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(54) LOCATING AND ANALYZING PERFORATOR FLAPS FOR PLASTIC AND RECONSTRUCTIVE SURGERY

(57) A method and an apparatus for preoperative identification of a perforator vessel for plastic and/or reconstructive surgery using ICG fluorescence angiography imaging are disclosed. Time-resolved image processing is used to highlight perforator locations and to enable visual discrimination among candidate perforators by various computed metrics. Based on these metrics, the surgeon is able to interactively locate and select perforator vessels suitable for plastic and reconstructive surgery

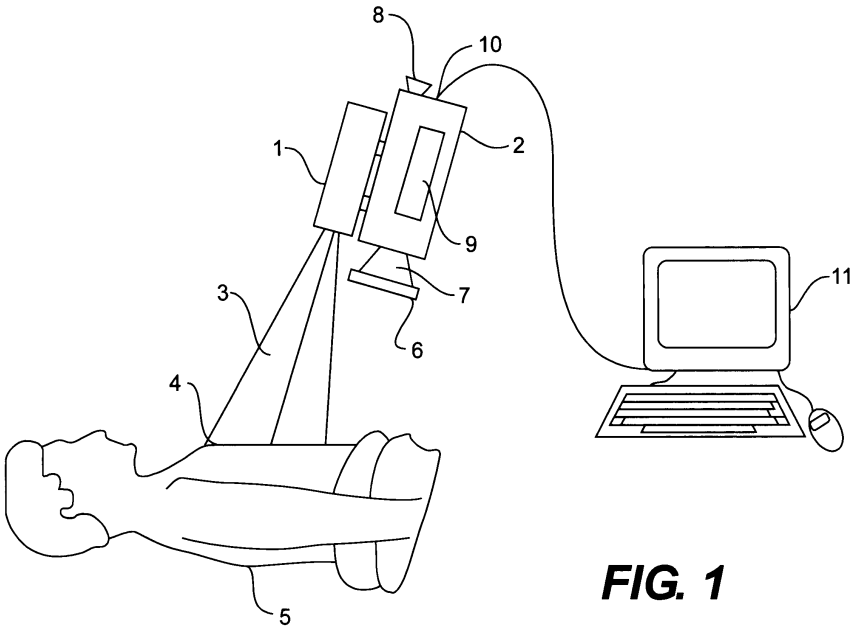


FIG. 1

EP 3 056 149 A2

Description

[0001] Plastic and reconstructive surgery often entails the localization and clinical evaluation of a flap of skin and subcutaneous tissue which is supplied by isolated perforator vessels and that is potentially suitable for grafting in another part of the body. Perforators pass from their source vessel to the skin surface, either through or between deep muscular tissues. Well-vascularised flaps are good candidates for grafts.

[0002] For example, abdominal donor-site flaps have become the standard for autologous breast reconstruction since the early 1980s. Within the abdomen, free fat options range from complete transverse rectus abdominis musculocutaneous (TRAM) flaps to isolated perforator flaps, such as the deep inferior epigastric artery (DIEA) perforator flap. Perforator flaps have allowed the transfer of the patient's own skin and fat in a reliable manner also in other areas of tissue reconstruction, with minimal donor-site morbidity. Flaps that relied on a random pattern blood supply were soon supplanted by pedicled, axial patterned flaps that could reliably transfer great amounts of tissue. The advent of free tissue transfer allowed an even greater range of possibilities to appropriately match donor and recipient sites. The increased use of perforator flaps has escalated the need for a pre-operative familiarity of an individual's particular anatomical feature of the DIEA and its perforating branches, particularly given the significant variation in that anatomy of the vascular supply to the abdominal wall.

[0003] Localization and evaluation of perforators is a painstaking and time-consuming process. Pre-operative computed tomography angiographic (CTA) imaging is often performed to do the localization. Such an approach entails considerable expense and has the additional complication that the surgeon must mentally correlate the images from the previously acquired 3D modality with the current 2D view of the patient now lying on the operating table. The search for a more favorable imaging modality is thus continuing, with recent interest in the use of indocyanine green (ICG) fluorescence imaging, wherein blood circulation is assessed through the skin on the basis of a fluorescence signal. Fluorescence in ICG with an emission peak around 830 nm occurs as a result of excitation by radiation in the near-infrared spectral range. Excitation light with a wavelength around 800 nm can be produced, for example, by a diode laser, light emitting diodes (LED), or other conventional illumination sources, such as arc lamps, halogen lamps with a suitable bandpass filter. The skin is transparent to this wavelength.

[0004] ICG strongly binds to blood proteins and has previously been used for cardiac output measurement, hepatic function evaluation, and ophthalmic angiography, with few adverse reactions. Evaluation of ICG fluorescence signals can be used to locate perforators. Since the skin surface near a perforator generally accumulates more blood and at a faster rate than the surrounding tissue, once ICG is injected, perforators tend to fluoresce brighter and faster than the surrounding tissue. This rapid, high-intensity fluorescence enables visual localization of the perforator. Often, however, the surgeon is interested not merely in localization but also in evaluation and comparison to support good clinical decision making. The surgeon needs to decide which of several perforators the best graft candidates are. Here, simple visual observation while fluorescence rapidly accumulates and dissipates does not suffice. For example, the tendency of residual ICG from successive injections to accumulate in tissue and to gradually raise the background brightness with each injection further confounds easy visual discrimination of the best candidate perforators. In addition, ICG sometimes moves exceedingly slowly over several minutes making such on-the-fly analysis very challenging and subjective. A surgeon will make an assessment by raising the following questions:

How much ICG-bound blood is in the tissue?
How long does it stay in the tissue?
How quickly does it move through the tissue?

[0005] After the bolus is injected, in which order do anatomical areas light up?

[0006] These questions are difficult to answer on a subjective basis. Accordingly, there is a need for more advanced image processing and display methods to apply objective standards to localize and evaluate perforators.

SUMMARY OF THE INVENTION

[0007] According to one aspect of the invention, a method for preoperative identification of a perforator vessel for plastic and/or reconstructive surgery using ICG fluorescence angiography imaging is disclosed, which includes time-resolved image processing to highlight perforator locations and to enable visual discrimination among candidate perforators by various computed metrics. The surgeon is able to select and compare the results of algorithms that analyze the time series and output the metrics according to at least one of the following processing acts:

Determine time-integrated fluorescence on a pixel-by-pixel basis.

[0008] Compute an average fluorescence by dividing the time-integrated fluorescence by the elapsed time.

[0009] Determine a rate of increase/wash-out in the fluorescence.

[0010] Determine the elapsed time to achieve peak fluorescence.

[0011] The various image processing steps process the image pixels independently and compute a unique numerical metric for each pixel in the input sequence observed across the entire time of the acquisition or a selected temporal sub-range. Each image output is thus

a numerical array having the same dimensions, i.e. number and arrangement of pixels, as a frame in the input image sequence. Thus, the processed image can be displayed, for example, as a three-dimensional representation, for example a contour map, of the computed pixel values across the imaged area, or as a color-coded two-dimensional image or a relief map. Such image representations facilitate rapid comprehension of image features and comparison between regions on the images, in this case the location of the perforators under the skin.

[0012] These and other features and advantages of the present invention will become more readily appreciated from the detailed description of the invention that follows.

BRIEF DESCRIPTION OF THE DRAWINGS

[0013] The following Figures depict certain illustrative embodiments of the invention in which like reference numerals refer to like elements. These depicted embodiments are to be understood as illustrative of the invention and not as limiting in any way.

FIG. 1 shows schematically a camera system for observing ICG fluorescence;
FIG. 2 shows an ICG fluorescence image of an area of skin, with the pixel values integrated over time;
FIG. 3 shows an ICG fluorescence image of an area of skin integrated over time, with the pixel values inversely weighted by elapsed time;
FIG. 4 shows an ICG fluorescence image of an area of skin, with the pixel values determined by the rate of increase of fluorescence;
FIG. 5 shows an ICG fluorescence image of an area of skin, with the pixel values determined by elapsed time to maximum fluorescence; and
FIG. 6 shows an ICG fluorescence image of an area of skin, with the pixel values determined by peak fluorescence;
FIG. 7 shows an overlay of the fluorescence image processed with a variable contrast transfer function;
FIG. 8 shows an overlay of the fluorescence image processed with another variable contrast transfer function;
FIG. 9 shows an overlay of the fluorescence image processed with yet another variable contrast transfer function;
FIG. 10A is a fluorescence image of the perfused region; and
FIG. 10B is a black/white rendition of a colored overlay corresponding to the fluorescence image of FIG. 10A, with markers indicating a normalized intensity.

DETAILED DESCRIPTION

[0014] The invention is directed to preoperative determination of the location of perforator vessels in perforator flaps by a non-invasive method, before any incision is made.

[0015] FIG. 1 shows schematically a device for a non-invasive, through the skin determination of tissue perfusion in operative, in particular preoperative, applications by ICG fluorescence imaging. An infrared light source, for example, one or more diode lasers or LEDs, with a peak emission of about 780-800 nm for exciting fluorescence in ICG is located inside housing 1. The fluorescence signal is detected by a CCD camera 2 having adequate near-IR sensitivity; such cameras are commercially available from several vendors (Hitachi, Hamamatsu, etc.). The CCD camera 2 may have a viewfinder 8, but the image may also be viewed during the operation on an external monitor which may be part of an electronic image processing and evaluation system 11.

