(19) Europäisches Patentamt
European Patent Office
Office européen des brevets

(11) EP 1 196 081 B1

(12) **EUROPEAN PATENT SPECIFICATION**

(45) Date of publication and mention of the grant of the patent:
21.08.2013 Bulletin 2013/34

(21) Application number: **00943361.6**

(22) Date of filing: **03.07.2000**

(51) Int Cl.:
A61B 5/00 *(2006.01)*

(86) International application number:
PCT/US2000/018221

(87) International publication number:
WO 2001/001854 (11.01.2001 Gazette 2001/02)

(54) **INTEGRATED IMAGING APPARATUS**

BILDERZEUGUNGSGERÄT ZUM INTEGRIEREN VERSCHIEDENER BILDMODALITÄTEN

DISPOSITIF D'IMAGERIE A MODALITE INTEGREE

(84) Designated Contracting States:
AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE

(30) Priority: **02.07.1999 US 142067 P**

(43) Date of publication of application:
17.04.2002 Bulletin 2002/16

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Description

Background of the Invention

1. Field of the Invention

[0001] The invention is directed to an imaging apparatus and methods for performing assessment and monitoring with interpreted imaging. Embodiments of the invention are particularly useful in surgery, clinical procedures, tissue assessment, diagnostic procedures, health monitoring, and medical evaluations.

2. Description of the Background

[0002] Spectroscopy, whether it is visible, near infrared, infrared or Raman, is an enormously powerful tool for the analysis of biomedical samples. The medical community, however, has a definite preference for imaging methods, as exemplified by methods such as MRI and CT scanning as well as standard X-ray photography and ultrasound imaging. This is entirely understandable as many factors need to be taken into account for a physician to make a clinical diagnosis. Imaging methods potentially can provide far more information to a physician than their non-imaging counterparts. With this medical reality in mind, there has been considerable effort put into combining the power and versatility of imaging method with the specificity of spectroscopic methods.

[0003] Xuegang et al. in SPIE 3545 pp. 574-577 (1998) teach multimodal imaging with image fusion, but without hyperspectral data.

[0004] Near-infrared (near-IR) spectroscopy and spectroscopic imaging can measure the balance between oxygen delivery and tissue oxygen utilization by monitoring the hemoglobin oxygen saturation in tissues (Sowa, M.G. et al., 1998, Proc. SPIE 3252, pp. 199-207; Sowa, G.W. et al., 1999, Journal of Surgical Research, 86:62-29; Sow, G.W. et al., 1999, Journal of Biomedical Optics, 4:474-481; Mansfield, J.R., et al., 2000, International Society of Optical Engineers, 3920:99-197). For in-vivo human studies, the forearm or leg has been the investigational site for many of the noninvasive near-IR studies. Non-imaging near-IR applications have examined the local response of tissue to manipulations of blood flow (De-Blasi, R.A. et al., 1992, Adv. Exp. Med. Biol, 317:771-777). Clinically, there are situations where the regional variations in oxygenation saturation are of interest (Stranc, M.F. et al, 1998, British Journal of Plastic Surgery, 51: 210-218). Near-IR imaging offers a means of accessing the spatial heterogeneity of the hemoglobin oxygenation saturation response to tissue perfusion. (Mansfield, J.R. et al., 1997, Analytical Chemistry, 69:3370-3374; Mansfield, J.R., et al., 1997, Computerized Medical Imaging and Graphics, 21:299-308; Salzer, R., et al., 2000, Fresenius Journal of Analytical Chemistry, 366:712-726; Shaw, R.A., et al., 2000, Journal of Molecular Structure (Theochem), 500:129-138; Shaw, R.A., et al., 2000, Journal of Inorganic Biochemistry, 79:285-293; Mansfield, J.R., et al., 1999, Proc. SPIE Int. Soc. Opt. Eng., 3597:222-233; Mansfield, J.R., et al., 1999, Applied Spectroscopy, 53:1323-1330; McIntosh, L.M., et al., 1999, Biospectroscopy, 5:265-275; Mansfield, R., et al., Vibrational Spectroscopy, 19:33-45; Payette, J.R., et al., 1999, American Clinical Laboratory, 18:4-6; Mansfield, J.R., et al., 1998, IEEE Transactions on Medical Imaging, 6: 1011-1018

[0005] Non-invasive monitoring of hemoglobin oxygenation exploits the differential absorption of HbO_2 and Hb, along with the fact that near-IR radiation can penetrate relatively deeply into tissues. Pulse oximetry routinely supplies a noninvasive measure of arterial hemoglobin oxygenation based on the differential red-visible and near infrared absorption of Hb and HbO_2. Visible/near-IR multispectral imaging permits the regional variations in tissue perfusion to be mapped on macro and micro scale. Unlike infrared thermography, hyperspectral imaging alone does not map the thermal emission of the tissues. Instead, this imaging method relies on the differential absorption of light by a chromophore, such as, Hb and HbO_2, resulting in differences in the wavelength dependence of the tissue reflectance depending on the hemoglobin oxygen saturation of the tissue. (Sowa, M.G., et al., 1997, Applied Spectroscopy, 51:143-152; Leventon, M., 2000, MIT Ph.D. Thesis)

[0006] Spectroscopic imaging methodologies and data are becoming increasingly common in analytical laboratories, whether it be magnetic resonance (MRI), mid-IR, Raman, fluorescence and optical microscopy, or near-IR/visible-based imaging. However, the volume of information contained in spectroscopic images can make standard data processing techniques cumbersome. Furthermore, there are few techniques that can demarcate which regions of a spectroscopic image contain similar spectra without a priori knowledge of either the spectral data or the sample's composition. The objective of analyzing spectroscopic images is not only to determine what the spectrum is at any particular pixel in the sample, but also to determine which regions of the sample contain similar spectra; i.e., what regions of the sample contain chemically related compounds. Multivariate analysis methodologies can be used to determine both the spectral and spatial characteristics of a sample within a spectroscopic imaging data set. These techniques can also be used to analyze variations in the temporal shape of a time series of images either derived for extracted from a time series of spectroscopic images.

[0007] There are few techniques that can demarcate which regions of a sample contain similar substances without a priori knowledge of the sample's composition. Spectroscopic imaging provides the specificity of spectroscopy while at the same time relaying spatial information by providing images of the sample that convey some chemical meaning. Usually the objective in analyzing heterogeneous systems is to identify not only the components present in the system, but their spatial distribution. The true power of this technique relative to traditional imaging methods lies in its inherent multivariate nature. Spatial relationships among many parameters can be assessed simultaneously. Thus, the chemical heterogeneity or regional similarity within a sample is captured in a high dimensional representation which can be projected onto a number of meaningful low dimensional easily interpretable representations which typically comprise a set of composite images each having a specific meaning.

[0008] While it is now clear that both spectroscopy and spectroscopic imaging can play roles in providing medically relevant information, the raw spectral or imaging measurement seldom reveals directly the property of clinical interest. For example using spectroscopy, one cannot easily determine whether the tissue is cancerous, or determine blood glucose concentrations and the adequacy of tissue perfusion. Instead, pattern recognition algorithms, clustering methods, regression and other theoretical methods provide the means to distill diagnostic information from the original analytical measurements.

