b)

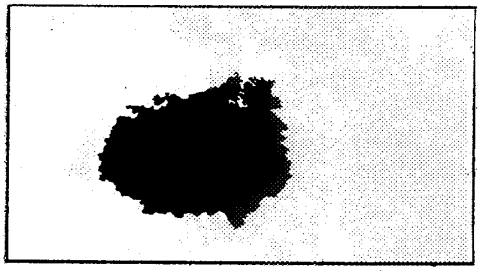


Fig. 6(e)

Fig. 6(c)

Fig. 6(f)

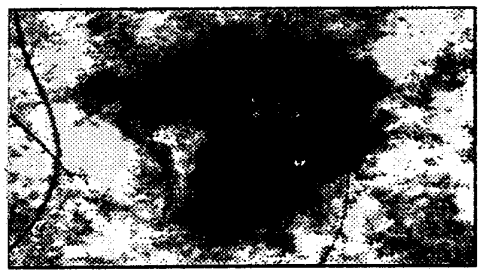


Fig. 7(a)

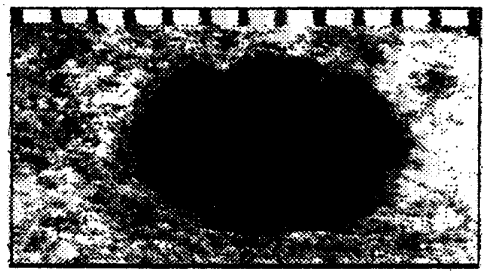


Fig. 7(d)

Fig. 7(b)

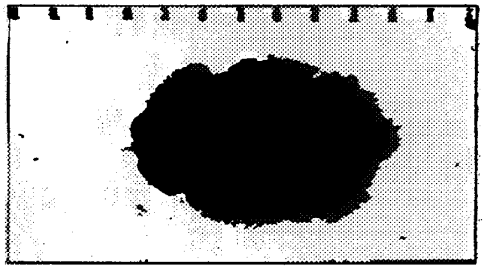


Fig. 7(e)

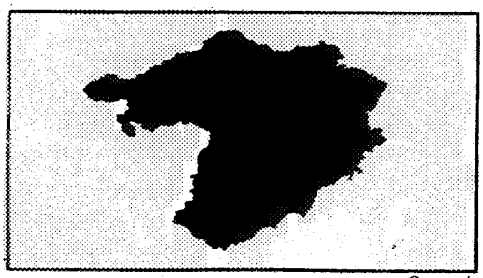


Fig. 7(c)

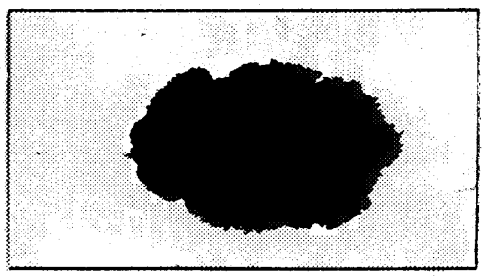


Fig. 7(f)

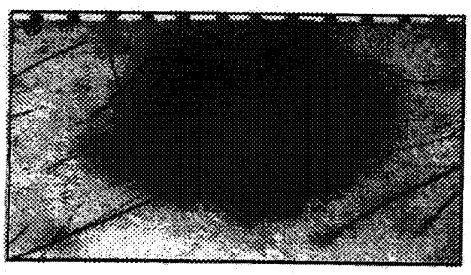


Fig. 8(a)

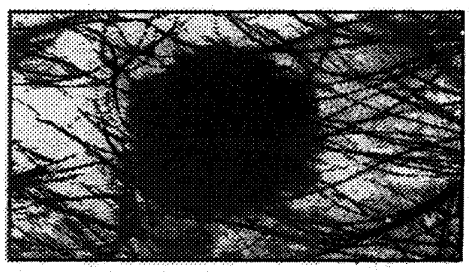


Fig. 8(e)

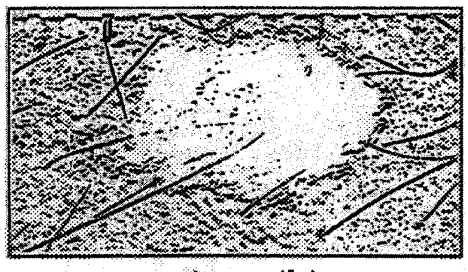


Fig. 8(b)

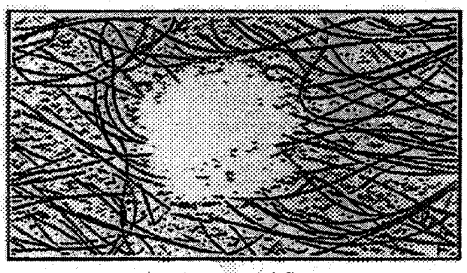


Fig. 8(f)

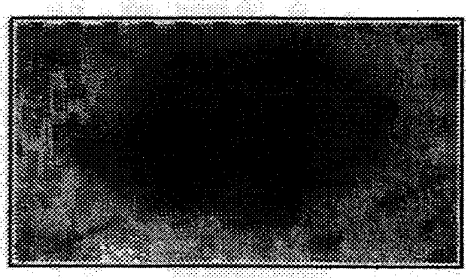


Fig. 8(c)

Fig. 8(g)

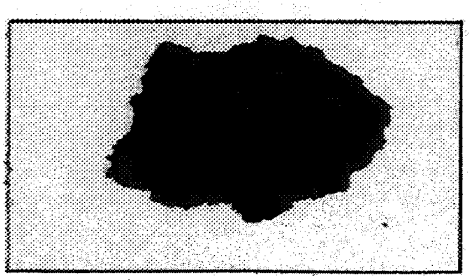


Fig. 8(d)

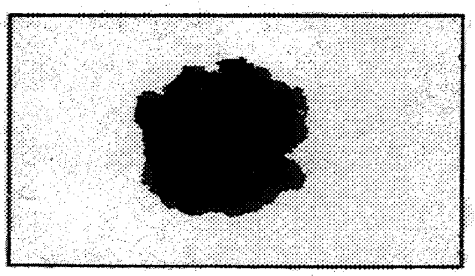


Fig. 8(h)

	I - 3	I - 2	I - 1	I	I + 1	I + 2	I + 3
J - 5	0	1	0	0	0	1	0
J - 4	0	1	1	0	1	1	0
J - 3	0	0	2	3	2	0	0
J - 2	1	0	0	1	0	0	1
J - 1	1	0	-3	-5	-3	0	1
J	1	1	-5	-8	-5	1	1
J + 1	1	0	-3	-5	-3	0	1
J + 2	1	0	0	1	0	0	1
J + 3	0	0	2	3	2	0	0
J + 4	0	1	1	0	1	1	0
J + 5	0	1	0	0	0	1	0

FIG. 9

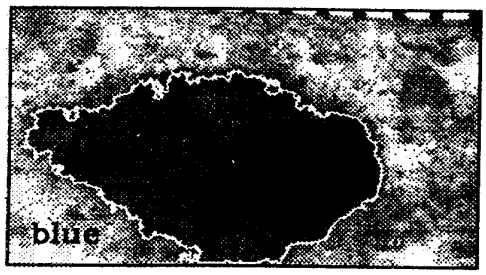


Fig. 10(a)

Fig. 10(d)

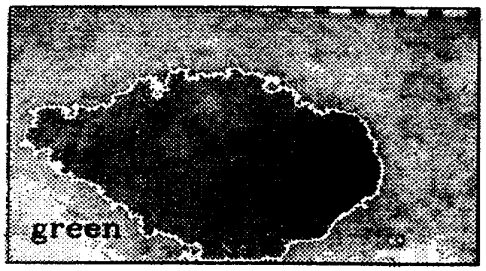


Fig. 10(b)

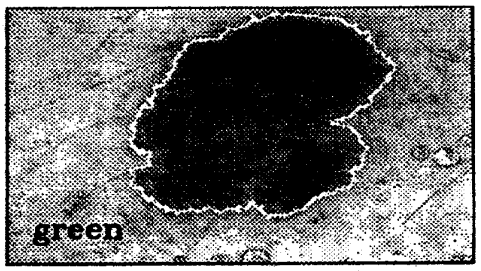


Fig. 10(e)

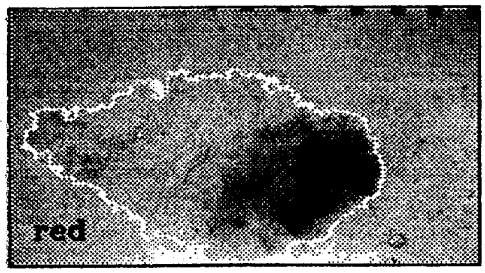


Fig. 10(c)

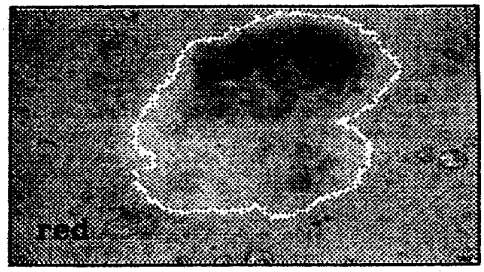


Fig. 10(f)

PARAMETER		DIAGNOSTIC ACCURACY (%)	SENSITIVITY (%)	SPECIFICITY (%)
ASYMMETRY:	A_{bin}	52	71	86
	A_b	48	68	84
	A_g	50	73	82
	A_r	62	78	89
BLOTCHINESS:	Bl_b	45	56	90
	Bl_g	40	68	72
	Bl_r	42	68	75
	C_b	37	80	55
	C_r	38	80	57
	Cl	44	78	70
BORDER:	B	44	66	81
	G_b	36	76	56
TEXTURE:	$T1_b$	38	88	49
	$T1_g$	49	61	90
	$T2_g$	41	66	76
	$T2_r$	43	73	72
	$T3_b$	39	80	59
	$T3_g$	38	63	74
	$T4_b$	38	68	69
	$T4_g$	39	56	83
	$T5_b$	36	76	58
	$T6_b$	38	90	46

FIG. 11

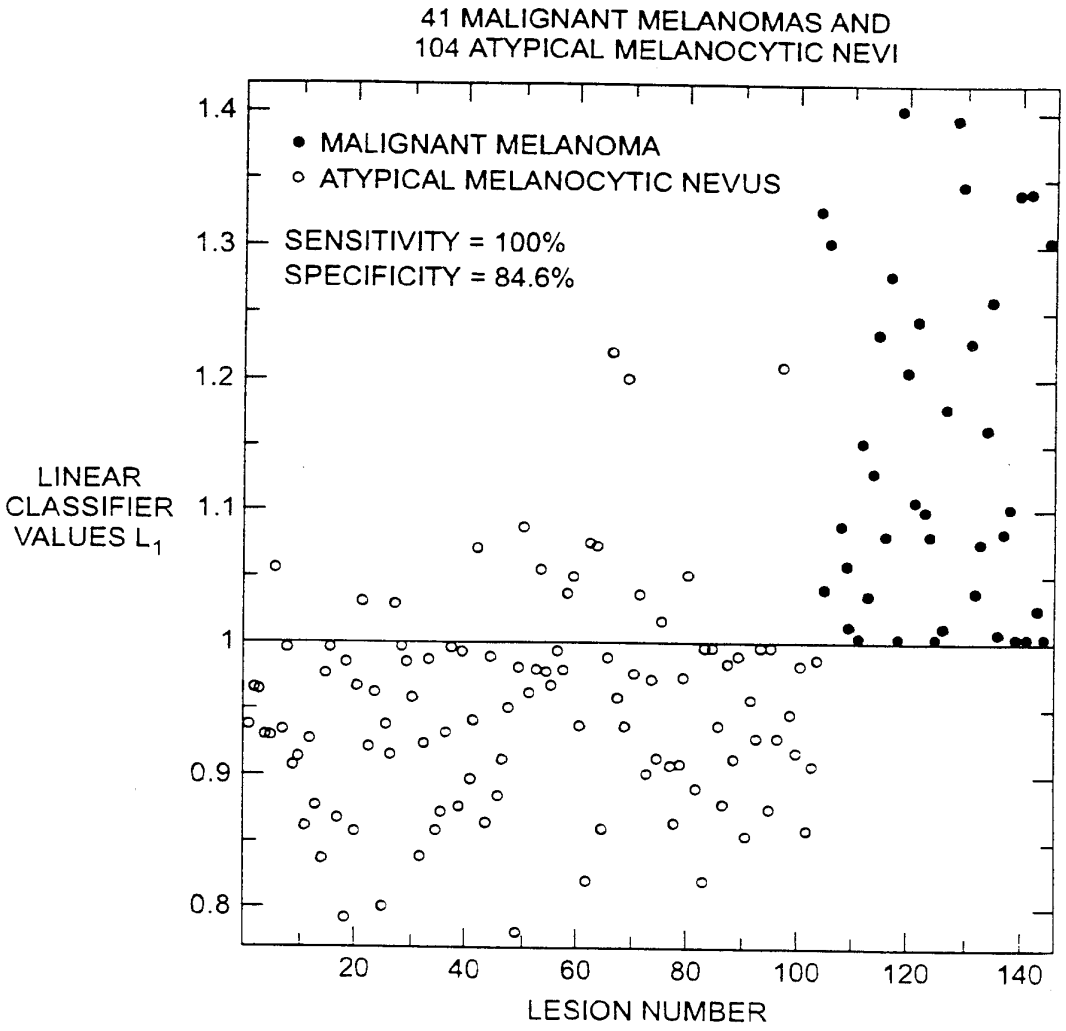


FIG. 12

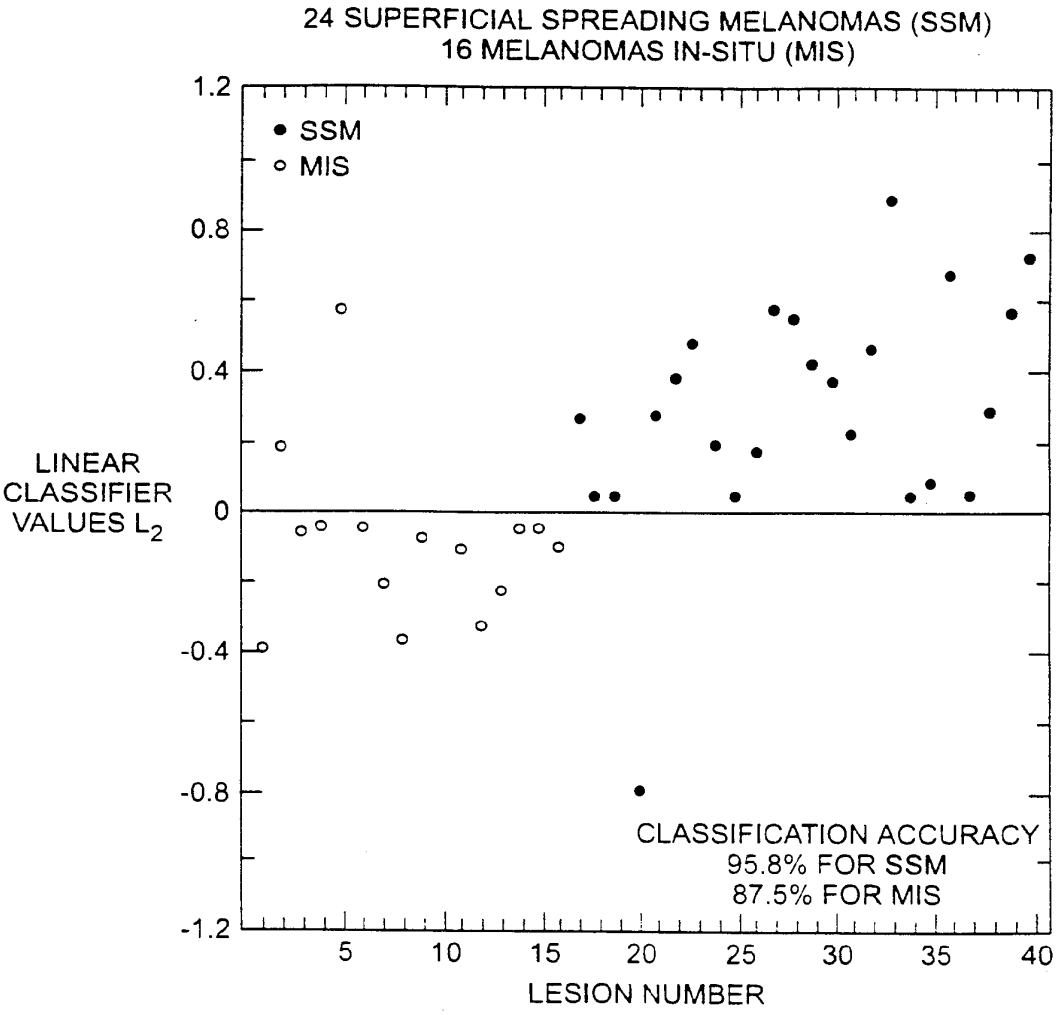


FIG. 13

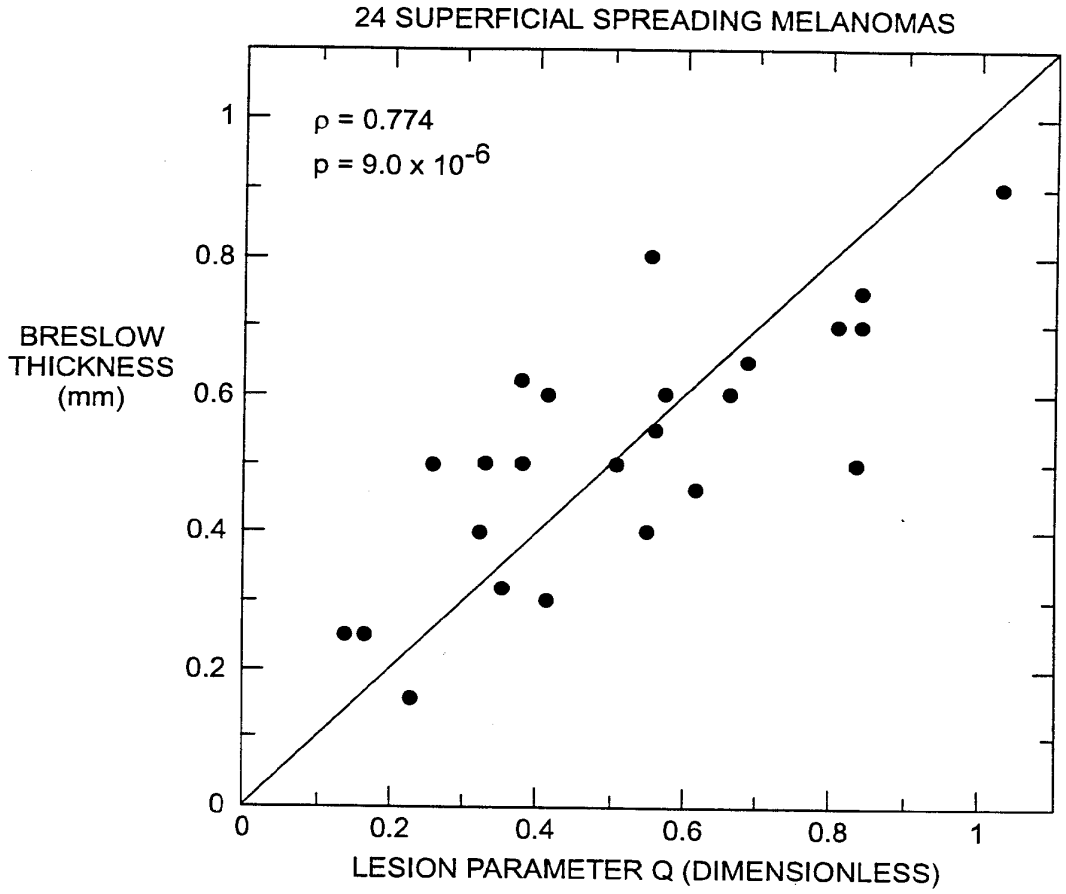


FIG. 14

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US99/04178

A. CLASSIFICATION OF SUBJECT MATTER

IPC(6) :G01B 9/02, G06K 9/00
US CL :382/128, 132, 173; 356/346
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 382/128, 173; 800/2; 356/346

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

IEEE Conferences, Journals and Standards; Journal of the American Academy of Dermatology

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

Please See Extra Sheet.

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 5,784,162 A (CABIB et al) 21 July 1998, col. 6, lines 1-3, cols. 7-12, col. 13, lines 1-15.	1, 2, 4, 6-14, 17-19, 23-33, 34 and 36
Y	US 5,799,100 A (CLARK et al) 25 August 1998, col. 4, lines 1-67, col. 5, lines 1-35	2, 6-14, 17-19, 23-34, and 36
Y	KOREN, I, Interactive Wavelet processing and Techniques Applied to Digital Mamography IEEE conference Proceedings, May 1996, Vol 3 ISBN 0-7803-3192-3, pages 1415-1418	1, 4, 6, 36
Y	AFROMOWITZ, M. A, Multispectral Imaging of Burn Wounds: A New Clinical Instrument for Evaluating Burn Depth IEEE Transaction on Biomedical Engineering 1988, Vol 35. No. 10, pages 842-850	9-12

[X] Further documents are listed in the continuation of Box C. [ ] See patent family annex.

*	Special categories of cited documents:	"T"	later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"A"	document defining the general state of the art which is not considered to be of particular relevance	"X"	document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"E"	earlier document published on or after the international filing date	"Y"	document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"L"	document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"&"	document member of the same patent family
"O"	document referring to an oral disclosure, use, exhibition or other means		
"P"	document published prior to the international filing date but later than the priority date claimed		

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Name and mailing address of the ISA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703) 305-3230	Authorized officer MEHRDAD DASTOURI Telephone No. (703) 305-2438

Form PCT/ISA/210 (second sheet)(July 1992) ★

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US99/04178

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	SCHINDERWOLF, T, Evaluation of Different Image Acquisition Techniques for a Computer Vision System in the Diagnosis of Malignant Melanoma Journal of the American Academy of Dermatology, July 1994, Vol 31, No. 1, Pages 33-41	13, 14, 17-19
Y	BOSTOCK, R.T.J, Toward a Neural Network Based System for Skin Cancer Diagnosis IEEE International Conference on Artificial Neural Network, 1993, ISBN 0-85296-573-7, pages 215-219	23, 24

Form PCT/ISA/210 (continuation of second sheet)(July 1992) ★

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US99/04178

B. FIELDS SEARCHED
Electronic data bases consulted (Name of data base and where practicable terms used):

APS
skin, texture, melanoma, malgnant, benign, burned skin, spectral band, wavelet maxima, rotationally and translationaly invarient, segmentation mask, intensity centroid, asymmetry, dermal papillae

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Remarks:
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(54) Systems and methods for the multispectral imaging and characterization of skin tissue

(57) Systems and methods for the multispectral imaging of skin tissue enables automatic characterization of the condition of a region of interest of the skin, based on direct digital imaging of the region of interest (Figures 1a, 2) or the digitization of color photographic slides of the region of interest, illuminated by appropriately filtered light. Preferably, a digital image at a low spectral band is automatically segmented and that segmented mask is used to segment the other images by a digital processor (Figure 3b). Parameters are estimated through wavelet maxima representation. Parameters related to the texture, asymmetry, blotchines and border irregularities are also automatically estimated (Figure 11). The region of interest is automatically characterized by the digital processor, based on those parameters. The region of interest may include a skin lesion, in which case the present invention enables the characterization of the lesion as malignant or benign (Figures 4a, 4b).

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Description

FIELD OF THE INVENTION

[0001] This invention relates to methods and systems for the computer controlled analysis of digital images of skin tissue at a plurality of wavelengths, which may include those outside of the red-green-blue bands. The methods and systems further include the automatic characterization of the condition of the skin tissue, based on automatically computed values of parameters which are functions of characteristics of the skin tissue, derived the digital images. Skin lesions can be analyzed for determining whether the lesion is a melanoma, for example. Systems for digitally imaging and analyzing skin tissue are disclosed, as well.

BACKGROUND OF THE INVENTION

[0002] Melanoma is a usually fatal skin cancer, unless it is detected and surgically removed in its earliest stages. Early detection of malignant melanoma is difficult because early melanomas, those having a Breslow thickness less than 1 mm, share many diagnostic features with benign lesions, such as dysplastic nevi or atypical melanocytic nevi.

[0003] To aid in the analysis of lesions, conventional photography, referred to as "clinical imaging", has been used to image the lesion for further study. The effectiveness of clinical imaging can be compromised, however, by specular reflection by the skin. Polarizers have been used for polarized imaging, which minimizes specular reflection.

[0004] Dermoscopy is another technique for examining skin, in which specular reflection is minimized. Dermoscopy also assists in clinically differentiating melanoma from its benign stimulants by enabling the observation of features of pigmented melanocytic lesions that are not discernible by the naked eye. In dermoscopy, the skin is made more transparent to light by providing an oil layer over the skin, in front of the optical system. A glass plate is placed over the oil layer. The oil has an index of refraction between the index of refraction of the horny layer of the skin and the glass plate. Standard magnifying optics may be used to enlarge the structures rendered visible on and under the surface of the skin by the oil layer. The region of interest can then be examined visually. Slides of the region of interest can be made, as well, for future study.

[0005] Despite their similarities, most malignant melanomas differ in certain of their characteristics from other melanocytic lesions. A major advance in characterizing skin lesions based on certain of the observable differences between malignant and other lesions is the "ABCD" rule, where A=asymmetry, B=border irregularity, C=color variability, and D=diameter greater than 6 mm. A corresponding ABCD rule, where "D" refers to dermoscopic structures, such as brown globules, black dots or pigment networks within the lesion, is applied to dermoscopic images. Because the clinical and dermoscopic applications of these rules are subjective, they are not very reliable.

[0006] When skin is illuminated by light, the light can be re-emitted by reflection, scattering or fluorescence. It is known in the art that re-emission of light absorbed at different wavelengths by the region of interest can provide different information. For example, as the wavelength of the light increases, its depth of penetration into the skin also increases. Chromophores at different depths in the tissue therefore absorb and re-emit light at various wavelengths. Melanin and hemoglobin are examples of such chromophores.

[0007] Since the unaided eye cannot perceive light outside of the visible region or low-contrast structure in visible-light images, information which may be useful in diagnosing a lesion may not be directly observable. Digital acquisition and processing of dermoscopic images may, therefore, improve diagnostic reliability by employing more of the information residing in such images that is not directly observable. There have therefore been attempts to use objective, computer-based, image analysis algorithms that can discern meaningful differences between benign and malignant melanocytic lesions with sufficient accuracy.

[0008] Computer processing of images requires that the image be in digital form. A digital image is an array of digital signals whose values are a function of certain characteristics of the subject of the image. When imaging skin lesions, the digital images comprise digital signals whose values are a function of the re-emission characteristics of the skin and lesion, at different spectral bands of the light. The array is obtained by spatial sampling and quantizing the intensity of images obtained with film or directly by electronic cameras. Practical limitations on the number of picture elements or pixels per unit area of image determine the achievable spatial resolution of the digital image. The digital image typically needs to be segmented to separate the digital signals which are a function of the skin lesion from the digital signals which are a function of the surrounding skin.

[0009] Computer aided analysis has also been used to classify skin lesions using quantitative values indicative of particular characteristics of lesions, referred to as parameters. Based on histopathological diagnosis of lesions, algorithms have been developed which use linear or non-linear classifiers to combine parameters provided by the operator of an imaging device or a physician or computed by a processor, to yield a value which can be used to classify the lesion. Because some of the steps in the computer-aided analysis of which we are aware depend on subjective judgments of an individual, such analysis may provide highly variable results.

[0010] The images heretofore available have been obtained with commercially available red-green-blue color imaging apparatus. Color photographic transparencies of skin lesions have been digitized and skin lesions have been directly imaged with "three-chip" digitizing cameras. Such cameras employ broad-band filter bandpasses that are ultimately based on the wavelength response of the human visual system and have large regions of overlap.

[0011] Electronic images may also be obtained in narrower, non-overlapping filter bandpasses, which may reveal additional, wavelength-dependent differences between the images of melanomas and of benign lesions. However, such devices have had poor resolution and/or poor signal-to-noise characteristics which prevent the acquisition of digital images of melanocytic skin lesions of sufficient quality for effective application of machine vision techniques for lesion diagnosis.

[0012] Existing imaging systems and processes also tend to suffer from an inability to provide the required repeatability of the value of extracted lesion parameters, due in part to a lack of standardization with respect to spatially varying artifacts, so that the parameters, therefore, lack invariance to lighting and image exposure conditions, for example. Obtaining high signal-to-noise ratios in images recorded in narrow filter bandpasses, when exposure times are sufficiently short that the skin is effectively "frozen" during the exposure sequence, has also been difficult. In addition, since the optimum wavelengths for automatic characterization may not be the optimum wavelengths for visual observation, it may be difficult to reconstruct high-fidelity color images from the digital images for visual interpretation by a clinician.

[0013] The assessment of wounds and burns through the appearance of color images present similar challenges. Existing technology for the imaging of skin *in vivo* for these purposes is also inadequate. Practical solutions to the problems of employing multispectral digital imaging of skin for the analysis of lesions, wounds, or other conditions, have not been found.

SUMMARY OF THE INVENTION

[0014] The methods and systems of the present invention provide for the acquisition of digital images of skin at a plurality of spectral bands to automatically characterize the condition of the tissue based on the digital images. Spectral wavelength bands within and outside of the visible band may be used. In accordance with the present invention, a pigmented skin lesion can be characterized as malignant or benign, for example. Wounds or bums can also be characterized with respect to their rate of healing. The digital images comprise a plurality of digital signals whose values are functions of the condition of the tissue. The digital images acquired are subjected to objective and quantitative analysis by a digital processor to detect and identify abnormalities. The analysis includes image segmentation, parameter estimation and characterization of the skin. The estimation and characterization steps are automatic. The segmentation step may be automatic, as well. Subjective judgments are therefore minimized or eliminated.

[0015] It has further been found that generating the segmentation mask from a digital image acquired with light in a spectral band which does not penetrate deeply into the skin, such as a spectral band with a center less than about 500 nanometers, provides superior results. After segmentation, estimated values which are functions of characteristics of the lesion, such as its texture, asymmetry, blotchiness, and border irregularities, are computed and used to automatically characterize the condition of the skin. Clinically significant dimensional parameters such as diameter may also be evaluated. Digital signals corresponding to hair or blob-like structures are preferably removed during segmentation. Some or all of the values may be estimated through wavelet maxima representations, as well.

[0016] In accordance with the present invention, a method for characterizing the condition of a region of interest of the skin, wherein the absorption and scattering of light in different spectral bands by the region of interest is a function of the condition of the skin, is disclosed. The method comprises illuminating the region of interest of the skin by light in at least three spectral bands and digitally imaging the region of interest at the at least three spectral bands with the light re-emitted by the skin to generate digital images comprising digital signals whose values are a function of the condition of the skin. The digital images are provided to a processor which segments the digital images by generating a segmentation mask from a digital image in any one of the at least three spectral bands. The processor estimates at least one rotationally and translationally invariant statistical measure of coefficient distributions of the multiscale wavelet maxim representations of the digital images in each spectral band, which are functions of the texture of the region of interest determined by the segmentation mask. The processor characterizes the condition of the skin based on the estimated values, and outputs the characterization of the condition of the skin. Preferably, the segmenting, estimating and characterizing steps are conducted without the intervention of an operator.

[0017] Additional parameters include measures of the texture, asymmetry, blotchiness and border irregularity of the portion of the region of interest.

[0018] The digital images may be obtained by directly imaging the region of interest with a digital camera, or digitally imaging color slides of the region of interest, through appropriately filtered light.

[0019] The characterizing step may include comparing a weighted combination of the parameter values against a threshold value. The weight coefficients for each parameter value and the threshold value may be selected based on a training set of images of lesions or other skin conditions, whose condition has been determined, preferably through

histological examination by a plurality of doctors. Preferably, for skin lesions, specificity is maximized under the constraint of 100% sensitivity to melanoma.

[0020] In accordance with another aspect of the invention, a system for characterizing the condition of a region of interest of skin includes means for illuminating the region of interest with light in at least three spectral bands and a camera for acquiring digital images of the region of interest based on the light re-emitted from the illuminated region of interest at each of the spectral bands. The digital image comprises digital signals whose values are a function of the condition of the region of interest. A digital processor segments the digital images by generating a segmentation mask from a digital image in any one of the at least three spectral bands. The processor estimates at least one rotationally and translationally invariant statistical measure of coefficient distributions of the multiscale wavelet maxim representations of the digital images in each spectral band, which are functions of the texture of the region of interest determined by the segmentation mask. The processor characterizes the skin condition based on the estimated value or values. The other parameters discussed above may be used, as well.