[0016] A light beam 3, which may be a divergent or a scanned beam, emerges from the housing 1 to illuminate an area of interest 4, i.e. the area where a flap with suitable perforator vessels is expected to be located. The area of interest may be about 10 cm x 10 cm, but may vary based on surgical requirements and the available illumination intensity and camera sensitivity.

[0017] A filter 6 is typically placed in front of the camera lens 7 to block excitation light from reaching the camera sensor, while allowing fluorescence light to pass through. The filter 6 may be an NIR long-wave pass filter (cut filter), which is only transparent to wavelengths greater than about 815 nm, or preferably a bandpass filter transmitting at peak wavelengths of between 830 and 845 nm and having a full width at half maximum (FWHM) transmission window of between about 10 nm and 25 nm, i.e. outside the excitation wavelength band. The camera 2 may also be designed to acquire a color image of the area of interest to allow real-time correlation between the fluorescence image and the color image.

[0018] In the context of the present invention, the device illustrated in FIG. 1 is used to identify/ locate perforator vessels prior to surgery- this will assist the surgeon in selecting the best flap or flap zone for use during the reconstruction.

[0019] In other post-operative applications, the device can be used to:

Validate anastomotic patency and arterial and venous flow - this can potentially improve outcomes to eliminate flap failure which can be a result of poor arterial flow and inadequate perfusion as well as poor venous return resulting in congestion.

[0020] Visualize and confirm complete tissue perfusion, as micro-vascular perfusion to the entire flap and native tissue is critical to flap survival.

[0021] With the invention, perforator locations are visualized by image processing and presentation techniques to enable easy and objective visual discrimination among candidate perforators. ICG is injected and the entire ICG fluorescence perfusion and wash-out cycle is captured by the imaging device. After image acquisition,

the entire sequence or some temporal sub-range of the images is processed by an image processing algorithm, which may be selected by the surgeon.

[0022] Processed results of the fluorescence measurements may be visualized, for example, as false color images or as a contour map, to enable rapid visual evaluation according to the applied algorithm metric. For example, the fluorescence intensity for each pixel may be rendered as a spectral color varying from blue ("cool" spots or low fluorescence-intensity or rate) to red ("hot" spots or high fluorescence- intensity or rate). Other spectral associations are easily accommodated. The output may be presented as a semi-transparent overlay on the original anatomical images. This enables visual correlation of "hot" spots with the underlying anatomy. The meaning of "hot" spots varies with the algorithm employed, such as integrated intensity, weighted or unweighted, rate of increase or wash-out.

[0023] The user is given interactive control over the "hot" to "cool" color mapping and can vary it in real time to explore finer or coarser sub-ranges of the dynamic range of each algorithm's output metric. As the color window is widened, the hottest regions are highlighted first, followed by the cooler regions. This kind of adjustment can be made by changing the mapping of luminosity or contrast between the acquired pixels and the pixels in the displayed image. Such mapping functions may be included in standard imaging programs. This windowing process based on the currently employed metric aids in discriminating between perforators and enhances perception and improves understanding by the surgeon of the applied ICG dynamics.

[0024] The invention also supports the simultaneous display and evaluation of two sequences from two different locations on the patient's skin. This enables comparison of candidate flaps that are separated by a distance greater than the imaging system's field of view.

[0025] FIG. 2 shows an image of an area of a patient's skin where suitable perforator vessels are to be identified. Each pixel represents the time integral of fluorescence intensity over the exposure time for the image sequence. This mode is typically referred to as "integration mode" in image processing and many image processors offer this mode as a standard feature. In practice, the pixel intensities (collected charges in a CCD) acquired during each frame in the image sequence are added on a pixel-by-pixel basis, for example in the image processor, and divided by the number of frames, whereafter the sum may be normalized to a fixed dynamic range, for example, from 1 to 255 (8-bits). The notion is that brighter pixels in an image represent an area of the skin infused with a greater volume of blood carrying ICG over a preset period of time. In FIG. 2, the perforator vessel 24 exhibits the highest integrated fluorescence intensity, with another perforator vessel exhibiting weaker fluorescence intensity shown as 26.

[0026] Note that the transparency of the image has been set such that the physician's marker 22 is visible through the transparent color overlay of the ICG fluorescence image at the upper right of the screen.

[0027] FIG. 3 shows an ICG fluorescence image of the same area of skin integrated over time, with the pixel values inversely weighted by elapsed time. This image processing algorithm is similar to the previously described integration, but instead of adding the measured intensities of each pixel directly, the measured intensity values are first divided by the elapsed time after start of the observation of ICG fluorescence, before being added. In this way, earlier fluorescence signals are given a greater significance that fluorescence signals acquired later. The "hottest" pixels are those pixels that in the sequence of image frames fluoresce earlier than other pixels which the ICG bolus reaches at a later time. The same perforator vessel 34 is identified as in FIG. 2, with another vessel 36 barely identifiable.

[0028] FIG. 4 shows an ICG fluorescence image, again of the same area of skin, with the pixel values in this image determined by the rate of increase of fluorescence intensity. In this image processing algorithm, a slope of the pixel intensity versus elapsed time is computed for each pixel in an image. For example, each pixel may have an assigned lowest intensity value (baseline) and an assigned highest intensity value (or another relatively high-intensity value). For each pixel, the time when the pixel intensity crosses the baseline and the time when the pixel intensity crosses the high-intensity value are noted. From this information, the image processing algorithm computes a rate of increase for each pixel in the image, with "hotter" pixels having a greater slope, i.e., they reach the high-intensity value faster than "cooler" pixels. This embodiment of the image processing algorithm thus highlights the speed at which the ICG bolus reaches the perforator vessels. The transparency has been turned off in FIG. 4, so that the surgeon's tool is not visible in the image.

[0029] The previously identified perforator vessel, shown here with the reference symbol 44, is much better defined, as are the vessel 46 (previously shown as 26 and 36) and another vessel 48.

[0030] FIG. 5 shows an ICG fluorescence image of the same area of skin, with the pixel values determined by elapsed time to maximum fluorescence. Unlike FIG. 4, which displays the time rate of change, the image processing algorithm of FIG. 5 displays the time at which pixels reach their maximum intensity, with the "hotter" pixels reaching their respective peak fluorescence intensity sooner than cooler pixels. The algorithm thus highlights areas of the image in the order in which perforators reach their peak intensity. In this image, the previously identified perforator vessels 24, 34, 44 is again clearly distinguishable, as are the vessels 56 and 58 which correspond to the vessels 46 and 48 of FIG. 4.

[0031] FIG. 6 shows an ICG fluorescence image of the same area of skin, with the pixel values determined by the peak fluorescence value at each pixel. Higher ("hot") fluorescence intensity values 64 may indicate a higher

ICG concentration or may be caused by perforator vessels located closer to the skin surface, which reduces absorption of the excitation light /fluorescence response. The vessels 66, 68 which were clearly visible in FIGS. 4 and 5, are barely distinguishable from the background.

[0032] While the images shown, for example, in FIGS. 2 and 6 are rendered with a linear contrast transfer function providing a 1:1 mapping of pixel values processed with the various algorithms described above to the displayed pixel intensities, images can also be rendered (as contour maps or false color overlays) with a variable contrast transfer function to enhance the visual differences in the image. In addition, labels may be placed in the overlay images, hereinafter referred to as ACR (accumulated or time-integrated intensity ratio) labels, which facilitate a quantitative comparison between two or more regions of the anatomy.

[0033] Because absolute pixel values in the image change when the dynamic range and slope of the variable contrast transfer function is modified, the ACR labels allow the user to compare the relative perfusion in different image regions as measured by any of the selected overlay techniques (e.g. accumulated/ time-averaged intensity, etc.).

[0034] The following approach is used to compute the ACR label values. For clarity, we assume that accumulated intensity is selected as overlay technique, although the same approach can be used with any of the available overlay techniques.

[0035] The accumulated intensity for all pixels for all images in the image sequence is computed over a time window.

[0036] The accumulated intensity is averaged over a region of the selected label (for example, a 5x5 pixel square matrix).

[0037] The averaged intensity is normalized to the maximum value of the accumulated intensity in the entire image.

[0038] The normalized averaged is intensity scaled, with the maximum value of the transfer function representing 100%.

[0039] By following this approach, the relative ratio of two different ACR labels remains unchanged even though the slope of the transfer function is modified. FIGS. 7 and 8 show a fluorescence image from the image sequence that has been processed with one of the aforementioned algorithms (upper part of the gray-scale image) and the false-color overlay image rendering the accumulated intensity from the sequence in color (from blue for low values to red for high values) for two different contrast functions. The pixel values in FIG. 7 are processed with a first contrast transfer function, giving two regions with 52% and 72% intensity, respectively, corresponding to a ratio of 52/72 = .72 between the two labeled regions. The second overlay image in FIG. 8 shows the same pixel values processed with a different contrast transfer function, with the intensity in the two regions now labeled 99% and 71%, respectively. However, their relative ratio remains essentially unchanged at 71/99 = 0.72.