[0009] There are however various methods for the collection of spectroscopic images. In all such cases, the result of a spectroscopic imaging experiment is something termed a spectral image cube, spectroscopic imaging data cube or just hypercube. This is a three dimensional array of data, consisting of two spatial dimensions (the imaging component), and one spectral dimension. It can be thought of as an array of spatially resolved individual spectra, with every pixel in the first image consisting of an entire spectrum, or as a series of spectrally resolved images. In either representation, the 3D data cube can be treated as a single entity containing enormous amounts of spatial and spectral information about the sample from which it was acquired.

[0010] As an extension of the three dimensional array acquired in a spectroscopic imaging experiment, one can collect data cubes as a function of additional parameters such as time, temperature or pH. Numerous algorithms can be used to analyze these multi-dimensional data sets so that chemical and spectral variations can be studied as additional parameters. However, taken together, they can allow one to more fully understand the variations in the data. This can be done in a gated or sequential fashion.

[0011] Multi-modal image fusion, or image registration, is an important problem frequently addressed in medical image analysis. Registration is the process of aligning data that arise from different sources into one consistent coordinate frame. For example, various tissues appear more clearly in different types of imaging methods. Soft tissue, for example, is imaged well in MR scans, while bone is more easily discernible in CT scans. Blood vessels are often highlighted better in an MR angiogram than in a standard MR scan. Multiple scans of the same patient will generally be unregistered when acquired, as the patient may be in different positions in each scanner, and each scanner has its own coordinate system. In order to fuse the information from all scans into one coherent frame, the scans must be registered. The very reason why multiple scans are useful is what makes the registration process difficult. As each modality images tissue differently and has its own artifacts and noise characteristics, accurately modeling the intensity relationship between the scans, and subsequently aligning them, is difficult.

[0012] The registration of two images consists of finding the transformation that best maps one image into the other. If I_1 and I_2 are two images of the same tissue and T is the correct transformation, then the voxel $I_1(x)$ corresponds to the same position in the sample as the voxel $I_2(T(x))$. In the simplest case, T is a rigid transformation consisting of three degrees of freedom of rotation and three degrees of freedom of translation. The need for rigid registration arises primarily from the patient being in different positions in the scanning devices used to image the anatomy. The information from all the images is best used when presented in one unified coordinate system. Without such image fusion, the clinician must mentally relate the information from the disparate coordinate frames.

[0013] One method of aligning the two images is to define an intermediate, patient-centered coordinate system, instead of trying to directly register the images to one another. An example of a patient-centered reference frame is the use of fiducial markers attached to a patient throughout the various image acquisitions. The fiducial markers define a coordinate system specific to the patient, independent of the scanner or choice of imaging modality. If the markers remain fixed and can be accurately localized in all the images, then the volumes can be registered by computing the best alignment of the corresponding fiducials (Horn, B.K.P., 1987, Journal of the Optical Society of America A, 4:629-642; Mandava, V.R., et al., Proc SPIE, 1992, 1652:271-282; Haralick, R.M., et al., 1993, Computer and Robot Vision*).* The main drawback of this method is that the markers must remain attached to the patient at the same positions throughout all image acquisitions. For applications such as change detection over months or years, this registration method is not suitable. Fiducial registration is typically used as ground-truth to evaluate the accuracy of other methods as careful placement and localization of the markers can provide very accurate alignment (West, J. et al., 1996, Proc SPIE, Newport Beach, California).

[0014] When fiducial markers are not available to define the patient coordinate frame, corresponding anatomical feature points can be extracted from the images and used to compute the best alignment (Maintz, J.B. Antione, et al.,

1995 Computer Vision, Virtual Reality and Robotics in Medicine, pp. 219-228; Maguire, Jr., G., et al., 1991, IEEE Computer Graphics Applications, 11:20-29). This approach depends greatly on the ability to automatically and accurately extract reliable image features. In general, methods of feature extraction such as intensity thresholding or edge detection do not work well on medical scans, due to non-linear gain fields and highly textured structures. Even manual identification of corresponding 3D anatomical points can be unreliable. Without the ability to accurately localize corresponding features in the images, alignment in this manner is difficult.

[0015] Instead of localizing feature points in the images, richer structures such as object surfaces can be extracted and used as a basis of registration. A common method of registering MR and CT of the head involves extracting the skin (or skull) surfaces from both images, and aligning the 3D head models (Jiang, H., et al., 1992 Proc. SPIE, 1808: 196-213; Lemoine, D. et al., 1994, Proc. SPIE, 2164:46-56). For PET/MR registration, the brain surface is typically used since the skull is not clearly visible in PET (Pelizzari, C., et al., J Comput Assist. Tomogr., 1989, 13:20-26). The 3D models are then rigidly registered using surface-based registration techniques (Ettinger, G., 1997, MIT Ph.D Thesis). The success of such methods relies on the structures being accurately and consistently segmented across modalities and the surfaces having rich enough structure to be unambiguously registered.

[0016] Voxel-based approaches to registration do not extract any features from the images, but use the intensities themselves to register the two images. Such approaches model the relationships between intensities of the two images when they are registered, and then search through the transformation space to find an alignment that best agrees with the model. Various intensity models are discussed, including correlation, mutual information. and joint intensity priors.

[0017] Correlation is a measure commonly used to compare two images or regions of images for computer vision problems such as alignment or matching. Given the intensity values of two image patches stacked in the vectors u and v, the normalized correlation measure is the dot product of unit vectors in the directions of u and v:

$$(u \bullet v) \; / \; (\|u\| \, \|v\|)$$

[0018] An advantage of correlation-based methods is that they can be computed quite efficiently using convolution operators. Correlation is applicable when one expects a linear relationship between the intensities in the two images. In computer vision problems, normalized correlation provides some amount of robustness to lighting variation over a measure such as sum of square differences (SSD), $|| u - v ||^2$. The primary reason for acquiring more than one medical scan of a patient stems from the fact that each scan provides different information to the clinician. Therefore, two images that have a simple linear intensity relationship may be straightforward to register, but do not provide any additional information than one scan by itself. On the other hand, if the images are completely independent (e.g. no intensity relationship exists between them), then they cannot be registered using voxel-based methods. In general, there is some dependence between images of different modalities and each modality does provide additional information.

[0019] One simplified model of the medical imaging process is that an internal image is a rendering function R of underlying tissue properties, P(x), over positions x. An image of modality A could be represented as a function $R_A(P)$ and a registered image of modality B of the same patient would be another function, say $R_B(P)$. Suppose a function F ($\times$) could be computed relating the two rendering functions such that the following is true (with the possible addition of some Gaussian noise, N):

$$F(R_B(P)) = R_A(P) + N$$

The function F would predict the intensity at a point in Image A given the intensity at the corresponding point in Image B. Such a function could be used to align a pair of images that are initially in different coordinate systems using SSD:

$$T^* = \text{argmin}_T \sum_x \; (F(R_B(P(x))) \; - R_A(P(x)))^2$$

where T is the transformation between the two sets of image coordinates. Van den Elsen et al. compute such a mapping that makes a CT image appear more like an MR, and then register the images using correlation (van den Elsen, P., et al., 1994, "Visualization in Biomedical Computing," 1994 Proc SPIE, 2359:227-237). In general, explicitly computing the function F that relates two imaging modalities is difficult and under-constrained.