[0021] The camera may be a single-chip or multiple-chip charge-coupled device which detects light in a plurality of spectral bands between the near ultraviolet to near infrared. The filter means may be a plurality of interference filters mounted on a wheel for stepping any filter into a position intercepting the light from the light source. Preferably, at least one of the spectral bands has a center which lies between about 350 and 500 nanometers, at least one of the spectral bands has a center which lies between about 500-600 nanometers, and at least one other spectral band has a center which lies between about 750-1000 nanometers.

DESCRIPTION OF THE FIGURES

[0022]

Fig. 1(a) is a schematic illustration of a method and system of imaging a region of interest of skin in accordance with the present invention;

Fig. 1(b) is a schematic illustration of a plurality of narrow spectral bandwidths which may be used to illuminate the skin in the embodiment of Fig. 1(a);

Fig. 1(c) is a schematic illustration of alternative methods and systems for digitizing and analyzing color photographic slides of a region of interest of skin;

Fig. 2 is a schematic illustration of preferred illumination and imaging portions of a computer controlled imaging system for direct imaging of a lesion;

Fig. 3(a) is a flow chart of a calibration procedure for use with the present invention;

Fig. 3(b) is a flow chart of a method of processing images for classifying lesions as malignant or benign, in accordance with the present invention;

Figs. 4(a) and 4(b) are histograms of a malignant melanoma and of an atypical melanocytic nevus, respectively, showing two peaks in each histogram;

Figs. 5(a) and 5(b) are histograms of another malignant melanoma and another atypical melanocytic nevus, respectively, showing three or more peaks in each histogram;

Figs. 6(a) and 6(d) are digital images in the blue spectral band of another malignant melanoma and another atypical melanocytic nevus, respectively;

Figs. 6(b) and 6(e) are digital images of the images of Figs. 6(a) and 6(d) respectively, after thresholding;

Figs 6(c) and 6(f) are digital images of the images of Figs. 6(a) and 6(d), respectively, after iterative thresholding;

Figs. 7(a) and 7(d) are digital images in the blue spectral band of another malignant melanoma and another atypical melanocytic nevus;

Figs. 7(b) and 7(e) are digital images of Figs. 7(a) and 7(d), respectively, resulting from iterative processing and showing dark blobs outside the lesion area;

Figs. 7(c) and 7(f) are digital image masks of Figs. 7(b) and 7(d), respectively, resulting from image cleaning;

Figs. 8(a) and 8(e) are digital images in the blue spectral band of another malignant melanoma and another atypical melanocytic nevus, respectively, showing hair;

Figs. 8(b) and 8(f) are reverse intensity contrast images of the lesions of Figs. 8(a) and 8(e), respectively;

Figs. 8(c) and 8(g) are digital images resulting from an averaging process applied to the images of Figs. 8(a) and 8(b), to remove hair;

Figs. 8(d) and 8(h) are binary lesion masks resulting from the segmentation of the images of Figs. 8(c) and 8(g), respectively;

Fig. 9 is a spatial filter used to remove hair;

Figs. 10(a) - 10(c) are segmented digital images in the blue, green and red spectral bands, of the malignant melanoma whose histogram is shown in Fig. 5(a);

Figs. 10(d) - 10(f) are segmented digital images in the blue, green and red spectral bands, of an atypical melanocytic

nevus whose histogram is shown in Fig. 5(b);
Fig. 11 is a chart of lesion parameters and their associated diagnostic accuracy, sensitivity and specificity when used individually;
Fig. 12 is a plot of linear classifier values versus lesion identification number, for 41 malignant melanomas and 104 atypical melanocytic nevi;
Fig. 13 is a plot of linear classifier values versus lesion identification number for 24 superficial spreading melanomas and 16 melanomas *in-situ; and*
Fig. 14 is a plot of lesion parameter versus Breslow thickness for 24 superficial spreading melanomas.

DESCRIPTION OF THE INVENTION

[0023] Fig. 1(a) is a schematic illustration of a method and system 1 in accordance with the present invention, by which images of the skin 2 are acquired by a camera nearly simultaneously at a plurality of spectral bands, λ_i, i=1,2,...M, that are preferably effectively non-overlapping, as shown schematically in FIG. 1(b). The skin is illuminated by a source of white light 3, which is filtered by narrow passband filters 4. The filtered light is preferably conveyed to the skin 2 through a fiberoptic illuminator 5. The light re-emitted by the illuminated skin through reflection, scattering or fluorescence is imaged by a low-noise, high-resolution monochrome camera 6, which is preferably an electronic charge-coupled ("CCD") camera. Digital images output by the camera 6 are provided to a computer 12 for processing.

[0024] The computer 12 includes a digital interface 12a, a memory 12b and a digital processor 12c. A display 19 is preferably provided as well. The computer 12 includes an input to a digital interface 12a for receiving the digital images. A memory 12b stores the digital images, and the software controlling operation of the imaging system, the image processing, and the classification and characterization of the lesion. The digital processor 12c, under control of the software, performs the calculations. The computer 12 has an output connected to a display 19, which can display the processed images and the results of the classification and characterization procedures for each image. The computer 12 also preferably has outputs connected to the source of light 3 and the camera 6, for controlling their illumination level and exposure times, respectively, as described below.

[0025] The image processing, classification or characterization and other programs can be implemented on a personal computer, using a programming language, such as FORTRAN or C. The memory 12b which stores the software can be any convenient media readable by the computer 12, such as the hard drive of the computer, read only memory, random access memory with a battery backup, electrically programmed ROM, electrically erasable ROM, floppy disc, or CD ROM. Other suitable media may be used, as well.

[0026] When the filter bandpasses have minimal overlap, as in FIG. 1(b), each monochromatic image will contain spectrally independent information. Such spectral separation is believed to be useful for differential diagnosis of skin lesions that contain varying amounts of melanin, and of hemoglobin in different oxidation states, for example. Spectral separation is also believed to be useful in distinguishing granulation of tissue and other structural details of wounds in various stages of healing. One or more of the wavelength bands may lie outside the visible region, such as in the near infrared and/or the near ultraviolet, as long as the wavelength is within the response range of the combined optical system including the electronic camera 6.

[0027] In accordance with another aspect of the invention, the digital images of skin lesions can be derived from color slides of the lesions obtained by clinical imaging, dermoscopy, or polarization imaging. Fig. 1(c) is a schematic illustration of alternative approaches to the acquisition and digitization of images of skin lesions from color slides. A photo camera 13 produces 35-mm color slides of a region of the skin 14. The camera 13 can be a Dermaphot ® camera from Heine, Optotechnik Gmbh & Co. AG, Germany, for example. The slides are typically stored in an archive 15. The slides are subsequently reimaged by a monochrome camera 16, which may be a CCD camera, that photographs each slide as it is illuminated by white light that has passed through a sequence of bandpass filters 17 to create a color filtered version of the image. The slides can be illuminated at broad or narrow blue (B), green (G) and red (R) wavelength bands, respectively. The broad wavelength bands may overlap somewhat. In one example, the blue wavelength band was about 400 nm $\pm$ 30 nm, the green wavelength band was about 550 nm $\pm$ 30 nm, and the red wavelength band was about 700 nm $\pm$ 30 nm.

[0028] Each of the filtered representations is recorded by the monochrome camera 16, which provides the resulting digital images 18 to an input of the computer 12. If an electronic camera is not used, the slide images could be digitized by any available commercial digitizer including three channels, one for red, one for green and one for blue, as long as the pixel size in the lesion plane after digitization is less than about 60 micrometers ("μm").

[0029] An appropriate CCD camera 16 is available from Electrim, Inc., Princeton, N.J. The camera 16 has a photographic macro-lens, wherein f#/2.8 and f=100 mm. Preferably, the spatial resolution of the CCD camera 16 provides pixels having a size about 10-30 μm in the lesion plane. The CCD camera 16 from Electrim, Inc., has 753 X 488 pixels. The spatial resolution with such a camera is approximately 21 x 24 μm at the lesion plane. Digital images of lesions obtained with this imaging system were used to classify lesions as malignant or benign, and to characterize lesions as

invasive or non-invasive, as described further, below. The Electrim, Inc., CCD camera 16 has rectangular pixels. A CCD camera with square pixels would simplify the calculating procedures.

[0030] Alternatively, a 3-chip CCD camera 20, indicated in phantom in Fig. 1c, may be used to reimage the slides of the region of interest. The CCD camera 20 provides digitized images for subsequent analysis by the computer 12. Broad bandpass filters, which are part of the CCD camera 20, produce a representation of the lesion as a set of three narrowband images. The filters are typically in accordance with CIE Standard Observer, wherein the bandwidths are broad.

[0031] Fig. 2 is a schematic illustration of the illumination and imaging portions of a preferred computer controlled imaging system 22 in accordance with the present invention, for imaging a region of interest of skin including a lesion. The electronic camera 23 may be a 10-bit monochromatic electronic CCD camera 23, such as the Xillix Model 1400, available from Xillix Technologies Corp., Canada. The Xillix camera is equipped with wide band, low distortion foreoptics, such as the XJP 1.9/0501, available from Jos. Schneider Werke, Germany. The lower distortion fore optics and the camera minimize chromatic aberrations of the optical system over the "multispectral" sequence of exposures, enabling registration of images with sub-pixel accuracy, over the entire field of view.

[0032] To ensure repeatability of imaging conditions and to minimize required intervention by the operator, it is preferred that the system be operated at a preset f/stop. For cameras such as the Xillix Model 1400, exposure times are preferably controlled by the computer 12 through an electromechanical shutter that can operate reliably between minimum and maximum exposure times t_{min} and t_{max}. Electronic shuttering may be more preferred for use with other cameras.

[0033] The imaging system provides low-noise, high-resolution digital images at high data transfer rates, with low distortion imaging over the entire range of wavelengths covered by the collection of filters. The Xillix camera, discussed above, has a resolution at the skin surface of about 20 microns per pixel. The CCD camera 23 is preferably contained in a hand-held unit, represented schematically as box 24. The illuminator source 25 is a tungsten-halogen lamp whose intensity is controlled by a light-stabilized power supply 26 whose setting is automatically adjusted by the computer 12. A 150 watt lamp, such as the Phillips EJA, available from Phillips Electronics North America Corporation, N.Y., may be used, for example. The output of the lamp 25 is white light. A narrowband filter 27 is provided between the source and an optical fiber 28. A plurality of narrowband filters, each one corresponding to a different spectral wavelength band, are mounted on a filter wheel 29. Preferred filter bandwidths are listed in Table 1, below. The filter wheel 29, which is driven by a stepping motor 29a, advances each filter to its proper position between the lamp 25 and the optical fiber 28, and holds each filter in position for a sufficient period of time. The computer 12 controls the motor 29a. More or fewer filters may be used. Appropriate lenses 14 are provided between the lamp 25 and the filter 27, and between the filter 27 and the optical fibers 28, as well. One or more fiber illuminators 30a, 30b are provided for conveying the light from the source to the lesion. Two such illuminators 30a, 30b are shown in Fig. 2 for simplicity. Although the fiber illuminator is illustrated as a bifurcated pair, a ring illuminator which provides more nearly uniform illumination at the skin surface, is preferred. An angle of illumination of about 20° is also preferred. A Fostec Model A0603 ring illuminator available from Fostec, Inc., N.Y., may be used, for example.

[0034] The hand-held portion of the system 24 of Fig. 2, which includes the camera 23, may be mounted on a cantilevered arm (not shown) that can be locked into position.

[0035] The digital signals making up each of the digital images output from the camera 23 are provided to the computer 12. The computer 12 conducts image processing procedures on the digital images to calibrate the images, and to objectively segment, estimate parameters, and classify the lesions based on the estimated parameters. Operator judgment is not required at any point in the process.

[0036] Control is maintained by the computer 12 over source intensity, filter position, and such camera settings as shutter timing, through the digital interface 12a. Key control parameters are empirically chosen on the basis of feedback from histograms of trial images. The intensity of the lamp 25 may be maintained at a stable value, commensurate with the 10-bit dynamic range of the camera 26, by monitoring a secondary light source, connected electrically in series with the primary light source 25. The light output from the secondary source may be monitored by a light sensor that is optically isolated from light reflections associated with the primary source. Such reflections may be caused by the filters that are located on the filter wheel, or from the housing of the primary light source. This method provides optical feedback which is sensitive to changes in light intensity caused by changes in lamp lead resistance, for example, while it is insensitive to the variable amounts of light reflected from the filters, for example. By means of a closed control loop, the optical feedback from the secondary source may be used to maintain constant light output from the primary source. In addition, the lamp intensity may be further stabilized by monitoring light reflected from a material of stable reflectance, such as Kodak "18% gray" card. If the intensity of the light detected by the camera deviates from a predetermined desired value, the intensity of the output of the lamp can be adjusted. The power, voltage or current supplied to the lamp 25, may also be monitored.

[0037] The apparatus of Fig. 2 can be used for either clinical imaging of the skin, wherein the skin is imaged directly, dermoscopic imaging, wherein a layer of oil is provided over the skin and a layer of glass placed over the oil layer, or polarized imaging, where a polarizer 31 is added to minimize specular reflection as shown in Fig. 2. In dermoscopic imaging, the index-matching oil sufficiently reduces the specular reflection to avoid the need for a polarizer. When imaging

wounds or bums, an additional polarizer 31a may be placed between the source of light 25 and the filter wheel 29, to be used in conjunction with the polarizer 31, to reject copolarized components of the light re-emitted from the region of interest, thereby reducing specular reflections, as is known in the art.

[0038] Instead of being positioned between the light source 25 and the optical fiber 28, the narrow bandpass filters 27 may be placed between the skin and the CCD camera 23 to filter the light reflected and scattered from the skin 2. Light re-emitted by the skin through fluorescence would also be filtered. In addition, instead of the filters 27, a monochromator, a plurality of lasers, each emitting at a single wavelength, multiline lasers, tunable lasers or light emitting diodes could also be used as the illumination source or sources, as is known in the art.

[0039] The front end of the system preferably consists of a flat glass plate (not shown) for being placed over the skin. Light pressure is applied through the glass, onto the skin, throughout the imaging process. This helps to stabilize the region of interest against unwanted motion which could blur an image or which could lead to spatial misregistration between images obtained in different filter bandpasses.

[0040] Preferably, the spectral bands span the range between the near ultraviolet to the near infrared. At least one spectral band preferably has a center which lies between about 350-500 nanometers, more preferably between about 400-450 nanometers, at least one of the bands preferably has a center which lies between about 500-600 nanometers, and at least one other spectral band preferably has a center which lies between about 750-1000 nanometers. The near infrared, between about 750-1000 nanometers, has been found to be useful in detecting invasive melanomas, because of its greater depth of penetration than the other spectral bands.

[0041] The preferred filters 27 for lesion imaging with a tungsten-halogen white light source 25 have the center wavelengths λ_i and bandwidths (FWHM) listed in Table 1, for i=1,2,...,M, M=10, wherein the bands are labeled by j=i-1 = 0,1,...M-1. Such filters are available, for example, from Intor, Inc., Tucson, AZ. In each band, the exposure time is preferably selected to avoid saturation of the detector elements of the CCD camera 23, as well as to maximize the linear dynamic range over which the image data are recorded. These exposure times should be constrained to be within limits t_{min} and t_{max} which are related to the electromechanical design of the shutter, optical throughput of the camera 23, and avoidance of image blur associated with motion during the exposure sequence. Suitable values of t_{min} and t_{max} could be 10 ms and 550 ms, respectively, for example. The choice of center wavelength and FWHM for the filter channels, as well as the corresponding exposure times, should preferably also take into account the following considerations:

(a) The center wavelength and FWHM for at least two channels should be chosen so that characteristic absorption lines can be differentiated, such as those associated with melanin and hemoglobin;
(b) For a given set of center wavelengths, there are upper limits on the associated bandwidths if spectral independence of data in different channels is to be maintained, as illustrated in FIG. 1(a);
(c) Bandpasses should be chosen in the red, green and blue portions of the spectrum which enable "true-color" reconstruction of skin images that are suitable for visualization by clinicians;
(d) The need for high signal-to-noise ratio in each image sets practical lower limits on the product of exposure time and filter bandwidth, especially at short wavelengths, where detector response falls off and lesion reflectance is low; and
(e) The total time taken to acquire the images in all filter bands is preferably less than about three seconds, to minimize patient discomfort and possible motion.

[0042] Based on considerations (d) and (e) above, and also taking into account the varying spectral reflectances of skin of different colors, the exposure times in each filter channel are preferably adjustable, with settings based on the dynamic range achieved on an empirical basis, with trial images. In this manner, both dynamic range and signal-to-noise ratio can be maximized for each filter channel. The preferred method is to choose t_{expi} by iteration, based on intensity histograms of images of the skin obtained with trial exposures at each wavelength band. The histograms are analyzed to determine the number of pixels at the saturation intensity level, $I_{sat} = 2^b-1$ (1023 for b=10 bits). The exposure time is decreased if the number of saturated pixels exceeds a predetermined amount, such as 0.01% of the total. Conversely, to maintain high signal-to-noise ratio, the exposure time is increased if a predetermined percentile in the histogram, 99.9%, for example, is reached at less than a preset threshold, such as 99.5% of I_{sat}. The iteration process typically converges after two or three trials.

[0043] It may be found to be useful to minimize fluorescence by restricting bandpasses to wavelengths of 400 nanometers and above.

[0044] The preferred exposure times at each wavelength for imaging skin of different colors to classify melanomas are listed in Table 1, for the embodiment of Fig. 2 with 10 filters. It has been found that for the blue channel centered at 450 nm, the optimal exposure time for dark skin is 273 ms, which is more than double the optimal 107 ms exposure time for light skin. On the other hand, in the near infrared channel centered at 780 nm, the exposure times listed are much shorter, between 24 and 35 ms, and vary relatively little with skin type. The optimal exposure time for dark skin in the deep blue channel at 430 nm is at t_{max} = 550 ms, due to the low skin reflectance and relatively low optical throughput

of the system at this short wavelength. Even with an exposure time this long, therefore, the image is less than fully exposed. Greater throughput at this wavelength could be achieved, at the expense of poorer response in the infrared.

[0045] In Table 1, the FWHM at 450 nm, is 100 nm, which is much broader than for other wavelengths. It has been found that where images are desired for visual analysis as well as computer processing, the broad wavelength band at 450 nm more closely matches the blue response of the human eye and is therefore preferred. In addition, the broad wavelength band provides data at a higher signal-to-noise ratio.

Table 1 appears below: Optimal Exposure Times (msec) vs. Skin Color

Filter Number (j=i-1)	Center Wavelength (nm)	Filter FWHM (nm)	Very Light Skin	Medium Skin	Tan Skin	Dark Skin
0	430	60	405.2	436.5	484.4	550.0
9	450	100	106.8	124.9	156.1	273.3
1	500	40	56.4	62.9	88.7	130.7
2	550	10	44.2	50.4	71.3	92.9
3	600	10	19.1	24.0	29.6	39.2
8	650	10	74.5	92.3	104.9	132.0
4	700	10	71.6	86.0	98.0	114.4
5	780	30	25.8	29.1	34.9	23.6
6	880	50	34.1	38.6	44.8	46.1
7	950	60	161.1	187.6	205.8	212.0

[0046] Tables similar to Table 1 can be readily constructed based on experimental results for other applications, where other spectral bands may be better suited. For example, in the analysis of wound healing, where it would be desirable to distinguish oxygenated from deoxygenated blood, other spectral bands could be better suited to identify the degree of oxygenated hemoglobin. In addition, the wavelengths and exposure times in Table 1 reflect a balance between the best results for subsequent analysis of the images by a computer, and the best results for visual observation of the images. If visual observation is not necessary, other wavelength bands and exposure times may be used.

[0047] FIG. 3(a) describes how the systems and methods of the present invention provide for calibration of the recorded images. The calibration procedure permits 10-bit image data to be recorded over a large linear dynamic range in each spectral band, independent of skin type. The recorded images can also be standardized for diffuse spectral reflectance. Consistent measures of reflectance ratios in different spectral bands can therefore be obtained, despite variations in illumination pattern with wavelength, changes in the position of the illuminator, or aging of the lamp, for example.

[0048] First, the effects of dark current and "fixed pattern noise" are removed in Step 1. N images are recorded by the camera without illumination. Preferably 8 such dark images are recorded. The average of these N dark images, I_D is calculated and stored in the computer 12.

[0049] Second, spatial in homogeneities in the illumination and in the response associated with each CCD pixel are removed in Step 2. A sequence ofN' images of an illuminated flat, diffuse reflectance standard, such as a white Spectralon® target (R>99%) recorded. As above, N' is preferably 8. The N' images are recorded at each wavelength band. To average over local inhomogeneities in the reflectance standard, the target is moved continuously during the integration time and between exposures. A small motor, such as a reciprocating motor, may be used. The integration time and/or lamp intensity are adjusted by the computer 12 at each wavelength band until negligibly few of the pixels are at or just below an intensity level corresponding to saturation. These N' "flat-field" images are averaged to reduce the effect of spatial non-uniformities in the reflectance standard, as well as to improve the detection signal-to-noise ratio. The resulting averages are stored in the computer as I_{wi}, where i=1,2,...M.

[0050] Next, monochromatic "raw data" images of the skin, I_{si}, are captured by the camera and digitally acquired by the computer 12 within each filter passband, i=1,2,...M. If dermoscopic imaging is used, where a thin layer of mineral oil is spread between the skin and a cover glass is fixed in position in front of the camera, each image of the skin preferably contains an image of a narrow strip of oil-free, diffusely reflecting gray material, held in place on the inside surface of the cover glass, and located along one edge of the field of view. The material may be cut out of a Kodak "18% gray" card. Dermoscopic imaging is preferred for melanocytic lesions. The alternative clinical imaging mode is preferred for the imaging of wounds and bums because contact with the wound or burn by a cover glass is not desired. Although FIG. 2 indicates a lesion present on the skin 2, it will be readily understood that the same method will apply when a wound or burn is present, instead. In the clinical imaging mode, it is preferable to reduce specular reflections by employing the polarizer 31, as indicated in FIG. 2.

[0051] In either the dermoscopic or clinical imaging techniques, a fourth step is preferably provided, in which the raw

data is compensated for dark current and fixed pattern noise and then normalized to the flat-field images. The dark-field compensation is performed by subtracting the stored average dark image I_D both from the flat-field image I_{wi} and from the raw data image I_{si}. The ratio of the results of these subtractions is then taken. This standardizes the dark-corrected raw data to the flat-field image, compensating for spatially varying illumination and pixel-to-pixel response variations. After the ratio is taken, the result is standardized to the maximum level, 2^b-1 which equals 1023 where b = 10 in a 10-bit data representation. The normalization process thus converts the image of the skin and the gray strip into a standardized diffuse reflectance map, with the result preserving a large linear recording dynamic range. In FIG. 3(a), the dark-field corrected and flat-field-normalized images, also referred to as "flat-field-calibrated" images, are denoted as I_{si}. In any image, standardization to maximum level can be reinterpreted directly in terms of equivalent diffuse reflectance on the basis of the average gray level over the image of the gray strip, $\langle I_{gray\ strip} \rangle_i$ and the measured average diffuse reflectance of the gray strip, which is approximately 0.2 and varies in a known and repeatable manner with wavelength.

[0052] Preferably, the average image intensity in the gray-strip region is also used to calculate weighting factors for combining three or more monochromatic images to provide "true-color" visualizations of lesion images on the computer 12 and display 19. This is preferably accomplished in Step 5, where the user selects the spectral bands to be used in the color visualization. Step 5 can take place prior to the imaging session. Four bands are currently preferred for such visualization. Filter bands j=3 and 8, in a 3:2 ratio, for the red (R) channel, filter band j=2 for the green (G) channel, and filter band j=9 for the blue (B) channel, in Table 1. As indicated in Step 6 of FIG. 3(a), the relative weights applied to the R:G:B channels are preferably inversely proportional to $\langle I_{gray\ strip} \rangle_i$ the average intensity over the portion occupied by the gray strip area in each image. This procedure tends to reconstruct the hues and saturations in the original scene to within accuracy limits associated with response nonlinearities of the display 19. To minimize the effects of such nonlinearities with display monitors such as the Sony Model GDM-175E1 Multiscan monitor, for example, the viewer may prefer to adjust the maximum brightness in the image to correspond to the maximum image intensity level of the monitor. A linear transformation step, which can be readily accomplished by commercial software such as Adobe Photoshop, may be used. If the digital images are derived from photographic slides, as in the embodiment of Fig. 1(c), steps 5 and 6 are not necessary.

[0053] As indicated by dashed lines in FIG. 3(a), either the normalized monochromatic images resulting from Step 4 or the color visualization provided from Step 6 can be displayed on the display 19. Any or all of the monochromatic raw images could be displayed as well.

[0054] Fig. 3(b) is a flow chart of a preferred method of processing images according to the present invention for characterizing the condition of a region of interest of the skin of a subject which includes a skin lesion. A skin lesion is selected in Step 50. Digital images of the lesions illuminated by light filtered at the desired wavelengths of λ_1 -λ_4..., are digitally recorded in Steps 52, 54, 56 and 57..., as described above. Each of these digital images is processed separately. In Step 58, the image taken in a spectral band wherein the amount of light re-emitted by abnormal skin is less than the amount of light re-emitted by normal skin, is used to create a mask for segmentation. Preferably, the image used for segmentation is the image of the shortest available spectral band. A blue spectral band is preferred. At Steps 60, 62, 64, 65..., each of the images of the lesion that correspond to different wavelengths are segmented by means of the segmented mask obtained at Step 58. Alternatively, one or all of the images may be separately segmented. Estimated values of lesion parameters are computed from each of the segmented images, in Step 66. Lesion parameters found to be useful for classifying and characterizing the lesion and statistical methods for computing the estimated values of the parameters, are discussed further, below. The estimated values of the parameters are provided to a linear classifier in Step 68. The linear classifier employs a linearly weighted sum of the individual parameters to derive a value used to classify the lesion as malignant or benign. A non-linear classifier such as a Gaussian quadratic classifier or an artificial neural-net classifier, each employing a suitable defined merit function, may be used as well. In either case, the numerical value produced by the classifier is subjected to a threshold test at Step 100, such that if the test is passed, the lesion is suspected to be malignant melanoma. If the test is failed, the lesion is declared not to be melanoma. The lesion could also be characterized as invasive or non-invasive with a different classifier.

[0055] If automatic segmentation is not successful in step 58, i.e., a closed boundary curve is not formed at the first spectral band chosen, the next lowest spectral band is used. This process may be repeated at a predetermined sequence of spectral bands. If segmentation cannot be completed automatically, the operator may intervene to complete the segmentation, as is known in the art.

I. SEGMENTATION

[0056] The segmentation algorithms will now be described. The function of the segmentation algorithms is to discriminate between the lesion and normal skin in the field-of-view of the imaging device. This is a complex function since not only is the lesion appearance highly variable but so is the appearance of healthy skin due, for example, to the presence of blotches, hair, wrinkles, etc. The automatic algorithm described here is based on the images in the blue spectral band, from about 400 nanometers (nm) to 500 nm. This spectral band was selected because melanin absorption increases

rapidly as the wavelength decreases. While the use of ultraviolet radiation could be advantageous, since ultraviolet radiation is carcinogenic, only low doses can be used.

[0057] Segmentation in blue consists of several automatic steps:

Location of major peaks in the histogram

[0058] First, the histogram of intensity levels in the whole image is determined. Then, given a sliding window with the range of $(2I_r + 1)$ intensity levels, the number of peaks Np in the histogram over that range is determined. IfNp < 2, the range is decreased by two levels and ifNp > 3, the range is increased by two levels and the process is repeated until Np = 2 or 3. For most of the images in the data base used in this study, there are two major peaks in the histogram. Examples of such histograms are shown in Fig. 4(a) for a malignant melanoma and in Fig. 4(b) for an atypical melanocytic nevus. The lesions correspond to the lower intensity peak, since it is darker than the surrounding skin due to strong absorption by melanin at 400 nm. However, some lesions are quite inhomogeneous, and the automatic procedure described can find 3 major peaks, as illustrated in Figs. 5(a) and 5(b).

Location of the intensity threshold

[0059] If two major peaks are found in the intensity histogram, then the threshold value I_{th} is selected to be at the histogram minimum between these two peaks, as indicated in Figs. 4(a) and 4(b). In the case of three peaks, it has been found that, if the middle peak is closer to the lowest intensity peak, the threshold value is at the minimum between the middle and the highest intensity peak. If the middle peak is closer to the highest intensity peak, then the threshold value is at the minimum between the middle and the lowest intensity peak, as shown in Figs. 5(a) and 5(b).

Iterative thresholding of the image

[0060] The next step in image segmentation is iterative thresholding of the images. Given the intensity threshold value, image thresholding has been typically accomplished as follows. The intensity *I(x,y)* of a pixel at location *(x,y)* is set to zero if it exceeds I_{th}, i.e.,

$$I_L(x,y) = \begin{cases} I(x,y), & if \quad I(x,y) < I_{th}; \\ 0, & otherwise. \end{cases} \tag{1}$$

[0061] Figs. 6(a) and 6(d) are examples of digital images of malignant melanoma and atypical melanocytic nevus in the blue spectral band, respectively. Figs. 6(b) and 6(e) are images resulting from the direct thresholding as in Eq. (1). As shown in Figs. 6(b) and 6(e), "holes" can appear within the lesion. Therefore, an iterative approach is preferably used. First, the intensity of pixels at the image edges is set to zero. Then as each iteration proceeds, the intensity *I(x, y)* of a pixel at location *(x,y)* is set to zero if it exceeds I_{th} and at least one of its nearest neighbors has zero intensity, i.e.,

$$I_L(x,y) = \begin{cases} 0, & if \quad I(x,y) \geq I_{th} \ and \ N_{nn} = 0; \\ I(x,y), & otherwise, \end{cases} \tag{2}$$

where

$$N_{nn} = \min[I(x-1,y), I(x+1,y), I(x,y-1), I(x,y+1),]. \tag{3}$$

This procedure is iterated until there are no pixels with $I(x,y) > I_{th}$ and a nearest neighbor with zero intensity. Typically, only a few iterations are required to complete this step. The resulting images are shown in Figs. 6(c) and 6(f).

[0062] Figs. 7(a) and 7(d) are other examples of digital images of malignant melanoma and atypical melanocytic nevus, respectively. Figs. 7(b) and 7(e) are images resulting from the iterative thresholding described above. Various dark blobs are seen in the images outside of the lesion area. These are removed in the following step.

Image cleaning

[0063] Some of the blobs in the thresholded images arise naturally due either to dark spots on the normal skin or to hair as in Fig. 7(b). Others are artifacts such as the film edge at the top of the nevus image in Fig. 7(e), or dark bands at the image edges from the slide mounts. These bands are removed by automatically testing for their presence and then setting the intensity of appropriate pixels to zero. The remaining blobs could also be removed by determining the overall number and size, i.e., number of pixels, of connected blobs, and then setting to zero the intensity of pixels belonging to the small ones. However, since the size of some lesions exceeds 100,000 pixels, this would be computationally very intensive. Therefore, in practice, this step is preferably carried out as follows. First, perimeter pixels for all blobs in the image are located. The number of such pixels is typically less than 10,000. Then, each of these perimeter pixels is assigned to a unique blob and its size, the number of perimeter pixels in the blob, is determined. The intensities of pixels belonging to blobs of size less than 30% of the maximum size for that image are set to zero. This process is iterated until all the small blobs are removed. Typically less than 10 iterations are needed. The intensity of all the nonzero pixels is then set to 1. The resulting binary lesion mask has the following property:

$$I_B(x,y) = \begin{cases} 1, & \text{if pixel at } (x,y) \text{ belongs to lesion ;} \\ 0, & \text{otherwise.} \end{cases} \qquad (4)$$

Figs. 7c) and 7(f) illustrate the resulting lesion masks.

[0064] In the images illustrated in Figs. 7(a) and 7(d), dark hairs were either absent or were not adjacent to the lesion. However, there are many images with prominent dark hair overlapping lesions. Segmentation of such images is described in the following section.

Segmentation of images in presence of hair

[0065] Figs. 8(a) and 8(e) are examples of lesion images with hair. Since the segmentation algorithm described in the previous section would leave some of these dark hairs connected to the lesion, images with hair require special preprocessing to allow for hair removal from the normal skin. Since hair is a problem because of its high contrast with respect to the normal skin in the blue, a spatial filter was designed to locate hairs. This filter, shown in Fig. 9, is magnification dependent. It is applied to every pixel of the original image and the result is thresholded at the 5% of maximum value in the whole filtered image. The filtered images are shown in Figs. 8(b) and 8(f) in reverse intensity contrast, wherein bright features are dark. Hairs are clearly located in the filtered images. It should be noted that the lesion interior is almost entirely blank, indicating poor contrast between hair and lesion.