[0040] The user can modify the transfer function so that a control region is labeled at 100%, wherein all other regions could then be compared to the control region.

[0041] FIG. 9 shows that the overlay is transparent where accumulated intensity pixels have a value less than the point where the bottom of the transfer function ramp intersects the horizontal pixel value axis. Further, this demonstrates that in this example 12% of the image area (Coverage number in the lower right of the bottom window) has accumulated intensity greater than 52% of the maximum accumulated intensity. The illustration shows several regions bounded by their 52% contours.

[0042] In the aforedescribed approach, the user could place labels on the image to compare relative perfusion of different tissue zones. These labels would normalize the accumulated intensity in a small region beneath the label to the accumulated intensity present in the zone at the top end of the color map range of interest. Although the value of individual labels would vary as the color mapping range was shifted, the ratios of the labels to one another would remain constant.

[0043] Practical trials have demonstrated that modifications in the aforedescribed methods would be desirable in order to better quantify the results and allow a more consistent comparison between profused areas.

[0044] Clinicians generally want to perform a consistent comparison of the perfusion of suspect tissue to that of well-perfused, "good" tissue. One way of doing that with the original technique described above is to go through the burdensome process of manually adjusting the color mapping range until a label placed on well-perfused tissue reaches 100%. This label may now be used as a "good" tissue reference.

[0045] Clinicians generally want to identify whether tissue which exhibits relative accumulated intensity at some percentage as compared to good tissue will suffer from necrosis. Inherent noise in the camera, variable conditions of illumination and surface reflectivity, and the presence of residual ICG in the patient make it difficult to ensure that the ratios are consistent.

[0046] Although the label ratios remained constant as the color mapping changed, clinicians found it confusing that the label values themselves vary in the process.

[0047] In one modified approach, two reference labels are placed on the image, either explicitly in a manual operation or implicitly through automatic computation as described below. The labels are denoted as the background or "0 Marker" and the reference or "100 Marker". Any additional labels placed on the accumulated intensity matrix are normalized to the range established by these markers.

[0048] Ideally, the "0 Marker" will be placed on native tissue outside the transplant flap. The accumulated intensity in a small region beneath this marker denotes background intensity that would result from background noise in the camera, possibly combined with signal from

some residual ICG in the patient from prior acquisitions.

[0049] Using clinical judgment, the operator places the "100 Marker" on tissue that the clinician has identified as being well-perfused, "good" tissue. This establishes the "good" tissue reference.

[0050] The two markers now support direct normalized quantitative comparison of regions of perfusion on the flap.

[0051] Labels values are computed using the following formula:

$$L = 100 * (Alabel - A0) / (A100 - A0),$$

where:

Alabel represents the accumulated intensity in the area beneath the label

AO represents the background accumulated intensity in the area beneath the "0 Marker"

A100 represents the reference accumulated intensity in the area beneath the "100 Marker"

All existing and newly placed label values are now normalized to the range between the "0 Marker" and "100 Marker". Label values can exceed 100% and now do not change as the color mapping range is shifted for enhanced visualization.

[0052] FIGS. 10A and 10B illustrate an exemplary embodiment of this technique. FIG. 10A is a fluorescence image of the perfused region, similar to those described above with reference to FIGS. 2 to 6. FIG. 10B is a black/white rendition of a colored overlay, with markers or label values computed with the formula:

$$L = 100 * (Alabel - A0) / (A100 - A0).$$

[0053] The "0 Marker" is denoted in the upper left corner by the circle enclosing a "0" and the "100 Marker" is denoted in the upper right corner by the circle enclosing a "100". Because all areas of the tissue show some perfusion, the "0 Marker" has been placed on a surgical clip within the field of view.

[0054] The following are additional/alternative options for deriving values for the "0 Marker" or accumulated background intensity:

If no separate "0 Marker" is explicitly placed, a value for the "0 Marker" can be derived by averaging the accumulated intensity present in the first frame captured prior to the arrival of the ICG bolus. The average accumulated intensity is then computed by multiplying initial frame values by the number of frames in the sequence.

[0055] Alternatively, in the absence of a separate "0 Marker", a value for the "0 Marker" can be derived by first automatically determining what pixels represent tissue and then examining the first frame to compute the average background intensity only for those tissue pixels. The changing pixels are those which receive blood with ICG. To locate these tissue pixels, the software locates pixels whose intensity changes to exceed a predetermined threshold value. Unchanged pixels are disregarded.

[0056] A physical reference standard or patch with a known near-infrared reflectance may be placed in the field of view. Several of these physical patches would be provided to simulate different skin tones with known reflectance in the visual spectrum. The "0 Marker" could then be explicitly placed over these markers to approximate the accumulated intensity underneath the tissue that is not perfused with ICG-laden blood. This would allow normalization to different illumination conditions in the operating room.

[0057] In summary, labels can be used to easily compare different perfusion boundaries to the perfusion that is present in known good tissue. These labels now correct for the effects of residual ICG, camera noise, and other NIR scattering effects.

[0058] The described embodiments detect a fluorescence signal emitted transcutaneously by ICG following excitation in the near-infrared spectral range. However, those of skill in the art will appreciate that other dyes which can be excited and emit fluorescence in a spectral range where tissue transmits light can also be used.

[0059] While the present invention has been described with reference to an example of arterial blood flow, i.e. supply of blood to the perforator vessel(s), the method may also detect graft failure due to venous congestion by quantifying and displaying the rate of change from peak intensity back down to the baseline. This will highlight venous return in the perfusion area.

[0060] While the invention is receptive to various modifications, and alternative forms, specific examples thereof have been shown in the drawings and are herein described in detail. It should be understood, however, that the invention is not limited to the particular forms or methods disclosed, but to the contrary, the invention is meant to cover all modifications, equivalents, and alternatives falling with the spirit and scope of the appended claims.

Claims

1. A method for evaluating tissue perfusion in a tissue of a subject, the method comprising:

   detecting a fluorescence response arising from a bolus of indocyanine green (ICG) in a bloodstream in the tissue;

   acquiring a temporal sequence of images of the fluorescence response over a period of time;

   independently processing the pixels in the temporal sequence of images to compute a tempo-

rally-based value for each pixel and generate a spatial map of the computed temporally-based values;
selecting a first region representing a well perfused tissue, and a second region representing background; and
processing at least part of the spatial map using the first and second regions to compute a quantitative representation of tissue perfusion in said at least part of the spatial map,

wherein preferably the first and second regions are used as reference regions having a reference value used in said computing.

2. The method of claim 1 wherein the tissue comprises a perforator flap.

3. The method of claims 1 or 2 wherein independently processing each pixel in the temporal sequence of images to compute the temporally-based value for each pixel comprises deriving a time-integrated intensity, a time-derivative of the intensity, or a combination thereof for each pixel, wherein preferably deriving the time-integrated intensity or the time-derivative of the intensity for each pixel comprises (i) adding on a pixel-by-pixel basis a plurality of pixel intensities acquired during each frame in the temporal sequence of images and dividing a sum of the pixel intensities by the number of frames in the temporal sequence of images; (ii) dividing each pixel intensity acquired during each frame in the temporal sequence of images by an elapsed time after ICG bolus administration and adding the divided pixels; (iii) dividing time-integrated intensity value for each pixel by an elapsed time after ICG bolus administration; (iv) determining an elapsed time after ICG bolus injection until time-integrated fluorescence intensity for each pixel reaches a peak value; or (v) computing for each pixel a slope of the pixel intensity versus elapsed time.

4. The method of any one of claims 1 to 3 wherein further comprising applying a contrast transfer function to the computed temporally-based value for each pixel in the spatial map to (i) enhance visual differences in the spatial map; (ii) transform the spatial map into an image representing different perfusion characteristics in different colours; or a combination of (i) and (ii) wherein preferably the contrast transfer function is a linear contrast transfer function or a non-linear contrast transfer function, and wherein more preferably the non-linear contrast transfer function is a function with regions of different slope, and wherein the different slopes and transition between the different slopes are adjusted while performing the method to evaluate tissue perfusion.

5. The method of any one of claims 1 to 4 further comprising displaying the spatial map as an image, a semi-transparent overlay on an anatomical image of the subject, a contour map, a relief map, a numerical representation, or a combination thereof.

6. The method of any one of claims 1 to 5 further comprising (i) displaying a quantitative representation of tissue perfusion in the target region; or (ii) simultaneously displaying a quantitative representation of tissue perfusion in the target region for two or more anatomical locations on the subject.

7. The method of any one of claims 1 to 6 wherein the second reference region representing background comprises background noise, a fluorescence response from residual ICG, a fluorescence response from tissue prior to arrival of the bolus of ICG in the tissue, or a combination thereof, wherein preferably the background noise, the fluorescence response from residual ICG, the fluorescence response from tissue prior to arrival of the bolus of ICG in the tissue or the combination thereof arise from unperfused tissue, wherein more preferably the unperfused tissue comprises a non-fluorescent object placed on the unperfused tissue.

8. The method of any one of claims 1 to 7 wherein the first region representing the well perfused tissue is designated as a "100 Marker" and the second region representing background is designated as a "0 Marker".