[0020] Maximization of mutual information (MI) is a general approach applicable to a wide range of multi-modality registration applications (Bell, A.J., et al., 1995 Advances in Neural Information Processing 7; Collignon, D., et al., 1995, First Conf. on Computer Vision, Virtual Reality and Robotics in Medicine Springer; Maes, F. et al, 1996, Mathematical Methods in Biomedical Image Analysis; Wells, W.M., et al., 1996, Medical Image Analysis, 1(1):35-51). One of the

strengths of using mutual information is that MI does not use any prior information about the relationship between joint intensity distributions. While mutual information does not explicitly model the function F that relates the two imaging modalities, it assumes that when the images are aligned, each image should explain the other better than when the images are not aligned.

[0021] Given two random variables U and V, mutual information is defined as (Bell, 1995):

$$MI(U, V) = H(U) + H(V) - H(U, V)$$

where H(U) and H(V) are the entropies of the two variables, and H(U,V) is the joint entropy. The entropy of a discrete random variable is defined as:

$$H(U) = - \sum P_u(u) \log P_u(u)$$

where $P_u(u)$ is the probability mass function associated with U. Similarly, the expression for joint entropy entropy operates over the joint PDF:

$$H(U, V) = - \sum\sum P_{u,v}(u,v) \log P_{u,v}(u,v)$$

[0022] When U and V are independent, H(U, V) = H(U) + H(V), which implies the mutual information is zero. When there is a one-to-one functional relationship between U and V, (i.e. they are completely dependent), the mutual information is maximized as:

$$MI(U, V) = H(U) = H(V) = H(U, V)$$

[0023] To operate on images over a transformation, we consider the two images, $I_1(x)$ and $I_2(x)$ to be random variables under a spatial parameterization, x. We seek to find the value of the transformation T that maximizes the mutual information (Wells, 1996):

$$T^* = \text{argmax}_T \; MI(I_1(x), I_2(T(x)))$$

$$T^* = \text{argmax}_T \; H(I_1(x)) + H(I_2(T(x))) - H(I_1(x), I_2(T(x))$$

The entropies of the two images encourage transformations that project I1 onto complex parts of I2. The third term, the (negative) joint entropy of I_1 and I_2, takes on large values when X explains Y well. Derivatives of the entropies with respect to the pose parameters can be calculated and used to perform stochastic gradient ascent (Wells, 1996). West et al. compare many multi-modal registration techniques and find mutual information to be one of the most accurate across all pairs of modalities (West, 1996).

[0024] Leventon et al. introduced an approach to multi-modal registration using statistical models derived from a training set of images (Leventon, M., et al., 1998, Medical Image Computing and Computer-assisted Intervention*).* The method involved building a prior model of the intensity relationship between the two scans being registered. The method requires a pair of registered training images of the same modalities as those to be registered in order to build the joint intensity model. To align a novel pair of images, the likelihood of the two images given a certain pose based on our model by sampling the intensities at corresponding points is computed. This current hypothesis can be improved by ascending the log likelihood function. In essence, one computes a probabilistic estimate of the function F (that relates the two imaging modalities) based on intensity co-occurrence. To align the novel images, the pose is found that maximizes the likelihood that those images arose from the same relation F.

[0025] Building a joint-intensity model does require having access to a registered pair of images of the same modality and approximately the same coverage as the novel pair to be registered. Mutual information approaches do not need to draw upon previously registered scans. However, when this information is available, the prior joint intensity model provides the registration algorithm with additional guidance which results in convergence on the correct alignment more quickly, more reliably and from more remote initial starting points.

Summary of the Invention

[0026] The present invention is defined in claims 1 and 10 and overcomes problems and disadvantages associated with current strategies and designs and provides methods and apparatus for imaging using real-time or near real-time assessment and monitoring. Embodiments of the device are useful in a plurality of settings including surgery, clinical procedures, tissue assessment, diagnostic procedures, forensic, health monitoring and medical evaluations.

[0027] One embodiment of the invention is directed to an imaging apparatus comprising integrating spatial, spectral and temporal features, and optionally other physiologic or relevant data, such as room temperature or ambient light, in a spectral and temporal multimodal imaging system for the evaluation of biological systems and stimuli and fusing one or more thermal images or other imaging modalities and hyperspectral data cube for assessment of biological processes. The integrated features may comprise two or more of visible or infrared hyperspectral images, visible or infrared brightfield images, thermal images, fluorescence images, Raman images and/or other relevant imaging modalities. The imaging apparatus may further comprise a specific UV, visible and/or infrared light source, and means for collecting two or more of visible or infrared hyperspectral images, visible or infrared brightfield images, thermal images, fluorescence images, Raman images, or standard video images.

[0028] Another embodiment of the invention is directed to methods for detecting a diseased condition comprising acquiring thermal images from a target, acquiring visible or infrared hyperspectral images from the same target, fusing the thermal images and visible or infrared hyperspectral images to analyze spatial distributions and/or feature determination of the target. Thermal images or hyperspectral images of the target and/or other data can be interlaced with a time dependent reference to determine changes which could influence and be correlated with results from other imaging modalities. Wavelengths can be selected to maximize diagnostic information for a specific tissue state or anticipated end diagnostic goal. The selection step involves performing multivariate image and spectral processing using multivariate image and spectral processing algorithms to extract information from the plurality of images and spectra for real-time or near real-time assessment. Multiple hyperspectral collection devices in a variety of wavelength regimens could be used simultaneously or sequentially or on an as needed basis. For instance a visible hyperspectral images could be combined with a near infrared hyperspectral imager (plus or minus a broad band thermal camera) to provide combined information from both wavelength regions. In this way, one can analyze tissue health mapping; skin sebum level mapping; skin dryness, skin texture, skin feel or skin color mapping; skin damage detection and mapping (UV damage, frostbite, bums, cuts, abrasions) impact of cosmetics or other substances applied to the skin bruise age, force of impact, peripheral vascular disease diagnosis, extent, determination or regionalization of ischemia, varicose veins or hemorrhage detection, local detection and mapping, systemic infection detection, differentiation between viral, bacterial and fungal, and more specific identification, such as between gram negative and gram positive bacterial infection, venous occlusion increase in total hemoglobin, hematocrit, and change in deoxyhemoglobin/oxyhemoglobin ratio, differentiate between ischemia and hypoxia, burn depth and wound healing evaluation, non-invasive diagnosis of shock by imaging uninjured skin, hemorrhagic shock, septic shock, burn shock, changes in a dynamic system as a function of time or other parameter, vascular occlusion, vaso-dilation and vaso-constriction changes related to the presence of cancer in primary tissue or lymph nodes, either surface or subsurface, changes related to a specific chemical, mechanical, thermal, pharmacological or physiological stimulus. Different levels of microvascular constriction and relaxation lead to different ratios of oxyhemoglobin/deoxyhemoglobin, to tissue perfusion, tissue abnormality, disease state or diagnostic condition, total hematocrit, differentiate differences in reperfusion state following occlusion where oxygenation levels may remain low although there is good perfusion.

[0029] Other technical advantages of the present invention are set forth in or will be apparent from drawings and the description of the invention which follows, or may be learned from the practice of the invention.

Description of the Drawings

[0030]

Figure 1 A schematic diagram of a common optical path shared by multiple modalities.

Description of the Invention

[0031] As embodied and broadly described herein, the present invention is directed to an imaging apparatus and methods for performing real-time or near real-time assessment and monitoring. Embodiments of the device are useful in a plurality of settings including surgery, clinical procedures, tissue assessment, diagnostic procedures, forensic, health monitoring and medical evaluations.