[0066] Hairs are removed by an averaging process. For every non-zero pixel at (x, *y)* in the filtered image one finds the locations of 4 nearest pixels (x_l,y), $(x_u,,y)$, (x,y_l), (x,y_u) (where $x_l < x < x_u$ *and* $y_l < y < y_u$) with zero intensity. Then the intensity of every pixel in the original image that has non-zero intensity in the filtered image is replaced as follows:

$$I_n(x,y) = \frac{1}{12}\sum_{k=1}^{3}[I(x_u + k, y) + I(x_l - k, y) + I(x, y_u + k) + I(x, y_l - k)]. \qquad (5)$$

The images averaged in this way are shown in Figs. 8(c) and 8(g). It is seen that the contrast between hairs and normal skin is considerably reduced in these images. After this preprocessing, the segmentation algorithm described in the previous section is applied to the averaged image. The final binary lesion masks are shown in Figs. 8(d) and 8(h).

[0067] The preprocessing step described above may be used for all lesion images, regardless of the presence of hair, enabling fully automated lesion segmentation. However, since this requires more computation and causes some border blurring, the need for preprocessing due to the presence of dark hair is preferably indicated interactively by an operator, and images preprocessed only when necessary.

Segmentation of images in other spectral bands

[0068] Since melanin absorption is strongest in the shortest-wavelength band, the lesion area, which appears as a dark region in the image, appears largest in the blue spectral band. Since longer wavelength radiation penetrates deeper into skin, if the thickness of the melanin-containing layer compensates for the weak absorption, that part of the lesion will appear dark even in the red spectral band. For thick melanomas, with Breslow thickness greater than 1 mm, one

expects dark lesions even in the infrared bands. This was observed, for example, by Marchesini et al., Photochemistry & Photobiology, "In vivo spectrophotometric evaluation of neoplastic and non-neoplastic skin pigmented lesions. III. CCD camera-based reflectance imaging," Vol. 62, 1995, pp. 151-154. However, for early malignant melanomas, with Breslow thickness less than 1 mm, great variability of images in the red spectral band has been found. There may be so little contrast between the lesion and the normal skin that direct segmentation is not possible. Therefore, segmentation of lesion images in all spectral bands with wavelength λ uses the binary lesion mask ofEq. (4), obtained in the shortest-wavelength band, here blue, i.e.,

$$I_L(x,y;\lambda) \equiv I(x,y;\lambda) \times I_B(x,y). \quad (6)$$

[0069] Figs. 10(a) - 10(f) are a series of images of the lesions, with their corresponding histograms shown in Figs. 5 (a) and 5(b), segmented in the blue, green, and red spectral bands, as indicated. The automatically determined lesion borders are superimposed on the original lesion images. The area of dark regions is largest in the blue.

II. LESION PARAMETER ESTIMATION

[0070] Objective and automatic lesion classification requires quantitative algorithms for lesion parameter estimation from their segmented images. Such parameters should be dimensionless, independent of lesion location and orientation in the image, and of the overall image brightness. It is convenient to separate the parameters used here into four broad classes: asymmetry, blotchiness, border, and texture. Parameters with the highest diagnostic accuracy for malignant melanoma are listed in Fig. 11, together with the values of diagnostic accuracy, sensitivity, and specificity, for a training set of images of 41 malignant melanomas and 104 atypical melanocytic nevi obtained with the imaging system described above, with respect to Fig. 1(a) wherein the monochrome camera 16 was used to digitize slides. The subscript *r, g,* or *b* refers to the red, green, or blue spectral band in which the parameter is evaluated. If additional spectral bands are used, then each of the parameters could be computed at the additional spectral bands, as well.

[0071] Specific algorithms for these parameters are described below. For simplicity it is assumed that the image pixels are square but the algorithms described below may be implemented for rectangular pixels as well.

Lesion Asymmetry

Asymmetry parameter

[0072] The lesion asymmetry parameter is based on moments of the intensity distribution. First, the lesion orientation angle is used to locate the principal axes, which are just the symmetry axes for symmetric lesions. The angle θ is computed from

$$\tan 2\theta = \frac{2 < (x - x_c)(y - y_c) >}{< (x - x_c)^2 > - < (y - y_c)^2 >}, \quad (7)$$

where the lesion intensity centroid is at

$$x_c = < x > \ and \ \ y_c = < y >. \quad (8)$$

[0073] The angular brackets in Eqs. (7) and (8) denote an intensity moment, which for any function *f (2, y)* of position in the image can be computed as follows:

$$< f(x,y) > \equiv \frac{\sum_x \sum_y f(x,y) I_L(x,y)}{\sum_x \sum_y I_L(x,y)}, \quad (9)$$

where $I_L(x,y)$ is the segmented lesion image. In order to compare properties of different lesions, the parameters used are independent of the orientation of the lesion in the image. Therefore, the lesion asymmetry is determined with respect to the principal axes. The measure of asymmetry described here requires rotation of the image by an angle θ so that principal axes are parallel to the image axes. In this principal-axis coordinate system the following asymmetry factors are defined:

$$A_x = \frac{\sum_n \sum_y |I_L(x_c + n, y) - I_L(x_c - n, y)|}{\sum_x \sum_y I_L(x,y)}, \tag{10a}$$

$$A_y = \frac{\sum_x \sum_n |I_L(x, y_c + n) - I_L(x, y_c - n)|}{\sum_x \sum_y I_L(x,y)}. \tag{10b}$$

The asymmetry parameter,

$$A = A_x + A_y, \tag{11}$$

is a measure of asymmetry in the geometric shape of a lesion as well as in the distribution of lesion pigmentation. Asymmetry parameters tend to be larger for malignant melanomas than for atypical melanocytic nevi.

Binary asymmetry parameter

[0074] If the intensity distribution I_L in Eqs. (10a) and (10b) is replaced by the binary intensity distribution ofEq. (4), then the corresponding asymmetry parameter A_{bin} is the fraction of the lesion pixels which do not have a counterpart on the other side of the principal axis. Thus, when based on the binary intensity distribution, parameter A_{bin} is a measure of the asymmetry of the geometric shape of the lesion.

Lesion Blotchiness

[0075] Visually, many early malignant melanomas appear blotchy. In multispectral images there may be darker and lighter regions or blotches of rather homogeneous intensity. In color images, in contrast, there may be regions of different colors. Therefore, it is of interest to quantify such blotchiness in order to differentiate malignant from benign lesions.

Blotchiness Parameter Based on Spatial Intensity Distribution

[0076] The lesion is divided into N_t "topographic" regions. If I_{max} and I_{min} are the maximum and minimum intensities in the lesion in some spectral band, respectively, then a pixel at (x,y) belongs to the nth region if

$$I_{\min} + (n-1)\frac{I_{\max} - I_{\min}}{N_I} \le I_L(x,y) < I_{\min} + n\frac{I_{\max} - I_{\min}}{N_t}. \tag{12}$$

[0077] For nth topographic region defined in Eq. (12), a distribution of distances of pixels in that region from the intensity centroid of the binary lesion mask

$$d_n(x,y) = \sqrt{(x_n - x_c)^2 + (y_n - y_c)^2} \tag{13}$$

is obtained and its mean value $< d_n >$ and variance $Var(d_n)$ are computed. The measure of lesion blotchiness based on spatial intensity distribution is

$$Bl = \frac{\sum_{n=1}^{N_t} \sqrt{Var(d_n)}}{\sum_{n=1}^{N_t} < d_n >} . \qquad (14)$$

This parameter can be evaluated in every spectral band.

Blotchiness Parameter Based on Centroids

[0078] The lesion is again divided into N_t "topographic" regions as defined in Eq. (12). An intensity centroid $(x_c(n), y_c(n))$, defined in Eqs. (8) and (9), is then computed for each such region separately. The blotchiness parameter based on the centroid is defined as

$$C = (X_{\max} - X_{\min})(Y_{\max} - Y_{\min}) / A_l \qquad (15)$$

where, for example, X_{max} is the maximum value of $x_c(n)$, and A_l is the lesion area in pixels. This blotchiness parameter is also determined in each spectral band separately.

Blotchiness Parameter Based on Spatial Color Distribution

[0079] The "color" in this analysis is not related to the visual perception of color. It is a quantitative descriptor of the relative intensities in red, blue, and green channels in a particular pixel.

[0080] All the other lesion parameters described here involve analysis of images in each spectral band separately. Therefore, absolute calibration of image intensities was not necessary. However, in order to describe the color distribution, normalization of intensities in red, green, and blue spectral bands is needed, so that intensities in the three channels are equal for white. In the spherical color coordinate system,

$$R(x,y) = \frac{I_R(x,y)}{I_R(x,y) + I_B(x,y) + I_G(x,y)},$$
$$G(x,y) = \frac{I_G(x,y)}{I_R(x,y) + I_B(x,y) + I_G(x,y)}, \qquad (16)$$

where the subscripts R, G, B refer to red, green, and blue spectral bands, are chosen as the independent variables. The lesion is then divided into color regions as follows. First $R(x,y)$ and $G(x,y)$ are divided into N_R and N_G topographic regions. A color region is defined as a particular combination of two topographic regions. The total number of color regions is

$$N_C = N_R \times N_G . \qquad (17)$$

The blotchiness parameter based on color is defined in analogy with Eq. (14):

$$Cl = \frac{\sum_{n=1}^{N_C} \sqrt{Var(d_n)}}{\sum_{n=1}^{N_C} < d_n >} \qquad (18)$$

Lesion border

Border Irregularity Parameter

[0081] Border irregularity is a well-known feature of malignant melanomas. It is typically defined as the ratio of the measured lesion perimeter to the perimeter of a circle with the same area as the lesion. Since perimeter is difficult to estimate reliably, a statistical descriptor of border irregularity is used here. In addition, many lesions are elongated and an ellipse is a better approximation for such lesions with regular borders than a circle.

[0082] Using the binary lesion mask of Eq. (4), the lesion intensity centroid from Eq. (8), orientation angle from Eq. (7), area, and the aspect ratio defined as

$$AR = \frac{\sqrt{< x' - x_c >^2}}{\sqrt{< y' - y_c >^2}}, \tag{19}$$

where primes refer to the coordinate system defined by the lesion principal axes, are determined. These values are then used to construct an ellipse that is the best regular approximation to the lesion border. For each lesion border pixel at (x_b,y_b), its angle with respect to the horizontal axis:

$$\phi = \tan^{-1} \frac{(x_b - x_c)}{(y_b - y_c)}, \tag{20}$$

and the location of the ellipse border for the same angle $(x_e(\phi), y_e(\phi))$ are determined. The distribution of distances between the ellipse border and lesion border:

$$d_{eb}(x_b, y_b) = d_b(x_b, y_b) - d_e(\phi), \tag{21}$$

where

$$d_b(x_b, y_b) = \sqrt{(x_b - x_c)^2 + (y_b - y_c)^2} \tag{22}$$

and

$$d_e(\phi) = \sqrt{x_e^2 + y_e^2}, \tag{23}$$

is obtained and the border irregularity parameter is defined as

$$B = \frac{\sqrt{Var(d_{eb})}}{< d_b >}. \tag{24}$$

Border Gradient Parameter

[0083] Another parameter that quantitatively characterizes lesion border is the measure of intensity gradients across the lesion borders over the length scale defined by n_g, in units of pixels. For each lesion border pixel at (x_b,y_b) one determines whether pixels at $(x_b \pm n_g, y_b \pm n_g)$ are at the border. If they are not, then the gradient is defined as

$$G(x_b, y_b) = \frac{1}{2}[\left|I(x+n_g, y) - I(x-n_g, y)\right| + \left|I(x, y+n_g) - I(x, y-n_g)\right|]; \quad (25a)$$

otherwise, if pixels at (x $\pm$ n_g,y) are not on the border,

$$G(x_b, y_b) = \left|I(x+n_g, y) - I(x-n_g, y)\right|, \quad (25b)$$

or, if pixels at $(x, y \pm n_g)$ are not on the border,

$$G(x_b, y_b) = \left|I(x, y+n_g) - I(x, y-n_g)\right|. \quad (25c)$$

The border gradient parameter is defined as

$$G = \frac{\sqrt{Var(G)}}{< G >} \quad (26)$$

Lesion Texture

[0084] The description of lesion texture is particularly vulnerable to subjective judgement. The quantitative evaluation of lesion texture parameters is possible only using computer-based image analysis. While many such parameters are possible, those found to be helpful in discriminating between malignant melanomas and atypical melanocytic nevi are described below.

Texture Parameters Based on Local Intensity Variations

[0085] Texture parameters are defined over a length scale n_t in units of pixels. For example, consider a pixel located at (x,y) in the lesion. Let I_l and I_u be the minimum and the maximum intensities in an image in the $2n_t + 1$ x $2n_t + 1$ window around this pixel, i.e., in the range $[x - n_t, x + n_t]$ and $[y - n_t, y + n_t]$. Consider a variable

$$C_1(x, y) = \frac{I_u - I_l}{I_l} \quad (27)$$

[0086] The first two texture parameters are defined as:

$$T1 = \frac{\sqrt{Var(C_1)}}{< C_1 >} \quad (28)$$

and

$$T2 = \sqrt{Var(C_1)} \quad (29)$$

[0087] Another texture parameter uses the following variable:

$$C_3(x,y) = 4w(0,0) + w(-n_t,0) + w(n_t,0) + w(0,-n_t) + w(0,n_t), \\ -2[w(-n_t,-n_t) + w(-n_t,n_t) + w(n_t,-n_t) + w(n_t,n_t)] \quad (30)$$

where

$$w(i,j) = I(x+i, y+j)/I(x,y). \quad (31)$$

If the value of C_3 is negative, it is set to zero and the corresponding texture parameter is

$$T3 = \frac{\sqrt{Var(C_3)}}{<C_3>}. \quad (32)$$

[0088] Another variable that leads to a texture parameter useful for classification of melanocytic lesions is:

$$C_4(x,y) = 8w(0,0) - w(-n_t,0) - w(n_t,0) - w(0,-n_t) - w(0,n_t) \\ -w(-n_t,-n_t) - w(-n_t,n_t) - w(n_t,-n_t) - w(n_t,n_t) \quad (33)$$

Again, if the value of the variable is negative it is set to zero and the corresponding texture parameter is

$$T4 = \frac{\sqrt{Var(C_4)}}{<C_4>}. \quad (34)$$

Texture Parameters Based on Pigmented Network

[0089] Texture parameters have also been developed by considering the properties of a pigmented network. These texture parameters are measures of variability in the area of the dermal papillae and in the aspect ratio (length/width) of the rete ridges.

[0090] Since dermal papillae appear as the brighter part of the network, one seeks all the local maxima over a $2n_t + 1$ x $2n_t + 1$ window. Starting from such a maximum at (x_m, y_m), one finds local one-dimensional minima in eight directions (2 vertical, 2 horizontal, and 4 diagonal) and locates the vertices of an octagonal region one pixel closer to the maximum intensity pixel than the minimum pixel. Such octagonal regions approximate the areas of dermal papillae A_{dp} which are computed from the known location of vertices; the corresponding texture parameter is

$$T5 = \frac{\sqrt{Var(A_{dp})}}{<A_{dp}>}. \quad (35)$$

Some of the areas determined by this algorithm are due to bubbles visible in some of these dermoscopic images. However, since there are typically on the order of hundreds of areas, and on the order of tens of bubbles, the statistical parameters should not be significantly biased by this artifact.

[0091] The aspect ratio of rete ridges is determined in a similar fashion, although one starts with local minima since rete ridges appear dark in the images. The vertices of an octagonal region are determined in this case from one-

dimensional maxima in the eight directions. The maximum and minimum extents of this region are then determined and the aspect ratio R is computed. This texture parameter then is

$$T6 = \frac{\sqrt{Var(R)}}{< R >}. \qquad (36)$$

III. LESION CLASSIFICATION

[0092] Selection of lesion parameters for classification was done by determining the maximum diagnostic accuracy for malignant melanoma for each parameter computed in every spectral band available for the training set of images. As mentioned above, diagnostic accuracy, sensitivity to malignant melanoma and specificity for the selected twenty two parameters are shown in Fig. 11. These parameters were then used as input to the linear classifier. Nonlinear classifiers may be used as well.

[0093] For each lesion k the linear classifier is

$$L(k) = \sum_{n=1}^{22} w_n X_n(k), \qquad (37)$$

where $X_n(_k)$ are the parameters for the kth lesion and weights w_n are to be determined so that a specified function $F(L)$ attains maximum value. The following functions $F(L)$ were used: 1) specificity under constraint of 100% sensitivity to malignant melanoma for the training set which included 41 malignant melanomas and 104 atypical melanocytic nevi; (2) classification accuracy for the 24 invasive and 16 noninvasive malignant melanomas of the training set; and 3) correlation with the Breslow thickness for the 24 invasive malignant melanomas.

[0094] Given any training set of lesion images and corresponding set of lesion image parameters, the weights that maximize $F(L)$ are found as follows. First, an initial range and resolution Δ for w_n are selected. For each allowed set of values of w_n, the values $L(k)$ are computed for each lesion. The value $F(L)$ is determined based on the input from histopathological evaluation of the lesion based on a biopsy, such as the diagnosis of the lesion as benign or malignant, and the Breslow thickness for a malignant melanoma. The range of w_n's is adjusted until the maximum value of $F(L)$ is inside the range. Then the resolution Δ is reduced by a factor of two, and the process is repeated until Δ reaches specified minimum value Δ_{min}. This procedure determines the weights w_n only up to a multiplicative constant. It is noted that the classifiers resulting from a particular training set are applicable only to images with a specific spatial and spectral resolution, and that lesion images obtained with a different imaging system may require the development of different classifiers, by the procedures described above.

[0095] Since detection of melanoma in its early stage significantly improves prognosis, there is a need for reliable methods of early detection. Clinical evaluation of melanocytic lesions is, however, a problem since reliable differentiation between early malignant melanoma with Breslow thickness less than 1 mm and atypical melanocytic nevus is difficult even for experienced dermatologists. In order to detect as many early melanomas as possible, weights in the linear classifier are preferably chosen to maximize specificity under the constraint of 100% sensitivity to malignant melanoma for the training set. For each set of weights, one finds the threshold value L_{th} of the linear classifier such that a L_{th} lesion is classified as suspicious of malignancy if $L(k) > L_{th}$, and as benign otherwise. The resulting classifier for the training set is

$$\begin{aligned} L_1 &= 0.025A_{bin} + 0.090A_b + 0.069A_g + 0.160A_r + 0.128C_b \\ &+ 0.095Cl + 0.038B + 0.107T1_g + 0.064T2_g + 0.018T2_r \\ &+ 0.111T3_b + 0.167T3_g + 0.268T5_b \end{aligned} \qquad (38)$$

where the weights are normalized so that the threshold value equals one. This classifier with sensitivity to malignant melanoma of 100% and specificity of 85% is shown in Fig. 12. Statistical significance of the specificity and sensitivity was assessed by considering the binomial probabilities for the value of L_1 to exceed the threshold for the 41 malignant melanomas and 104 atypical melanocytic nevi of the training set separately. At the 95% confidence level, one finds that sensitivity is not less than 93% while specificity is not less than 79%. Since there are several melanomas very close to

the threshold value, a practical classifier may use a threshold value that is less than one. It has been found that this set of 145 images is sufficient to yield statistically significant results. A greater number of images may be used, as well.

[0096] Some of the noninvasive melanomas, called melanomas in-situ, are confined to epidermis and are 100% curable by surgery. The invasive melanomas, i.e., superficial spreading melanomas in our data base, require more extensive surgery. Therefore, it is of clinical interest to differentiate between invasive and noninvasive melanomas and a linear classifier was trained to perform this task. This classifier, with weights chosen to maximize the overall classification accuracy for the 24 superficial spreading melanomas and 16 melanomas in-situ of the training set is

$$L_2 = -1.00A_b - 0.14Bl_g - 2.47Bl_r - 0.4C_b - 0.98Cl \\ -1.17T2_r + 0.53T4_b + 1.98T5_b + 1.58T6_b - 0.73 \quad (39)$$

where a constant was subtracted from the classifier values to obtain the threshold value of zero. This classifier, with overall classification accuracy of 92.5%, is shown in Fig. 13.

[0097] Since prognosis for invasive melanomas correlates strongly with the Breslow thickness, a linear function of lesion parameters Q was trained to maximize the Pearson correlation coefficient between Q and the Breslow thickness for a set 24 superficial spreading melanomas. This function is

$$Q = 0.955A_g - 1.391A_r + 2.791Bl_b - 1.320Bl_g + 0.146C_b \\ + 0.267C_r - 0.506B + 0.202T1_g + 1.476T2_r - 0.485 \quad (40)$$

and is shown in Fig. 14. Even though there are only 24 superficial spreading melanomas in the data base, the high correlation of 0.77 is statistically very significant since $p = 9 \times 10^{-6}$.

[0098] The classifiers ofEqs. (38)-(40) are applicable to the imaging system described above, with respect to Fig. 1 (a) wherein the monochrome camera 16 was used to digitize slides.

[0099] For other imaging systems, having different spatial and spectral resolution, different classifiers may need to be developed, based on a sufficient data base of lesion images obtained with that imaging system, in accordance with the procedures described above.

[0100] The segmentation, parameter estimation and classification programs described in Sections I-III, above, can be implemented on any personal computer, using a programming language, such as FORTRAN or C. The program can be stored on any convenient media readable by a computer, such as read only memory, ("ROM"), random access memory with a battery backup, electrically programmed ROM (EPROM), electrically erasable ROM (EEPROM), floppy disc, CD ROM, or a hard disc. Other suitable media may be used, as well.

[0101] While the procedures of Sections I-III were described with respect to digital images obtained by imaging color photographic slides of skin lesions with a monochrome CCD camera 16 in accordance with the system of Fig. 1c, these procedures are readily adaptable to the analysis of digital images of skin lesions acquired directly from the region of interest of the skin with a digital electronic camera, such as the monochrome CCD camera 6 of Fig. 1a and Fig. 2. Preferred parameters for direct digital imaging of a region of interest of skin are described, below.

[0102] In the process described in Sections I-III, above, segmentation was conducted in the blue wavelength band. The segmented mask in blue was then applied to images in the red and green wavelength bands. Where images at additional wavelengths are provided, segmentation is preferably first attempted at the shortest available spectral band in which the amount of light re-emitted by skin is different within skin having an abnormal condition than within skin having a normal condition. The contrast between the melanocytic lesion and normal skin tends to be highest at the shortest spectral band because melanin close to the skin surface generally has the highest absorption and causes the greatest scattering. In other skin conditions, such as wounds or bums, other chromophores, such as hemoglobin, tend to produce strong absorption and scattering.

SECTION IV

ESTIMATION OF OTHER PARAMETERS

[0103] In addition to the new parameters defined in Section II, above, the values of conventional dermoscopic parameters may also be incorporated into the classifier. For example, a dimensional parameter which is a function of the length of a principal axis of the segmented image, may additionally be used. Whether or not the length of the principal axis of

a skin lesion exceeds a suitable threshold, such as 6 mm, may be incorporated into the classifier.

[0104] Values for the standard deviation of reflectance and the mean reflectance may also be used. The ratio between the standard deviation and the mean has been found to be useful.

[0105] Wavelet maxima representations may also be used to compute estimated values of the texture and other parameters of a skin lesion or other skin condition, separately or in conjunction with the non-wavelet derived parameters described, above. Values of lesion parameters may be estimated by the following steps:

(1) segmenting each of the digital images in each spectral band, preferably automatically;
(2) subdividing each digital image into border and interior regions of the lesion;
(3) applying the dyadic, multiscale, continuous wavelet transformation ("CWT") to the digital image in each spectral band;
(4) producing wavelet maxima representations ("WMRs") of the CWT in the border and interior regions of each image at each spectral band; and
(5) computing estimated values for rotation-and translation-invariant statistical parameters from the WMRs, to characterize the textures of the border and inside regions, for each image.

[0106] Preferably, the segmentation mask is created in one spectral band in accordance with the procedure described in Section I, above, separating the skin lesion from the remaining skin in the region of interest. Then, that segmentation mask is used to define the lesion/skin "border region" separately, in each of the spectral bands. Any or all of the images may be segmented and subdivided independently, as well.

[0107] To define the border region, pixels assigned to the lesion (within the segmentation mask), which border on pixels assigned to normal skin (outside of the segmentation mask), are used to define centers of circular regions. For skin lesions, the center preferably has a fixed 8-pixel radius and a 17-pixel diameter. All pixels lying within such circular regions are assigned to the border of the lesion in each digital image.

[0108] All pixels in the neighborhood of each pixel of the image contribute to the CWTs centered within the border and interior regions of each digital image. Each pixel in each region serves as a center of a "mother" wavelet. Each mother wavelet is scaled to span six different "scale wavelets," which play the role of local band-pass spatial filters that can selectively zoom in on different scales in the lesion structures of interest. See, for example, Daubechies, I, "The Wavelet transform, time-frequency localization and signal analysis.", IEEE Trans Inform Theory 36:961-1005 (1990); Aldroubi, A. et al., Wavelet in Medicine and Biology, C&C Press, NY, pp 11-15 (1996). The fine/coarse filtering that the scale wavelets provide also reduces background noise.

[0109] Wavelet maxima representations ("WMRs") are "multiscale" spatial maps that indicate the locations of local maxima of changes in image intensity and provide a quantitative measure of those changes. They are, therefore, suitable for characterizing textures at different "scales". See, for example, Mallat S, Hwang, W L. "Singularity detection and processing with wavelets., "IEEE Trans Inform Theory 38:617-643, 1992; Mallat S, Zhong S. "Wavelet maxima representation." Wavelets and Applications, Springer-Verlag, Y. Meyer (ed.), NY, pp. 207-284, (1992); Mallat S, Zhong S., "Characterization of signals from multiscale edges.", IEEE Trans Patt Anal Mach Intell 14:710-732 (1992). WMRs are used here to represent the border and the interior regions of each lesion, in each of the spectral bands separately. Differences in texture between the border and interior regions correspond to differences in activity of the wavelet maxima at coarse scale and at finer scale.

[0110] The coefficient distributions of the WMRs are used to estimate values of statistical parameters for each lesion which are translation- and rotation-invariant. These parameters summarize the image structure in each region and in each spectral band through statistical properties of the wavelet coefficient distribution at each of the spatial-scale levels.

[0111] The large number of candidates of wavelet parameters are used individually to train and then to test a classifier, as described in Section III, above. The classifier can be the linear classifier of Equation 37 above, preferably under the constraint of maximizing specificity subject to 100% sensitivity. A non-linear classifier such as a Gaussian quadratic classifier which is designed to minimize a cost function which is a linearly weighted sum of the fraction of missed melanomas, and of the total misclassification error, may also be used. One such Gaussian quadratic classifier is as defined in Fukunaga, K, Introduction to Statistical Pattern Recognition, Academic Press, Boston, pp 19-96, 125 (1990). In the process of selecting the best subset of these parameters for classification, the training and testing of the classifier was based on a "leave-one-out" strategy, for selection of the training set. *Id.* at 219-221.

[0112] When using the quadratic Gaussian classifier, the parameters are modeled as elements of a p-dimensional vector, $X=(x_1, x_2, ..., x_p)$, each of which is normally distributed over the malignant (melanoma) and benign (AMN) classes, with (vector) means $M_1=(m_{1\,1}, m_{1\,2},..., m_{1\,p})$ and $M_2=(m_{2\,1}, m_{2\,2}, ..., m_{2\,p})$, respectively, and with covariance matrices Σ_1 and Σ_2 (which are generally different), for $p \leq 12$, for example. The quadratic Gaussian classifier that discriminates between the two classes employs normalized "distances" defined (in standard matrix notation) by:

$$(X\text{-}M_i)^T \Sigma_i^{-1}(X\text{-}M_i),$$

where $\Sigma i\text{-}_1$ is the matrix inverse to Σ_i. Mi and Σ_i , are estimated from the available data. In practice, each classifier is developed on the basis of the means and covariances estimated over a training set, and the resulting classifier is then exercised over a testing set. The performance of the classifier is analyzed by studying the sensitivity and specificity achieved as one varies the threshold function:

$$h(X)=f(X,M_1, \Sigma_1) - f(X,M_2, \Sigma_2)$$

where:

$$f(X,M_i, \Sigma_i) = \tfrac{1}{2}(X\text{-}M_i)^T\Sigma_i^{-1} (X\text{-}M_i) + \tfrac{1}{2}\ln|\Sigma_i|, \; i=1,2,$$

and M_i and Σ_i are estimators of M_i and Σ_i that are obtained from the sampled data sets.

[0113] Minimization of the following *cost* function is used to rank parameters that are candidates for use in the classifier:

Cost = α (1-Sensitivity) + (1-α)(1-GlobalError), where Sensitivity = (Number of correctly classified melanomas)/(Total melanomas), GlobalError = (Number of incorrectly classified lesions)/(Total lesions) and α is a constant, preferably between 0.4 and 0.6, and more preferably 0.45.

[0114] A limited database of images obtained by directly imaging skin lesions with the system of Fig. 1a was used to develop non-linear and linear classifiers and determine the most useful parameters. The wavelet parameters found most useful in characterizing the skin lesion based on the available database were: 1) the number of maxima per unit area (per pixel); 2) the mean value of the WMR coefficients, 3) the root-mean-square value of the WMR coefficients, 4) the mean absolute deviation about the WMR coefficients, and 5) the skewness of the WMR coefficients. Preferably, in addition to the number of maxima per pixel, the ratio of the mean value of the WMR coefficients to their standard deviation, the ratio of the mean value to their mean absolute deviation, and the skewness normalized to the cube of the standard deviation, are used.

[0115] Two additional wavelet related parameters are referred to as a goodness of fit measure and an intercept measure. The intercept measure is a measurement of the degree of change of a statistic of the wavelet coefficient distribution with increment in wavelet level. The statistic is preferably the average rate of change of the number of wavelet maxima per unit area. One way to compute this average is to determine the level 0 intercept of the best linear fit of the number of wavelet maxima per unit area, with respect to wavelet level.

[0116] The goodness of fit measure quantifies the degree of deviation of the intercept measure from linearity. Preferably, the deviation of the number of wavelet maxima per unit area, with respect to level, is estimated.

[0117] Another parameter is the slope of the best fit linear trend of the variation in wavelet maxima per unit area, versus wavelet level. This parameter has not been found to be as useful as the other parameters described, based on the limited database of available images.

[0118] The large number of wavelet parameters per spectral band, wavelet level and region (border and interior) were evaluated in the same manner as described in Section III above, with linear and non-linear classifiers. It has been found that a combination of certain of the non-wavelet parameters discussed in Section II, above, and parameters estimated through the wavelet maxima representations, gives the best specificity at 100% sensitivity for the data available to date for a quadratic Gaussian classifier.

[0119] Table 2, below, indicates the most useful non-wavelet parameters and their center wavelength ("CWL"), the wavelet parameters ("WMR") and their CWL, and the best combination of WMR and non-wavelet parameters and their associated CWL. Each sequence adds the indicated parameter to the parameter or parameters in the prior sequences. For example, the best single non-wavelet parameter was T1, (texture, Type 1) defined in Equation 28, above, at a wavelength of 950 nm. Better results were obtained when T5, defined in Equation 35, above, at wavelength 500 nm, was added in sequence 2. The parameters of sequences 1-12 identify the twelve best parameters found for characterizing skin lesions with the quadratic Gaussian classifier, above. The other columns of Table 2 are similarly interpreted. The definitions of the abbreviations used in the Table 2 appear below the Table.

[0120] When the 12 non-wavelet parameters of Table 2 were used alone, and the threshold in the nonlinear quadratic

Guassian classifier was chosen such that all the melanomas in the database were correctly classified (100% sensitivity), the specificity of correct classification of benign lesions was 64%. When 12 WMR parameters were used alone, the specificity was 86%. When the 12 parameters of both types were used, the specificity was 90%.