9. The method of any one of claims 1 to 8 wherein the computed temporally-based values are averaged over a predefined region of the temporal sequence of images and normalized to a maximum value of the computed temporally-based values in the temporal sequence of images, wherein the normalized averaged temporally-based value is preferably scaled using a maximum value of a contrast transfer function.

10. ICG for use in the method of any one of claims 1 to 9.

11. A system for evaluating tissue perfusion in a tissue of a subject, the system comprising:

means for detecting a fluorescence response arising from a bolus of indocyanine green (ICG) in a bloodstream in the tissue;
means for acquiring a temporal sequence of images of the fluorescence response over a period of time; and
means for independently processing the pixels in the temporal sequence of images of the tissue to:

compute a temporally-based value for each pixel and generate a spatial map of the computed temporally-based values,
select a first region representing a well perfused tissue, and a second region representing background, and
process at least part of the spatial map using the first and second regions to compute a quantitative representation of tissue perfusion in the said part of the spatial map.

12. The system of claim 11 wherein means for independently processing each pixel in the temporal sequence of images to compute the temporally-based value for each pixel is configured to derive a time-integrated intensity, a time-derivative of the intensity, or a combination thereof for each pixel,
wherein preferably derivation of the time-integrated intensity or the time-derivative of the intensity for each pixel comprises (i) addition on a pixel-by-pixel basis a plurality of pixel intensities acquired during each frame in the temporal sequence of images and division of a sum of the pixel intensities by the number of frames in the temporal sequence of images; (ii) division of each pixel intensity acquired during each frame in the temporal sequence of images by an elapsed time after ICG bolus administration and addition of the divided pixels; (iii) division of the time-integrated intensity value for each pixel by an elapsed time after ICG bolus administration; (iv) determination of an elapsed time after ICG bolus administration until time-integrated fluorescence intensity for each pixel reaches a peak value; or (v) computation for each pixel of a slope of the pixel intensity versus elapsed time.

13. The system of any one of claims 11 to 12 wherein a contrast transfer function is applied to the computed temporally-based value for each pixel in the spatial map to (i) enhance visual differences in the map; (ii) transform the spatial map into an image representing different perfusion characteristics in different colours; or a combination of (i) and (ii), wherein preferably the contrast transfer function is a linear contrast transfer function or a non-linear contrast transfer function, and wherein more preferably the non-linear contrast transfer function is a function with regions of different slope, and wherein the different slopes and transition between the different slopes are adjusted while using the system of any one of claims 11 or 12 to evaluate tissue perfusion.

14. The system of any one of claims 11 to 13 further comprising means for displaying the spatial map as an image, a semi-transparent overlay on an anatomical image of the subject, a contour map, a relief map, a numerical representation, or a combination thereof.

15. The system of any one of claims 11 to 14 further comprising means for (i) displaying a quantitative representation of tissue perfusion in the target region; or (ii) simultaneously displaying a quantitative representation of tissue perfusion in the target region for two or more anatomical locations on the subject.

16. The system of any one of claims 11 to 15 wherein the second reference region representing background comprises background noise, a fluorescence response from residual ICG, a fluorescence response from tissue prior to arrival of the bolus of ICG in the tissue, or a combination thereof, wherein preferably the background noise, the fluorescence response from residual ICG, the fluorescence response from tissue prior to arrival of the bolus of ICG in the tissue or the combination thereof arise from unperfused tissue, wherein more preferably the unperfused tissue comprises a non-fluorescent object placed on the unperfused tissue.

17. The system of any one of claims 11 to 16 wherein the first reference region representing the well perfused tissue is designated as a "100 Marker" and the second reference region representing background is designated as a "0 Marker".

18. The system of any one of claims 11 to 17 wherein the computed temporally-based values are averaged over a predefined region of the temporal sequence of images and normalized to a maximum value of the computed temporally-based values in the temporal sequence of images, wherein preferably the normalized averaged temporally-based value is scaled using a maximum value of a contrast transfer function.

19. A method for evaluating tissue perfusion in a tissue of a subject, preferably according to any one of claims 1 - 10, the method comprising:

detecting a fluorescence response arising from a bolus of indocyanine green (ICG) in the bloodstream in the tissue;
acquiring a temporal sequence of images of the fluorescence response over a period of time;
independently processing each pixel in the temporal sequence of images of the tissue to compute a temporally-based value for each pixel and generate a spatial map of the computed temporally-based values;
selecting in the spatial map a target tissue, a first reference region representing native tissue different from the target tissue, and a second reference region representing tissue achieving a predetermined tissue perfusion; and
normalizing at least one additional reference region to a range established by the first and sec-

ond reference regions,
the method preferably further comprising displaying the spatial map as a colour or black-and-white image, and displaying the first reference region,
the second reference region and the at least one additional reference region on the spatial map.