[0032] It has been surprisingly found that the pairing of hyperspectral imaging data with data obtained from other single-image imaging methodologies, (examples of which include thermal imaging or fluorescence imaging) provides a

sensitive and accurate assessment measure of a physiological condition. This is particularly appealing in terms of tissue assessment in that both thermal perfusion assessments and various multi-modal tissue signatures which incorporate things such as oxyhemoglobin/deoxyhemoglobin ratios and other indices of tissue physiology, pathology or function are interrelated. By fusing data from multiple collection devices and multiple spectral modalities, such as a broad band thermal camera and one or more hyperspectral cameras, or a single imaging device that can respond in multiple discreet bands, data can be obtained to provide medically relevant information. Additionally, pixel to pixel registration for fusion will benefit from methodologies designed to permit this. Included among these technologies are Automatic Target Recognition (ATR), a technology developed within the military for automatic analysis and pattern recognition of signature data, and gating of images relative to repetitive physiological parameters such as heart rate or respiration. In an embodiment of the invention, an ATR is used to maintain image centering. The addition of such novel features as a common optical path optimizes data collection and minimizes processing requirements for a fused image. Image fusion between hyperspectral image datasets (also referred to as cubes) and other imaging modalities would allow for the extraction of more medically-relevant features and diagnostic information than any of the modalities alone. Addition of physiologically or medically related scalar variables to the data set of one or more hyperspectral imaging sets with or without formal image fusion being required allows for the enhancement of diagnostic algorithms.

[0033] Incorporation of a stable broad band light source with the ability to be filtered to provide illumination, either singly or in multiples of different spectral regions, an electronically tunable imaging spectrometer, a video camera, a CCD, and a parfocal infrared focal plane array or other camera with the same field of view as the CCD.

[0034] Image fusion using beam splitters for the simultaneous acquisition of multiple discreet images incorporating spectral data, each discreet image providing a unique information set, and these various information sets are combined in a variety of manners to allow for enhanced and more unique signatures. Enhancement results in a broader and more discernible identification methodology. If desired, data analysis can be enhanced by triangulation with two cameras. Polarizing imagers may be used as desired to enhance signatures for various targets. Temporal analysis is included in a signature. Temporal alterations or heterogeneity, with or without a meaningful pattern, is acquired with or without gating.

[0035] Thermal images or hyperspectral images, either singly or in combination with other modal images, may be used as an interlaced, time dependent reference to identify changes in the dynamic system. These changes may influence and be correlated with the results from all modalities.

[0036] Referring to Figure 1, signal beam 110 is acquired and IR Beam-splitter 160 is placed in the path of signal beam 110 and accordingly, splits or diverts a portion of the infra-red signal beam 110 to infra-red focal plane array 120. 90/10 Visible Beam-splitter 130 is placed in signal beam 110 behind IR Beamsplitter 160. Visible Beam-splitter 130 splits the visible spectrum of signal beam 110 into two portions, wherein one portion is received by video camera 150, and the other is received by visible camera 140. One or multiple mirrors can be used for the beam splitter. This allows for the simultaneous acquisition of data from multiple modalities.

[0037] Fusion of broad band infrared and hyperspectral imaging methodologies may be useful to devise algorithms for wavelength selection that maximize the diagnostic information for a specific tissue state; employ various multivariate image processing algorithms to extract information from the hyperspectral images and spectra and the thermal images for real-time or near real-time assessment of tissue state; devise image processing algorithms to assess the size and shape of abnormal tissue regions or domains; acquire sequential hyperspectral imaging cubes, thermal images or other physiological data to examine changes in a dynamic system as a function of time. Utility is extended by pairing more superficial data from hyperspectral imaging cubes with deeper perfusion data.

[0038] According to an embodiment of the present invention, a method for determining a total hematocrit comprises measuring a spatial distribution of oxyhemoglobin, deoxyhemoglobin and methemoglobin using hyperspectral imaging methods within the visible range or infrared range of the electro-magnetic spectrum; determining total hematocrit by calculating the area under the oxyhemoglobin, deoxyhemoglobin and methemoglobin spectrum or the intensity at their respective wavelengths; and pairing this with perfusion data from broad band thermal camera to permit assessment of total blood volume.

[0039] Alternatively, the invention may be used to determine blood flow within a patient. For example, a thermal camera demonstrates a state of perfusion and a hyperspectral camera demonstrates a state of oxygen extraction. Spatial characteristics relative to blood vessel assist diagnosis, i.e., like mottling visible in skin, and can see more or less heterogeneity under certain thermal, neurohumoral, physiological or pathological circumstances and in specific spatial patterns. In addition, the present invention may be used to determine a static or dynamic response of tissue or musculature when applying an active stimulus, such as a thermal change, drug injection, and electromagnetic or mechanical stimulus.

[0040] Different levels of microvascular constriction lead to different ratios of blood oxy/deoxygenation or signature of tissue vs. artery vs. vein. In addition to heme and heme-containing or related components, many chemicals and substances can be identified including, for example, glucose, enzymes and metabolic effluents, and moisture content and distribution can be determined and calibrated with artery verses vein. Arterial occlusion causes a decrease in perfusion and total hemoglobin and increase in deoxyhemoglobin/oxyhemoglobin ratio. The time course will be useful as well as including both first and second derivatives. Arterial reperfusion causes increase in perfusion and total hemoglobin. This

increase in perfusion, leads to decreased differences between artery and tissue and vein for both hemoglobin saturation and thermal differences. This is due to a decreased resistance to flow at the arteriolar level. Venous occlusion causes an increase in total hemoglobin, hematocrit, and an increase in deoxyhemoglobin/oxyhemoglobin ratio. The time course also varies with arterial occlusion and oxyhemoglobin/deoxyhemoglobin ratios.

[0041] Artery and vein measurements can be used as internal calibration on a given picture for tissue levels of oxyhemoglobin/deoxyhemoglobin or thermal image or signature. Further, one can add thermal data by fusing thermal image just as one of the wavelengths in series in hyperspectral cube, i.e., an extra plane. Alternatively, thermal images can be fused to each wavelength image in series. Alternatively or in addition, generic processed analysis of thermal image (degree of variation) weights an image of each wavelength plane or impacts hyperspectral algorithmic analysis. Scalar data presenting physiologic or other relevant data can be also incorporated as described above.

[0042] According to an embodiment of the present invention, correction for a patient's motion is done by tissue stabilization or in the case of repetitive motions by gating image frames with a patient's cardiac or respiration cycle. Frames at the specific wavelengths selected for a particular diagnostic module are acquired at the same position in sequential cardiac cycles. The timing of the cardiac cycle is provided by electrocardiogram or cardiac ultrasound or other method. The respiratory variation is timed with an external sensor of respiration or with either the ventilating mechanism or a sensor mechanism of an artificial respirator.