TABLE 2

Sequence	Non Wavelet	CWL (nm)	WMR	CWL (nm)	Combined	CWL (nm)
1	T1	950	b, I*,	650	b, I*,	650
2	T5	500	b, L3K,	950	T3,	430
3	ASY,	450	b, 1W,	430	b, L6S	600
4	T6,	450	b, L6K,	430	b, L1K,	700
5	T5,	600	I, L6K,	430	T5,	550
6	GRD	430	b, L1K,	430	b, L3K,	650
7	CE,	950	b, L5S,	780	T3,	500
8	STR,	500	I, L3W,	550	B1,	950
9	STR,	430	I, L3A	450	STR,	550
10	T6,	500	b, L5A,	780	I, L3W,	780
11	STR,	550	I, L3A,	430	b, L6W,	650
12	SMR,	789	b, I*,	600	T2,	950

Key to Non-Wavelet Parameters

[0121]

ASY = Asymmetry, BI = Blotchiness, CE = Centroid, GRD = Gradient,
SMR = (Std Dev of Reflectance) / (Mean Reflectance),
STR = Std Dev of Reflectance, Tp = Texture, type p

Key to WMR Parameters

[0122] b = border region, I = interior region, Ln = Level n = 1,2,...,6

[0123] Statistics:

A = (mean coef. magnitude) / (mean absolute deviation)
I* = intercept measure (extrapolated over levels n=1-4)
K = skewness
S = (mean coef. magnitude) / (Std Dev of coef. magnitude)
W = number of wavelet maxima per pixel

Table 3 is a comparable table of preferred parameters with the linear classifier of Equation 37. The abbreviations for parameters not defined above, appear below Table 3.

TABLE 3

Sequence	Non Wavelet	CWL (nm)	WMR Code	CWL (nm)	Combined Codes	CWL (nm)
1	ASY,	450	I, L1K,	550	b, L4S,	880
2	BLr,	430	b, L3A,	780	I, L6A,	880
3	T5,	780	I, L5S,	780	b, L3S,	700
4	T6,	780	I, L6K,	880	I, L1K,	600
5	T2,	500	I, L1K,	950	b, L5S	650
6	T2,	550	I, L3W,	450	b, L2S,	700
7	GRD,	780	I, L5K,	450	ASY,	450
8	R1,	950	b, L1K,	780	GRD,	430
9	BL,	950	b, F*,	780	I, L2K,	600

(continued)

Sequence	Non Wavelet	CWL (nm)	WMR Code	CWL (nm)	Combined Codes	CWL (nm)
10	T6,	430	b, L4A,	430	T5,	550
11	T5,	430	I, L2K,	600	CE,	450
12	T3,	950	b, L4S,	880	---	---

Key to Additional Non-Wavelet Parameters

[0124]

BIr = Border Irregularity,
GRD = Gradient, R1 = Mean Reflectance,

Key to Additional WMR Parameters

[0125] Statistics:

F* = goodness-of-fit measure (levels n=1,2,3,4)

[0126] When the 12 non-wavelet parameters of Table 3 were used alone, and the threshold within the linear classifier was chosen such that all available melanomas are correctly classified (100% sensitivity), the specificity was 91%. With only the wavelet parameters, the specificity was 95%. With the combination of wavelet and non-wavelet parameters, the specificity was 97%. Although these results seem to indicate that the linear classifier separates the two classes of lesions better than the nonlinear one, it should be recognized that sampling bias effects tend to be greater for a linear classifier.

[0127] When a similar analysis of the combination of non-wavelet and wavelet parameters was applied to the digitized images obtained with the system of Fig. 1(c), the linear classifier in Section III, which includes only the non wavelet parameters, was found to be superior than a linear classifier including wavelet parameters. Non-linear classifiers showed superior results with the non-wavelet parameters with the digitized images, as well.

[0128] The systems and methods of the present invention may also be used to differentiate between melanoma and different types of benign pigmented lesions. Classification is preferably accomplished through a multiple-step process. For example, if two classes of benign lesion share very different parameter values, as is the case for nevi and seborrheic keratoses, then a two-step classification may be used. Two different linear classifiers (with different weights) are trained as described in Section III, above, to have 100% sensitivity to melanoma; one to differentiate between melanoma and keratosis and the other to differentiate between melanoma and nevus. A lesion is then declared to be benign if at least one of its classifier values is below threshold and malignant if both of its classifier values are above threshold. In general, if there are N types of benign lesions, the *N*-step classification may be used. In this case the lesion is declared to be malignant if all *N* of its classifier values are above threshold and benign otherwise.

[0129] If other conditions of skin or tissue are to be characterized, the preferred spectral band for generating the mask may be the one in which the amount of light re-emitted is greater within abnormal tissue than for normal tissue. Preferably, the segmented mask is then applied to the images in the other wavelength bands, as shown in the flowchart of Fig. 3b. In addition, while the parameters are described in the terms of the red, green and blue wavelength bands in Sections I-III, parameters can be derived at any of the wavelengths actually used, in accordance with the procedures described in Sections I-III. The parameters in the additional wavelength bands can be readily used to develop an appropriate classifier, also by the processes described in Section I-III.

[0130] The condition of a region of interest of skin including wound or bums may be characterized by a quantitative measure of tissue abnormality with respect to normal skin. Classifiers may be developed based on images of wounds of different types or bums of varying degrees of severity, in an analogous manner as described above with respect to skin lesions. The condition of the region of interest could then be characterized as a percentage relative to normal skin, for example, to indicate the extent to which healing has occurred.

[0131] The references cited above are incorporated by reference, herein.

[0132] While preferred systems and methods for practicing the present invention have been described above, it is understood that departures may be made from the systems and methods, without departing from the scope of the present invention, which is defined by the following claims.

[0133] Although the present invention is defined in the attached claims, it should be understood that the present invention can also (alternatively) be defined in accordance with the following embodiments:

1. A method of characterizing the condition of a region of interest of skin, wherein the absorption and scattering of light in different spectral bands by the region of interest is a function of the condition of the skin, the method comprising:

illuminating a portion of the skin including the region of interest by light in at least three spectral bands;
digitally imaging a portion of the skin including the region of interest at the at least three spectral bands with the light re-emitted by the portion of the skin to generate digital images comprising digital signals whose values are a function of the condition of the region of interest of the skin; and
providing the digital images to a processor, wherein the processor:

segments the digital images by generating a segmentation mask defining the boundary of the region of interest from a digital image in any one of the at least three spectral bands;
estimates at least one rotationally and translationally invariant statistical measure of coefficient distributions of the multiscale wavelet maxima representations of the digital images in each spectral band, which are functions of the texture of the region of interest determined by the segmentation mask;
characterizes the condition of the skin based on the estimated values; and
outputs the characterization of the condition of the skin.

2. The method of embodiment 1, wherein the at least one statistical measure is calculated separately within either of a border region and an interior region of the digital image, wherein:

the border region encompasses the envelope of circles of fixed radius centered on the boundary of the segmentation mask; and
the inside region comprises all points of the image that are within the segmentation mask boundary but not included in the border region.

3. The method of embodiment 2, wherein the computing step comprises estimating at an individual level at least one value which is a statistical measure of texture of the portion of the region of interest within the border region and interior region, chosen from the group consisting of :

the number of wavelet maxima per unit area;
the ratio of the mean coefficient magnitude to the absolute deviation of the coefficient magnitudes from the mean value;
the ratio of the mean coefficient magnitude to the standard deviation of the coefficient magnitude; and
the skewness of the coefficient magnitude, normalized to the cube of the standard deviation.

4. The method of embodiment 1, further comprising estimating either of the degree of change of a statistic of the wavelet coefficient distribution with increment of wavelet level, and the degree of deviation of such change from linearity.

5. The method of embodiment 2, further comprising estimating the average rate of change, with respect to level, of the number of wavelet maxima per unit area.

6. The method of embodiment 1, further comprising comparing the estimated texture values to the threshold derived from statistical analysis of a multiscale wavelet transformation of the digital image.

7. The method of embodiment 1, wherein the estimating and characterizing steps are conducted without the intervention of an operator.

8. The method of embodiment 1, wherein the segmenting step is conducted without the intervention of an operator.

9. The method of embodiment 1, wherein the illuminating step further comprises illuminating a region of interest including a bum.

10. The method of embodiment 9, wherein the characterizing step comprises characterizing the condition of the burn with respect to the condition of normal skin.

11. The method of embodiment 1, wherein the illuminating step further comprises illuminating a region of interest including a wound.

12. The method of embodiment 11, wherein the characterizing step comprises characterizing the condition of the wound with respect to the condition of normal skin.

13. The method of embodiment 1, further comprising:

photographing the region of interest with a color camera to form color photographic slides; and
illuminating the color photographic slides with light in each spectral band;
wherein the digital imaging step comprises digitally imaging the illuminated color photographic slides of the region of interest with a digital camera.

14. The method of embodiment 1, wherein the computing step further comprises estimating a value which is a function of the asymmetry of the segmented image in each spectral band, for two principal axis of the segmented image.

15. The method of embodiment 1, wherein the computing step further comprises:

locating the principal axes by computing an orientation angle;
computing the intensity centroid;
rotating the digital image such that the principal axes are parallel to the image axes;
estimating asymmetry values for each principal axis based on the intensity centroid; and
summing the estimated asymmetry values for the two principal axes.

16. The method of embodiment 1, wherein the computing step further comprises computing the intensity moment with a binary intensity distribution.

17. The method of embodiment 1, wherein the computing step further comprises estimating at least one value which is a function of the blotchiness of the segmented digital image, the estimated blotchiness value being defined through statistical properties of the spatial distribution of topographic regions of the digital images at each spectral band.

18. The method of embodiment 17, wherein the computing step further comprises determining the centroids of topographic regions of the segmented digital image at each spectral band.

19. The method of embodiment 1, wherein the computing step comprises estimating a value which is a statistical measure of the deviation of the border of the region of interest from the border of an ellipse of the same area, aspect ratio, and orientation as the segmentation mask.

20. The method of embodiment 1, wherein the computing step comprises estimating a statistical measure of the gradient values of the intensity of the digital images across the border of the segmented images, at each spectral band.

21. The method of embodiment 1, wherein the computing step comprises estimating values based on the ratio of standard deviation of the areas of dermal papillae to their mean within the segmentation mask.

22. The method of embodiment 1, wherein the computing step comprises estimating values of the average and standard deviation of the thickness of rete ridges within the segmentation mask.

23. The method of embodiment 1, wherein the characterizing step comprises distinguishing multiple times between melanoma and several types of benign lesion.

24. The method of embodiment 1, wherein the condition of the region of interest to be characterized is the presence of a melanoma and the processor compares a weighted combination of parameter values against a threshold value for melanoma and different types of benign lesions, multiple times.

25. The method of embodiment 1, wherein the segmentation mask is generated from a digital image in a spectral band in which the amount of light reemitted by skin is less within skin having an abnormal condition than within skin having a normal condition.

26. The method of embodiment 1, wherein the segmenting step further comprises segmenting the digital images by generating a segmentation mask in more than one spectral band.

27. A system for characterizing the condition of a region of interest of skin, comprising:

a source of illumination of light in at least three spectral bands;
a camera for acquiring digital images of the region of interest based on the light re-emitted from the illuminated region of interest at each of the spectral bands, the digital image comprising digital signals whose values are a function of the condition of the region of interest;
memory for storing the digital images provided by the camera;
a digital processor programmed to perform the steps of :

segmenting the digital images stored in memory by generating a segmentation mask from a digital image in any one of the at least three spectral bands;
estimating at least one rotationally and translationally invariant statistical measure of coefficient distributions for the multiscale wavelet maxima representations of the digital images in each spectral band, which are functions of the texture of the region of interest determined by the segmentation mask;
characterizing the condition of the skin based on the estimated values; and
outputting the characterization of the region of interest.

28. The system of embodiment 27, further comprising means for suppressing specular reflections from the region of interest.

29. The system of embodiment 27, wherein the camera records monochromatic images and the illumination means comprises:

a tungsten halogen light source with feedback to stabilize the intensity in each wavelength band;
means for sequentially filtering the light; and
an optical fiber ring illuminator to distribute the filtered light.

30. The system of embodiment 29, further comprising a feedback loop for stabilizing the intensity of the light source by the processor.

31. The system of embodiment 30, further comprising a material of stable reflectance for being illuminated by the light source, wherein the feedback loop includes the monitoring by the processor, of the intensity of light reflected from the material by the processor and the adjustment of the intensity of the light source if the monitored intensity varies from a desired value.

32. The system of embodiment 31, wherein the power, voltage or current supplied to the light source is monitored.

33. The system of embodiment 27, wherein the source of illumination is at least one laser.

34. The system of embodiment 28, wherein the processor estimates the statistical measures separately within either of a border region and an interior region of the digital image, wherein:

the border region encompasses the envelope of circles of fixed radius centered on the boundary of the segmentation mask; and
the inside region comprises all points of the image that are within the segmentation mask boundary but not included in the border region.

35. The system of embodiment 34, wherein the processor estimates at an individual level at least one value which is a statistical measure of texture of the portion of the region of interest within the border region and interior region, chosen from the group consisting of :

the number of wavelet maxima per unit area;
the ratio of the mean coefficient magnitude to the absolute deviation of the coefficient magnitudes from the mean value;
the ratio of the mean coefficient magnitude to the standard deviation of the coefficient magnitude; and
the skewness of the coefficient magnitude, normalized to the cube of the standard deviation.

36. The system of embodiment 35, wherein the processor further estimates either of the degree of change of a

statistic of the wavelet coefficient distribution with increment of wavelet level, and the degree of deviation of such change from linearity.

37. The system of embodiment 35, wherein the processor further estimates the average rate of change, with respect to level, of the number of wavelet maxima per unit area.

Claims

1. An apparatus comprising
a camera (6, 16, 20, 23) for acquiring digital images of a skin lesion based on light re-emitted from the skin lesion illuminated in each of at least three spectral bands,
a memory (12b) for storing the digital images; and
a digital processor (12c), and
characterized in that the digital processor (12c) is programmed to:

segment the digital images stored in memory (12b), estimate, from the segmented digital images, based on wavelet maxima representations, values that are functions of characteristics of the lesion,
based on the estimated values, automatically classify the lesion with respect to malignant melanoma, the specificity of the classification being maximized under a constraint of 100% sensitivity to melanoma on a training set of images for which the lesions have been **characterized** with respect to malignant melanoma; and
cause a display of a result of the classification.

2. The apparatus of claim 1 in which the digital processor is programmed to estimate at least one rotationally and translationally invariant statistical measure of coefficient distributions of the wavelet maxima representations of the digital images in each spectral band, the measures being functions of a texture of a region of interest determined by the segmentation.

3. The apparatus of claim 1 in which at least one statistical measure is calculated separately for either of a border region and an interior region of each of the digital images, the border region encompassing an envelope of circles of fixed radius centered on a boundary of the segmentation mask used for the segmenting; and the inside region comprises all points of the digital image that are within the segmentation mask boundary but not included in the border region.

4. The apparatus of claim 2 in which the digital processor is programmed to estimate at least one value which is a statistical measure of texture of a portion of the region of interest within the border region and interior region, and is one of the following: the number of wavelet maxima per unit area; the ratio of the mean coefficient magnitude to the absolute deviation of the coefficient magnitudes from the mean value; the ratio of the mean coefficient magnitude to the standard deviation of the coefficient magnitude; and the skewness of the coefficient magnitude, normalized to the cube of the standard deviation.

5. The apparatus of claim 1 in which the digital processor is programmed to estimate either a degree of change of a statistic of the wavelet coefficient distribution with an increment of a wavelet level, or the degree of deviation of such change from linearity.

6. The apparatus of claim 2 in which the digital processor is programmed to compare estimated texture values to the threshold derived from statistical analysis of a wavelet transformation of the digital image.

7. The apparatus of claim 1 in which the segmenting is conducted without the intervention of an operator.

8. The apparatus of claim 1 in which the digital processor is configured to estimate a value which is a function of the asymmetry of the segmented image in each spectral band, for two principal axes of the segmented object in the image.

9. The apparatus of claim 1 in which the digital processor is configured to estimate at least one value which is a function of a blotchiness of the segmented digital image, the estimated blotchiness value being defined by statistical properties of the spatial distribution of topographic regions of the digital images at each spectral band.

10. The apparatus of claim 1 in which the digital processor is configured to estimate a value which is a statistical measure

of the deviation of the border of the region of interest from the border of an ellipse of the same area, aspect ratio, and orientation as a segmentation mask used for the segmenting.

11. The apparatus of claim 1 in which the digital processor is configured to estimate a statistical measure of the gradient values of the intensity of the digital images across the border of the segmented images, at each spectral band.

12. The apparatus of claim 1 in which the digital processor is configured to estimate values based on the ratio of standard deviation of the areas of dermal papillae to their mean within a segmentation mask used for the segmenting.

13. The apparatus of claim 1 in which the digital processor is configured to estimate values of the average and standard deviation of the thickness of rete ridges within a segmentation mask used for the segmenting.

14. The apparatus of claim 1 in which the digital processor is configured to classify multiple times between melanoma and different types of benign lesions.

15. The apparatus of claim 1 in which a segmentation mask is generated for the segmenting from a digital image in a spectral band in which the amount of light re-emitted by skin is less within skin having an abnormal condition than within skin having a normal condition.

