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(54) Title: SYSTEM AND METHOD FOR USING COLOR CHERENKOV IMAGING AND COLOR REFLECTANCE IMAGING TO CORRECT AND MAP RADIATION DOSAGE AND MONITOR RADIATION DAMAGE DURING RADIATION TREATMENTS

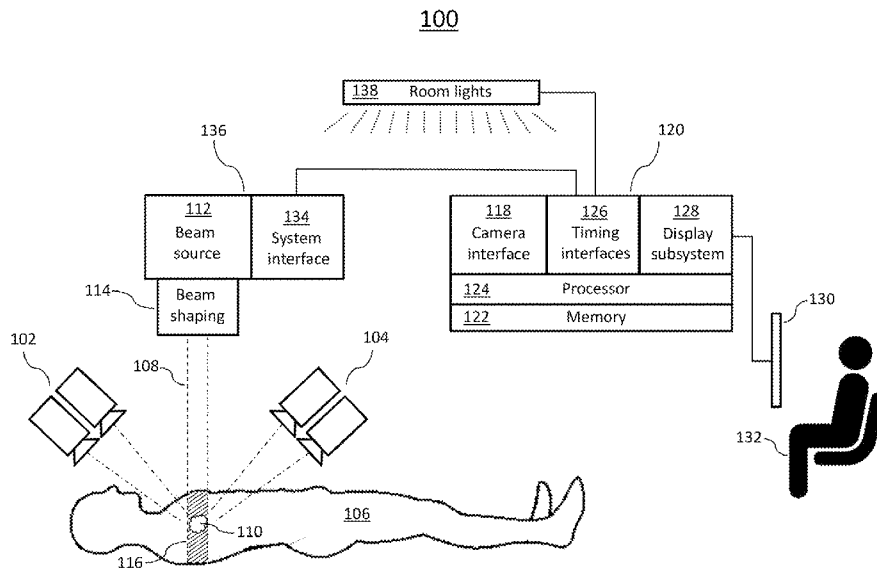


Fig. 2

(57) Abstract: A radiation treatment observation system has a camera configured to image Cherenkov light emissions in multiple spectral bands including a band having a center wavelength between 750 and 900 nanometers from a treatment zone to generate Cherenkov images, and an image processor. The image processor determines Cherenkov spectral correction parameters at pixels of the Cherenkov images based on differences between imaged intensity of Cherenkov light in the spectral bands at pixels of the Cherenkov images, and determines a corrected dosage map of the subject based upon at least the Cherenkov images and the Cherenkov spectral correction parameters. A method of monitoring radiation treatment of diffuse media includes determining surface coloration; determining subsurface optical parameters; and using the surface color and optical parameters, determining dose correction functions. The method includes

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obtaining and totalizing color Cherenkov images, and using the dose correction function to give corrected dose images.

**SYSTEM AND METHOD FOR USING COLOR CHERENKOV IMAGING AND COLOR REFLECTANCE
IMAGING TO CORRECT AND MAP RADIATION DOSAGE AND MONITOR RADIATION DAMAGE
DURING RADIATION TREATMENTS**

Government Rights

[0001] This invention was made with government support under grant number R01 EB023909 awarded by the National Institutes of Health (NIH). The government has certain rights in the invention.

Cross Reference to Related Applications

[0002] The present application claims priority to U.S. Provisional Patent Application 63/523,860. Background information for the present case, such as the use of optical imaging of Cherenkov radiation to estimate radiation dose received by a subject, can be found in Patent Application PCT/US19/14242 filed January 18, 2019. The entire contents of the aforementioned provisional patent application and PCT/US19/14242 are incorporated herein by reference.

[0003] Background information for the present case, such as the use of optical imaging of Cherenkov radiation to estimate radiation dose received by a subject, can be found in Patent Application PCT/US19/14242 filed January 18, 2019. The entire contents of PCT/US19/14242 is incorporated herein by reference for disclosure purposes. Additional background information can be found in Color Cherenkov imaging of clinical radiation therapy, Daniel A Alexander, Anthony Nomezine, Lesley A Jarvis, David J. Gladstone, Brian W. Pogue and Petr Bruza, Science & Applications (2021) 10:226 (Alexander), incorporated herein by reference for disclosure purposes.

Background

[0004] Patients are often exposed to high energy beams of ionizing radiation during radiation treatment of cancers, and for other purposes. Such treatments are typically planned to irradiate particular portions of the patient with beams of predetermined shape, and to verify that the actual beams have that predetermined shape. During radiation treatments for cancer, it is desirable to verify the radiation dose received by the patient matches planned dosage since underdosing may permit survival and regrowth of cancer cells, and overdosing may cause excessive damage to noncancerous tissues leading to debility or other consequences including possible patient death.