[0043] The present invention may be used to provide signatures of tissue viability or cancer. Markers of cell viability include hyperspectral signatures of oxyhemoglobin and deoxyhemoglobin or other chromaphores, thermal signatures, or fused signatures. The present invention is used to determine drug impact on vasodilitation, neurohumoral response, physiology, and pathology. The present invention is used to identify and classify a large variety of chemical species, for example, those other than oxyhemoglobin and deoxyhemoglobin. Sensor/image fusion permits additional data acquisition and incorporation into diagnostic assessment. This is facilitated by the use of multiple optical paths properly aligned to optimize registration. Inclusion of simultaneous recording of standard video camera images facilitates registration and provides additional data. False color imaging may be added real-time to facilitate the rapid understanding of the data presented to the surgeon or other user. On board CCD chip filters can be provided to increase processing speed. Input for physiologic monitoring systems, such as blood pressure, heart rate, peripheral oxygenation, can be added to the data acquired and fed into diagnostic algorithms. A recording system can be included to log the real-time or near real-time output of imaging systems.

[0044] In an embodiment of the present invention, a split frame video display is used to show all modes simultaneously. For example, parameters of wound healing may be displayed, such as: oxyhemoglobin or deoxyhemoglobin independently or as a ratio; signatures associated with rapidly dividing cells or dead cells, or particular types of cells; fluid content; hydration/dehydration or edema of tissue; or tissue performance. Tissue perfusion data provided by a thermal camera increases accuracy, delivers information about underlying vascular, beds, and/or provides data that will minimize the hyperspectral data processing requirements. Thermal images are used provide a baseline to track oxygen extraction or signature changes induced by tissue exposure.

[0045] Increased heterogeneity and spatial features can be important in a diagnosis. For example, in vasoconstriction, it allows identification of areas that are less well perfused small micro areas that manifest as heterogeneity, to be diagnosed. Differences in oxyhemoglobin and deoxyhemoglobin ratios with spatial characteristics provide an image of micromottling. If vasodilated are more uniform, the patterns of vasoconstriction are helpful in diagnosis of infection in general and can aid in the identification of specific infection. Other patterns of heterogeneity are seen with cancers, and for example are associated with areas of increased metabolism or necrosis.

[0046] The present invention may be used to analyze tissue health mapping; skin sebum level mapping; skin dryness, skin texture, skin feel or skin color mapping; skin damage detection and mapping (UV damage, frostbite, bums, cuts, abrasions) impact of cosmetics or other substances applied to the skin bruise age, force of impact, peripheral vascular disease diagnosis, extent, determination or regionalization of ischemia, varicose veins or hemorrhage detection, local detection and mapping, systemic infection detection, differentiation between viral, bacterial and fungal, and more specific identification, such as between gram negative and gram positive bacterial infection, venous occlusion increase in total hemoglobin, hematocrit, and change in deoxyhemoglobin/oxyhemoglobin ratio, differentiate between ischemia and hypoxia, burn depth and wound healing evaluation, non-invasive diagnosis of shock by imaging uninjured skin, hemorrhagic shock, septic shock, burn shock, changes in a dynamic system as a function of time or other parameter, vascular occlusion, vaso-dilation and vaso-constriction changes related to the presence of cancer in primary tissue or lymph nodes, either surface or subsurface, changes related to a specific chemical, mechanical, thermal, pharmacological or physiological stimulus. Different levels of microvascular constriction and relaxation lead to different ratios of oxyhemoglobin/deoxyhemoglobin, to tissue perfusion, tissue abnormality, disease state or diagnostic condition, total hematocrit, differentiate differences in reperfusion state following occlusion where oxygenation levels may remain low although there is good perfusion.

[0047] In an embodiment of the present invention, motion artifacts of the measurements are used to measure heterogeneity. With motion, a homogeneous tissue will continue to produce the same spectral signature, whereas heteroge-

neous tissue will demonstrate a variety of different signatures. Extraneous motion artifacts can be reduced by mechanical stabilization of field of regard, for example, by clamping tissue or region of interest. Even in the absence of discrete spatial information, the simple range of spectra obtained, demonstrating the heterogeneity per se can be useful. Dilation makes thermal imaging more uniform and constriction more heterogeneous. The latter correlates with ischemia, microvascular mottling or the edge of larger vessels. Different changes would be detected in association with tumors, immunologic response to infection or other stimulus. Spatial patterns will vary with pathological or physiological differences. Motion artifacts are used as an indicator of inhomogeneous distributions of oxygenation and perfusion. Increases or decreases in artifacts not related to motion are used to assess heterogeneity of oxygenation and perfusion, and, hence, viability.

[0048] The present invention may be used to look for signs of perfusion vs. viability. Integration of spatial and spectral and temporal features allows for the diagnosis of viability by creating a perfusion viability matrix. Because blood flow has a temporal component, the amount of blood that gets to tissue may be measured. This can be useful in the assessment of viability, cancer or infection.

[0049] In an embodiment of the present invention, images are correlated with pain and drug response to provide pain feedback with infusion; other drug levels, to provide positive/negative feedback. Surface heterogeneity is correlated with infection, to provide determine time of infection, severity, systemic vs. local infection, type of organism, bacterial vs. viral, gram positive versus gram negative The present invention is also used to detect drug usage.

[0050] The present invention may also be used for the assessment of metabolism and nutrition. Tissue structure and function, and hence signature, are influenced by nutritional status. The present invention may also be used to define adequacy of regional anesthesia or evaluation of pain response and the response to drug therapy with or without an automatic feedback component. It may also be used to identify and evaluate the presence of a drug substance and evaluate the initial response and/or therapeutic efficacy of a variety of pharmaceuticals. It can be used to track die agents and quantify their presence in association with blood flow parameters.

[0051] Other embodiments and uses of the invention will be apparent to those skilled in the art from consideration of the specification and practice of the invention disclosed herein. Reference is made to U.S. Patent Nos. 5,441,053, 5,553,614, 5,377,003, 5,528,368, 6,937,885, 6,741,884, and WO 99/22640 and WO 00/13578. The specification and examples should be considered exemplary only within the scope of the invention.

Claims

1. A multimodal imaging apparatus for examining changes in a dynamic system as a function of time comprising:

   a first collection device for collecting spectral data of a sample and for creating a hyperspectral data cube;
   a means for registering and analyzing multiple hyperspectral data cubes created over time;
   one or more additional collection devices for collecting thermal image data or other image modality data from said sample; and
   a means for fusing said multiple hyperspectral data cubes created over time with said thermal image data or other image modality data
   wherein the multiple hyperspectral data cubes comprise three dimensional arrays of data comprising data from two spatial dimensions and one spectral dimension.

2. The imaging apparatus of claim 1, wherein the other image modality data comprise data from one or more of visible or infrared hyperspectral images, visible or infrared brightfield images, fluorescence images, Raman images, and a combination thereof.

3. The imaging apparatus of claim 1 or 2, further comprising
   a means for integration of physiologic data with said multiple hyperspectral data cubes; and/or
   a means for integration of calibration data with said multiple hyperspectral data cubes.

4. The imaging apparatus of any of claims 1 to 3, further comprising a light source and, preferably, wherein the light source is a visible light source or an infrared light source.

5. The imaging apparatus of claim 4, wherein the light source emits a signal beam at one or more predetermined wavelengths and, preferably, wherein the imaging apparatus further comprises one or more beam splitters for splitting said signal beam into a plurality of wavelengths.

6. The imaging apparatus of any of claims 1 to 5, further comprising a collection optic that is an endoscope.

7. The imaging apparatus of any of claims 1 to 6, further comprising one or more inputs for signals from one or more instruments monitoring one or more biological functions of a patient and, preferably, wherein the one or more biological functions is selected from the group consisting of respiration, cardiac cycle, muscle contraction, heart rate, and a combination thereof.