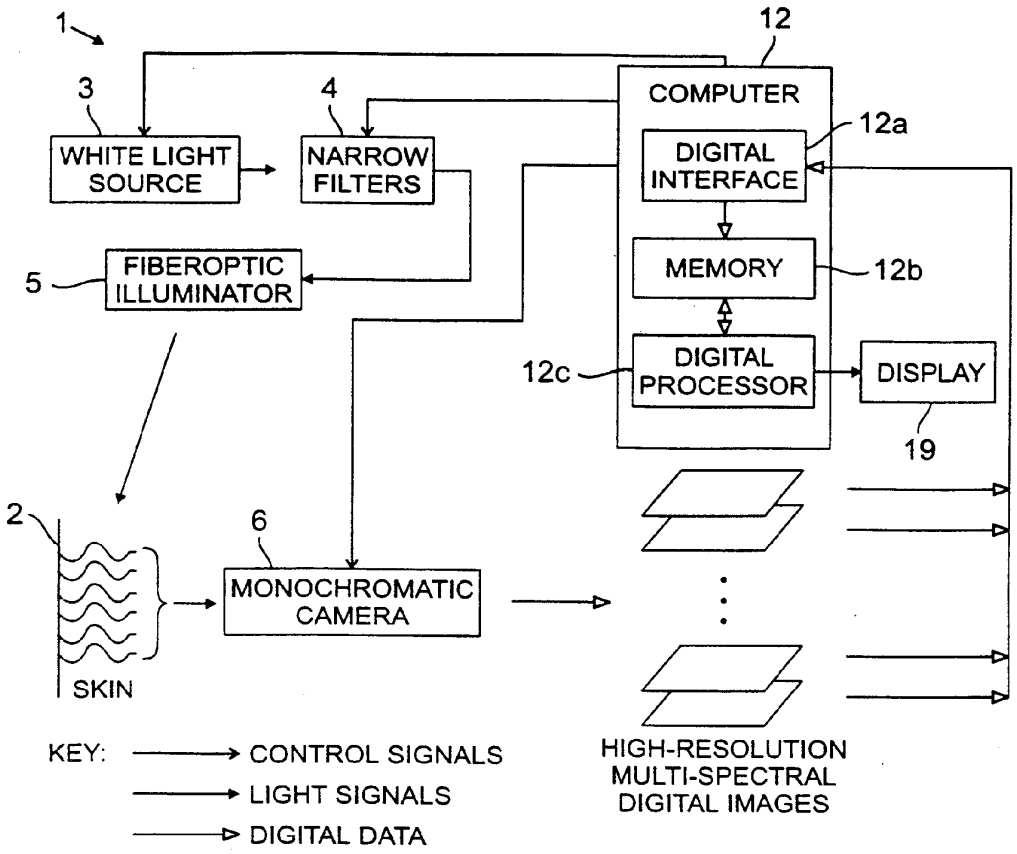

FIG. 1a

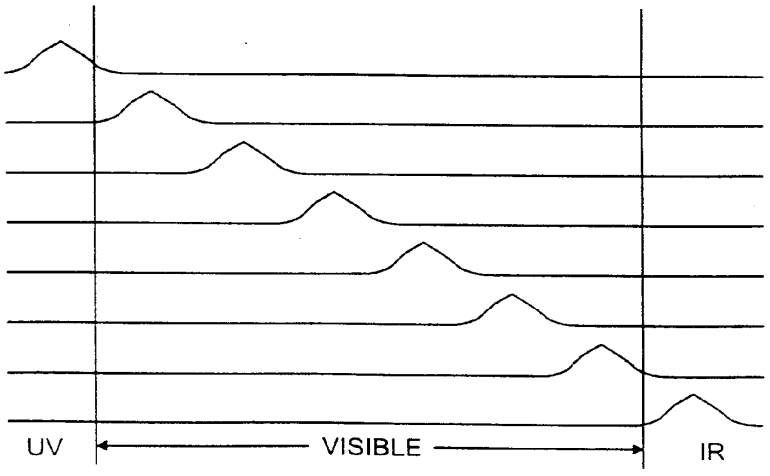

FIG. 1b

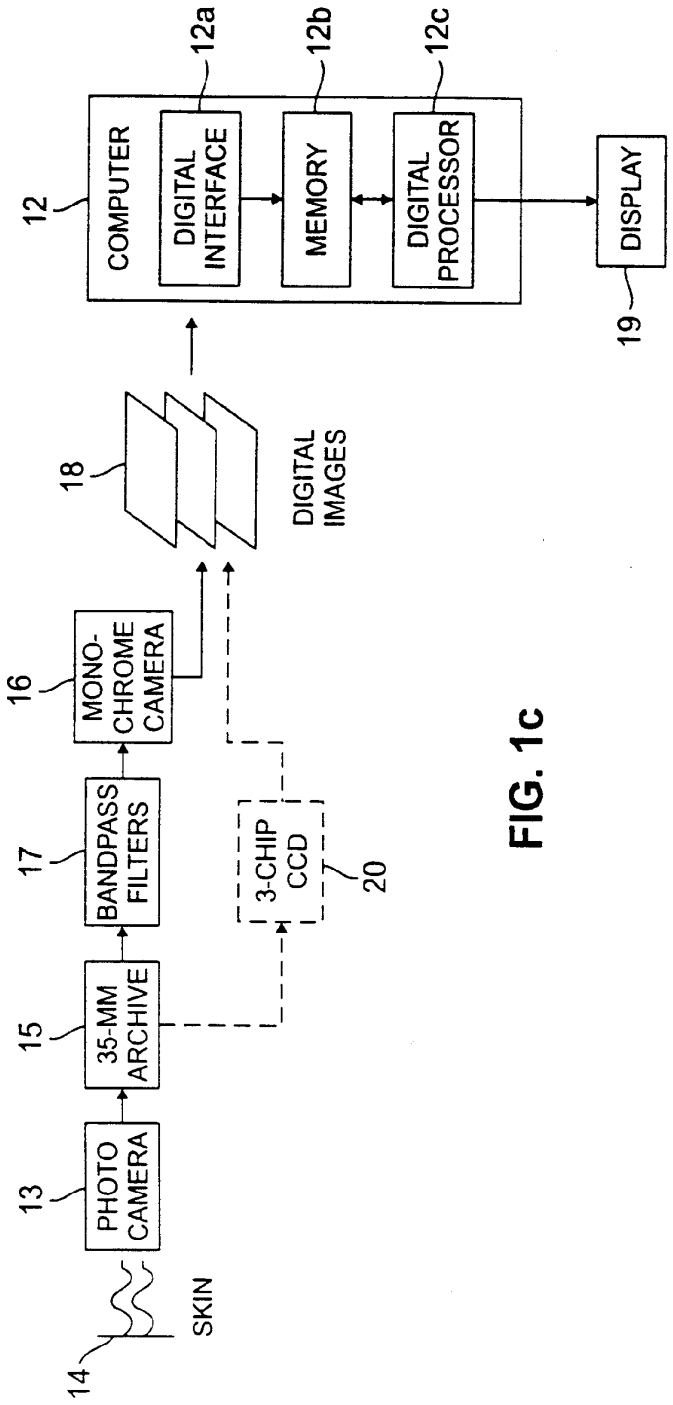

FIG. 1c

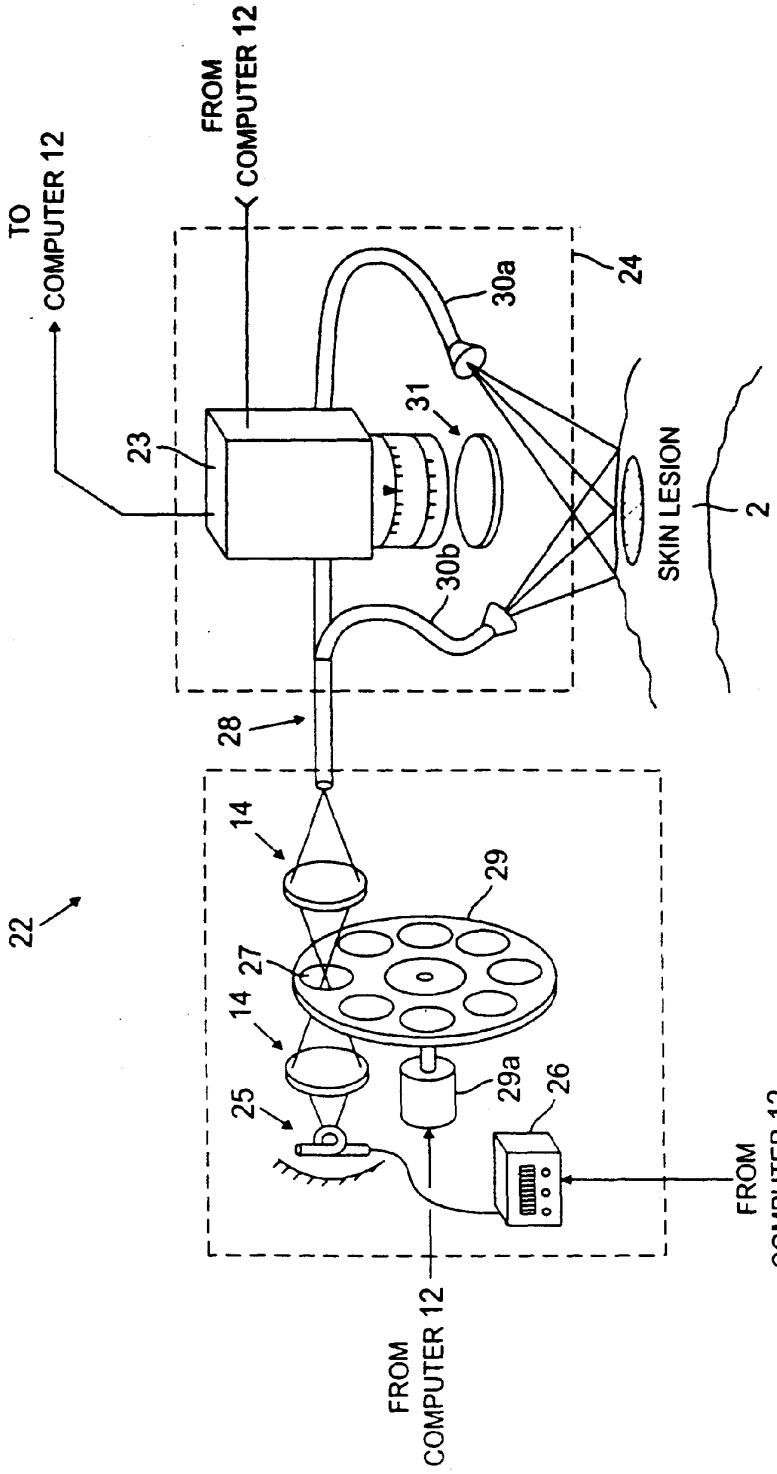

FIG. 2

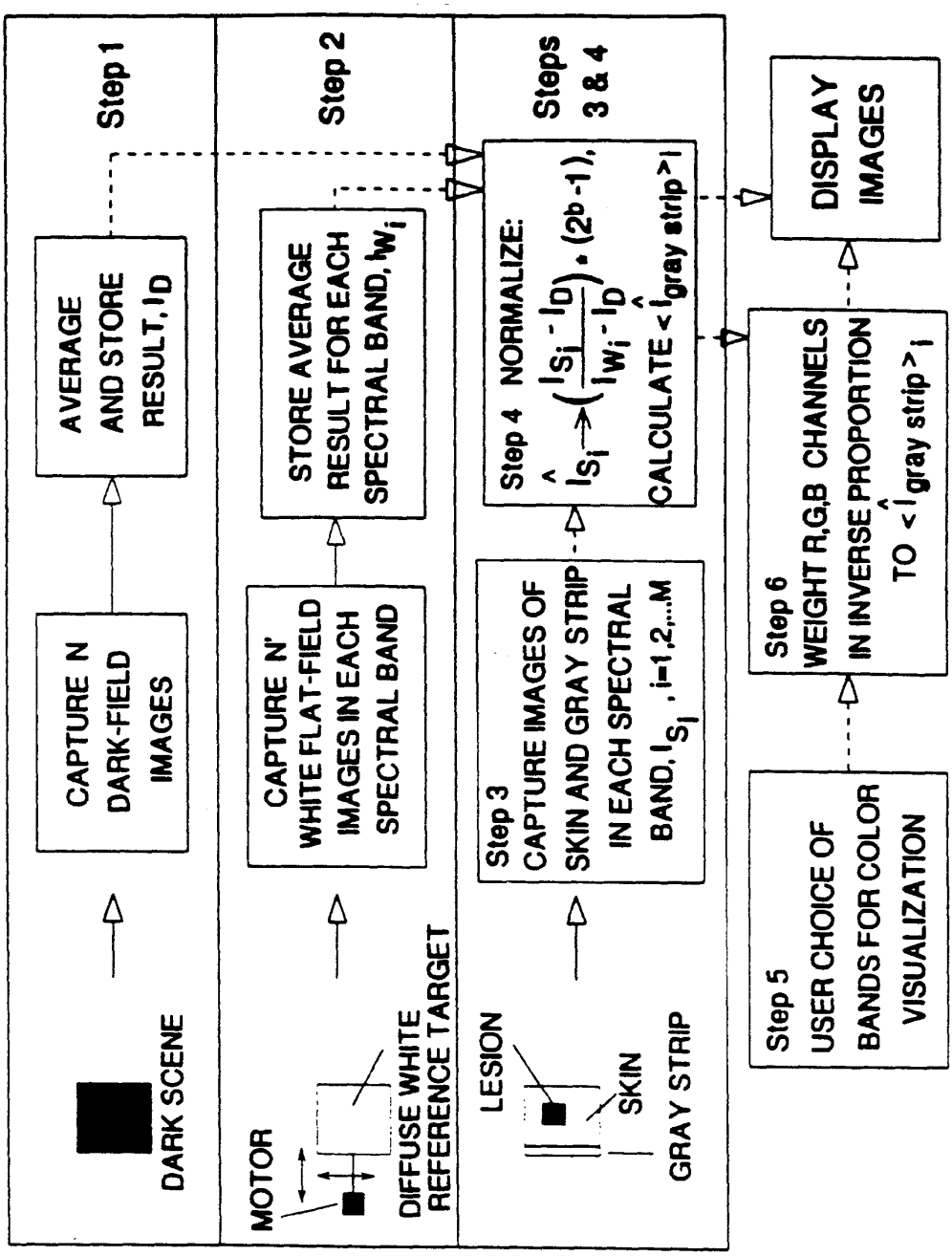

FIG. 3a

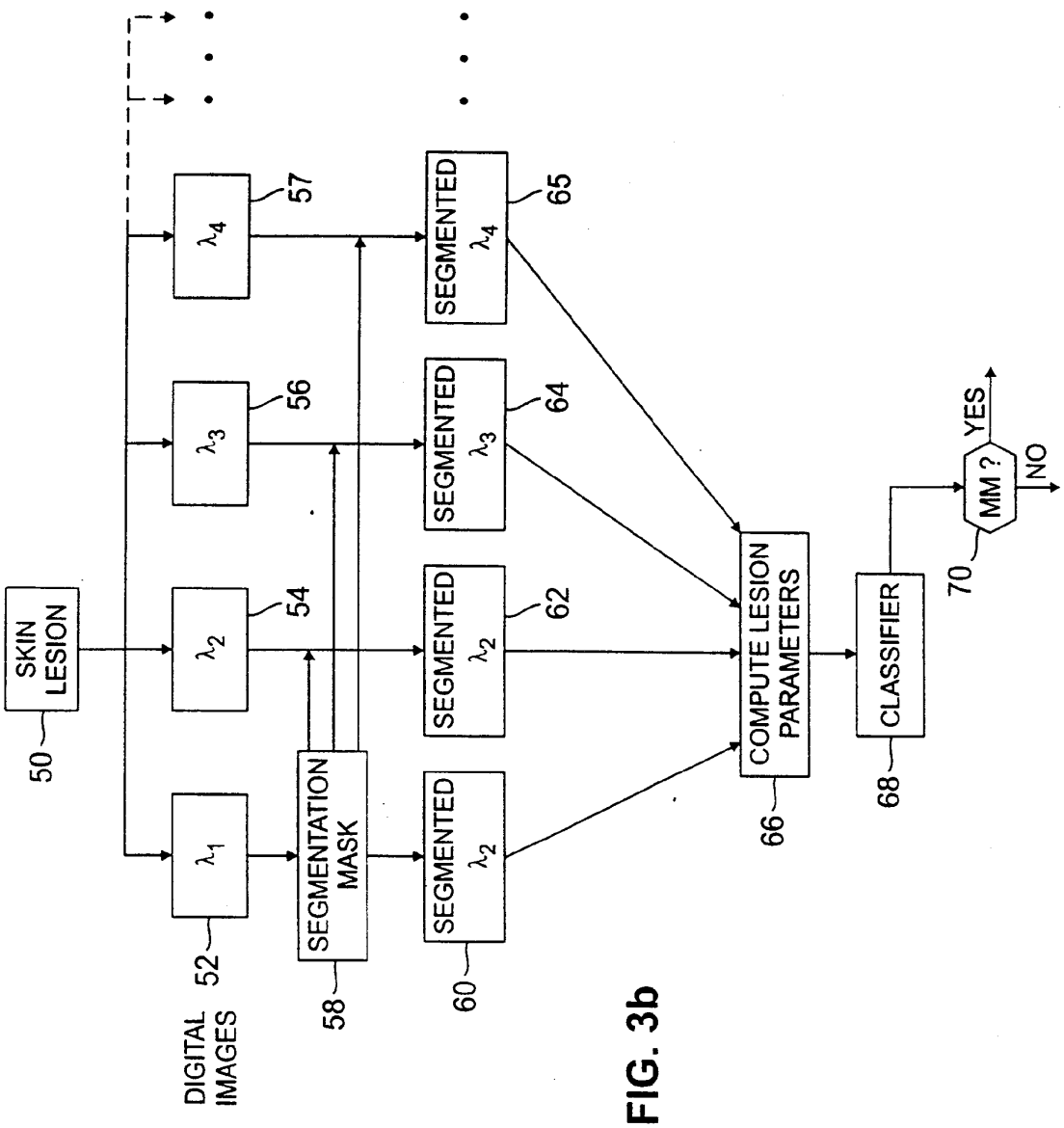

FIG. 3b

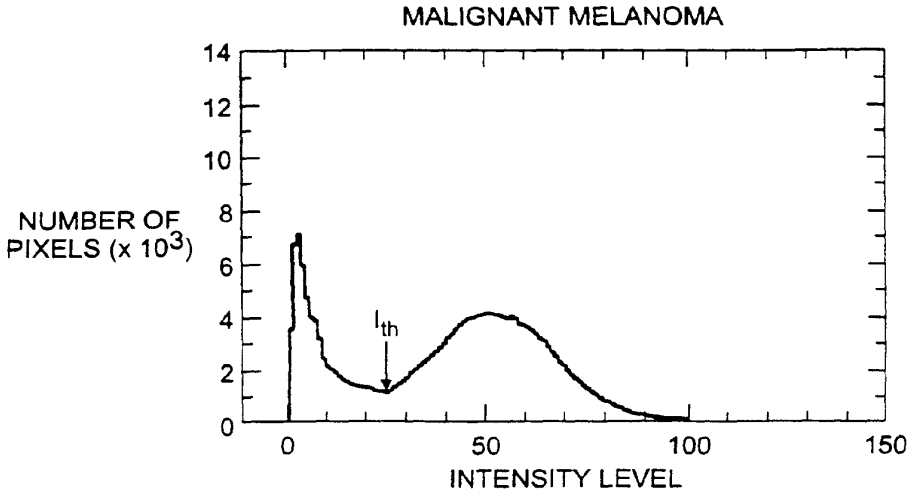

FIG. 4a

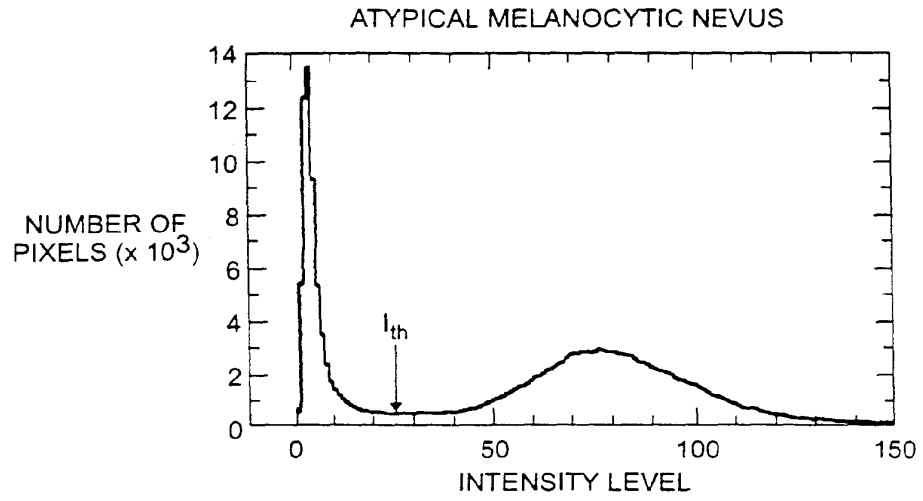

FIG. 4b

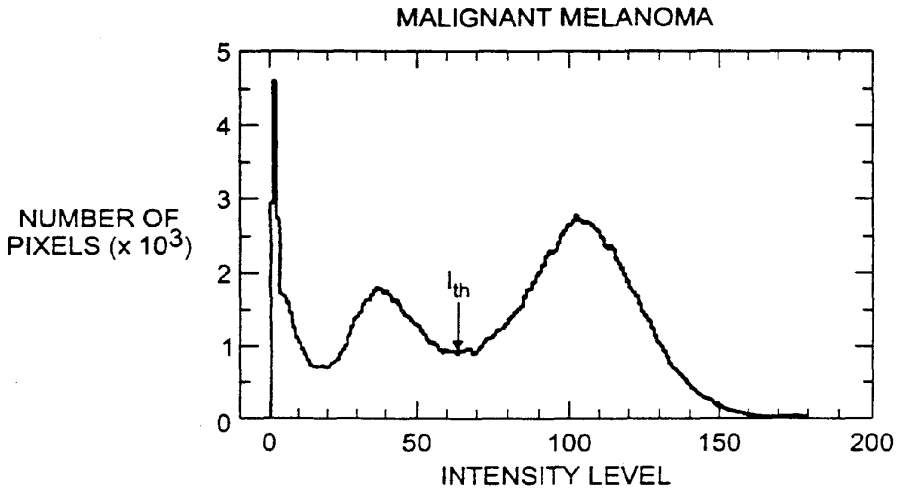

FIG. 5a

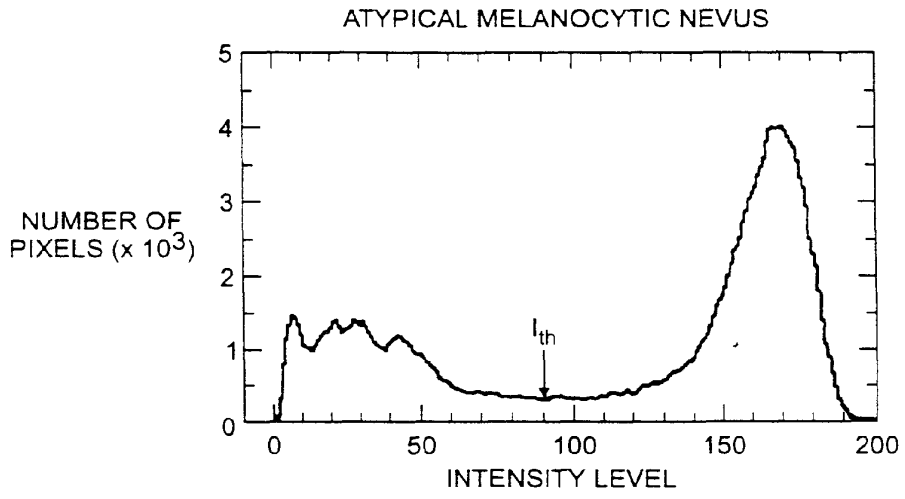

FIG. 5b

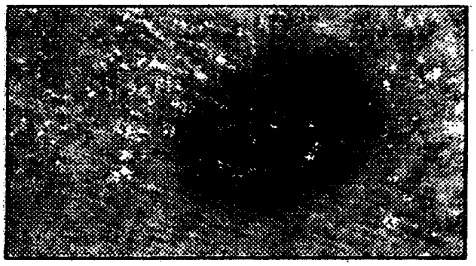

Fig. 6(a)

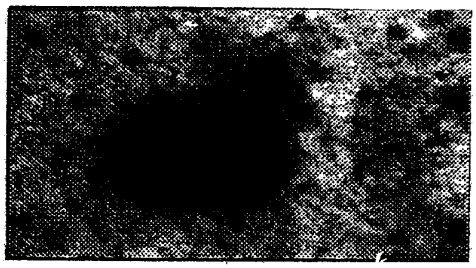

Fig. 6(d)

Fig. 6(b)

Fig. 6(e)

Fig. 6(c)

Fig. 6(f)

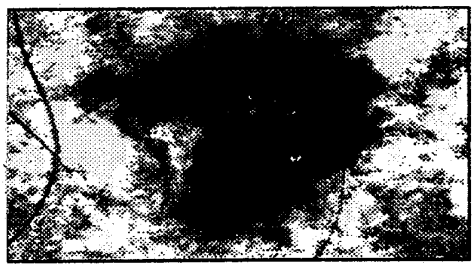

Fig. 7(a)

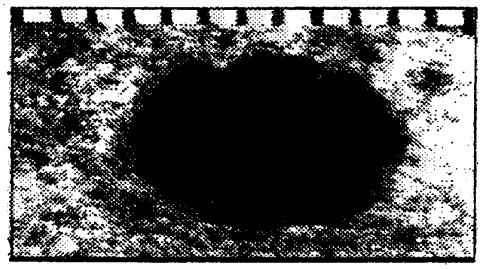

Fig. 7(d)

Fig. 7(b)

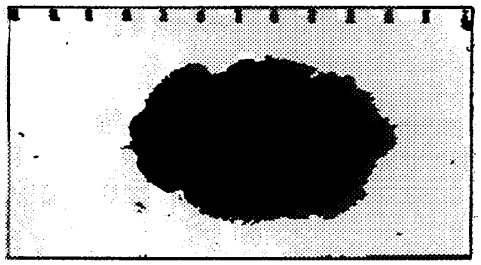

Fig. 7(e)

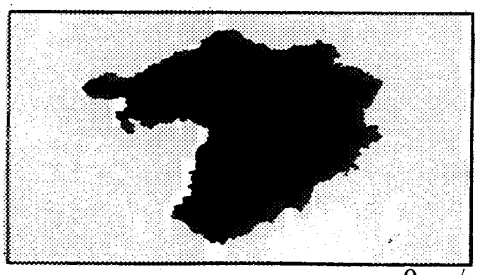

Fig. 7(c)

Fig. 7(f)

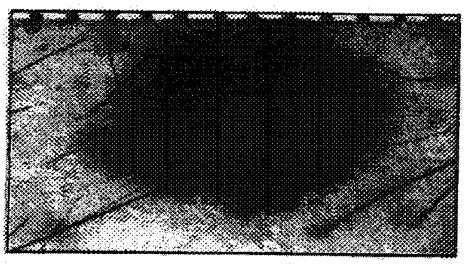

Fig. 8(a)

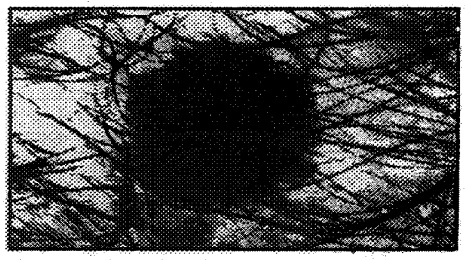

Fig. 8(e)

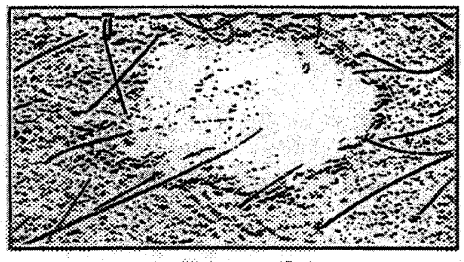

Fig. 8(b)

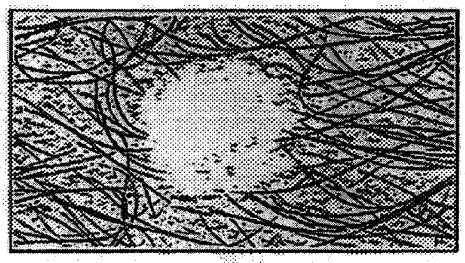

Fig. 8(f)

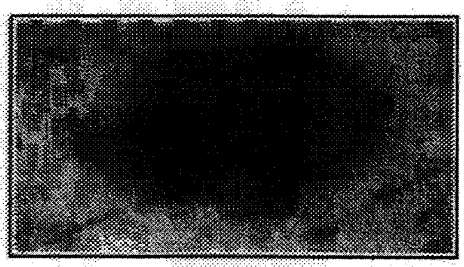

Fig. 8(c)

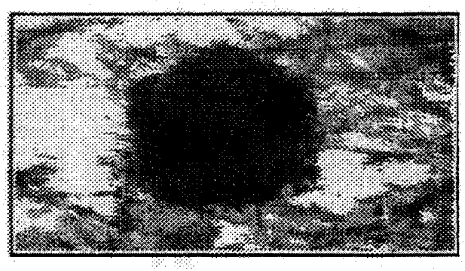

Fig. 8(g)

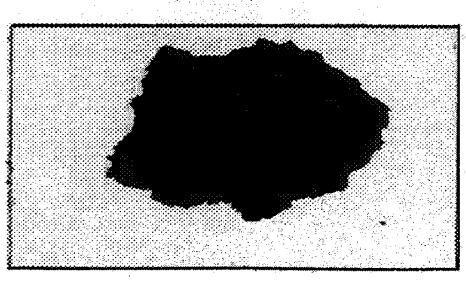

Fig. 8(d)

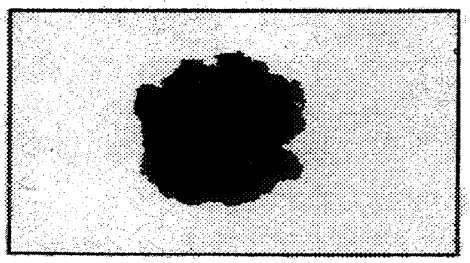

Fig. 8(h)

J - 5	0	1	0	0	0	1	0
J - 4	0	1	1	0	1	1	0
J - 3	0	0	2	3	2	0	0
J - 2	1	0	0	1	0	0	1
J - 1	1	0	-3	-5	-3	0	1
J	1	1	-5	-8	-5	1	1
J + 1	1	0	-3	-5	-3	0	1
J + 2	1	0	0	1	0	0	1
J + 3	0	0	2	3	2	0	0
J + 4	0	1	1	0	1	1	0
J + 5	0	1	0	0	0	1	0
	I - 3	I - 2	I - 1	I	I + 1	I + 2	I + 3

FIG. 9

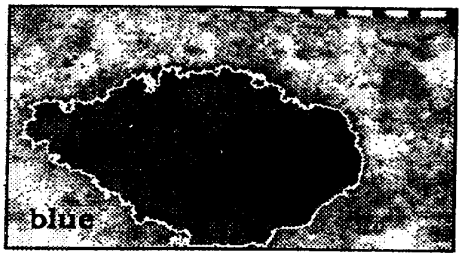

Fig. 10(a)

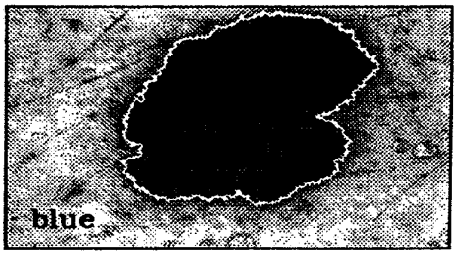

Fig. 10(d)

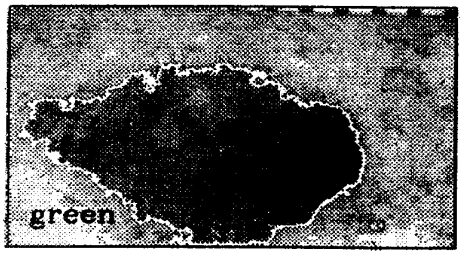

Fig. 10(b)

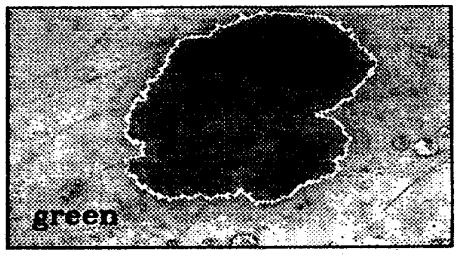

Fig. 10(e)

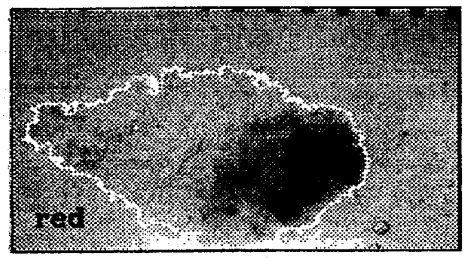

Fig. 10(c)

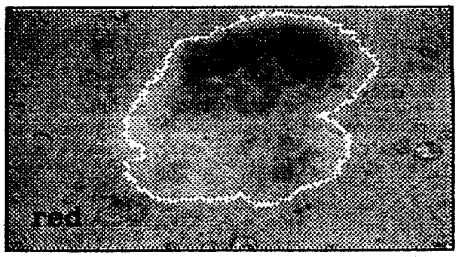

Fig. 10(f)

PARAMETER		DIAGNOSTIC ACCURACY (%)	SENSITIVITY (%)	SPECIFICITY (%)
ASYMMETRY:	A_{bin}	52	71	86
	A_b	48	68	84
	A_g	50	73	82
	A_r	62	78	89
BLOTCHINESS:	Bl_b	45	56	90
	Bl_g	40	68	72
	Bl_r	42	68	75
	C_b	37	80	55
	C_r	38	80	57
	Cl	44	78	70
BORDER:	B	44	66	81
	G_b	36	76	56
TEXTURE:	$T1_b$	38	88	49
	$T1_g$	49	61	90
	$T2_g$	41	66	76
	$T2_r$	43	73	72
	$T3_b$	39	80	59
	$T3_g$	38	63	74
	$T4_b$	38	68	69
	$T4_g$	39	56	83
	$T5_b$	36	76	58
	$T6_b$	38	90	46

FIG. 11

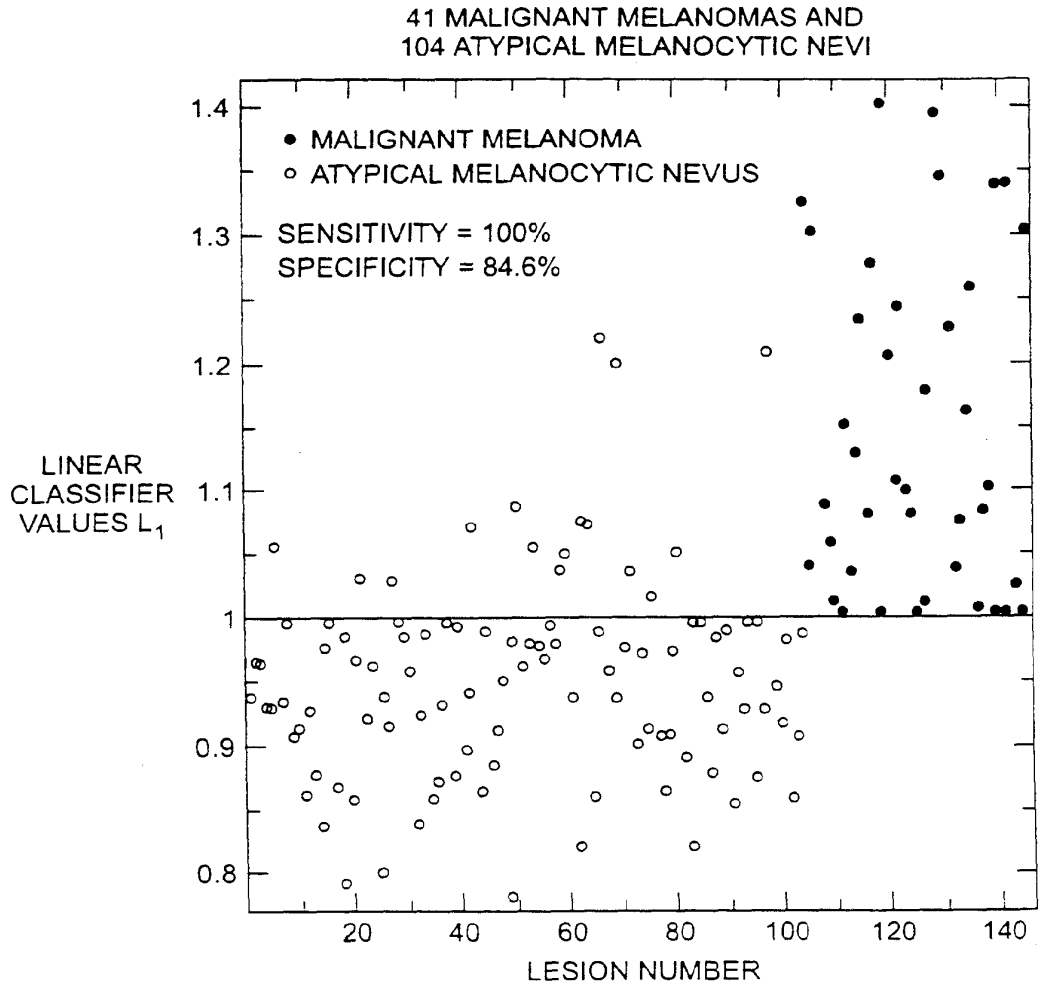

FIG. 12

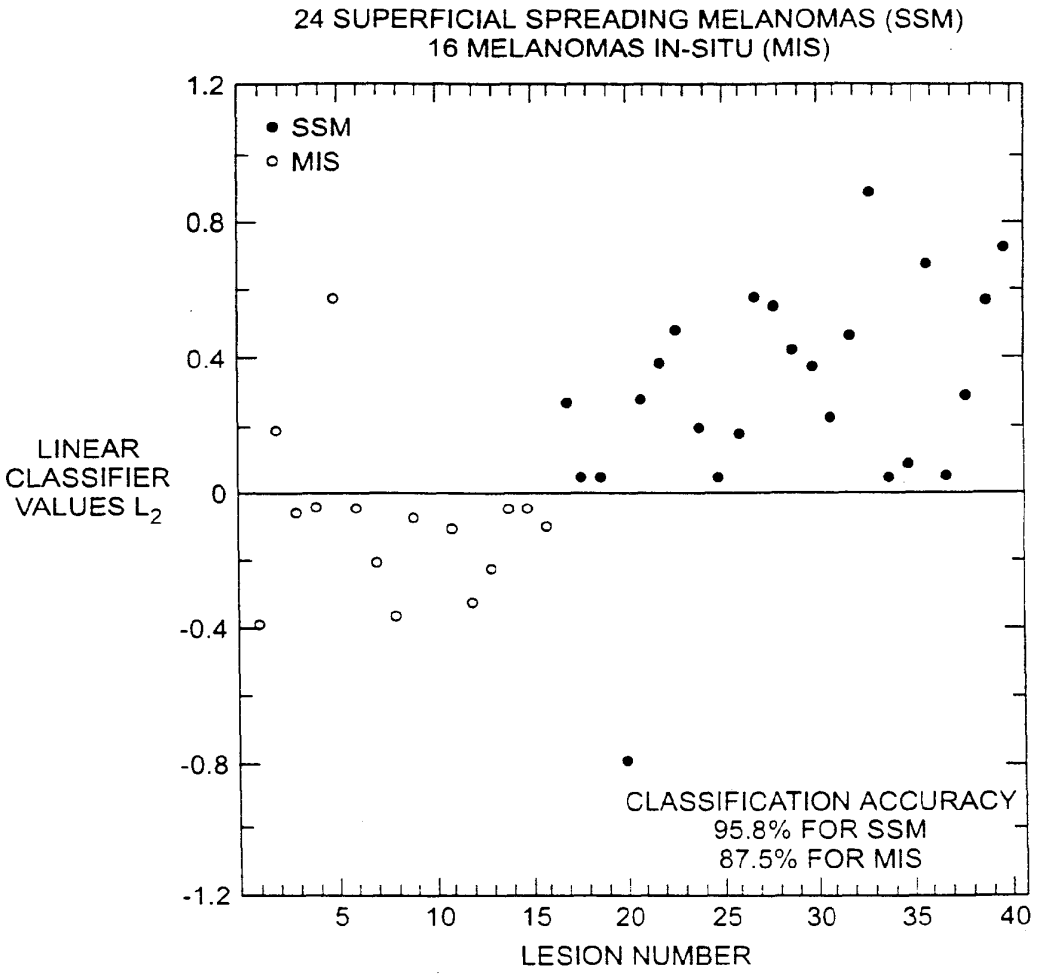

FIG. 13

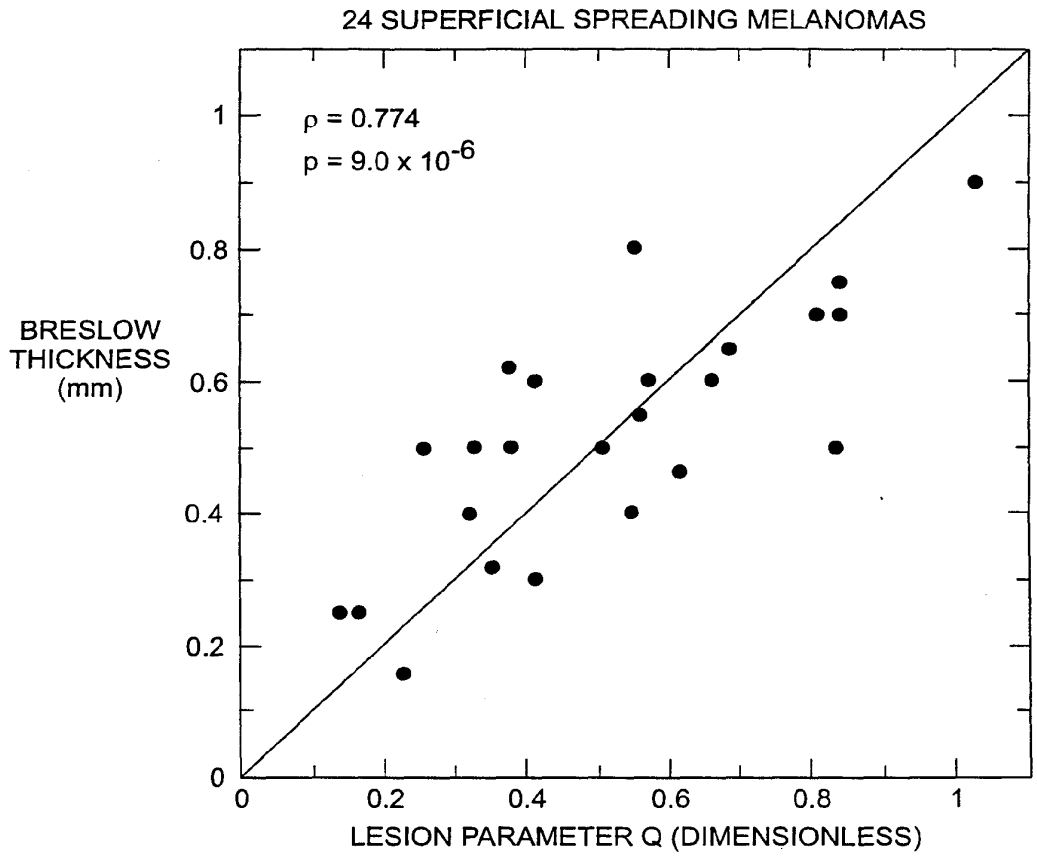

FIG. 14

REFERENCES CITED IN THE DESCRIPTION

This list of references cited by the applicant is for the reader's convenience only. It does not form part of the European patent document. Even though great care has been taken in compiling the references, errors or omissions cannot be excluded and the EPO disclaims all liability in this regard.

Non-patent literature cited in the description

- **Marchesini et al.** Photochemistry & Photobiology. *In vivo spectrophotometric evaluation of neoplastic and non-neoplastic skin pigmented lesions. III. CCD camera-based reflectance imaging,* 1995, vol. 62, 151-154 **[0068]**
- **Daubechies, I.** The Wavelet transform, time-frequency localization and signal analysis. *IEEE Trans Inform Theory,* 1990, vol. 36, 961-1005 **[0108]**
- **Aldroubi, A. et al.** Wavelet in Medicine and Biology. C&C Press, 1996, 11-15 **[0108]**
- **Mallat S ; Hwang, W L.** Singularity detection and processing with wavelets. *IEEE Trans Inform Theory,* 1992, vol. 38, 617-643 **[0109]**
- Wavelet maxima representation. **Mallat S ; Zhong S.** Wavelets and Applications. Springer-Verlag, 1992, 207-284 **[0109]**
- **Mallat S ; Zhong S.** Characterization of signals from multiscale edges. *IEEE Trans Patt Anal Mach Intell,* 1992, vol. 14, 710-732 **[0109]**
- **Fukunaga, K.** Introduction to Statistical Pattern Recognition. Academic Press, 1990, 19-96125 **[0111]**

Electronic Acknowledgement Receipt

EFS ID:	11339678
Application Number:	13069124
International Application Number:	
Confirmation Number:	9532
Title of Invention:	Image Capture and Identification System and Process
First Named Inventor/Applicant Name:	Wayne C. Boncyk
Customer Number:	24392
Filer:	Martin Fessenmaier/Laryssa Weiland
Filer Authorized By:	Martin Fessenmaier
Attorney Docket Number:	101044.0001US14
Receipt Date:	04-NOV-2011
Filing Date:	22-MAR-2011
Time Stamp:	15:02:54
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	no

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Information Disclosure Statement (IDS) Form (SB08)	IDS_Mela_References.pdf	611973 e134b6ac36fa3cea8e87086ab08a8fecdceabfbe	no	4

Warnings:	
Information:	

2	Foreign Reference	WO0201143.pdf	246244 2e58c1cda2a9b576c57e31f8776b1fe2607e526f	no	12
Warnings:					
Information:					
3	Foreign Reference	WO9837811.pdf	1432941 11d4ee3f94737de7f7e435c6ea302d9224bbeade	no	65
Warnings:					
Information:					
4	Foreign Reference	WO9944010.pdf	1453329 e9a3735eb2813405c04a8e6478652d0fffa9f94d	no	70
Warnings:					
Information:					
5	Foreign Reference	EP2264669.pdf	1506568 8feceb1e88b0133e67b6b8765ed2e0f085131f22	no	45
Warnings:					
Information:					
			Total Files Size (in bytes):	5251055	

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New Applications Under 35 U.S.C. 111
If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

National Stage of an International Application under 35 U.S.C. 371
If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office
If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
P.O. BOX 1450
ALEXANDRIA, VA 22313-1450

Appl No.:	**13/069124**	Confirmation No. **9532**
Applicant:	**Boncyk, Wayne C.**	
Filed:	**3/22/2011**	
TC/A.U.:		
Examiner:		
Docket No.:	**101044.0001US14**	
Customer No.:	**24392**	

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

PRELIMINARY AMENDMENT

Sir:

Please amend the above-identified application as follows:

Amendments to the Specification begin on page 2 of this paper

Remarks/Arguments begin on page 3 of this paper.

REMARKS/ARGUMENTS

Specification Amendments

The specification was amended to correctly identify the priority chain.