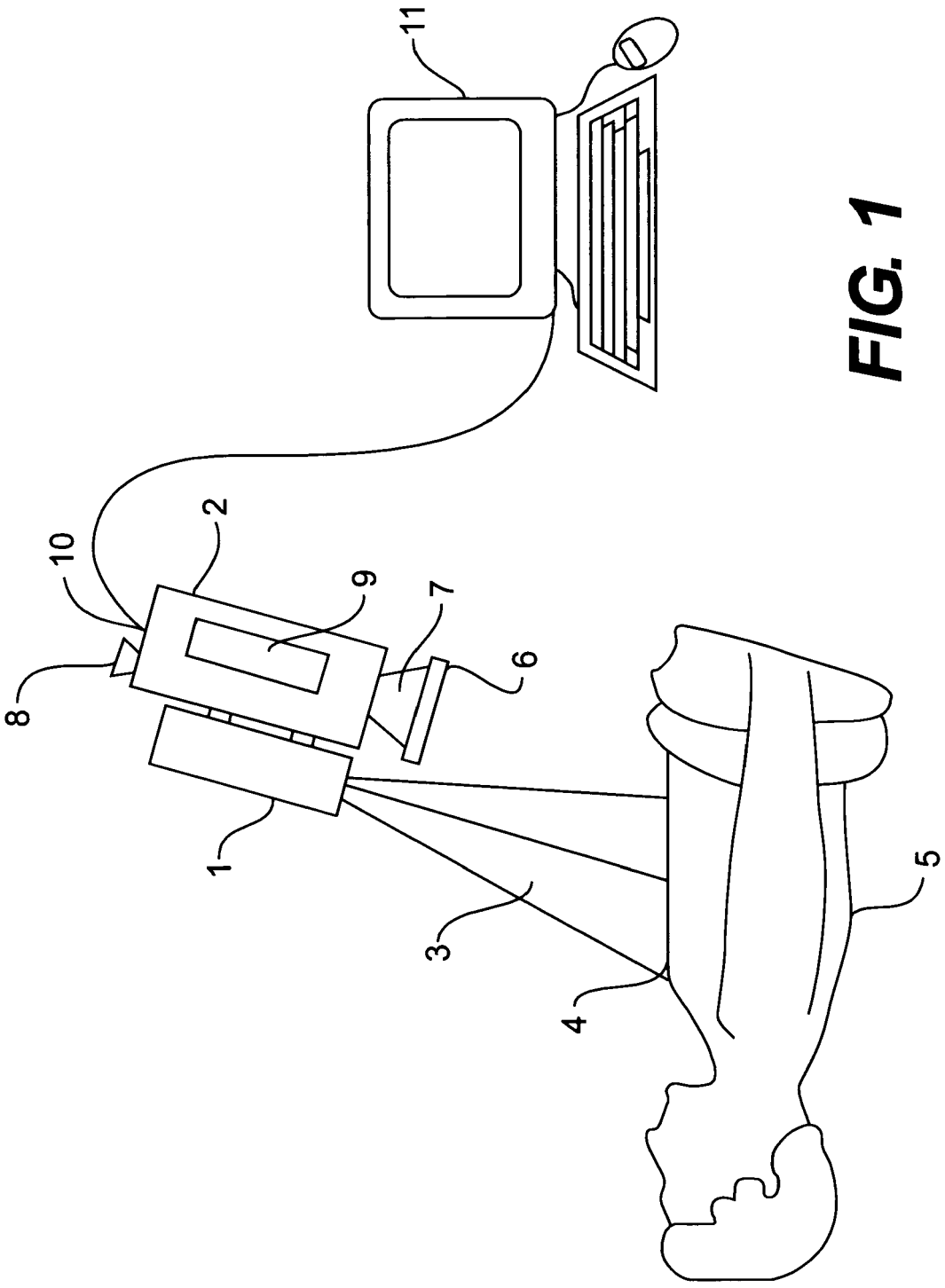


FIG. 1

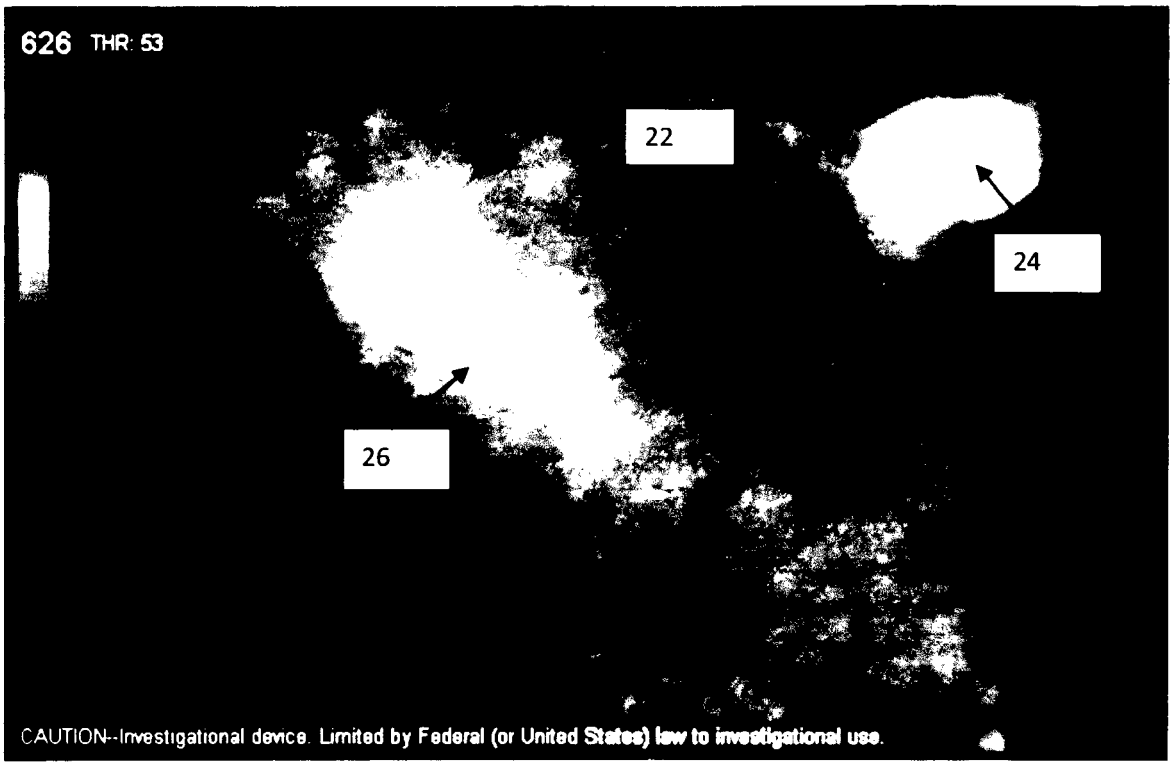

626 THR: 53
22
24
26
CAUTION--Investigational device. Limited by Federal (or United States) law to investigational use.

FIG. 2

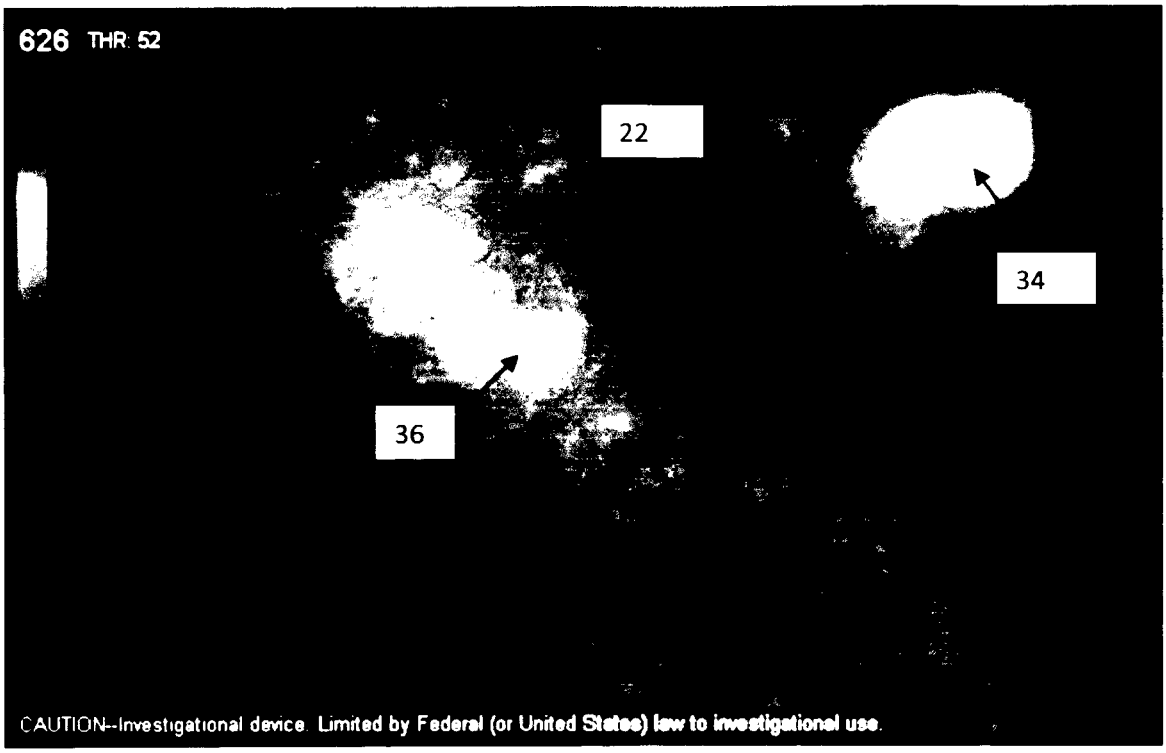

626 THR: 52
22
34
36
CAUTION--Investigational device. Limited by Federal (or United States) law to investigational use.

FIG. 3

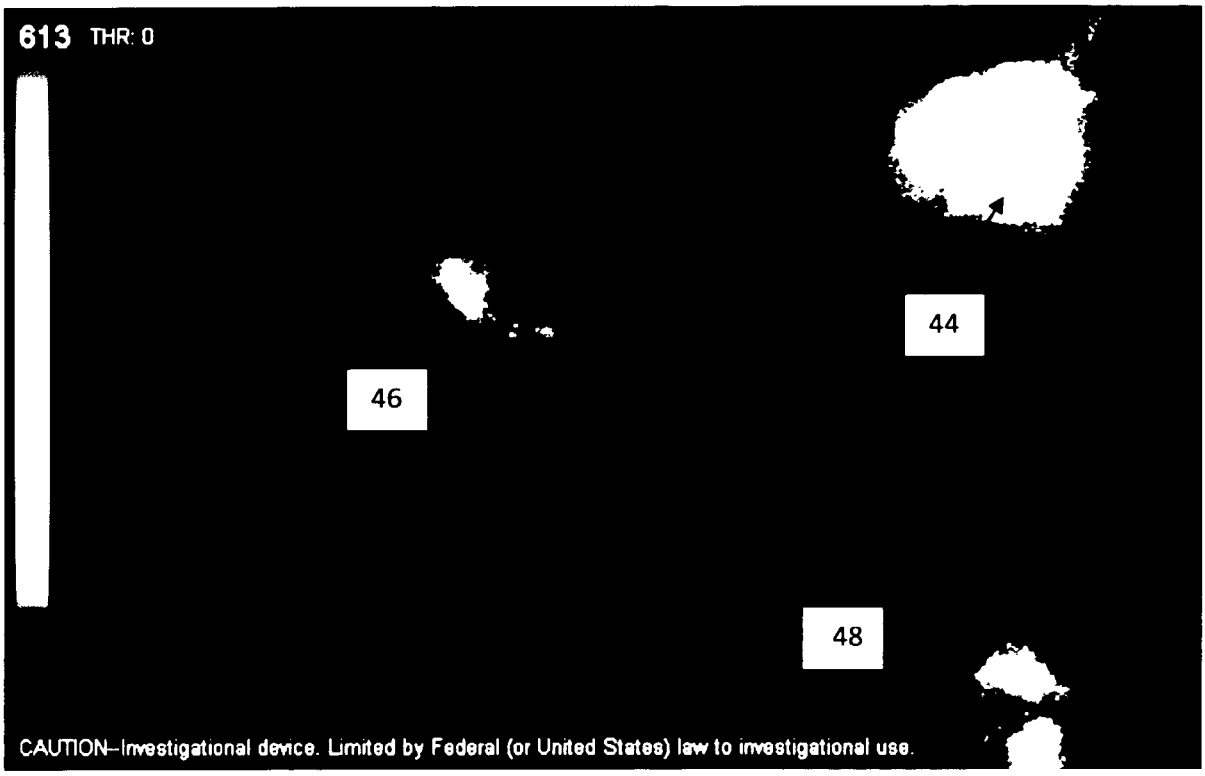

613 THR: 0
44
46
48