8. The imaging apparatus of any of claims 1 to 7, further comprising:

a video camera; and/or
an on-board CCD chip filter, processing electronics to perform data operations prior to transmission of signal, and one or more inputs for physiological monitoring systems; and/or
one or more devices for image fusion and alignment, means for aligning optical paths, a video display for displaying data and for camera alignment and aiming, and a storage system for recording and logging real-time or near real-time output.

9. The imaging apparatus of any of claims 1 to 8, further comprising:

means for stabilizing and integrating said data and said image modality data in a temporally and geometrically dynamic environment; and/or
an image registration device to maintain image alignment; and/or
a reference frame device; and/or
a tracked imaging device comprising a means of creating a unified spatial mosaic of hyperspectral image cubes taken at one or more locations or times.

10. A method for analyzing a sample comprising the steps of:

collecting multiple hyperspectral data cubes over time, each respective hyperspectral data cube in the multiple hyperspectral data cubes comprising a plurality of spectral images of said sample;
registering each respective spectral image in the plurality of spectral images; and
registering one or more thermal images of said sample with said multiple hyperspectral data cubes taken over time,
wherein the multiple hyperspectral data cubes comprise three dimensional arrays of data comprising data from two spatial dimensions and one spectral dimension.

11. The method of claim 10, wherein the step of registering one or more thermal images of said sample with said multiple hyperspectral data cubes comprises registering a single thermal image with each respective hyperspectral data cube in the plurality of hyperspectral data cubes.

12. The method claim 10, wherein the step of registering one or more thermal images of said sample with said multiple hyperspectral data cubes comprises registering a thermal image with each respective spectral image in the plurality of spectral images.

13. The method of any of claims 10 to 12, further comprising the step of selecting a wavelength to obtain diagnostic information of said sample and, preferably, wherein the selection step is performed by one or more multivariate image and spectral processing algorithms to extract information from the plurality of spectral images for real-time or near real-time assessment.

14. The method of any of claims 10 to 13 wherein the sample is a biological sample and comprises skin, an organ, a tissue or combination thereof.

15. The method of any of claims 10 to 14, wherein total hematocrit is determined by measuring a spatial distribution of oxyhemoglobin, deoxyhemoglobin and methemoglobin of said sample and, preferably, wherein total blood volume is determined by further measuring perfusion data.

16. The method of any of claims 13 to 15, further comprising the step of gating each respective spectral image in the plurality of spectral images and the corresponding one or more thermal images to a biological function and, preferably, wherein the biological function is selected from the group consisting of cardiac cycle, breathing, pulse, muscle contraction, and a combination thereof.

17. The method of any of claims 10 to 16 wherein the method further comprises identifying a chemical species other than hemoglobin.

18. The method of any of claims 10 to 17, further comprising the step of using one or more automatic feature extraction techniques to localize landmarks in the multiple hyperspectral data cubes.

19. The method of claim 10, further comprising the step of registering a three dimensional spatial medical image with said multiple hyperspectral data cubes taken over time and, preferably, wherein the three dimensional spatial medical image is selected from the group consisting of MR, CT, PET, SPECT, ultrasound, and combinations thereof.

Patentansprüche

1. Ein multimodaler bildgebender Apparat zum Untersuchen von Veränderungen in einem dynamischen System als eine Funktion der Zeit, umfassend:

   ein erstes Sammelgerät zum Sammeln spektraler Daten einer Probe und zum Schaffen eines Hyperspektraldatenwürfels;
   ein Mittel zum Registrieren und Analysieren multipler Hyperspektraldatenwürfel, die über die Zeit geschaffen werden;
   ein oder mehrere zusätzliche Sammelgeräte zum Sammeln von Wärmebilddaten oder anderen Bildmodalitätsdaten von genannter Probe; und
   ein Mittel zum Fusionieren genannter multipler Hyperspektraldatenwürfel, die über die Zeit geschaffen wurden, mit genannten Wärmebilddaten oder anderen Bildmodalitätsdaten
   wobei die multiplen Hyperspektraldatenwürfel dreidimensionale Arrays von Daten umfassen, die Daten von zwei räumlichen Dimensionen und einer spektralen Dimension umfassen.

2. Der bildgebende Apparat von Anspruch 1, wobei die anderen Bildmodalitätsdaten Daten von einem oder mehreren von sichtbaren oder infraroten Hyperspektralbildern, sichtbaren oder infraroten Hellfeldbildern, Fluoreszenzbildern, Raman-Bildern, und eine Kombination davon umfassen.

3. Der bildgebende Apparat von Anspruch 1, weiter umfassend
   ein Mittel zur Integration physiologischer Daten mit genannten multiplen Hyperspektraldatenwürfeln; und/oder
   ein Mittel zur Integration von Kalibrierungsdaten mit genannten multiplen Hyperspektraldatenwürfeln.

4. Der bildgebende Apparat irgendeines der Ansprüche 1 bis 3, weiter umfassend eine Lichtquelle und, vorzugsweise, wobei die Lichtquelle eine Quelle sichtbaren Lichts oder eine Infrarotlichtquelle ist.

5. Der bildgebende Apparat von Anspruch 4, wobei die Lichtquelle einen Signalstrahl mit einer oder mehreren vorbestimmten Wellenlängen emittiert und, vorzugsweise, wobei der bildgebende Apparat weiter einen oder mehrere Strahlenteiler zum Teilen genannten Signalstrahls in eine Vielzahl von Wellenlängen umfasst.

6. Der bildgebende Apparat irgendeines der Ansprüche 1 bis 5, weiter umfassend eine Sammeloptik, die ein Endoskop ist.

7. Der bildgebende Apparat irgendeines der Ansprüche 1 bis 6, weiter umfassend einen oder mehrere Inputs für Signale von einem oder mehreren Instrumenten, die ein oder mehrere biologische Funktionen eines Patienten überwachen und, vorzugsweise, wobei die eine oder mehreren biologischen Funktionen ausgewählt ist aus der Gruppe bestehend aus Atmung, Herzzyklus, Muskelkontraktion, Herzfrequenz, und eine Kombination davon.

8. Der bildgebende Apparat irgendeines der Ansprüche 1 bis 7, weiter umfassend:

   eine Videokamera; und/oder
   einen On-Board-CCD-Chip-Filter, Prozessierungselektronik um Datenoperationen vor vor Signalübertragung durchzuführen, und ein oder mehrere Inputs für physiologische Überwachungssysteme; und/oder
   ein oder mehrere Geräte zur Bildfusion und -ausrichtung, Mittel zum Ausrichten optischer Wege, ein Videodisplay zum Zeigen von Daten und zur Kameraausrichtung und -Positionierung, und ein Speichersystem zum Aufneh-

men und Erfassen von Echtzeit- oder annähernd Echtzeit-Output..

9. Der bildgebende Apparat irgendeines der Ansprüche 1 bis 8, weiter umfassend:

Mittel zum Stabilisieren und Integrieren genannter Daten und genannter Bildmodalitätsdaten in einer temporär und geometrisch dynamischen Umgebung; und/oder
ein Bildregistrationsgerät um Bildausrichtung aufrechtzuerhalten; und/oder ein Referenzrahmengerät; und/oder ein Bildverfolgungsgerät umfassend ein Mittel zum Schaffen eines vereinheitlichten räumlichen Mosaiks von Hyperspektralbildwürfeln, die an einer oder mehreren Positionen oder Zeiten aufgenommen werden.