Respectfully submitted,

FISH & ASSOCIATES, PC

By /Nicholas J. Witchey/
Nicholas J. Witchey
Reg. No. 63481
Tel.: (949) 943-8300

Electronic Acknowledgement Receipt

EFS ID:	11497430
Application Number:	13069124
International Application Number:	
Confirmation Number:	9532
Title of Invention:	Image Capture and Identification System and Process
First Named Inventor/Applicant Name:	Wayne C. Boncyk
Customer Number:	24392
Filer:	Martin Fessenmaier/Lindsey Ripley
Filer Authorized By:	Martin Fessenmaier
Attorney Docket Number:	101044.0001US14
Receipt Date:	29-NOV-2011
Filing Date:	22-MAR-2011
Time Stamp:	13:14:21
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	no

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Application Data Sheet	US_ADS_Form_SB_14_corrected_priority.pdf	964984 e783cf24783195c1124dd3deddd8d446f6afa281	no	5
Warnings:					
Information:					

2	Preliminary Amendment	Preliminary_Amendment_correct_priority.pdf	81669 26101cbd81ecc8c94e6314e06bdbb07612fa1b8d	no	3
Warnings:					
Information:					
			Total Files Size (in bytes):	1046653	

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New Applications Under 35 U.S.C. 111
If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

National Stage of an International Application under 35 U.S.C. 371
If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office
If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

PTO/SB/14 (02-07)
Approved for use through 02/28/2007. OMB 0651-0032
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

Application Data Sheet 37 CFR 1.76	Attorney Docket Number	101044.0001US14
	Application Number	
Title of Invention	Image Capture and Identification System and Process	

The application data sheet is part of the provisional or nonprovisional application for which it is being submitted. The following form contains the bibliographic data arranged in a format specified by the United States Patent and Trademark Office as outlined in 37 CFR 1.76.
This document may be completed electronically and submitted to the Office in electronic format using the Electronic Filing System (EFS) or the document may be printed and included in a paper filed application.

Secrecy Order 37 CFR 5.2

☐ Portions or all of the application associated with this Application Data Sheet may fall under a Secrecy Order pursuant to 37 CFR 5.2 (Paper filers only. Applications that fall under Secrecy Order may not be filed electronically.)

Applicant Information:

Applicant 1 Remove

Applicant Authority ◉ Inventor ○ Legal Representative under 35 U.S.C. 117 ○ Party of Interest under 35 U.S.C. 118

Prefix	Given Name	Middle Name	Family Name	Suffix
	Wayne	C.	Boncyk	

Residence Information (Select One) ◉ US Residency ○ Non US Residency ○ Active US Military Service

City	Evergreen	State/Province	CA	Country of Residence [i]	US

Citizenship under 37 CFR 1.41(b) [i] US

Mailing Address of Applicant:

Address 1	32059 Quarterhorse Road		
Address 2			
City	Evergreen	State/Province	CO
Postal Code	80439	Country [i]	US

Applicant 2 Remove

Applicant Authority ◉ Inventor ○ Legal Representative under 35 U.S.C. 117 ○ Party of Interest under 35 U.S.C. 118

Prefix	Given Name	Middle Name	Family Name	Suffix
	Ronald	H.	Cohen	

Residence Information (Select One) ◉ US Residency ○ Non US Residency ○ Active US Military Service

City	Pasadena	State/Province	CA	Country of Residence [i]	US

Citizenship under 37 CFR 1.41(b) [i] US

Mailing Address of Applicant:

Address 1	2445 E. Del Mar Blvd., #416		
Address 2			
City	Pasadena	State/Province	CA
Postal Code	91107	Country [i]	US

All Inventors Must Be Listed - Additional Inventor Information blocks may be generated within this form by selecting the **Add** button. Add

Correspondence Information:

Enter either Customer Number or complete the Correspondence Information section below.
For further information see 37 CFR 1.33(a).

PTO/SB/14 (02-07)
Approved for use through 02/28/2007. OMB 0651-0032
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE
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Application Data Sheet 37 CFR 1.76	Attorney Docket Number	101044.0001US14
	Application Number	
Title of Invention	Image Capture and Identification System and Process	

☐ An Address is being provided for the correspondence Information of this application.			
Customer Number	24392		
Email Address	nwitchey@fishiplaw.com	Add Email	Remove Email

Application Information:

Title of the Invention	Image Capture and Identification System and Process		
Attorney Docket Number	101044.0001US14	**Small Entity Status Claimed**	☒
Application Type	Nonprovisional		
Subject Matter			
Suggested Class (if any)		**Sub Class (if any)**	
Suggested Technology Center (if any)			
Total Number of Drawing Sheets (if any)	7	**Suggested Figure for Publication (if any)**	2
Publication Information:			
☐ Request Early Publication (Fee required at time of Request 37 CFR 1.219)			
☐ Request Not to Publish. I hereby request that the attached application not be published under 35 U.S.C. 122(b) and certify that the invention disclosed in the attached application has not been and will not be the subject of an application filed in another country, or under a multilateral agreement, that requires publication at eighteen months after filing.			

Representative Information:

Representative information should be provided for all practitioners having a power of attorney in the application. Providing this information in the Application Data Sheet does not constitute a power of attorney in the application (see 37 CFR 1.32). Enter either Customer Number or complete the Representative Name section below. If both sections are completed the Customer Number will be used for the Representative Information during processing.

Please Select One:	◉ Customer Number	○ US Patent Practitioner	○ US Representative (37 CFR 11.9)
Customer Number	24392		

Domestic Priority Information:

This section allows for the applicant to claim benefit under 35 U.S.C. 119(e), 120, 121, or 365(c). Providing this information in the application data sheet constitutes the specific reference required by 35 U.S.C. 119(e) or 120, and 37 CFR 1.78(a)(2) or CFR 1.78(a)(4), and need not otherwise be made part of the specification.

Prior Application Status	Pending		Remove
Application Number	Continuity Type	Prior Application Number	Filing Date (YYYY-MM-DD)
	Division of	13/037317	2011-02-28
Prior Application Status	Pending		Remove

PTO/SB/14 (02-07)
Approved for use through 02/28/2007. OMB 0651-0032
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE
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Application Data Sheet 37 CFR 1.76	Attorney Docket Number	101044.0001US14
	Application Number	
Title of Invention	Image Capture and Identification System and Process	

Application Number	Continuity Type	Prior Application Number	Filing Date (YYYY-MM-DD)
13/037317	Division of	12/333630	2008-12-12
Prior Application Status	Patented		Remove

Application Number	Continuity Type	Prior Application Number	Filing Date (YYYY-MM-DD)	Patent Number	Issue Date (YYYY-MM-DD)
12/333630	Division of	10/492243	2004-04-09	747780	2008-12-22
Prior Application Status	Expired				Remove

Application Number	Continuity Type	Prior Application Number	Filing Date (YYYY-MM-DD)
12/333630	a 371 of international	PCT/US02/35047	2002-11-05

Additional Domestic Priority Data may be generated within this form by selecting the **Add** button. Add

Foreign Priority Information:

This section allows for the applicant to claim benefit of foreign priority and to identify any prior foreign application for which priority is not claimed. Providing this information in the application data sheet constitutes the claim for priority as required by 35 U.S.C. 119(b) and 37 CFR 1.55(a).

Remove

Application Number	Country [i]	Parent Filing Date (YYYY-MM-DD)	Priority Claimed
			◉ Yes ○ No

Additional Foreign Priority Data may be generated within this form by selecting the **Add** button. Add

Assignee Information:

Providing this information in the application data sheet does not substitute for compliance with any requirement of part 3 of Title 37 of the CFR to have an assignment recorded in the Office.

Assignee 1 Remove

If the Assignee is an Organization check here. ☐

Prefix	**Given Name**	Middle Name	**Family Name**	Suffix

Mailing Address Information:

Address 1			
Address 2			
City		**State/Province**	
Country [i]		Postal Code	
Phone Number		Fax Number	
Email Address			

Additional Assignee Data may be generated within this form by selecting the **Add** button. Add

Signature:

A signature of the applicant or representative is required in accordance with 37 CFR 1.33 and 10.18. Please see 37 CFR 1.4(d) for the form of the signature.

PTO/SB/14 (02-07)
Approved for use through 02/28/2007. OMB 0651-0032
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

Application Data Sheet 37 CFR 1.76	Attorney Docket Number	101044.0001US14
	Application Number	
Title of Invention	Image Capture and Identification System and Process	

Signature	/Nicholas J. Witchey/			Date (YYYY-MM-DD)	2011-11-30
First Name	Nicholas J.	Last Name	Witchey	Registration Number	63481

This collection of information is required by 37 CFR 1.76. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 23 minutes to complete, including gathering, preparing, and submitting the completed application data sheet form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

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The information provided by you in this form will be subject to the following routine uses:

1. The information on this form will be treated confidentially to the extent allowed under the Freedom of Information Act (5 U.S.C. 552) and the Privacy Act (5 U.S.C. 552a). Records from this system of records may be disclosed to the Department of Justice to determine whether the Freedom of Information Act requires disclosure of these records.

2. A record from this system of records may be disclosed, as a routine use, in the course of presenting evidence to a court, magistrate, or administrative tribunal, including disclosures to opposing counsel in the course of settlement negotiations.

3. A record in this system of records may be disclosed, as a routine use, to a Member of Congress submitting a request involving an individual, to whom the record pertains, when the individual has requested assistance from the Member with respect to the subject matter of the record.

4. A record in this system of records may be disclosed, as a routine use, to a contractor of the Agency having need for the information in order to perform a contract. Recipients of information shall be required to comply with the requirements of the Privacy Act of 1974, as amended, pursuant to 5 U.S.C. 552a(m).

5. A record related to an International Application filed under the Patent Cooperation Treaty in this system of records may be disclosed, as a routine use, to the International Bureau of the World Intellectual Property Organization, pursuant to the Patent Cooperation Treaty.

6. A record in this system of records may be disclosed, as a routine use, to another federal agency for purposes of National Security review (35 U.S.C. 181) and for review pursuant to the Atomic Energy Act (42 U.S.C. 218(c)).

7. A record from this system of records may be disclosed, as a routine use, to the Administrator, General Services, or his/her designee, during an inspection of records conducted by GSA as part of that agency's responsibility to recommend improvements in records management practices and programs, under authority of 44 U.S.C. 2904 and 2906. Such disclosure shall be made in accordance with the GSA regulations governing inspection of records for this purpose, and any other relevant (i.e., GSA or Commerce) directive. Such disclosure shall not be used to make determinations about individuals.

8. A record from this system of records may be disclosed, as a routine use, to the public after either publication of the application pursuant to 35 U.S.C. 122(b) or issuance of a patent pursuant to 35 U.S.C. 151. Further, a record may be disclosed, subject to the limitations of 37 CFR 1.14, as a routine use, to the public if the record was filed in an application which became abandoned or in which the proceedings were terminated and which application is referenced by either a published application, an application open to public inspections or an issued patent.

9. A record from this system of records may be disclosed, as a routine use, to a Federal, State, or local law enforcement agency, if the USPTO becomes aware of a violation or potential violation of law or regulation.

Amendment to the Specification

Please replace the first paragraph beginning on line 1 of page 1 of the application with the following statement of priority:

[0001] This application is a divisional of 13/037317 filed February 28, 2011 which is a divisional of 12/333630 filed December 12, 2008 which is a divisional of 10/492243 filed April 9, 2004 which is a National Phase of PCT/US02/35407 filed November 5, 2002 ~~which is an International Patent application of 09/992942 filed November 5, 2001 which claims priority to provisional application number 60/317521 filed Sept. 5, 2001 and provisional application number 60/246295 filed Nov. 6, 2000~~. These and all other referenced patents and applications are incorporated herein by reference in their entirety. Where a definition or use of a term in a reference that is incorporated by reference is inconsistent or contrary to the definition of that term provided herein, the definition of that term provided herein is deemed to be controlling.

Following is a clean replacement paragraph:

[0001] This application is a divisional of 13/037317 filed February 28, 2011 which is a divisional of 12/333630 filed December 12, 2008 which is a divisional of 10/492243 filed April 9, 2004 which is a National Phase of PCT/US02/35407 filed November 5, 2002. These and all other referenced patents and applications are incorporated herein by reference in their entirety. Where a definition or use of a term in a reference that is incorporated by reference is inconsistent or contrary to the definition of that term provided herein, the definition of that term provided herein is deemed to be controlling.

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
13/069,124	03/22/2011	Wayne C. Boncyk	101044.0001US14	9532

24392 7590 11/09/2012

FISH & ASSOCIATES, PC
ROBERT D. FISH
2603 Main Street
Suite 1000
Irvine, CA 92614-6232

EXAMINER	
SHERALI, ISHRAT I	
ART UNIT	**PAPER NUMBER**
2667	

NOTIFICATION DATE	DELIVERY MODE
11/09/2012	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

rfish@fishiplaw.com
patents@fishiplaw.com

Office Action Summary	Application No.	Applicant(s)	
	13/069,124	BONCYK ET AL.	
	Examiner	Art Unit	
	ISHRAT I. SHERALI	2667	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ An election was made by the applicant in response to a restriction requirement set forth during the interview on _____; the restriction requirement and election have been incorporated into this action.

4)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

5)☒ Claim(s) 1-38 is/are pending in the application.

5a) Of the above claim(s) _____ is/are withdrawn from consideration.

6)☐ Claim(s) _____ is/are allowed.

7)☒ Claim(s) 1-38 is/are rejected.

8)☐ Claim(s) _____ is/are objected to.

9)☐ Claim(s) _____ are subject to restriction and/or election requirement.

* If any claims have been determined allowable, you may be eligible to benefit from the **Patent Prosecution Highway** program at a participating intellectual property office for the corresponding application. For more information, please see http://www.uspto.gov/patents/init_events/pph/index.jsp or send an inquiry to PPHfeedback@uspto.gov.

Application Papers

10)☐ The specification is objected to by the Examiner.

11)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)

2) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.

3) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .

4) ☐ Other: _____.

DETAILED ACTION

Double Patenting

1. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

2. Claim 1-38 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-47 of U.S. Patent No. 8,218,874. Although the conflicting claims are not identical, they are not patentably distinct from each other because they claim the same subject matter. Claim 1 of US Patent No. 8,218,874 includes all of the limitations recited in claim 1. Furthermore dependent claims 2-38 are also similarly rejected in view of claims 1-16 of US Patent 8,218,874.

Communication

3. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sherali Ishrat whose telephone number is 571-272-7398. The examiner can normally be reached on 8:00 AM - 4:30PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Matthew Bella can be reached on 571-272-7778. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see

http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Sherali Ishrat/

Primary Examiner, Art Unit 2624

November 4, 2012

Notice of References Cited	Application/Control No. 13/069,124	Applicant(s)/Patent Under Reexamination BONCYK ET AL.	
	Examiner ISHRAT I. SHERALI	Art Unit 2667	Page 1 of 1

U.S. PATENT DOCUMENTS

*		Document Number Country Code-Number-Kind Code	Date MM-YYYY	Name	Classification
*	A	US-8,218,874	07-2012	Boncyk et al.	382/181
	B	US-			
	C	US-			
	D	US-			
	E	US-			
	F	US-			
	G	US-			
	H	US-			
	I	US-			
	J	US-			
	K	US-			
	L	US-			
	M	US-			

FOREIGN PATENT DOCUMENTS

*		Document Number Country Code-Number-Kind Code	Date MM-YYYY	Country	Name	Classification
	N					
	O					
	P					
	Q					
	R					
	S					
	T					

NON-PATENT DOCUMENTS

*		Include as applicable: Author, Title Date, Publisher, Edition or Volume, Pertinent Pages)
	U	
	V	
	W	
	X	

*A copy of this reference is not being furnished with this Office action. (See MPEP § 707.05(a).)
Dates in MM-YYYY format are publication dates. Classifications may be US or foreign.

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (**Not for submission under 37 CFR 1.99)**		
	Application Number	13069124
	Filing Date	2011-03-22
	First Named Inventor	Wayne C. Boncyk
	Art Unit	2622
	Examiner Name	to be assigned
	Attorney Docket Number	101044.0001US14

U.S.PATENTS						Remove
Examiner Initial*	Cite No	Patent Number	Kind Code[1]	Issue Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
	1	6081612		2000-06-27	Gutkowicz-Krusin et al.	
	2	6208749		2001-03-27	Gutkowicz-Krusin et al.	
	3	6307957		2001-10-23	Gutkowicz-Krusin et al.	
	4	7127094		2006-10-24	Elbaum et al.	

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INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
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	First Named Inventor	Wayne C. Boncyk
	Art Unit	2622
	Examiner Name	to be assigned
	Attorney Docket Number	101044.0001US14

	1	98/37811	WO		1998-09-03	Electro-Optical Sciences, Inc.		☐
	2	99/44010	WO		1999-09-02	Gutkowicz-Krusin et al.		☐
	3	02/01143	WO		2002-01-03	Electro-Optical Sciences, Inc.		☐
	4	2264669	EP		2010-12-22	MELA Sciences, Inc.		☐

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Examiner Initials*	Cite No	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc), date, pages(s), volume-issue number(s), publisher, city and/or country where published.	T[5]
	1		☐

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EXAMINER SIGNATURE

Examiner Signature	/Ishrat Sherali/	Date Considered	11/04/2012

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through a citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

[1] See Kind Codes of USPTO Patent Documents at www.USPTO.GOV or MPEP 901.04. [2] Enter office that issued the document, by the two-letter code (WIPO Standard ST.3). [3] For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. [4] Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. [5] Applicant is to place a check mark here if English language translation is attached.

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	Art Unit	2622
	Examiner Name	to be assigned
	Attorney Docket Number	101044.0001US14

CERTIFICATION STATEMENT

Please see 37 CFR 1.97 and 1.98 to make the appropriate selection(s):

☐ That each item of information contained in the information disclosure statement was first cited in any communication from a foreign patent office in a counterpart foreign application not more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e)(1).

OR

☒ That no item of information contained in the information disclosure statement was cited in a communication from a foreign patent office in a counterpart foreign application, and, to the knowledge of the person signing the certification after making reasonable inquiry, no item of information contained in the information disclosure statement was known to any individual designated in 37 CFR 1.56(c) more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e)(2).

☐ See attached certification statement.

☐ The fee set forth in 37 CFR 1.17 (p) has been submitted herewith.

☒ A certification statement is not submitted herewith.

SIGNATURE

A signature of the applicant or representative is required in accordance with CFR 1.33, 10.18. Please see CFR 1.4(d) for the form of the signature.

Signature	/Nicholas J. Witchey/	Date (YYYY-MM-DD)	2011-11-04
Name/Print	Nicholas J. Witchey	Registration Number	63481

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 1 hour to complete, including gathering, preparing and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

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The Privacy Act of 1974 (P.L. 93-579) requires that you be given certain information in connection with your submission of the attached form related to a patent application or patent. Accordingly, pursuant to the requirements of the Act, please be advised that: (1) the general authority for the collection of this information is 35 U.S.C. 2(b)(2); (2) furnishing of the information solicited is voluntary; and (3) the principal purpose for which the information is used by the U.S. Patent and Trademark Office is to process and/or examine your submission related to a patent application or patent. If you do not furnish the requested information, the U.S. Patent and Trademark Office may not be able to process and/or examine your submission, which may result in termination of proceedings or abandonment of the application or expiration of the patent.

The information provided by you in this form will be subject to the following routine uses:

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3. A record in this system of records may be disclosed, as a routine use, to a Member of Congress submitting a request involving an individual, to whom the record pertains, when the individual has requested assistance from the Member with respect to the subject matter of the record.

4. A record in this system of records may be disclosed, as a routine use, to a contractor of the Agency having need for the information in order to perform a contract. Recipients of information shall be required to comply with the requirements of the Privacy Act of 1974, as amended, pursuant to 5 U.S.C. 552a(m).

5. A record related to an International Application filed under the Patent Cooperation Treaty in this system of records may be disclosed, as a routine use, to the International Bureau of the World Intellectual Property Organization, pursuant to the Patent Cooperation Treaty.

6. A record in this system of records may be disclosed, as a routine use, to another federal agency for purposes of National Security review (35 U.S.C. 181) and for review pursuant to the Atomic Energy Act (42 U.S.C. 218(c)).

7. A record from this system of records may be disclosed, as a routine use, to the Administrator, General Services, or his/her designee, during an inspection of records conducted by GSA as part of that agency's responsibility to recommend improvements in records management practices and programs, under authority of 44 U.S.C. 2904 and 2906. Such disclosure shall be made in accordance with the GSA regulations governing inspection of records for this purpose, and any other relevant (i.e., GSA or Commerce) directive. Such disclosure shall not be used to make determinations about individuals.

8. A record from this system of records may be disclosed, as a routine use, to the public after either publication of the application pursuant to 35 U.S.C. 122(b) or issuance of a patent pursuant to 35 U.S.C. 151. Further, a record may be disclosed, subject to the limitations of 37 CFR 1.14, as a routine use, to the public if the record was filed in an application which became abandoned or in which the proceedings were terminated and which application is referenced by either a published application, an application open to public inspections or an issued patent.

9. A record from this system of records may be disclosed, as a routine use, to a Federal, State, or local law enforcement agency, if the USPTO becomes aware of a violation or potential violation of law or regulation.

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BIB DATA SHEET

CONFIRMATION NO. 9532

SERIAL NUMBER	FILING or 371(c) DATE	CLASS	GROUP ART UNIT	ATTORNEY DOCKET NO.
13/069,124	03/22/2011 RULE	382	2667	101044.0001US14

APPLICANTS

Wayne C. Boncyk, Evergreen, CA;
Ronald H. Cohen, Pasadena, CA;

**** CONTINUING DATA **************************

This application is a DIV of 13/037,317 02/28/2011 PAT 8,224,078
which is a DIV of 12/333,630 12/12/2008 PAT 7,899,243
which is a DIV of 10/492,243 05/20/2004 PAT 7,477,780 *
which is a 371 of PCT/US02/35407 11/05/2002
which is a CON of 09/992,942 11/05/2001 PAT 7,016,532
which claims benefit of 60/246,295 11/06/2000
and claims benefit of 60/317,521 09/05/2001
(*)Data provided by applicant is not consistent with PTO records.

**** FOREIGN APPLICATIONS **************************

**** IF REQUIRED, FOREIGN FILING LICENSE GRANTED **** ** SMALL ENTITY **
04/01/2011

Foreign Priority claimed ☐ Yes ☑ No 35 USC 119(a-d) conditions met ☐ Yes ☑ No Verified and Acknowledged /ISHRAT I SHERALI/ Examiner's Signature	☐ Met after Allowance Initials	STATE OR COUNTRY	SHEETS DRAWINGS	TOTAL CLAIMS	INDEPENDENT CLAIMS
		CA	7	38	1

ADDRESS

FISH & ASSOCIATES, PC
ROBERT D. FISH
2603 Main Street
Suite 1000
Irvine, CA 92614-6232
UNITED STATES

TITLE

Image Capture and Identification System and Process

FILING FEE RECEIVED		
930	FEES: Authority has been given in Paper No._____ to charge/credit DEPOSIT ACCOUNT No._____ for following:	☐ All Fees ☐ 1.16 Fees (Filing) ☐ 1.17 Fees (Processing Ext. of time) ☐ 1.18 Fees (Issue) ☐ Other _____ ☐ Credit

BIB (Rev. 05/07).

Search Notes	Application/Control No.	Applicant(s)/Patent Under Reexamination
	13069124	BONCYK ET AL.
	Examiner	Art Unit
	ISHRAT I SHERALI	2667

SEARCHED

Class	Subclass	Date	Examiner
382	181, 162, 165, 100, 305. 224, 115-118	11/4/12	IS
705	26.1-27.2, 23	11/4/12	IS
348	239, 211.2-211.6, 207.1, 460, 552	11/4/12	IS
713	186, 168	11/4/12	IS
455	414.2-414.3, 412.1, 411	11/4/12	IS
709	201-203, 217-219, 250	11/4/12	IS

SEARCH NOTES

Search Notes	Date	Examiner
SEARCH EAST/IEEE/INVENTOR/ASSIGNEE	11/4/12	IS

INTERFERENCE SEARCH

Class	Subclass	Date	Examiner

Doc code: IDS
Doc description: Information Disclosure Statement (IDS) Filed

PTO/SB/08a (01-10)
Approved for use through 07/31/2012. OMB 0651-0031
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

INFORMATION DISCLOSURE STATEMENT BY APPLICANT
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First Named Inventor	Boncyk, Wayne C.
Art Unit	
Examiner Name	
Attorney Docket Number	101044.0001US14

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Examiner Initial*	Cite No	Patent Number	Kind Code[1]	Issue Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
	1	5933829	A	1999-08-03	Durst et al.	
	2	5815411	A	1998-09-29	Ellenby et al.	
	3	5742521	A	1998-04-21	Ellenby et al.	
	4	5682332	A	1997-10-28	Ellenby et al.	
	5	5625765	A	1997-04-29	Ellenby et al.	

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	1	9942947	WO	A2	1999-08-26	ELLENBY		☐
	2	9942946	WO	A2	1999-08-26	ELLENBY		☐
	3	02073818	WO	A1	2002-09-19	ELLENBY		☐
	4	02059716	WO	A2	2002-08-01	ELLENBY		☐
	5	1354260	EP	A2	2003-10-22	ELLENBY		☐
	6	1012725	EP	A1	2000-06-28	ELLENBY		☐
	7	0171282	WO	A1	2001-09-27	ELLENBY		☐
	8	0163487	WO	A1	2001-08-30	ELLENBY		☐

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	Art Unit	
	Examiner Name	
	Attorney Docket Number	101044.0001US14

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EXAMINER SIGNATURE

Examiner Signature	/Ishrat Sherali/	Date Considered	11/04/2012

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[1] See Kind Codes of USPTO Patent Documents at www.USPTO.GOV or MPEP 901.04. [2] Enter office that issued the document, by the two-letter code (WIPO Standard ST.3). [3] For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. [4] Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. [5] Applicant is to place a check mark here if English language translation is attached.

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U.S.PATENTS						Remove
Examiner Initial*	Cite No	Patent Number	Kind Code[1]	Issue Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
	1	7916138	B2	2011-03-29	John et al.	
	2	7889193	B2	2011-02-15	Platonov et al.	
	3	7768534	B2	2010-08-03	Pentenrieder et al.	
	4	7765126	B2	2010-07-27	Hudetz et al.	
	5	7696905	B2	2010-04-13	Ellenby et al.	
	6	7641342	B2	2010-01-05	Eberl et al.	
	7	7430588	B2	2006-07-13	Hunter	
	8	7383209	B2	2005-11-03	Hudetz et al.	

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	9	7245273	B2	2002-08-01	Eberl et al.	
	10	7031875	B2	2006-04-18	Ellenby et al.	
	11	7031536	B2	2006-04-18	Kajiwara	
	12	6993573	B2	2006-01-31	Hunter	
	13	6865608	B2	2005-03-08	Hunter	
	14	6804726	B1	2004-10-12	Ellenby et al.	
	15	6766363	B1	2004-07-20	Rothschild	
	16	6690370	B2	2004-02-10	Ellenby et al.	
	17	6675165	B1	2004-01-06	Rothschild	
	18	6651053	B1	2003-11-18	Rothschild	
	19	6542933	B1	2003-04-01	Durst, Jr. et al.	

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	Examiner Name	
	Attorney Docket Number	101044.0001US14

	20	6535210	B1	2003-03-18	Ellenby et al.	
	21	6522292	B1	2003-02-18	Ellenby et al.	
	22	6434561	B1	2002-08-13	Durst, Jr. et al.	
	23	6430554	B1	2002-08-06	Rothschild	
	24	6414696	B1	2002-07-02	Ellenby et al.	
	25	6396475	B1	2002-05-28	Ellenby et al.	
	26	6307556	B1	2001-10-23	Ellenby et al.	
	27	6278461	B1	2001-08-21	Ellenby et al.	
	28	6199048	B1	2001-03-06	Hudetz et al.	
	29	6173239	B1	2001-01-09	Ellenby	
	30	6108656	A	2000-08-22	Durst et al.	

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	Attorney Docket Number	101044.0001US14

	31	6098118	A	2000-08-01	Ellenby et al.	
	32	6064398	A	2000-05-16	Ellenby et al.	
	33	6037936	A	2000-03-14	Ellenby et al.	
	34	6031545	A	2000-02-29	Ellenby et al.	
	35	5991827	A	1999-11-23	Ellenby et al.	
	36	5978773	A	1999-11-02	Hudetz et al.	

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Examiner Initial*	Cite No	Publication Number	Kind Code[1]	Publication Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
	1	20100188638	A1	2010-07-29	Eberl et al.	
	2	20100045933	A1	2010-02-25	Eberl et al.	
	3	20080157946	A1	2008-07-03	Eberl et al.	

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INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	13069124 13069124 - GAU: 2667
	Filing Date	2011-03-22
	First Named Inventor	Boncyk, Wayne C.
	Art Unit	
	Examiner Name	
	Attorney Docket Number	101044.0001US14

	4	20070182739	A1	2007-08-09	Platonov et al.	
	5	20070146391	A1	2007-06-28	PENTENRIEDER et al.	
	6	20070109619	A1	2007-05-17	Eberl et al.	
	7	20060190812	A1	2006-08-24	Ellenby et al.	
	8	20060161379	A1	2006-07-20	Ellenby et al.	
	9	20050024501	A1	2005-02-03	Ellenby et al.	
	10	20020163521	A1	2002-11-07	Ellenby et al.	
	11	20010047426	A1	2001-11-29	Hunter	
	12	20010044824	A1	2001-11-22	Hunter et al.	
	13	20010032252	A1	2001-10-18	Durst et al.	
	14	20010011276	A1	2001-08-02	DURST JR. et al.	

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	First Named Inventor	Boncyk, Wayne C.
	Art Unit	
	Examiner Name	
	Attorney Docket Number	101044.0001US14

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INFORMATION DISCLOSURE STATEMENT BY APPLICANT
(Not for submission under 37 CFR 1.99)

Application Number	13069124
Filing Date	2011-03-22
First Named Inventor	Wayne C. Boncyk
Art Unit	
Examiner Name	to be assigned
Attorney Docket Number	101044.0001US14

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Examiner Initial*	Cite No	Patent Number	Kind Code[1]	Issue Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
	1	5579471		1996-11-26	Barber et al.	
	2	5615324		1997-03-25	Kuboyama	
	3	5724579		1998-03-03	Suzuki	
	4	5751286		1998-05-12	Barber et al.	
	5	5768633		1998-06-16	Allen et al.	
	6	5926116		1999-07-20	Kitano et al.	
	7	5933823		1999-08-03	Cullen et al.	
	8	5933829		1999-08-03	Durst et al.	

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	First Named Inventor	Wayne C. Boncyk
	Art Unit	
	Examiner Name	to be assigned
	Attorney Docket Number	101044.0001US14

	9	5978773		1999-11-02	Hudetz et al.	
	10	6055536		2000-04-25	Shimakawa et al.	
	11	6144848		2000-11-07	Walsh et al.	
	12	6181817		2001-01-30	Zabih et al.	
	13	6182090		2001-01-30	Peairs	
	14	6256409		2001-07-03	Wang	
	15	6286036		2001-09-01	Rhoads	
	16	6393147		2002-05-21	Danneels et al.	
	17	6396537		2002-05-28	Squilla et al.	
	18	6411725		2002-06-25	Rhoads	
	19	6453361		2002-09-17	Morris	

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	First Named Inventor	Wayne C. Boncyk
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	Examiner Name	to be assigned
	Attorney Docket Number	101044.0001US14

	20	6522889		2003-02-18	Aarnio	
	21	6532298		2003-03-11	Cambier et al.	
	22	6567122		2003-05-20	Anderson et al.	
	23	6651053		2003-11-18	Rothschild	
	24	6674923		2004-01-06	Shih et al.	
	25	6674993		2004-01-06	Tarbouriech	
	26	6691914		2004-02-17	Isherwood et al.	
	27	6714969		2004-03-30	Klein et al.	
	28	6724914		2004-04-20	Brundage et al.	
	29	6738630		2004-05-18	Ashmore	
	30	6842181		2005-01-11	Acharya	

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	31	6885771		2005-04-26	Takahashi	
	32	7016532		2006-03-21	Boncyk et al.	
	33	7362922		2008-04-22	Nishiyama et al.	