CAUTION–Investigational device. Limited by Federal (or United States) law to investigational use.

FIG. 4

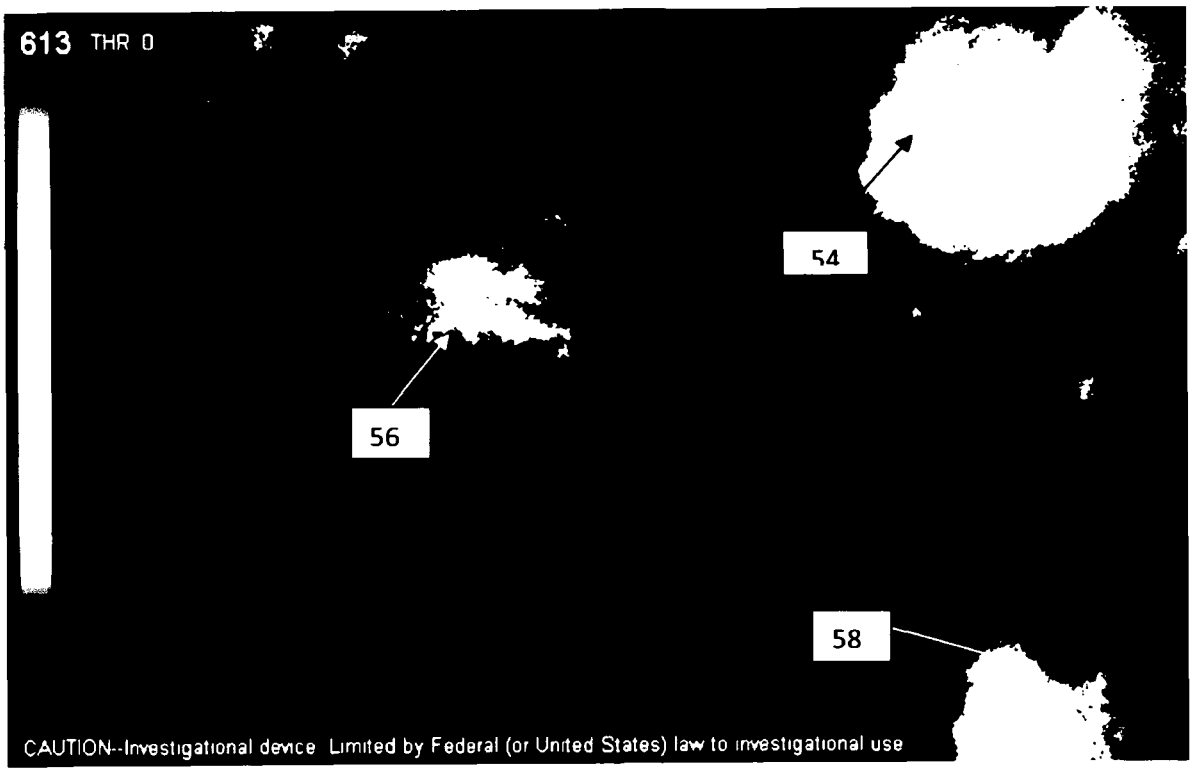

613 THR 0
54
56
58
CAUTION--Investigational device Limited by Federal (or United States) law to investigational use

FIG. 5

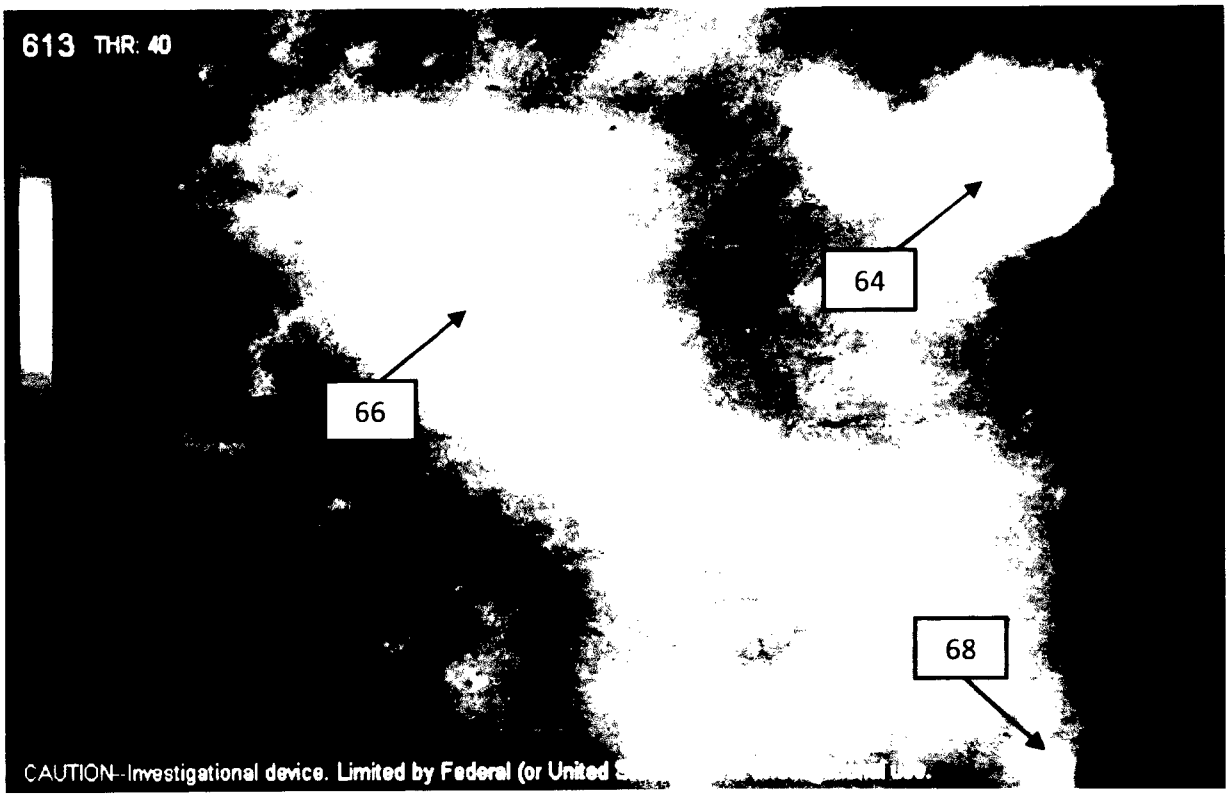
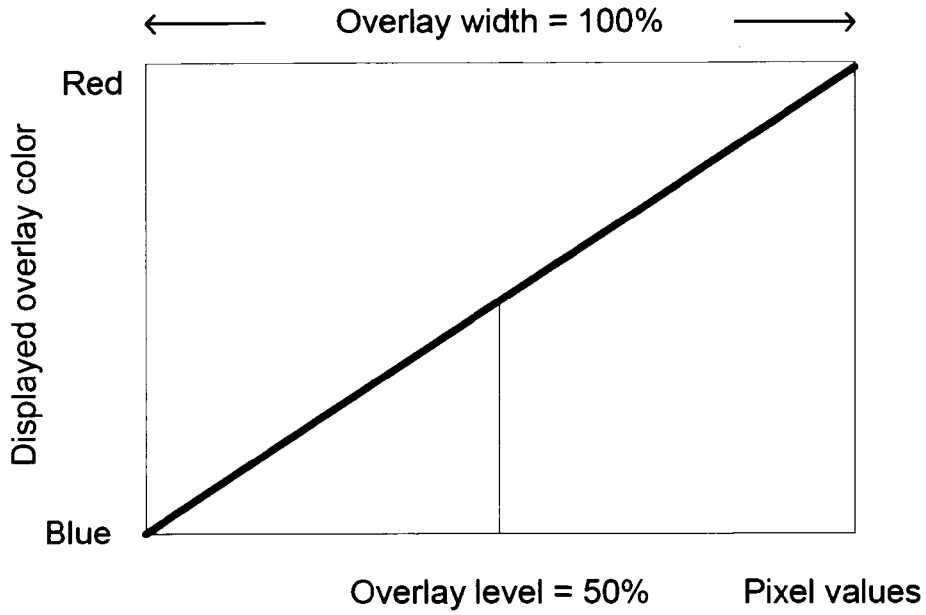

613 THR: 40
64
66
68
CAUTION--Investigational device. Limited by Federal (or United

FIG. 6


Overlay width = 100%
Red
Displayed overlay color
Blue
Overlay level = 50%
Pixel values