10. Ein Verfahren zum Analysieren einer Probe umfassend die Schritte von:

Sammeln von multiplen Hyperspektraldatenwürfeln über Zeit, wobei jeder jeweilige Hyperspektraldatenwürfel in den multiplen Hyperspektraldatenwürfeln eine Vielzahl spektraler Bilder genannter Probe umfasst;
Registrieren jedes jeweiligen spektralen Bildes in der Vielzahl spektraler Bilder; und Registrieren eines oder mehrerer Wärmebilder genannter Probe mit genannten multiplen Hyperspektraldatenwürfeln, die über die Zeit aufgenommen wurden,
wobei die multiplen Hyperspektraldatenwürfel dreidimensionale Anordnungen von Daten umfassen, die Daten von zwei räumlichen Dimensionen und einer spektralen Dimension umfassen.

11. Das Verfahren von Anspruch 10, wobei der Schritt von Registrieren eines oder mehrerer Wärmebilder genannter Probe mit genannten multiplen Hyperspektraldatenwürfeln Registrieren eines einzelnen Wärmebildes mit jedem jeweiligen Hyperspektraldatenwürfel in der Vielzahl von Hyperspektraldatenwürfeln umfasst.

12. Das Verfahren von Anspruch 10, wobei der Schritt von Registrieren eines oder mehrerer Wärmebilder genannter Probe mit genannten multiplen Hyperspektraldatenwürfeln Registrieren eines Wärmebildes mit jedem jeweiligen spektralen Bild in der Vielzahl von spektralen Bildern umfasst.

13. Das Verfahren irgendeines der Ansprüche 10 bis 12, weiter umfassend den Schritt von Auswählen einer Wellenlänge um diagnostische Information von genannter Probe zu erhalten und, vorzugsweise, wobei der Auswahlschritt durch einen oder mehrere multivariate Bild- und spektralprozessierende Algorithmen durchgeführt wird um Information von der Vielzahl spektraler Bilder für Echtzeit- oder annähernd Echtzeit-Bewertung zu extrahieren.

14. Das Verfahren irgendeines der Ansprüche 10 bis 13, wobei die Probe eine biologische Probe ist und Haut, ein Organ, ein Gewebe, oder Kombination davon umfasst.

15. Das Verfahren irgendeines der Ansprüche 10 bis 14, wobei totaler Hämatokrit bestimmt wird durch Messen einer räumlichen Verteilung von Oxyhämoglobin, Desoxyhämoglobin und Methämoglobin von genannter Probe und, vorzugsweise, wobei totales Blutvolumen weiter durch Messen von Perfusionsdaten bestimmt wird.

16. Das Verfahren irgendeines der Ansprüche 13 bis 15, weiter umfassend den Schritt von Ansteuern jedes jeweiligen spektralen Bildes in der Vielzahl spektraler Bilder und des korrespondierenden einen oder mehreren Wärmebildern zu einer biologischen Funktion und, vorzugsweise, wobei die biologische Funktion ausgewählt ist aus der Gruppe bestehend aus Herzzyklus, Atmung, Puls, Muskelkontraktion, und eine Kombination davon.

17. Das Verfahren irgendeines der Ansprüche 10 bis 16, wobei das Verfahren weiter Identifizieren einer chemischen Spezies außer Hämoglobin umfasst.

18. Das Verfahren irgendeines der Ansprüche 10 bis 17, weiter umfassend den Schritt von Verwenden einer oder mehrerer automatischer Merkmalauszugstechniken um Orientierungspunkte in den multiplen Hyperspektraldatenwürfeln zu lokalisieren.

19. Das Verfahren von Anspruch 10, weiter umfassend den Schritt von Registrieren eines dreidimensionalen räumlichen medizinischen Bildes mit genannten multiplen Hyperspektraldatenwürfeln, die über die Zeit aufgenommen wurden und, vorzugsweise, wobei das dreidimensionale räumliche medizinische Bild ausgewählt ist aus der Gruppe bestehend aus MR, CT, PET, SPECT, Ultraschall, und Kombinationen davon.

Revendications

1. Appareil d'imagerie multimodale pour examiner des modifications d'un système dynamique en fonction du temps, comprenant :

   un premier dispositif de collecte pour collecter les données spectrales d'un échantillon et pour créer un cube de données hyperspectrales ;
   des moyens pour recaler et analyser de multiples cubes de données hyperspectrales créés dans le temps ;
   un ou plusieurs dispositifs de collecte supplémentaires pour collecter des données d'images thermiques ou d'autres données de modalité d'images à partir dudit échantillon ; et
   des moyens pour fusionner lesdits multiples cubes de données hyperspectrales créés dans le temps avec lesdites données d'images thermiques ou autres données de modalité d'images
   dans lequel les multiples cubes de données hyperspectrales comprennent des matrices tridimensionnelles de données comprenant des données provenant de deux dimensions spatiales et d'une dimension spectrale.

2. Appareil d'imagerie selon la revendication 1, dans lequel les autres données de modalité d'images comprennent des données provenant d'un ou plusieurs types d'images parmi les images hyperspectrales visibles ou infrarouges, les images visibles ou infrarouges en fond clair, les images de fluorescence, les images de Raman et une combinaison de celles-ci.

3. Appareil d'imagerie selon la revendication 1 ou 2, comprenant en outre

   des moyens d'intégration des données physiologiques avec lesdits multiples cubes de données hyperspectrales ; et/ou
   des moyens d'intégration de données d'étalonnage avec lesdits multiples cubes de données hyperspectrales.

4. Appareil d'imagerie selon l'une quelconque des revendications 1 à 3, comprenant en outre une source de lumière et, de préférence, dans lequel la source de lumière est une source de lumière visible ou une source de lumière infrarouge.

5. Appareil d'imagerie selon la revendication 4, dans lequel la source de lumière émet un faisceau de signal à une ou plusieurs longueurs d'onde prédéterminées et, de préférence, dans lequel le dispositif d'imagerie comprend en outre un ou plusieurs séparateurs de faisceaux pour séparer ledit faisceau de signal en une pluralité de longueurs d'onde.

6. Appareil d'imagerie selon l'une quelconque des revendications 1 à 5, comprenant en outre une optique de collecte qui est un endoscope.

7. Appareil d'imagerie selon l'une quelconque des revendications 1 à 6, comprenant en outre une ou plusieurs entrées pour des signaux provenant d'un ou plusieurs instruments surveillant une ou plusieurs fonctions biologiques d'un patient et, de préférence, dans lequel les une ou plusieurs fonctions biologiques sont choisies dans le groupe constitué de la respiration, du cycle cardiaque, de la contraction musculaire, de la fréquence cardiaque, et d'une combinaison de ceux-ci.

8. Appareil d'imagerie selon l'une quelconque des revendications 1 à 7, comprenant en outre :

   une caméra vidéo ; et/ou
   un filtre embarqué à puce CCD, une électronique de traitement pour effectuer des opérations sur des données avant la transmission d'un signal, et une ou plusieurs entrées pour des systèmes de surveillance physiologique ; et/ou
   un ou plusieurs dispositifs de fusion et d'alignement des images, des moyens d'alignement de trajets optiques, un dispositif d'affichage vidéo pour afficher des données et pour l'alignement et l'orientation de la caméra, et un système de stockage pour enregistrer et consigner les sorties en temps réel ou en temps quasi réel.