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Examiner Initial*	Cite No	Publication Number	Kind Code[1]	Publication Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
	1	20020019819		2002-02-14	Sekiguchi et al.	
	2	20020055957		2002-05-09	Ohsawa	
	3	20020089524		2002-07-11	Ikeda	
	4	20020090132		2002-07-11	Boncyk et al.	
	5	20020102966		2002-08-01	Lev et al.	
	6	20020103813		2002-08-01	Frigon	

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	First Named Inventor	Wayne C. Boncyk
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	Examiner Name	to be assigned
	Attorney Docket Number	101044.0001US14

	7	20020140988		2002-10-03	Cheatle et al.	
	8	20020156866		2002-10-24	Schneider	
	9	20030095681		2003-05-22	Burg et al.	
	10	20040208372		2004-10-21	Boncyk et al.	
	11	20050015370		2005-01-20	Stavely et al.	
	12	20050162523		2005-07-28	Darrell et al.	
	13	20050185060		2005-08-25	Neven, Sr.	
	14	20080021953		2008-01-24	Gil	

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Examiner Initial*	Cite No	Foreign Document Number[3]	Country Code[2] i	Kind Code[4]	Publication Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear	T[5]
	1	0920179	EP		1999-06-02	Eastman Kodak Company		☐

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	First Named Inventor	Wayne C. Boncyk
	Art Unit	
	Examiner Name	to be assigned
	Attorney Docket Number	101044.0001US14

	2	1355258	EP		2003-10-22	Fujitsu Limited		☐
	3	2407230	GB		2005-04-20	OpenBlue Limited		☐
	4	1091634	JP		1998-04-10	写真画像検索システム		☐
	5	10289243	JP		1998-10-27	Casio Comput Co Ltd.		☐
	6	2001101191	JP		2001-04-13	Dacix Inc.		☐
	7	2001282825	JP		2001-10-12	Eighting:KK		☐
	8	0124050	WO		2001-04-05	Cadix Inc.		☐
	9	0173603	WO		2001-10-04	Kabushiki Kaisha Eighting		☐
	10	02082799	WO		2002-10-17	Lev et al.		☐
	11	0149056	WO		2001-07-05	Nokia Corporation		☐
	12	97/49060	WO		1997-12-24	Norand Corporation		☐

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	Examiner Name	to be assigned
	Attorney Docket Number	101044.0001US14

	13	9916024	WO		1999-04-01	Raytheon Company		☐

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Examiner Signature	/Ishrat Sherali/	Date Considered	11/04/2012

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Index of Claims	Application/Control No.	Applicant(s)/Patent Under Reexamination
	13069124	BONCYK ET AL.
	Examiner	**Art Unit**
	ISHRAT I SHERALI	2667

✓	Rejected	-	Cancelled	N	Non-Elected	A	Appeal
=	Allowed	÷	Restricted	I	Interference	O	Objected

☐ Claims renumbered in the same order as presented by applicant ☐ CPA ☐ T.D. ☐ R.1.47

CLAIM		DATE								
Final	Original	11/05/2012								
	1	✓								
	2	✓								
	3	✓								
	4	✓								
	5	✓								
	6	✓								
	7	✓								
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	30	✓								
	31	✓								
	32	✓								
	33	✓								
	34	✓								
	35	✓								
	36	✓								

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	Examiner	**Art Unit**
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=	Allowed	÷	Restricted	I	Interference	O	Objected

☐ Claims renumbered in the same order as presented by applicant ☐ CPA ☐ T.D. ☐ R.1.47

CLAIM		DATE								
Final	Original	11/05/2012								
	37	✓								
	38	✓								

PTO/SB/80 (11-08)
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U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

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I hereby revoke all previous powers of attorney given in the application identified in the attached statement under 37 CFR 3.73(b).

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☑ Practitioners associated with the Customer Number: 24392

OR

☐ Practitioner(s) named below (if more than ten patent practitioners are to be named, then a customer number must be used):

Name	Registration Number	Name	Registration Number

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Telephone		Email	

Assignee Name and Address:

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11755 Wilshire Boulevard, Suite 2000
Los Angeles, CA 90025

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SIGNATURE of Assignee of Record

The individual whose signature and title is supplied below is authorized to act on behalf of the assignee

Signature		Date	7/19/12
Name	Charles Kenworthy	Telephone	310-405-7998
Title	Manager, Nant Holdings IP, LLC		

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7. A record from this system of records may be disclosed, as a routine use, to the Administrator, General Services, or his/her designee, during an inspection of records conducted by GSA as part of that agency's responsibility to recommend improvements in records management practices and programs, under authority of 44 U.S.C. 2904 and 2906. Such disclosure shall be made in accordance with the GSA regulations governing inspection of records for this purpose, and any other relevant (*i.e.*, GSA or Commerce) directive. Such disclosure shall not be used to make determinations about individuals.
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TERMINAL DISCLAIMER TO OBVIATE A DOUBLE PATENTING REJECTION OVER A "PRIOR" PATENT	Docket Number (Optional) 101044-0001US14

In re Application of: Wayne C. Boncyk

Application No.: 13/069124

Filed: 03/22/2011

For: Image Capture and Identification System and Process

The owner*, Nant Holdings IP, LLC, of 100 percent interest in the instant application hereby disclaims, except as provided below, the terminal part of the statutory term of any patent granted on the instant application which would extend beyond the expiration date of the full statutory term of **prior patent** No. 8218874 as the term of said **prior patent** is presently shortened by any terminal disclaimer. The owner hereby agrees that any patent so granted on the instant application shall be enforceable only for and during such period that it and the **prior patent** are commonly owned. This agreement runs with any patent granted on the instant application and is binding upon the grantee, its successors or assigns.

In making the above disclaimer, the owner does not disclaim the terminal part of the term of any patent granted on the instant application that would extend to the expiration date of the full statutory term of the **prior patent**, "as the term of said **prior patent** is presently shortened by any terminal disclaimer," in the event that said **prior patent** later:

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I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

2. ☑ The undersigned is an attorney or agent of record. Reg. No. 63481

/Nicholas J. Witchey/ — Signature

2013-02-05 — Date

Nicholas J. Witchey — Typed or printed name

949-943-8300 — Telephone Number

☑ Terminal disclaimer fee under 37 CFR 1.20(d) included.

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Electronic Patent Application Fee Transmittal

Application Number:	13069124
Filing Date:	22-Mar-2011
Title of Invention:	Image Capture and Identification System and Process
First Named Inventor/Applicant Name:	Wayne C. Boncyk
Filer:	Martin Fessenmaier/Marutzzella Castro
Attorney Docket Number:	101044.0001US14

Filed as Large Entity

Utility under 35 USC 111(a) Filing Fees

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
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Claims:				
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Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Miscellaneous:				
Statutory or terminal disclaimer	1814	1	160	160
		Total in USD ($)		**160**

Electronic Acknowledgement Receipt	
EFS ID:	14880968
Application Number:	13069124
International Application Number:	
Confirmation Number:	9532
Title of Invention:	Image Capture and Identification System and Process
First Named Inventor/Applicant Name:	Wayne C. Boncyk
Customer Number:	24392
Filer:	Martin Fessenmaier/Marutzzella Castro
Filer Authorized By:	Martin Fessenmaier
Attorney Docket Number:	101044.0001US14
Receipt Date:	05-FEB-2013
Filing Date:	22-MAR-2011
Time Stamp:	16:02:18
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	yes
Payment Type	Deposit Account
Payment was successfully received in RAM	$160
RAM confirmation Number	2687
Deposit Account	500341
Authorized User	
The Director of the USPTO is hereby authorized to charge indicated fees and credit any overpayment as follows: Charge any Additional Fees required under 37 C.F.R. Section 1.21 (Miscellaneous fees and charges)	

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1		101044-0001US14_Response-01b.pdf	31541 88a961a084bbf19491d5def973e2336d9ba6b951	yes	7
	Multipart Description/PDF files in .zip description				
	Document Description		**Start**	**End**	
	Amendment/Req. Reconsideration-After Non-Final Reject		1	1	
	Claims		2	5	
	Applicant Arguments/Remarks Made in an Amendment		6	7	
Warnings:					
Information:					
2	Assignee showing of ownership per 37 CFR 3.73.	101044-0001US14_StmtOwner.pdf	136482 246f67fa9bb26a64e3cf92adec22cf3eabdeac0f	no	3
Warnings:					
Information:					
3	Power of Attorney	POA_signed.pdf	804515 f53b869c4af2913fe35231489c5f0cdd88f94023	no	2
Warnings:					
The page size in the PDF is too large. The pages should be 8.5 x 11 or A4. If this PDF is submitted, the pages will be resized upon entry into the Image File Wrapper and may affect subsequent processing					
Information:					
4	Terminal Disclaimer Filed	101044-0001US14_TerminalDisclaimer.pdf	374193 1527932f945fdbd8532e777534c38d31451d4461	no	2
Warnings:					
Information:					
5	Fee Worksheet (SB06)	fee-info.pdf	29834 2d7c92f11e0a0aa3554fd24a96662872cbf585a0	no	2
Warnings:					
Information:					
		Total Files Size (in bytes):	1376565		

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New Applications Under 35 U.S.C. 111
If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

National Stage of an International Application under 35 U.S.C. 371
If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office
If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
P.O. BOX 1450
ALEXANDRIA, VA 22313-1450

Appl No.:	**13/069,124**
Applicant:	**Boncyk, Wayne C., et al.**
Filing Date:	**March 22, 2011**
Art Unit:	**2667**
Examiner:	**Sherali, Ishrat I.**
Attorney Docket No.:	**101044.0001US14**
Title	**Image Capture and Identification System and Process**

Mail Stop Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

RESPONSE TO OFFICE ACTION

Sir:

This paper responds to the Office Action dated November 9, 2012. This document is accompanied by a terminal disclaimer. Please enter the amendments shown herein.

- Claim amendments begin on page 2.
- Remarks begin on page 6.

AMENDMENTS TO THE CLAIMS

This listing of claims replaces all prior versions, and listings, of claims in the application:

1. (original) A transaction system comprising:

a mobile device configured to acquire data related to an object;

an object identification platform configured to obtain the acquired data, recognize the object as a target object based on the acquired data, and determine object information associated with the target object; and

a content platform configured to obtain the object information, and initiate a transaction associated with the target object with a selected account over a network based on the object information.

2. (original) The system of claim 1, wherein the mobile device is configured to operate, at least in part, as the object identification platform.

3. (original) The system of claim 2, wherein the object identification platform is distributed between the mobile device and at least one remote server coupled with the mobile device via a network.

4. (original) The system of claim 1, wherein a remote server coupled with the mobile device over a network is configured to operate as the object identification platform.

5. (original) The system of claim 1, wherein the mobile device comprises the content platform.

6. (original) The system of claim 1, wherein at least one remote server coupled with the mobile device over a network operates as the content platform.

7. (original) The system of claim 1, wherein the content platform is further configured to provide content information pertinent to the target object to the mobile device based on the object information.

8. (currently amended) The system of claim 7, wherein the content information comprises video data.

9. (original) The system of claim 8, wherein the content information comprises a video stream.

10. (currently amended) The system of claim 7, wherein the content information comprises audio data.

11. (currently amended) The system of claim [[8]]10, wherein the audio data comprises an audio recording.

12. (currently amended) The system of claim [[8]]10, wherein the audio data comprises an audio stream.

13. (original) The system of claim 1, wherein the transaction comprises a commercial transaction.

14. (original) The system of claim 13, wherein the commercial transaction includes a purchase related to the target object.

15. (original) The system of claim 14, wherein the purchase relates to at least one of the following: audio data, video data, the object, the target object, a ticket, an item on a screen, a disc, a fare, and a vending machine product.

16. (original) The system of claim 1, wherein the selected account comprises an on-line account.

17. (original) The system of claim 1, wherein the selected account comprises an account linked with the mobile device.

18. (original) The system of claim 1, wherein the selected account comprises an account linked to a user of the mobile device.

19. (original) The system of claim 1, wherein the selected account comprises a bank account.

20. (original) The system of claim 1, wherein the selected account comprises a credit card account.

21. (original) The system of claim 1, wherein the acquired data comprises an image.

22. (currently amended) The system of claim [[21]]1, wherein the acquired data comprises image data.

23. (original) The system of claim 1, wherein the acquired data comprises a digital representation relating to a person.

24. (currently amended) The system of claim 23, wherein the digital representation comprises a representation of a human face.

25. (currently amended) The system of claim 1, wherein the acquired data comprises a user ~~identify~~identity.

26. (currently amended) The system of claim 1, wherein the acquired data comprises a location of the mobile device.

27. (original) The system of claim 1, wherein the acquired data comprises screen content.

28. (original) The system of claim 1, wherein the acquired data comprises a user voice command.

29. (original) The system of claim 1, wherein the acquired data comprises symbol content.

30. (original) The system of claim 29, wherein the symbol content comprises alphanumeric data.

31. (original) The system of claim 1, wherein the object information comprises an object identity.

32. (currently amended) The system of claim 31, wherein the object ~~identify~~identity comprises an object classification.

33. (original) The system of claim 1, wherein the object information comprises an object status.

34. (original) The system of claim 1, wherein the object information comprises decoded symbol information.

35. (original) The system of claim 1, wherein the object information comprises an object attribute.

36. (original) The system of claim 1, wherein the mobile device comprises a mobile telephone.

37. (original) The system of claim 36, wherein the mobile device comprises a camera equipped mobile telephone.

38. (original) The system of claim 1, wherein the mobile device comprises a vehicle.

REMARKS/ARGUMENTS

Claim Amendments

Claims 8, 10-12, 22, 24-26, and 32 have been amended to address minor informalities or for clarity. No new matter has been added.

Double Patenting

The office rejected claims 1-38 on the ground of non-statutory obviousness-type double patenting as being unpatentable over claims 1-47 of co-owned U.S. Patent No. 8,218,874. In response, the Applicants submit the accompanying terminal disclaimer with respect to U.S. 8,218,874.

Thus, Applicant respectfully requests allowance of pending Claims 1-38.

Request For Allowance

Claims 1-38 are pending in this application. The applicant requests allowance of all pending claims.

Respectfully submitted,
Fish & Associates, PC

Date: January 29, 2013

By: /Rosie H. Kim/
Rosie H. Kim
Reg. No. 67,139

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Irvine, CA 92614-6232
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PTO/AIA/96 (08-12)
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STATEMENT UNDER 37 CFR 3.73(c)

Applicant/Patent Owner: Wayne C. Boncyk, et al.

Application No./Patent No.: 13/069124 Filed/Issue Date: March 22, 2011

Titled: Image Capture and Identification System and Process

Nant Holdings IP, LLC, a limited liability company

(Name of Assignee) (Type of Assignee, e.g., corporation, partnership, university, government agency, etc.)

states that, for the patent application/patent identified above, it is (choose **one** of options 1, 2, 3 or 4 below):

1. ☑ The assignee of the entire right, title, and interest.

2. ☐ An assignee of less than the entire right, title, and interest (check applicable box):

   ☐ The extent (by percentage) of its ownership interest is _____%. Additional Statement(s) by the owners holding the balance of the interest must be submitted to account for 100% of the ownership interest.

   ☐ There are unspecified percentages of ownership. The other parties, including inventors, who together own the entire right, title and interest are:

   Additional Statement(s) by the owner(s) holding the balance of the interest must be submitted to account for the entire right, title, and interest.

3. ☐ The assignee of an undivided interest in the entirety (a complete assignment from one of the joint inventors was made). The other parties, including inventors, who together own the entire right, title, and interest are:

   Additional Statement(s) by the owner(s) holding the balance of the interest must be submitted to account for the entire right, title, and interest.

4. ☐ The recipient, via a court proceeding or the like (*e.g.*, bankruptcy, probate), of an undivided interest in the entirety (a complete transfer of ownership interest was made). The certified document(s) showing the transfer is attached.

The interest identified in option 1, 2 or 3 above (not option 4) is evidenced by either (choose **one** of options A or B below):

A. ☐ An assignment from the inventor(s) of the patent application/patent identified above. The assignment was recorded in the United States Patent and Trademark Office at Reel _____, Frame _____, or for which a copy thereof is attached.

B. ☑ A chain of title from the inventor(s), of the patent application/patent identified above, to the current assignee as follows:

1. From: Wayne C. Boncyk, Ronald H. Cohen To: Evryx Technologies

   The document was recorded in the United States Patent and Trademark Office at
   Reel 026260, Frame 0027, or for which a copy thereof is attached.

2. From: Evryx Technologies To: Evryx Acquisition, LLC

   The document was recorded in the United States Patent and Trademark Office at
   Reel 026260, Frame 0146, or for which a copy thereof is attached.

PTO/AIA/96 (08-12)
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U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

STATEMENT UNDER 37 CFR 3.73(c)

3. From: Evryx Acquisition, LLC To: Nant Holdings IP, LLC

The document was recorded in the United States Patent and Trademark Office at
Reel 026354, Frame 0291, or for which a copy thereof is attached.

4. From: _____ To: _____

The document was recorded in the United States Patent and Trademark Office at
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5. From: _____ To: _____

The document was recorded in the United States Patent and Trademark Office at
Reel _____, Frame _____, or for which a copy thereof is attached.

6. From: _____ To: _____

The document was recorded in the United States Patent and Trademark Office at
Reel _____, Frame _____, or for which a copy thereof is attached.

☐ Additional documents in the chain of title are listed on a supplemental sheet(s).

☑ As required by 37 CFR 3.73(c)(1)(i), the documentary evidence of the chain of title from the original owner to the assignee was, or concurrently is being, submitted for recordation pursuant to 37 CFR 3.11.

[NOTE: A separate copy (i.e., a true copy of the original assignment document(s)) must be submitted to Assignment Division in accordance with 37 CFR Part 3, to record the assignment in the records of the USPTO. See MPEP 302.08]

The undersigned (whose title is supplied below) is authorized to act on behalf of the assignee.

/Nicholas J. Witchey/	February 5, 2013
Signature	Date
Nicholas J. Witchey	63481
Printed or Typed Name	Title or Registration Number

Privacy Act Statement

The **Privacy Act of 1974 (P.L. 93-579)** requires that yoube given certain informationin connection with your submission of the attached form related to a patent application or patent. Accordingly, pursuant to the requirements of the Act, pleasebe advised that: (1) the general authority forthe collection of thisinformation is 35 U.S.C. 2(b)(2); (2) furnishing of the information solicited is voluntary; and(3) the principal purpose forwhich the information isused by the U.S. Patent and Trademark Office is to process and/or examine your submission related to a patent applicationor patent. If you do not furnish the requested information,the U.S. Patent and Trademark Office may not be able to process and/or examineyour submission,which may result in termination of proceedings or abandonment of the applicationor expiration of the patent.

The informationprovided by you in this form will be subject to the following routine uses:

1. The information on this form will be treated confidentially to the extent allowed under the Freedom of Information Act (5 U.S.C. 552) and the Privacy Act (5 U.S.C 552a). Records from this system of records may be disclosed to the Department of Justice to determine whether disclosure of these records is required by the Freedom of Information Act.
2. A record from this system of records may be disclosed, as a routine use, in the course of presenting evidence to a court, magistrate, or administrative tribunal, including disclosures to opposing counsel in the course of settlement negotiations.
3. A record in this system of records may be disclosed, as a routine use, to a Member of Congress submitting a request involving an individual, to whom the record pertains, when the individual has requested assistance from the Member with respect to the subject matter of the record.
4. A record in this system of records may be disclosed, as a routine use, to a contractor of the Agency having need for the informationin order to perform a contract. Recipients of information shall be required to comply with the requirements of the Privacy Act of 1974, as amended, pursuant to 5 U.S.C. 552a(m).
5. A record related to an InternationalApplication filed under the Patent Cooperation Treaty in this system of records may be disclosed, as a routine use, to the International Bureau of the World Intellectual Property Organization, pursuant to the Patent Cooperation Treaty.
6. A record in this system of records may be disclosed, as a routine use, to another federal agency for purposes of National Security review (35 U.S.C. 181) and for review pursuant to the Atomic Energy Act (42 U.S.C. 218(c)).
7. A record from this system of records may be disclosed, as a routine use, to the Administrator, General Services, or his/her designee, during an inspection of records conducted by GSA as part of that agency's responsibility to recommend improvements in records management practices and programs, under authority of 44 U.S.C. 2904 and 2906. Such disclosure shall be made in accordance with the GSA regulations governing inspection of records for this purpose, and any other relevant (*i.e.*, GSA or Commerce) directive. Such disclosure shall not be used to make determinations about individuals.
8. A record from this system of records may be disclosed, as a routine use, to the public after either publication of the application pursuant to 35 U.S.C. 122(b) or issuance of a patent pursuant to 35 U.S.C. 151. Further, arecord may be disclosed, subject to the limitations of 37 CFR 1.14, as a routine use, to the public if the record was filed in an application which became abandoned or in which the proceedings were terminated and which application is referenced by either a published application, an application open to public inspection or an issued patent.
9. A record from thissystem of records may be disclosed, as a routine use, to a Federal, State, or local law enforcement agency, if the USPTO becomes aware of a violation or potential violation of law or regulation.

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PATENT APPLICATION FEE DETERMINATION RECORD

Substitute for Form PTO-875

Application or Docket Number	Filing Date	☐ To be Mailed
13/069,124	03/22/2011	

APPLICATION AS FILED – PART I

	(Column 1)	(Column 2)	SMALL ENTITY ☒		OR	OTHER THAN SMALL ENTITY	
FOR	NUMBER FILED	NUMBER EXTRA	RATE ($)	FEE ($)		RATE ($)	FEE ($)
☐ BASIC FEE (37 CFR 1.16(a), (b), or (c))	N/A	N/A	N/A			N/A	
☐ SEARCH FEE (37 CFR 1.16(k), (i), or (m))	N/A	N/A	N/A			N/A	
☐ EXAMINATION FEE (37 CFR 1.16(o), (p), or (q))	N/A	N/A	N/A			N/A	
TOTAL CLAIMS (37 CFR 1.16(i))	minus 20 =	*	X $ =		OR	X $ =	
INDEPENDENT CLAIMS (37 CFR 1.16(h))	minus 3 =	*	X $ =			X $ =	
☐ APPLICATION SIZE FEE (37 CFR 1.16(s))	If the specification and drawings exceed 100 sheets of paper, the application size fee due is $250 ($125 for small entity) for each additional 50 sheets or fraction thereof. See 35 U.S.C. 41(a)(1)(G) and 37 CFR 1.16(s).						
☐ MULTIPLE DEPENDENT CLAIM PRESENT (37 CFR 1.16(j))							
* If the difference in column 1 is less than zero, enter "0" in column 2.			TOTAL			TOTAL	

APPLICATION AS AMENDED – PART II

AMENDMENT	02/05/2013	(Column 1) CLAIMS REMAINING AFTER AMENDMENT		(Column 2) HIGHEST NUMBER PREVIOUSLY PAID FOR	(Column 3) PRESENT EXTRA	SMALL ENTITY RATE ($)	ADDITIONAL FEE ($)	OR	OTHER THAN SMALL ENTITY RATE ($)	ADDITIONAL FEE ($)
	Total (37 CFR 1.16(i))	* 38	Minus	** 38	= 0	X $31 =	0	OR	X $ =	
	Independent (37 CFR 1.16(h))	* 1	Minus	***3	= 0	X $125 =	0	OR	X $ =	
	☐ Application Size Fee (37 CFR 1.16(s))									
	☐ FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j))							OR		
						TOTAL ADD'L FEE	0	OR	TOTAL ADD'L FEE	

AMENDMENT		(Column 1) CLAIMS REMAINING AFTER AMENDMENT		(Column 2) HIGHEST NUMBER PREVIOUSLY PAID FOR	(Column 3) PRESENT EXTRA	RATE ($)	ADDITIONAL FEE ($)	OR	RATE ($)	ADDITIONAL FEE ($)
	Total (37 CFR 1.16(i))	*	Minus	**	=	X $ =		OR	X $ =	
	Independent (37 CFR 1.16(h))	*	Minus	***	=	X $ =		OR	X $ =	
	☐ Application Size Fee (37 CFR 1.16(s))									
	☐ FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j))							OR		
						TOTAL ADD'L FEE		OR	TOTAL ADD'L FEE	

* If the entry in column 1 is less than the entry in column 2, write "0" in column 3.

** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 20, enter "20".

*** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 3, enter "3".

The "Highest Number Previously Paid For" (Total or Independent) is the highest number found in the appropriate box in column 1.

Legal Instrument Examiner:
/NICOLE C. LAWRENCE/

Application Number	Application/Control No.	Applicant(s)/Patent under Reexamination	
	13/069,124	BONCYK ET AL.	

Document Code - DISQ	Internal Document – DO NOT MAIL

TERMINAL DISCLAIMER	☒ APPROVED	☐ DISAPPROVED
Date Filed : 2/05/13	This patent is subject to a Terminal Disclaimer	

Approved/Disapproved by:

jean proctor

U.S. Patent and Trademark Office

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APPLICATION NUMBER	FILING OR 371(C) DATE	FIRST NAMED APPLICANT	ATTY. DOCKET NO./TITLE
13/069,124	03/22/2011	Wayne C. Boncyk	101044.0001US14

CONFIRMATION NO. 9532

POA ACCEPTANCE LETTER

24392
FISH & ASSOCIATES, PC
ROBERT D. FISH
2603 Main Street
Suite 1000
Irvine, CA 92614-6232

OC000000059189440

Date Mailed: 02/13/2013

NOTICE OF ACCEPTANCE OF POWER OF ATTORNEY

This is in response to the Power of Attorney filed 02/05/2013.

The Power of Attorney in this application is accepted. Correspondence in this application will be mailed to the above address as provided by 37 CFR 1.33.

/ttkim/

Office of Data Management, Application Assistance Unit (571) 272-4000, or (571) 272-4200, or 1-888-786-0101

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NOTICE OF ALLOWANCE AND FEE(S) DUE

24392 7590 02/15/2013

FISH & ASSOCIATES, PC
ROBERT D. FISH
2603 Main Street
Suite 1000
Irvine, CA 92614-6232

EXAMINER
SHERALI, ISHRAT I

ART UNIT	PAPER NUMBER
2667	

DATE MAILED: 02/15/2013

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
13/069,124	03/22/2011	Wayne C. Boncyk	101044.0001US14	9532

TITLE OF INVENTION: IMAGE CAPTURE AND IDENTIFICATION SYSTEM AND PROCESS

APPLN. TYPE	SMALL ENTITY	ISSUE FEE DUE	PUBLICATION FEE DUE	PREV. PAID ISSUE FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	YES	$885	$300	$0	$1185	05/15/2013

THE APPLICATION IDENTIFIED ABOVE HAS BEEN EXAMINED AND IS ALLOWED FOR ISSUANCE AS A PATENT. PROSECUTION ON THE MERITS IS CLOSED. THIS NOTICE OF ALLOWANCE IS NOT A GRANT OF PATENT RIGHTS. THIS APPLICATION IS SUBJECT TO WITHDRAWAL FROM ISSUE AT THE INITIATIVE OF THE OFFICE OR UPON PETITION BY THE APPLICANT. SEE 37 CFR 1.313 AND MPEP 1308.

THE ISSUE FEE AND PUBLICATION FEE (IF REQUIRED) MUST BE PAID WITHIN THREE MONTHS FROM THE MAILING DATE OF THIS NOTICE OR THIS APPLICATION SHALL BE REGARDED AS ABANDONED. THIS STATUTORY PERIOD CANNOT BE EXTENDED. SEE 35 U.S.C. 151. THE ISSUE FEE DUE INDICATED ABOVE DOES NOT REFLECT A CREDIT FOR ANY PREVIOUSLY PAID ISSUE FEE IN THIS APPLICATION. IF AN ISSUE FEE HAS PREVIOUSLY BEEN PAID IN THIS APPLICATION (AS SHOWN ABOVE), THE RETURN OF PART B OF THIS FORM WILL BE CONSIDERED A REQUEST TO REAPPLY THE PREVIOUSLY PAID ISSUE FEE TOWARD THE ISSUE FEE NOW DUE.

HOW TO REPLY TO THIS NOTICE:

I. Review the SMALL ENTITY status shown above.

If the SMALL ENTITY is shown as YES, verify your current SMALL ENTITY status:

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If the SMALL ENTITY is shown as NO:

A. Pay TOTAL FEE(S) DUE shown above, or

B. If applicant claimed SMALL ENTITY status before, or is now claiming SMALL ENTITY status, check box 5a on Part B - Fee(s) Transmittal and pay the PUBLICATION FEE (if required) and 1/2 the ISSUE FEE shown above.

II. PART B - FEE(S) TRANSMITTAL, or its equivalent, must be completed and returned to the United States Patent and Trademark Office (USPTO) with your ISSUE FEE and PUBLICATION FEE (if required). If you are charging the fee(s) to your deposit account, section "4b" of Part B - Fee(s) Transmittal should be completed and an extra copy of the form should be submitted. If an equivalent of Part B is filed, a request to reapply a previously paid issue fee must be clearly made, and delays in processing may occur due to the difficulty in recognizing the paper as an equivalent of Part B.

III. All communications regarding this application must give the application number. Please direct all communications prior to issuance to Mail Stop ISSUE FEE unless advised to the contrary.

IMPORTANT REMINDER: Utility patents issuing on applications filed on or after Dec. 12, 1980 may require payment of maintenance fees. It is patentee's responsibility to ensure timely payment of maintenance fees when due.

PART B - FEE(S) TRANSMITTAL

Complete and send this form, together with applicable fee(s), to: Mail **Mail Stop ISSUE FEE**
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Alexandria, Virginia 22313-1450
or Fax (571)-273-2885

INSTRUCTIONS: This form should be used for transmitting the ISSUE FEE and PUBLICATION FEE (if required). Blocks 1 through 5 should be completed where appropriate. All further correspondence including the Patent, advance orders and notification of maintenance fees will be mailed to the current correspondence address as indicated unless corrected below or directed otherwise in Block 1, by (a) specifying a new correspondence address; and/or (b) indicating a separate "FEE ADDRESS" for maintenance fee notifications.

CURRENT CORRESPONDENCE ADDRESS (Note: Use Block 1 for any change of address)

24392 7590 02/15/2013
FISH & ASSOCIATES, PC
ROBERT D. FISH
2603 Main Street
Suite 1000
Irvine, CA 92614-6232

Note: A certificate of mailing can only be used for domestic mailings of the Fee(s) Transmittal. This certificate cannot be used for any other accompanying papers. Each additional paper, such as an assignment or formal drawing, must have its own certificate of mailing or transmission.

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I hereby certify that this Fee(s) Transmittal is being deposited with the United States Postal Service with sufficient postage for first class mail in an envelope addressed to the Mail Stop ISSUE FEE address above, or being facsimile transmitted to the USPTO (571) 273-2885, on the date indicated below.

(Depositor's name)
(Signature)
(Date)

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
13/069,124	03/22/2011	Wayne C. Boncyk	101044.0001US14	9532

TITLE OF INVENTION: IMAGE CAPTURE AND IDENTIFICATION SYSTEM AND PROCESS

APPLN. TYPE	SMALL ENTITY	ISSUE FEE DUE	PUBLICATION FEE DUE	PREV. PAID ISSUE FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	YES	$885	$300	$0	$1185	05/15/2013

EXAMINER	ART UNIT	CLASS-SUBCLASS
SHERALI, ISHRAT I	2667	382-165000

1. Change of correspondence address or indication of "Fee Address" (37 CFR 1.363).

❑ Change of correspondence address (or Change of Correspondence Address form PTO/SB/122) attached.

❑ "Fee Address" indication (or "Fee Address" Indication form PTO/SB/47; Rev 03-02 or more recent) attached. **Use of a Customer Number is required.**

2. For printing on the patent front page, list

(1) the names of up to 3 registered patent attorneys or agents OR, alternatively,

(2) the name of a single firm (having as a member a registered attorney or agent) and the names of up to 2 registered patent attorneys or agents. If no name is listed, no name will be printed.

1 _____

2 _____

3 _____

3. ASSIGNEE NAME AND RESIDENCE DATA TO BE PRINTED ON THE PATENT (print or type)

PLEASE NOTE: Unless an assignee is identified below, no assignee data will appear on the patent. If an assignee is identified below, the document has been filed for recordation as set forth in 37 CFR 3.11. Completion of this form is NOT a substitute for filing an assignment.

(A) NAME OF ASSIGNEE (B) RESIDENCE: (CITY and STATE OR COUNTRY)

Please check the appropriate assignee category or categories (will not be printed on the patent) : ❑ Individual ❑ Corporation or other private group entity ❑ Government

4a. The following fee(s) are submitted:

❑ Issue Fee

❑ Publication Fee (No small entity discount permitted)

❑ Advance Order - # of Copies _____

4b. Payment of Fee(s): **(Please first reapply any previously paid issue fee shown above)**

❑ A check is enclosed.

❑ Payment by credit card. Form PTO-2038 is attached.

❑ The Director is hereby authorized to charge the required fee(s), any deficiency, or credit any overpayment, to Deposit Account Number _____ (enclose an extra copy of this form).

5. **Change in Entity Status** (from status indicated above)

❑ a. Applicant claims SMALL ENTITY status. See 37 CFR 1.27.

❑ b. Applicant is no longer claiming SMALL ENTITY status. See 37 CFR 1.27(g)(2).