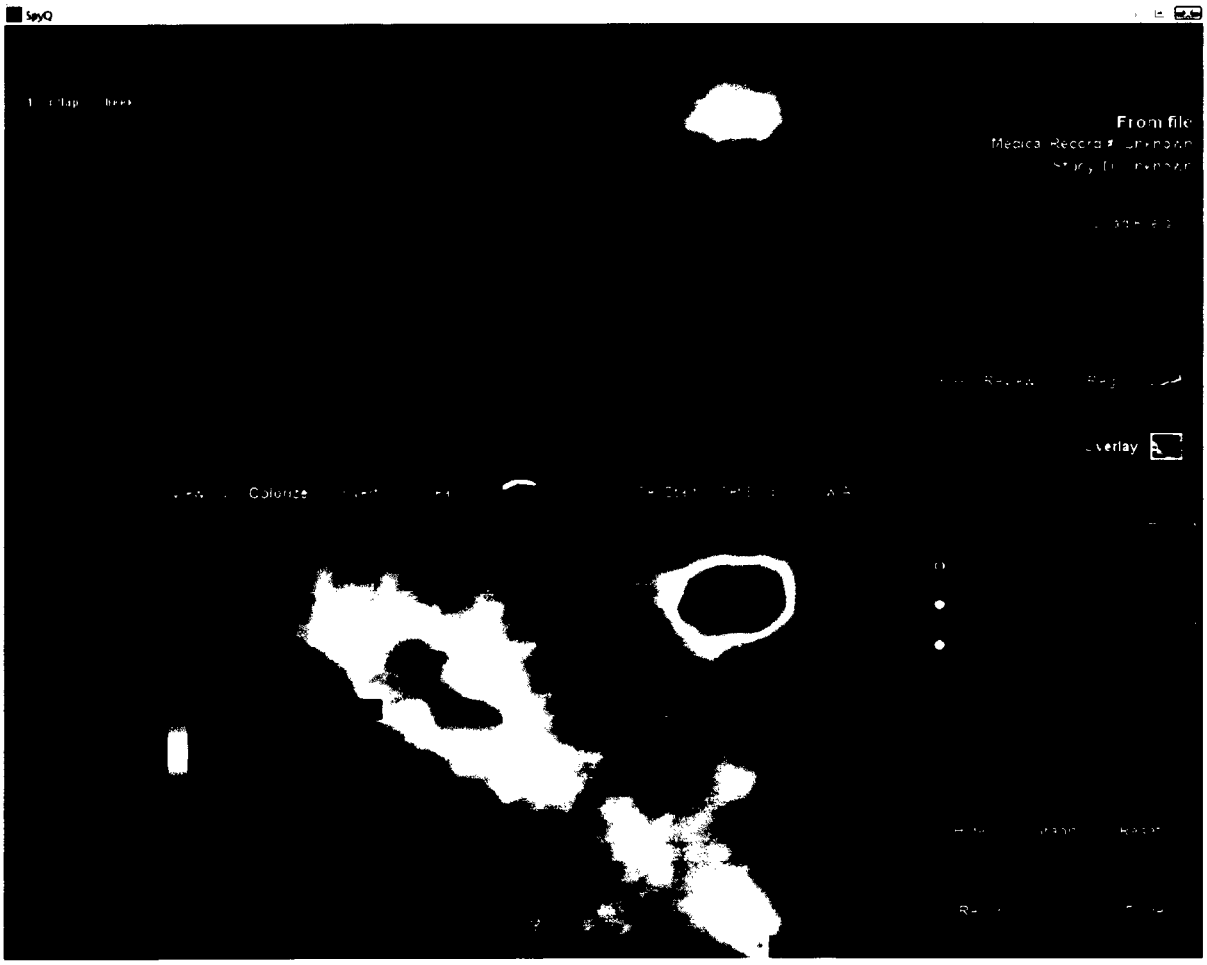
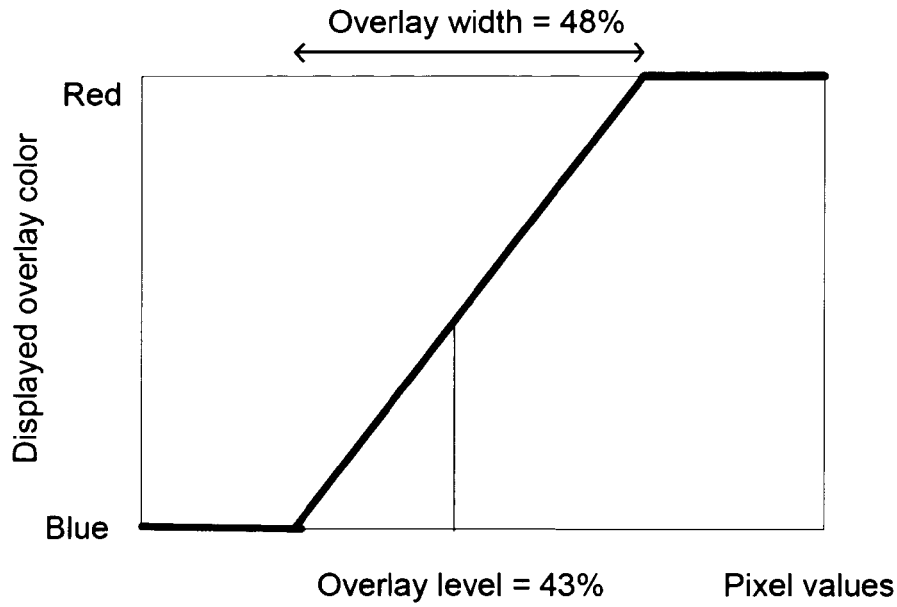

From file
Overlay

FIG. 7


Overlay width = 48%
Red
Displayed overlay color
Blue
Overlay level = 43%
Pixel values

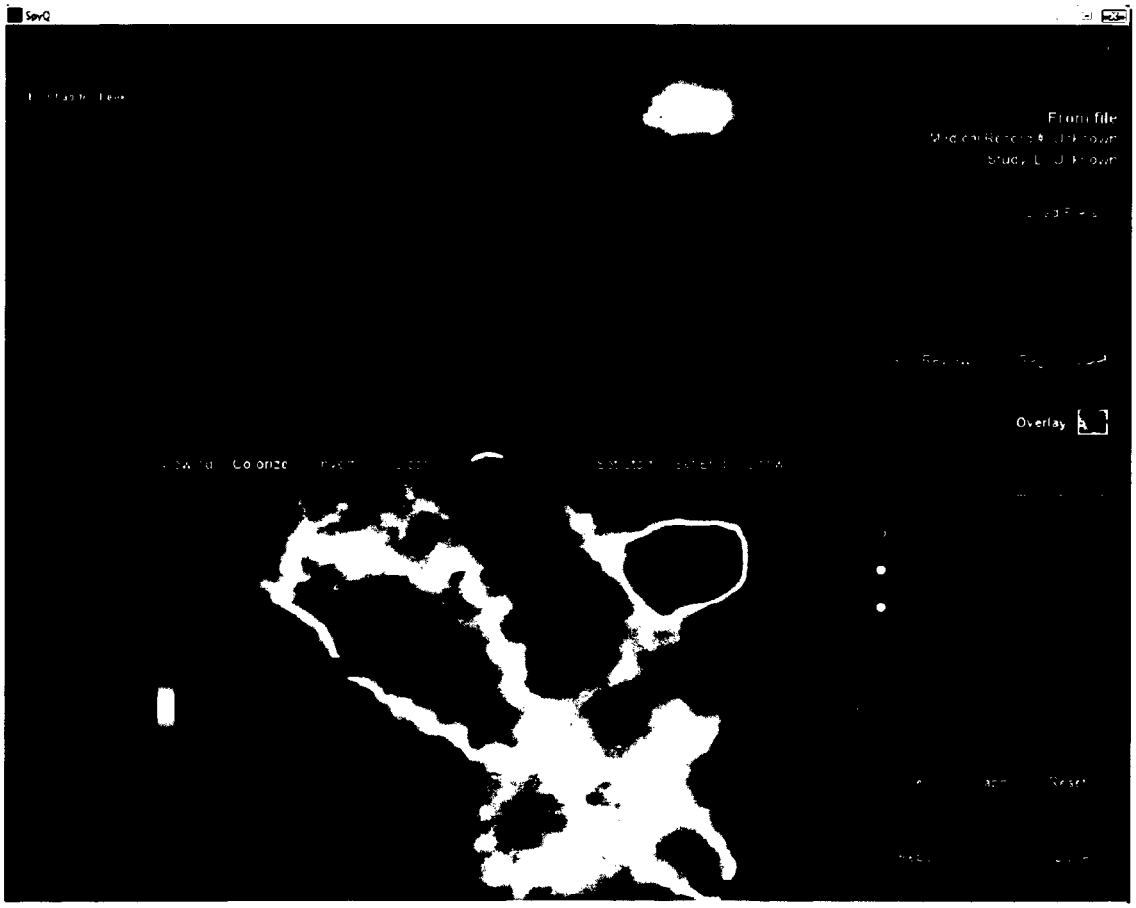
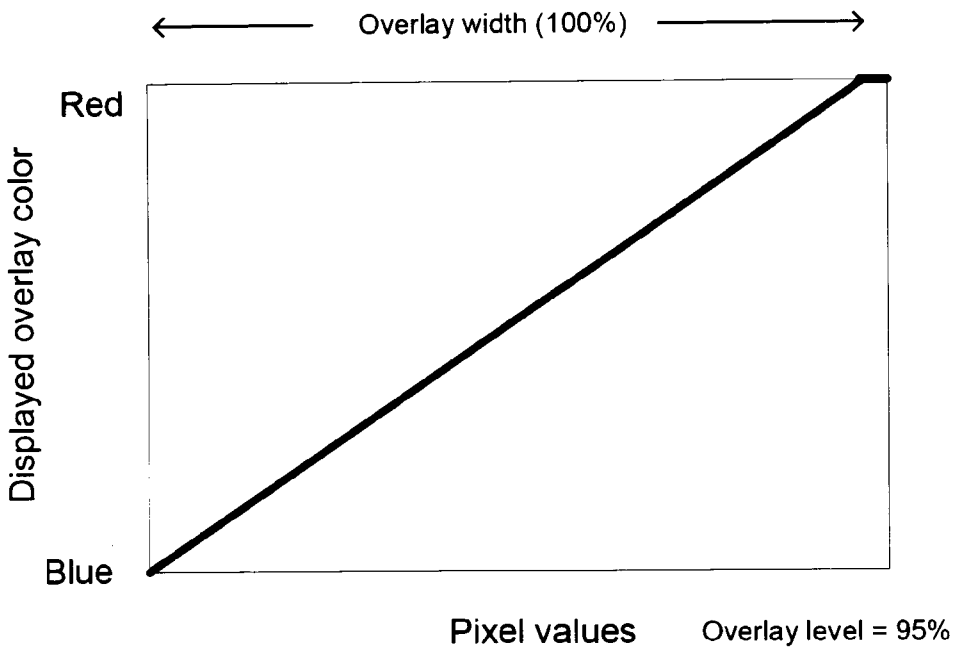