9. Appareil d'imagerie selon l'une quelconque des revendications 1 à 8, comprenant en outre :

   des moyens pour stabiliser et intégrer lesdites données et lesdites données de modalité d'images dans un milieu temporellement et géométriquement dynamique ; et/ou

un dispositif de recalage d'image pour maintenir l'alignement des images ; et/ou
un dispositif de cadre de référence ; et/ou
un dispositif d'imagerie de suivi comprenant des moyens pour créer une mosaïque spatiale unifiée de cubes d'images hyperspectrales pris à un ou plusieurs lieux ou moments.

10. Procédé d'analyse d'un échantillon, comprenant les étapes suivantes :

la collecte de multiples cubes de données hyperspectrales dans le temps, chaque cube de données hyperspectrales respectif des multiples cubes de données hyperspectrales comprenant une pluralité d'images spectrales dudit échantillon ;
le recalage de chaque image spectrale respective de la pluralité d'images spectrales ; et
le recalage d'une ou plusieurs images thermiques dudit échantillon avec lesdits multiples cubes de données hyperspectrales pris dans le temps,
dans lequel les multiples cubes de données hyperspectrales comprennent des matrices tridimensionnelles de données comprenant des données provenant de deux dimensions spatiales et d'une dimension spectrale.

11. Procédé selon la revendication 10, dans lequel l'étape de recalage d'une ou plusieurs images thermiques dudit échantillon avec lesdits multiples cubes de données hyperspectrales comprend le recalage d'une seule image thermique avec chaque cube de données hyperspectrales respectif de la pluralité de cubes de données hyperspectrales.

12. Procédé selon la revendication 10, dans lequel l'étape de recalage d'une ou plusieurs images thermiques dudit échantillon avec lesdits multiples cubes de données hyperspectrales comprend le recalage d'une image thermique avec chaque image spectrale respective de la pluralité d'images spectrales.

13. Procédé selon l'une quelconque des revendications 10 à 12, comprenant en outre l'étape de sélection d'une longueur d'onde pour obtenir des informations de diagnostic dudit échantillon et, de préférence, dans lequel l'étape de sélection est effectuée par un ou plusieurs algorithmes de traitement d'images multivariées et de traitement spectral pour extraire des informations de la pluralité d'images spectrales à des fins d'évaluation en temps réel ou en temps quasi réel.

14. Procédé selon l'une quelconque des revendications 10 à 13, dans lequel l'échantillon est un échantillon biologique et comprend de la peau, un organe, un tissu ou une combinaison de ceux-ci.

15. Procédé selon l'une quelconque des revendications 10 à 14, dans lequel l'hématocrite total est déterminé par mesure de la répartition spatiale de l'oxyhémoglobine, de la désoxyhémoglobine et de la méthémoglobine dudit échantillon et, de préférence, dans lequel le volume sanguin total est déterminé en outre par la mesure des données de perfusion.

16. Procédé selon l'une quelconque des revendications 13 à 15, comprenant en outre l'étape de synchronisation de chaque image spectrale respective de la pluralité d'images spectrales et de l'une ou plusieurs images thermiques correspondantes avec une fonction biologique et, de préférence, dans lequel la fonction biologique est choisie dans le groupe constitué du cycle cardiaque, de la respiration, du pouls, de la contraction musculaire, et d'une combinaison de ceux-ci.

17. Procédé selon l'une quelconque des revendications 10 à 16, dans lequel le procédé comprend en outre l'identification d'une espèce chimique autre que l'hémoglobine.

18. Procédé selon l'une quelconque des revendications 10 à 17, comprenant en outre l'étape d'utilisation d'une ou plusieurs techniques d'extraction automatiques pour localiser des repères dans les multiples cubes de données hyperspectrales.

19. Procédé selon la revendication 10, comprenant en outre l'étape de recalage d'une image médicale spatiale tridimensionnelle avec lesdits multiples cubes de données hyperspectrales pris dans le temps et, de préférence, dans lequel l'image médicale spatiale tridimensionnelle est choisie dans le groupe constitué de la résonance magnétique, de la tomodensitométrie, de la tomographie par émission de positons, de la tomographie d'émission monophotonique, des ultrasons et de leurs combinaisons.

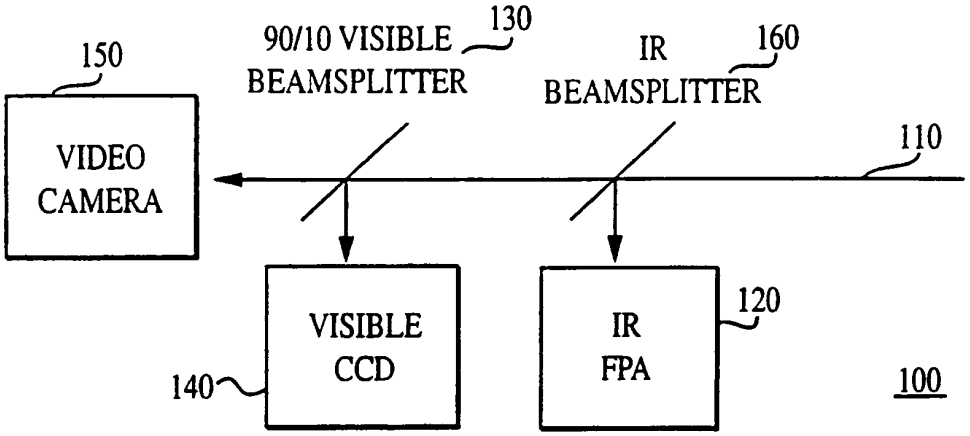
150
90/10 VISIBLE
BEAMSPLITTER
130
IR
BEAMSPLITTER
160
110
VIDEO
CAMERA
VISIBLE
CCD
140
IR
FPA
120
100

FIG.1

REFERENCES CITED IN THE DESCRIPTION

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专利名称(译)	集成成像设备		
公开(公告)号	EP1196081B1	公开(公告)日	2013-08-21
申请号	EP2000943361	申请日	2000-07-03
[标]申请(专利权)人(译)	超级医药成像有限公司		
申请(专利权)人(译)	超声波成像有限公司		
当前申请(专利权)人(译)	HYPERMED IMAGING，INC.		
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发明人	FREEMAN, JENNY, E. LEVENTON, MICHAEL HOPMEIER, MICHAEL J. MANSFIELD, JAMES LEWIS, EDGAR N.		
IPC分类号	A61B5/00 A61B10/00 A61B5/103 A61B5/145 A61B5/1455 G06T1/00		
CPC分类号	A61B5/442 A61B5/0059 A61B5/0071 A61B5/0073 A61B5/0077 A61B5/015 A61B5/14535 A61B5/1455 A61B5/415 A61B5/418 A61B5/441 A61B5/444 A61B5/445		
代理机构(译)	Grund的，MARTIN		
优先权	60/142067 1999-07-02 US		
其他公开文献	EP1196081A2		
外部链接	Espacenet		

摘要(译)

本发明涉及用于执行实时或近实时评估和监视的成像设备。该装置的实施例可用于多种设置，包括手术，临床程序，组织评估，诊断程序，法医，健康监测和医疗用途。