NOTE: The Issue Fee and Publication Fee (if required) will not be accepted from anyone other than the applicant; a registered attorney or agent; or the assignee or other party in interest as shown by the records of the United States Patent and Trademark Office.

Authorized Signature _____ Date _____

Typed or printed name _____ Registration No. _____

This collection of information is required by 37 CFR 1.311. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 12 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, Virginia 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450.

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
13/069,124	03/22/2011	Wayne C. Boncyk	101044.0001US14	9532

24392 7590 02/15/2013

FISH & ASSOCIATES, PC
ROBERT D. FISH
2603 Main Street
Suite 1000
Irvine, CA 92614-6232

EXAMINER	
SHERALI, ISHRAT I	

ART UNIT	PAPER NUMBER
2667	

DATE MAILED: 02/15/2013

Determination of Patent Term Adjustment under 35 U.S.C. 154 (b)
(application filed on or after May 29, 2000)

The Patent Term Adjustment to date is 171 day(s). If the issue fee is paid on the date that is three months after the mailing date of this notice and the patent issues on the Tuesday before the date that is 28 weeks (six and a half months) after the mailing date of this notice, the Patent Term Adjustment will be 171 day(s).

If a Continued Prosecution Application (CPA) was filed in the above-identified application, the filing date that determines Patent Term Adjustment is the filing date of the most recent CPA.

Applicant will be able to obtain more detailed information by accessing the Patent Application Information Retrieval (PAIR) WEB site (http://pair.uspto.gov).

Any questions regarding the Patent Term Extension or Adjustment determination should be directed to the Office of Patent Legal Administration at (571)-272-7702. Questions relating to issue and publication fee payments should be directed to the Customer Service Center of the Office of Patent Publication at 1-(888)-786-0101 or (571)-272-4200.

Privacy Act Statement

The Privacy Act of 1974 (P.L. 93-579) requires that you be given certain information in connection with your submission of the attached form related to a patent application or patent. Accordingly, pursuant to the requirements of the Act, please be advised that: (1) the general authority for the collection of this information is 35 U.S.C. 2(b)(2); (2) furnishing of the information solicited is voluntary; and (3) the principal purpose for which the information is used by the U.S. Patent and Trademark Office is to process and/or examine your submission related to a patent application or patent. If you do not furnish the requested information, the U.S. Patent and Trademark Office may not be able to process and/or examine your submission, which may result in termination of proceedings or abandonment of the application or expiration of the patent.

The information provided by you in this form will be subject to the following routine uses:

1. The information on this form will be treated confidentially to the extent allowed under the Freedom of Information Act (5 U.S.C. 552) and the Privacy Act (5 U.S.C 552a). Records from this system of records may be disclosed to the Department of Justice to determine whether disclosure of these records is required by the Freedom of Information Act.
2. A record from this system of records may be disclosed, as a routine use, in the course of presenting evidence to a court, magistrate, or administrative tribunal, including disclosures to opposing counsel in the course of settlement negotiations.
3. A record in this system of records may be disclosed, as a routine use, to a Member of Congress submitting a request involving an individual, to whom the record pertains, when the individual has requested assistance from the Member with respect to the subject matter of the record.
4. A record in this system of records may be disclosed, as a routine use, to a contractor of the Agency having need for the information in order to perform a contract. Recipients of information shall be required to comply with the requirements of the Privacy Act of 1974, as amended, pursuant to 5 U.S.C. 552a(m).
5. A record related to an International Application filed under the Patent Cooperation Treaty in this system of records may be disclosed, as a routine use, to the International Bureau of the World Intellectual Property Organization, pursuant to the Patent Cooperation Treaty.
6. A record in this system of records may be disclosed, as a routine use, to another federal agency for purposes of National Security review (35 U.S.C. 181) and for review pursuant to the Atomic Energy Act (42 U.S.C. 218(c)).
7. A record from this system of records may be disclosed, as a routine use, to the Administrator, General Services, or his/her designee, during an inspection of records conducted by GSA as part of that agency's responsibility to recommend improvements in records management practices and programs, under authority of 44 U.S.C. 2904 and 2906. Such disclosure shall be made in accordance with the GSA regulations governing inspection of records for this purpose, and any other relevant (i.e., GSA or Commerce) directive. Such disclosure shall not be used to make determinations about individuals.
8. A record from this system of records may be disclosed, as a routine use, to the public after either publication of the application pursuant to 35 U.S.C. 122(b) or issuance of a patent pursuant to 35 U.S.C. 151. Further, a record may be disclosed, subject to the limitations of 37 CFR 1.14, as a routine use, to the public if the record was filed in an application which became abandoned or in which the proceedings were terminated and which application is referenced by either a published application, an application open to public inspection or an issued patent.
9. A record from this system of records may be disclosed, as a routine use, to a Federal, State, or local law enforcement agency, if the USPTO becomes aware of a violation or potential violation of law or regulation.

Notice of Allowability	Application No.	Applicant(s)	
	13/069,124	BONCYK ET AL.	
	Examiner	Art Unit	
	ISHRAT I. SHERALI	2667	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to *2/5/2013*.

2. ☐ An election was made by the applicant in response to a restriction requirement set forth during the interview on _____; the restriction requirement and election have been incorporated into this action.

3. ☒ The allowed claim(s) is/are *1-38*. As a result of the allowed claim(s), you may be eligible to benefit from the **Patent Prosecution Highway** program at a participating intellectual property office for the corresponding application. For more information, please see http://www.uspto.gov/patents/init_events/pph/index.jsp or send an inquiry to PPHfeedback@uspto.gov .

4. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
   a) ☐ All b) ☐ Some* c) ☐ None of the:
      1. ☐ Certified copies of the priority documents have been received.
      2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
      3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

   * Certified copies not received: _____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.
THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

5. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
   ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.

   Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).

6. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

1. ☐ Notice of References Cited (PTO-892)
2. ☐ Information Disclosure Statements (PTO/SB/08), Paper No./Mail Date _____
3. ☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material
4. ☐ Interview Summary (PTO-413), Paper No./Mail Date _____ .
5. ☐ Examiner's Amendment/Comment
6. ☐ Examiner's Statement of Reasons for Allowance
7. ☐ Other _____.

/ISHRAT I SHERALI/
Primary Examiner, Art Unit 2667

Search Notes	Application/Control No.	Applicant(s)/Patent Under Reexamination
	13069124	BONCYK ET AL.
	Examiner	Art Unit
	ISHRAT I SHERALI	2667

CPC- SEARCHED		
Symbol	Date	Examiner

CPC COMBINATION SETS - SEARCHED		
Symbol	Date	Examiner

US CLASSIFICATION SEARCHED			
Class	Subclass	Date	Examiner
382	181, 162, 165, 100, 305. 224, 115-118	2/10/13	IS
705	26.1-27.2, 23	2/10/13	IS
348	239, 211.2-211.6, 207.1, 460, 552	2/10/13	IS
713	186, 168	2/10/13	IS
455	414.2-414.3, 412.1, 411	2/10/13	IS
709	201-203, 217-219, 250	2/10/13	IS

SEARCH NOTES		
Search Notes	Date	Examiner
SEARCH EAST/IEEE/INVENTOR/ASSIGNEE	2/10/13	IS

INTERFERENCE SEARCH			
US Class/ CPC Symbol	US Subclass / CPC Group	Date	Examiner
SEARCH	EAST INTERFERENCE	2/10/13	IS

Index of Claims	Application/Control No.	Applicant(s)/Patent Under Reexamination
	13069124	BONCYK ET AL.
	Examiner	**Art Unit**
	ISHRAT I SHERALI	2667

✓	Rejected	-	Cancelled	N	Non-Elected	A	Appeal
=	Allowed	÷	Restricted	I	Interference	O	Objected

☐ Claims renumbered in the same order as presented by applicant ☐ CPA ☒ T.D. ☐ R.1.47

CLAIM		DATE								
Final	Original	11/05/2012	02/10/2013							
1	1	✓	=							
2	2	✓	=							
3	3	✓	=							
4	4	✓	=							
5	5	✓	=							
6	6	✓	=							
7	7	✓	=							
8	8	✓	=							
9	9	✓	=							
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26	26	✓	=							
27	27	✓	=							
28	28	✓	=							
29	29	✓	=							
30	30	✓	=							
31	31	✓	=							
32	32	✓	=							
33	33	✓	=							
34	34	✓	=							
35	35	✓	=							
36	36	✓	=							

Index of Claims	Application/Control No.	Applicant(s)/Patent Under Reexamination
	13069124	BONCYK ET AL.
	Examiner	Art Unit
	ISHRAT I SHERALI	2667

✓	Rejected	-	Cancelled	N	Non-Elected	A	Appeal
=	Allowed	÷	Restricted	I	Interference	O	Objected

☐ Claims renumbered in the same order as presented by applicant ☐ CPA ☒ T.D. ☐ R.1.47

CLAIM		DATE								
Final	Original	11/05/2012	02/10/2013							
37	37	✓	=							
38	38	✓	=							

Issue Classification	Application/Control No.	Applicant(s)/Patent Under Reexamination
	13069124	BONCYK ET AL.
	Examiner	**Art Unit**
	ISHRAT I SHERALI	2667

CPC		
Symbol	**Type**	**Version**

CPC Combination Sets				
Symbol	**Type**	**Set**	**Ranking**	**Version**

US ORIGINAL CLASSIFICATION		INTERNATIONAL CLASSIFICATION									
CLASS	**SUBCLASS**	**CLAIMED**					**NON-CLAIMED**				
382	165	G	0	6	K	9 / 00 (2006.01.01)					
CROSS REFERENCE(S)											
CLASS	**SUBCLASS (ONE SUBCLASS PER BLOCK)**										

NONE		**Total Claims Allowed:**	
(Assistant Examiner)	(Date)	38	
/ISHRAT I SHERALI/ Primary Examiner.Art Unit 2667	2/10/13	O.G. Print Claim(s)	O.G. Print Figure
(Primary Examiner)	(Date)	1	1

Issue Classification	Application/Control No.	Applicant(s)/Patent Under Reexamination
	13069124	BONCYK ET AL.
	Examiner	**Art Unit**
	ISHRAT I SHERALI	2667

NONE (Assistant Examiner)	(Date)	**Total Claims Allowed:** 38	
/ISHRAT I SHERALI/ Primary Examiner.Art Unit 2667 (Primary Examiner)	2/10/13 (Date)	O.G. Print Claim(s) 1	O.G. Print Figure 1

U.S. Patent and Trademark Office

Part of Paper No. 20130210

Issue Classification	Application/Control No.	Applicant(s)/Patent Under Reexamination
	13069124	BONCYK ET AL.
	Examiner	**Art Unit**
	ISHRAT I SHERALI	2667

☐ Claims renumbered in the same order as presented by applicant ☐ CPA ☒ T.D. ☐ R.1.47

Final	Original	Final	Original	Final	Original	Final	Original	Final	Original	Final	Original	Final	Original	Final	Original
1	1	17	17	33	33										
2	2	18	18	34	34										
3	3	19	19	35	35										
4	4	20	20	36	36										
5	5	21	21	37	37										
6	6	22	22	38	38										
7	7	23	23												
8	8	24	24												
9	9	25	25												
10	10	26	26												
11	11	27	27												
12	12	28	28												
13	13	29	29												
14	14	30	30												
15	15	31	31												
16	16	32	32												

NONE (Assistant Examiner)	(Date)	**Total Claims Allowed:** 38	
/ISHRAT I SHERALI/ Primary Examiner.Art Unit 2667 (Primary Examiner)	2/10/13 (Date)	O.G. Print Claim(s) 1	O.G. Print Figure 1

PART B - FEE(S) TRANSMITTAL

Complete and send this form, together with applicable fee(s), to: Mail **Mail Stop ISSUE FEE**
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450
or Fax (571)-273-2885

INSTRUCTIONS: This form should be used for transmitting the ISSUE FEE and PUBLICATION FEE (if required). Blocks 1 through 5 should be completed where appropriate. All further correspondence including the Patent, advance orders and notification of maintenance fees will be mailed to the current correspondence address as indicated unless corrected below or directed otherwise in Block 1, by (a) specifying a new correspondence address; and/or (b) indicating a separate "FEE ADDRESS" for maintenance fee notifications.

CURRENT CORRESPONDENCE ADDRESS (Note: Use Block 1 for any change of address)

24392 7590 02/15/2013
FISH & ASSOCIATES, PC
ROBERT D. FISH
2603 Main Street
Suite 1000
Irvine, CA 92614-6232

Note: A certificate of mailing can only be used for domestic mailings of the Fee(s) Transmittal. This certificate cannot be used for any other accompanying papers. Each additional paper, such as an assignment or formal drawing, must have its own certificate of mailing or transmission.

Certificate of Mailing or Transmission
I hereby certify that this Fee(s) Transmittal is being deposited with the United States Postal Service with sufficient postage for first class mail in an envelope addressed to the Mail Stop ISSUE FEE address above, or being facsimile transmitted to the USPTO (571) 273-2885, on the date indicated below.

Marutzzella Castro	(Depositor's name)
/Marutzzella Castro/	(Signature)
May 14, 2013	(Date)

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
13/069,124	03/22/2011	Wayne C. Boncyk	101044.0001US14	9532

TITLE OF INVENTION: IMAGE CAPTURE AND IDENTIFICATION SYSTEM AND PROCESS

APPLN. TYPE	SMALL ENTITY	ISSUE FEE DUE	PUBLICATION FEE DUE	PREV. PAID ISSUE FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	YES	$885	$300	$0	$1185	05/15/2013

EXAMINER	ART UNIT	CLASS-SUBCLASS
SHERALI, ISHRAT I	2667	382-165000

1. Change of correspondence address or indication of "Fee Address" (37 CFR 1.363).
- ☐ Change of correspondence address (or Change of Correspondence Address form PTO/SB/122) attached.
- ☐ "Fee Address" indication (or "Fee Address" Indication form PTO/SB/47; Rev 03-02 or more recent) attached. **Use of a Customer Number is required.**

2. For printing on the patent front page, list
(1) the names of up to 3 registered patent attorneys or agents OR, alternatively,
(2) the name of a single firm (having as a member a registered attorney or agent) and the names of up to 2 registered patent attorneys or agents. If no name is listed, no name will be printed.

1 Fish & Associates, PC
2
3

3. ASSIGNEE NAME AND RESIDENCE DATA TO BE PRINTED ON THE PATENT (print or type)

PLEASE NOTE: Unless an assignee is identified below, no assignee data will appear on the patent. If an assignee is identified below, the document has been filed for recordation as set forth in 37 CFR 3.11. Completion of this form is NOT a substitute for filing an assignment.

(A) NAME OF ASSIGNEE: Nant Holdings IP, LLC

(B) RESIDENCE: (CITY and STATE OR COUNTRY): Culver City, CA

Please check the appropriate assignee category or categories (will not be printed on the patent) : ☐ Individual ☒ Corporation or other private group entity ☐ Government

4a. The following fee(s) are submitted:
- ☒ Issue Fee
- ☒ Publication Fee (No small entity discount permitted)
- ☐ Advance Order - # of Copies _____

4b. Payment of Fee(s): **(Please first reapply any previously paid issue fee shown above)**
- ☐ A check is enclosed.
- ☐ Payment by credit card. Form PTO-2038 is attached.
- ☒ The Director is hereby authorized to charge the required fee(s), any deficiency, or credit any overpayment, to Deposit Account Number 500341 (enclose an extra copy of this form).

5. **Change in Entity Status** (from status indicated above)
- ☐ a. Applicant claims SMALL ENTITY status. See 37 CFR 1.27.
- ☒ b. Applicant is no longer claiming SMALL ENTITY status. See 37 CFR 1.27(g)(2).

NOTE: The Issue Fee and Publication Fee (if required) will not be accepted from anyone other than the applicant; a registered attorney or agent; or the assignee or other party in interest as shown by the records of the United States Patent and Trademark Office.

Authorized Signature /Nicholas J. Witchey/ Date May 14, 2013

Typed or printed name Nicholas J. Witchey Registration No. 63481

This collection of information is required by 37 CFR 1.311. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 12 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, Virginia 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450.

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Electronic Patent Application Fee Transmittal

Application Number:	13069124
Filing Date:	22-Mar-2011
Title of Invention:	IMAGE CAPTURE AND IDENTIFICATION SYSTEM AND PROCESS
First Named Inventor/Applicant Name:	Wayne C. Boncyk
Filer:	Martin Fessenmaier/Marutzzella Castro
Attorney Docket Number:	101044.0001US14

Filed as Large Entity

Utility under 35 USC 111(a) Filing Fees

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Basic Filing:				
Pages:				
Claims:				
Miscellaneous-Filing:				
Petition:				
Patent-Appeals-and-Interference:				
Post-Allowance-and-Post-Issuance:				
Utility Appl Issue Fee	1501	1	1780	1780
Publ. Fee- Early, Voluntary, or Normal	1504	1	300	300

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Extension-of-Time:				
Miscellaneous:				
			Total in USD ($)	**2080**

Electronic Acknowledgement Receipt	
EFS ID:	15777935
Application Number:	13069124
International Application Number:	
Confirmation Number:	9532
Title of Invention:	IMAGE CAPTURE AND IDENTIFICATION SYSTEM AND PROCESS
First Named Inventor/Applicant Name:	Wayne C. Boncyk
Customer Number:	24392
Filer:	Martin Fessenmaier/Marutzzella Castro
Filer Authorized By:	Martin Fessenmaier
Attorney Docket Number:	101044.0001US14
Receipt Date:	14-MAY-2013
Filing Date:	22-MAR-2011
Time Stamp:	20:00:46
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	yes
Payment Type	Deposit Account
Payment was successfully received in RAM	$2080
RAM confirmation Number	6611
Deposit Account	500341
Authorized User	
The Director of the USPTO is hereby authorized to charge indicated fees and credit any overpayment as follows: Charge any Additional Fees required under 37 C.F.R. Section 1.16 (National application filing, search, and examination fees) Charge any Additional Fees required under 37 C.F.R. Section 1.17 (Patent application and reexamination processing fees)	

Charge any Additional Fees required under 37 C.F.R. Section 1.19 (Document supply fees) Charge any Additional Fees required under 37 C.F.R. Section 1.20 (Post Issuance fees) Charge any Additional Fees required under 37 C.F.R. Section 1.21 (Miscellaneous fees and charges)

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Issue Fee Payment (PTO-85B)	PTOL-85_IssueFeeTransmittal.pdf	120295 6c8e79c7a0179463b07ae6651051eb134aa86fcd	no	1
Warnings:					
Information:					
2	Fee Worksheet (SB06)	fee-info.pdf	32242 542a83f4d1178b8530cc0bb45ad7c6e6f827a4c7	no	2
Warnings:					
Information:					
		Total Files Size (in bytes):	152537		

This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.

New Applications Under 35 U.S.C. 111
If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

National Stage of an International Application under 35 U.S.C. 371
If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office
If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (**Not for submission under 37 CFR 1.99)**		
	Application Number	13069124
	Filing Date	2011-03-22
	First Named Inventor	Boncyk, Wayne C.
	Art Unit	
	Examiner Name	
	Attorney Docket Number	101044.0001US14

U.S.PATENTS Remove

Examiner Initial*	Cite No	Patent Number	Kind Code[1]	Issue Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
	1	7916138	B2	2011-03-29	John et al.	
	2	7889193	B2	2011-02-15	Platonov et al.	
	3	7768534	B2	2010-08-03	Pentenrieder et al.	
	4	7765126	B2	2010-07-27	Hudetz et al.	
	5	7696905	B2	2010-04-13	Ellenby et al.	
	6	7641342	B2	2010-01-05	Eberl et al.	
Change(s) applied to document, /C.L.V./ 3/15/2013	7	7430588	B2	~~2008-07-13~~ 09/2008	Hunter	
	8	7383209	B2	~~2005-11-03~~ 06/2008	Hudetz et al.	

EFS Web 2.1.17

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /I.S./

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APPLICATION NO.	ISSUE DATE	PATENT NO.	ATTORNEY DOCKET NO.	CONFIRMATION NO.
13/069,124	06/11/2013	8463030	101044.0001US14	9532

24392 7590 05/22/2013

FISH & ASSOCIATES, PC
ROBERT D. FISH
2603 Main Street
Suite 1000
Irvine, CA 92614-6232

ISSUE NOTIFICATION

The projected patent number and issue date are specified above.

Determination of Patent Term Adjustment under 35 U.S.C. 154 (b)
(application filed on or after May 29, 2000)

The Patent Term Adjustment is 171 day(s). Any patent to issue from the above-identified application will include an indication of the adjustment on the front page.

If a Continued Prosecution Application (CPA) was filed in the above-identified application, the filing date that determines Patent Term Adjustment is the filing date of the most recent CPA.

Applicant will be able to obtain more detailed information by accessing the Patent Application Information Retrieval (PAIR) WEB site (http://pair.uspto.gov).

Any questions regarding the Patent Term Extension or Adjustment determination should be directed to the Office of Patent Legal Administration at (571)-272-7702. Questions relating to issue and publication fee payments should be directed to the Application Assistance Unit (AAU) of the Office of Data Management (ODM) at (571)-272-4200.

APPLICANT(s) (Please see PAIR WEB site http://pair.uspto.gov for additional applicants):

Wayne C. Boncyk, Evergreen, CA;
Ronald H. Cohen, Pasadena, CA;

PTO/SB/44 (09-07)
Approved for use through 08/31/2013. OMB 0651-0033
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

(Also Form PTO-1050)

UNITED STATES PATENT AND TRADEMARK OFFICE
CERTIFICATE OF CORRECTION

PATENT NO. : 8,463,030

APPLICATION NO.: 13/069,124

ISSUE DATE : June 11, 2013

INVENTOR(S) : Wayne C. Boncyk, Ronald H. Cohen

It is certified that an error appears or errors appear in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

Please replace Related U.S. Application Data (60):

(60) Division of application No. 13/037,317, filed on Feb. 28, 2011, now Pat. No. 8,224,078, which is a division of application No. 12/333,630, filed on Dec. 12, 2008, now Pat. No. 7,899,243, which is a division of application No. 10/492,243, filed as application No. PCT/US02/35407 on Nov. 5, 2002, now Pat. No. 7,477,780, which is a continuation of application No. 09/992,942, filed on Nov. 5, 2001, now Pat. No. 7,016,532.

with:

(60) Division of application No. 13/037,317, filed on Feb. 28, 2011, now Pat. No. 8,224,078, which is a division of application No. 12/333,630, filed on Dec. 12, 2008, now Pat. No. 7,899,243, which is a division of application No. 10/492,243, filed as application No. PCT/US02/35407 on Nov. 5, 2002, now Pat. No. 7,477,780, which is a continuation-in-part of application No. 09/992,942, filed on Nov. 5, 2001, now Pat. No. 7,016,532.

MAILING ADDRESS OF SENDER (Please do not use customer number below):

Fish & Tsang LLP
2603 Main Street, Suite 1000
Irvine, CA 92614

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The **Privacy Act of 1974 (P.L. 93-579)** requires that you be given certain information in connection with your submission of the attached form related to a patent application or patent. Accordingly, pursuant to the requirements of the Act, please be advised that: (1) the general authority for the collection of this information is 35 U.S.C. 2(b)(2); (2) furnishing of the information solicited is voluntary; and (3) the principal purpose for which the information is used by the U.S. Patent and Trademark Office is to process and/or examine your submission related to a patent application or patent. If you do not furnish the requested information, the U.S. Patent and Trademark Office may not be able to process and/or examine your submission, which may result in termination of proceedings or abandonment of the application or expiration of the patent.

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2. A record from this system of records may be disclosed, as a routine use, in the course of presenting evidence to a court, magistrate, or administrative tribunal, including disclosures to opposing counsel in the course of settlement negotiations.
3. A record in this system of records may be disclosed, as a routine use, to a Member of Congress submitting a request involving an individual, to whom the record pertains, when the individual has requested assistance from the Member with respect to the subject matter of the record.
4. A record in this system of records may be disclosed, as a routine use, to a contractor of the Agency having need for the information in order to perform a contract. Recipients of information shall be required to comply with the requirements of the Privacy Act of 1974, as amended, pursuant to 5 U.S.C. 552a(m).
5. A record related to an International Application filed under the Patent Cooperation Treaty in this system of records may be disclosed, as a routine use, to the International Bureau of the World Intellectual Property Organization, pursuant to the Patent Cooperation Treaty.
6. A record in this system of records may be disclosed, as a routine use, to another federal agency for purposes of National Security review (35 U.S.C. 181) and for review pursuant to the Atomic Energy Act (42 U.S.C. 218(c)).
7. A record from this system of records may be disclosed, as a routine use, to the Administrator, General Services, or his/her designee, during an inspection of records conducted by GSA as part of that agency's responsibility to recommend improvements in records management practices and programs, under authority of 44 U.S.C. 2904 and 2906. Such disclosure shall be made in accordance with the GSA regulations governing inspection of records for this purpose, and any other relevant (*i.e.*, GSA or Commerce) directive. Such disclosure shall not be used to make determinations about individuals.
8. A record from this system of records may be disclosed, as a routine use, to the public after either publication of the application pursuant to 35 U.S.C. 122(b) or issuance of a patent pursuant to 35 U.S.C. 151. Further, a record may be disclosed, subject to the limitations of 37 CFR 1.14, as a routine use, to the public if the record was filed in an application which became abandoned or in which the proceedings were terminated and which application is referenced by either a published application, an application open to public inspection or an issued patent.
9. A record from this system of records may be disclosed, as a routine use, to a Federal, State, or local law enforcement agency, if the USPTO becomes aware of a violation or potential violation of law or regulation.

PTO/SB/44 (09-07)
Approved for use through 08/31/2013. OMB 0651-0033
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

(Also Form PTO-1050)

UNITED STATES PATENT AND TRADEMARK OFFICE
CERTIFICATE OF CORRECTION

PATENT NO. : 8,463,030

APPLICATION NO.: 13/069,124

ISSUE DATE : June 11, 2013

INVENTOR(S) : Wayne C. Boncyk, Ronald H. Cohen

It is certified that an error appears or errors appear in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

Please also replace lines 4-8 on page 1:

This application is a divisional of Ser. No. 13/037,317 filed Feb. 28, 2011 which is a divisional of Ser. No. 12/333,630 filed Dec. 12, 2008 which is a divisional of Ser. No. 10/492, 243 filed Apr. 9, 2004 which is a National Phase of PCT/US02/35407 filed Nov. 5, 2002.

with:

This application is a divisional of Ser. No. 13/037,317 filed Feb. 28, 2011 which is a divisional of 12/333,630 filed Dec. 12, 2008 and issued Mar. 1, 2011 as US7899243, which is a divisional of 10/492,243 filed May 20, 2004 and issued Jan. 13, 2009 as US7477780, which is a National Phase of PCT/US02/35407 filed Nov. 5, 2002, which is an International Patent application and a continuation-in-part of 09/992942 filed November 5, 2001 and issued March 21, 2006 as US7016532, which claims priority to provisional application number 60/317521 filed September 5, 2001 and provisional application number 60/246295 filed November 6, 2000.

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Fish & Tsang LLP
2603 Main Street, Suite 1000
Irvine, CA 92614

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The **Privacy Act of 1974 (P.L. 93-579)** requires that you be given certain information in connection with your submission of the attached form related to a patent application or patent. Accordingly, pursuant to the requirements of the Act, please be advised that: (1) the general authority for the collection of this information is 35 U.S.C. 2(b)(2); (2) furnishing of the information solicited is voluntary; and (3) the principal purpose for which the information is used by the U.S. Patent and Trademark Office is to process and/or examine your submission related to a patent application or patent. If you do not furnish the requested information, the U.S. Patent and Trademark Office may not be able to process and/or examine your submission, which may result in termination of proceedings or abandonment of the application or expiration of the patent.

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1. The information on this form will be treated confidentially to the extent allowed under the Freedom of Information Act (5 U.S.C. 552) and the Privacy Act (5 U.S.C 552a). Records from this system of records may be disclosed to the Department of Justice to determine whether disclosure of these records is required by the Freedom of Information Act.
2. A record from this system of records may be disclosed, as a routine use, in the course of presenting evidence to a court, magistrate, or administrative tribunal, including disclosures to opposing counsel in the course of settlement negotiations.
3. A record in this system of records may be disclosed, as a routine use, to a Member of Congress submitting a request involving an individual, to whom the record pertains, when the individual has requested assistance from the Member with respect to the subject matter of the record.
4. A record in this system of records may be disclosed, as a routine use, to a contractor of the Agency having need for the information in order to perform a contract. Recipients of information shall be required to comply with the requirements of the Privacy Act of 1974, as amended, pursuant to 5 U.S.C. 552a(m).
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6. A record in this system of records may be disclosed, as a routine use, to another federal agency for purposes of National Security review (35 U.S.C. 181) and for review pursuant to the Atomic Energy Act (42 U.S.C. 218(c)).
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9. A record from this system of records may be disclosed, as a routine use, to a Federal, State, or local law enforcement agency, if the USPTO becomes aware of a violation or potential violation of law or regulation.

Electronic Patent Application Fee Transmittal

Application Number:	13069124
Filing Date:	22-Mar-2011
Title of Invention:	IMAGE CAPTURE AND IDENTIFICATION SYSTEM AND PROCESS
First Named Inventor/Applicant Name:	Wayne C. Boncyk
Filer:	Rosie H. Kim/Laryssa Weiland
Attorney Docket Number:	101044.0001US14

Filed as Large Entity

Filing Fees for Utility under 35 USC 111(a)

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Basic Filing:				
Pages:				
Claims:				
Miscellaneous-Filing:				
Petition:				
Patent-Appeals-and-Interference:				
Post-Allowance-and-Post-Issuance:				
Certificate of Correction	1811	1	100	100

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Extension-of-Time:				
Miscellaneous:				
		Total in USD ($)		**100**

Electronic Acknowledgement Receipt	
EFS ID:	21799313
Application Number:	13069124
International Application Number:	
Confirmation Number:	9532
Title of Invention:	IMAGE CAPTURE AND IDENTIFICATION SYSTEM AND PROCESS
First Named Inventor/Applicant Name:	Wayne C. Boncyk
Customer Number:	24392
Filer:	Rosie H. Kim/Laryssa Weiland
Filer Authorized By:	Rosie H. Kim
Attorney Docket Number:	101044.0001US14
Receipt Date:	17-MAR-2015
Filing Date:	22-MAR-2011
Time Stamp:	19:11:53
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	yes
Payment Type	Deposit Account
Payment was successfully received in RAM	$100
RAM confirmation Number	5365
Deposit Account	500341
Authorized User	
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File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Request for Certificate of Correction	Certificate_Correction.pdf	165760 eba00b73bee28424554988a0bef12fe588ad7162	no	2
Warnings:					
Information:					
2	Request for Certificate of Correction	Certificate_Correction_2.pdf	165974 82a3259d9f934054f96f3b1939d2d33f8639e23e	no	2
Warnings:					
Information:					
3	Fee Worksheet (SB06)	fee-info.pdf	30424 b52dc6dcffe5ddb14a53042dbce2de256944d273	no	2
Warnings:					
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		Total Files Size (in bytes):	362158		

This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.

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If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

National Stage of an International Application under 35 U.S.C. 371
If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office
If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

UNITED STATES PATENT AND TRADEMARK OFFICE

CERTIFICATE OF CORRECTION

PATENT NO. : 8,463,030 B2
APPLICATION NO. : 13/069124
DATED : June 11, 2013
INVENTOR(S) : Wayne C. Boncyk and Ronald H. Cohen

It is certified that error appears in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

Title Page

Please replace Related U.S. Application Data item (60):

(60) Division of application No. 13/037,317, filed on Feb. 28, 2011, now Pat. No. 8,224,078, which is a division of application No. 12/333,630, filed on Dec. 12, 2008, now Pat. No. 7,899,243, which is a division of application No. 10/492,243, filed as application No. PCT/US02/35407 on Nov. 5, 2002, now Pat. No. 7,477,780, which is a continuation of application No. 09/992,942, filed on Nov. 5, 2001, now Pat. No. 7,016,532.

with:

(60) Division of application No. 13/037,317, filed on Feb. 28, 2011, now Pat. No. 8,224,078, which is a division of application No. 12/333,630, filed on Dec. 12, 2008, now Pat. No. 7,899,243, which is a division of application No. 10/492,243, filed as application No. PCT/US02/35407 on Nov. 5, 2002, now Pat. No. 7,477,780, which is a continuation-in-part of application No. 09/992,942, filed on Nov. 5, 2001, now Pat. No. 7,016,532.

Signed and Sealed this
Sixteenth Day of June, 2015

Michelle K. Lee

Michelle K. Lee
Director of the United States Patent and Trademark Office