Overlay

FIG. 8


Overlay width (100%)
Red
Displayed overlay color
Blue
Pixel values
Overlay level = 95%

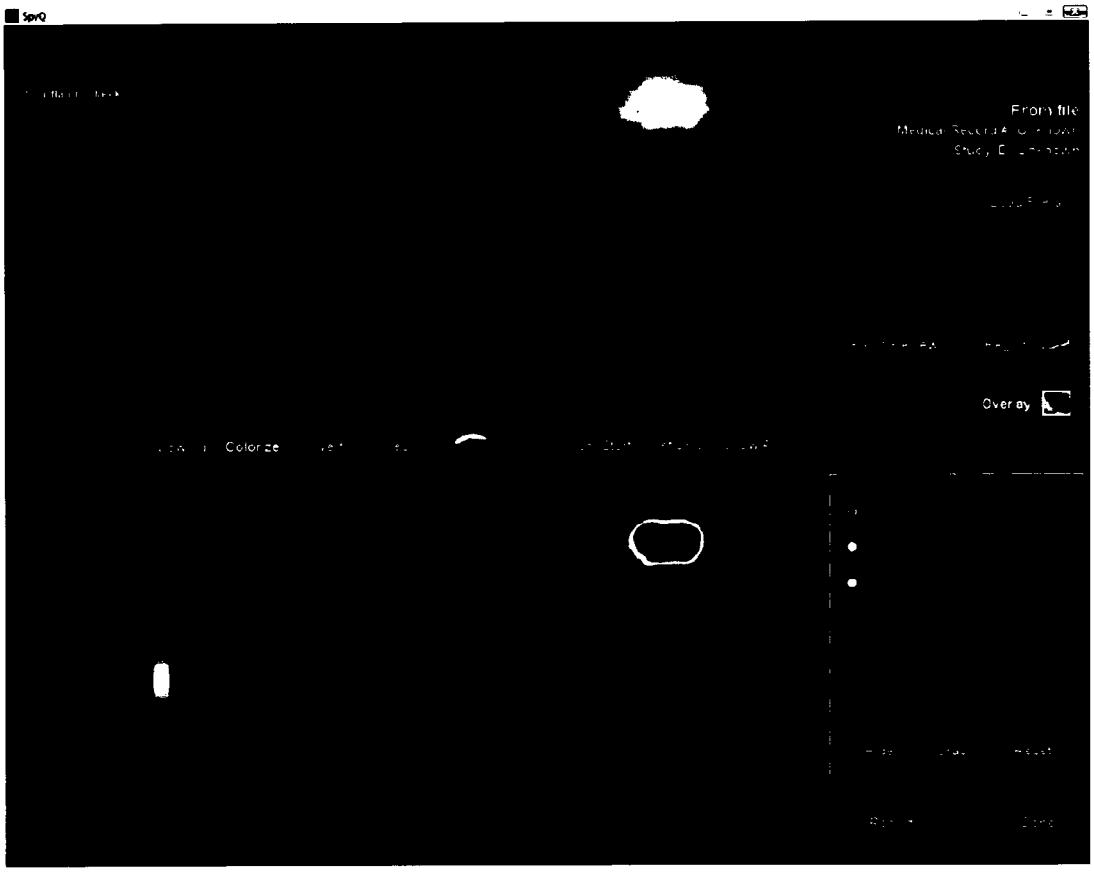

From file
Overlay
Colorize

FIG. 9

FIG. 10A

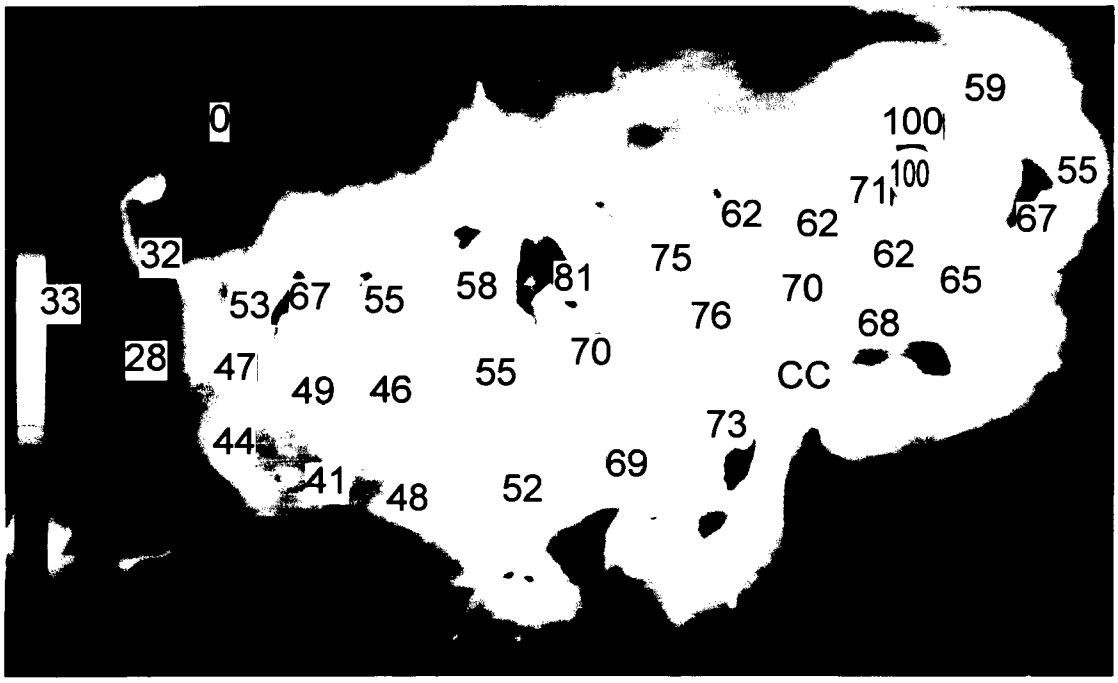


FIG. 10B

专利名称(译)	定位和分析穿孔器皮瓣，用于整形和重建手术		
公开(公告)号	EP3056149A2	公开(公告)日	2016-08-17
申请号	EP2016163909	申请日	2011-09-20
[标]申请(专利权)人(译)	诺瓦达克技术公司		
申请(专利权)人(译)	NOVADAQ科技股份有限公司.		
当前申请(专利权)人(译)	NOVADAQ科技股份有限公司.		
[标]发明人	DVORSKY PETER GOYETTE DAVID MARK HENRI FERGUSON JR BRUCE T CHEN CHENG		
发明人	DVORSKY, PETER GOYETTE, DAVID MARK HENRI FERGUSON JR., BRUCE T. CHEN, CHENG		
IPC分类号	A61B6/00 A61B5/00 A61B6/03		
CPC分类号	A61B5/0059 A61B5/413 A61B5/489 A61B2017/00792		
优先权	12/933477 2010-09-20 US PCT/IB2011/002381 2011-09-20 WO		
其他公开文献	EP3056149B1 EP3056149A3		
外部链接	Espacenet		

摘要(译)

公开了一种使用ICG荧光血管造影成像术前识别用于塑料和/或重建手术的穿支血管的方法和装置。时间分辨图像处理用于突出穿孔器位置并且通过各种计算的度量来实现候选穿孔器之间的视觉区分。基于这些指标，外科医生能够交互式地定位和选择适合于整形和重建手术的穿孔器血管

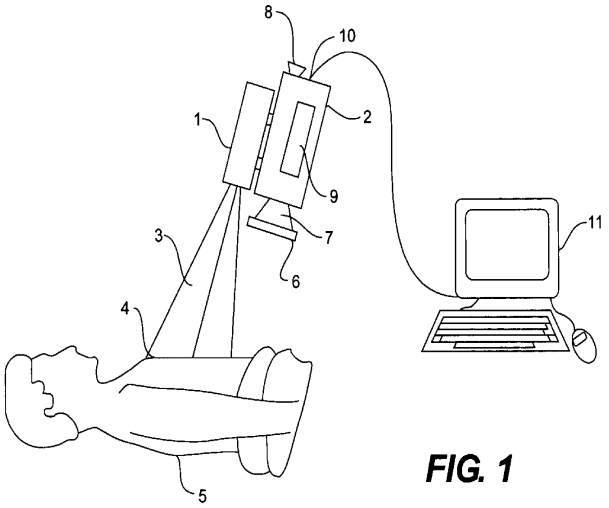


FIG. 1