[0005] High energy radiation beams of charged particles, such as ions or electrons, having velocities below that of light in a vacuum but above that of light in patient tissues, interact with patient tissues to produce Cherenkov light emissions, PCT/US19/14242 discussed capturing images of these light emissions with an electronic camera synchronized to pulses of pulsed radiation beams and using

those images to map the interface of beam to tissue and estimate skin dosage. Similarly, high energy gamma radiation beams may cause ionization in patient tissues, some of these ions being fast enough to produce Cherenkov light.

[0006] Both Cherenkov light generated by radiation beams interacting with tissue of a patient, and radiation of the radiation beams themselves, can also cause some scintillation within, and excite endogenous or exogenous fluorophores within the patient, causing additional optical emissions from the patient.

[0007] Materials that scintillate when exposed to radiation beams have also been applied to a patient. When these materials are used, they may also be optically imaged to map beam shape and estimate radiation dose administered to the patient.

[0008] While some Cherenkov light and other light emissions from a patient exposed to radiation treatments is from skin, radiation beams of high energies can penetrate deep into the body—not all light generated by beams interacting with the patient is generated in the skin. Light generated by beam-tissue interactions both at skin level and deep within a patient may be scattered or attenuated as light propagates to and through the skin. We have previously shown in Alexander, that it is possible to image Cherenkov emissions in color with a three-color, intensified, camera. We proposed in Alexander that, since tissue blood concentration and oxygen saturation can affect color of Cherenkov emissions, it may be possible to monitor erythema in patients undergoing radiation treatments. We also observed a general trend of decreasing Cherenkov intensity during the radiotherapy course as shown in Fig. 3.

Summary

[0009] In a first embodiment, A radiation treatment observation system has an optical camera system configured to image Cherenkov light emissions from a treatment zone to generate Cherenkov images, the optical camera system being configured to record light intensity separately in each of a plurality of spectral bands including a spectral band having a center wavelength between 750 and 900 nanometers, and an image processor. The image processor determines Cherenkov spectral correction parameters at pixels of the Cherenkov images based on differences between imaged intensity of Cherenkov light in the spectral bands at pixels of the Cherenkov images, and determine a corrected dosage map of the subject based upon at least the Cherenkov images and the Cherenkov spectral correction parameters.

[00010] In another embodiment, A radiation treatment observation system includes an optical camera system configured to image Cherenkov light emissions from the treatment zone to generate Cherenkov images, the optical camera system configured to record light intensity separately in each of several spectral band including at least one spectral band having a center wavelength between

750 and 900 nanometers, and where spectral Cherenkov images from an initial treatment session are stored in a database as initial spectral Cherenkov images, and the image processor is configured to compare current spectral Cherenkov images to the initial spectral Cherenkov images to determine tissue response images.

[00011] In another embodiment, A method of monitoring radiation treatment of diffuse media includes determining skin or surface coloration from color images; determining subsurface optical parameters of the diffuse media; obtaining color or hyperspectral Cherenkov images of the diffuse media with a high-sensitivity camera; using determined skin or surface coloration and subsurface optical parameters of the diffuse media, determining dose correction functions; totalizing the color Cherenkov images to prepare a totalized color Cherenkov image; and applying the determined dose correction function to the totalized color Cherenkov images to give corrected dose images.

Brief Description of the Figures

[00012] Figs 1A-1D are PRIOR ART as published in Alexander. Fig. 1A illustrates a patient subject to radiation treatments while being observed by a camera. Fig. 1B illustrates gated camera timing synchronized to radiation pulse timing through an intensifier gate, Fig. 1C is a photograph of a prototype tricolor, intensified, gated, camera capable of color imaging of Cherenkov radiation emissions, and Fig. 1D is a block diagram of the camera of Fig. 1C.

[00013] Fig. 2 is a block diagram illustrating a system having multiple cameras disposed to view an intersection of a pulsed radiation beam with a subject.

[00014] Fig. 3 is a plot of relative observed Cherenkov light emissions intensity versus treatment session for a number of patients illustrating that Cherenkov intensities as observed by a camera tend to decrease with successive treatments because of increased light absorption in the patient.

[00015] Fig. 4 is an illustration of wavelength dependence of light absorption of various chromophores in tissue.

[00016] Fig. 5A-5E are illustrations of multiple alternative imaging systems such as may also be used to provide a color or hyperspectral image stack.

[00017] Fig. 6 is an illustration of a camera that uses four filters having different passband characteristics with a prism to direct images through each filter to different regions of a common image sensor.

[00018] Fig. 7 illustrates absorption of Cherenkov light by melanin in skin.

[00019] Fig. 8 is a flowchart of the herein-disclosed method of determining a corrected dose map and, if necessary, aborting treatment when a maximum dose threshold is reached or a significant deviation from planned dose is reached.

[00020] Fig. 9A is an illustration of loss versus wavelength for several substances, including oxygenated and deoxygenated hemoglobin, fat, and water, with expected Cherenkov source spectra.

[00021] Fig. 9B is an illustration of a sample loss spectra for a composite media including the substances of Fig. 9A and showing a composite emissions spectrum for the composite media.

Detailed Description of the Embodiments

[00022] We desire to use optical sensors such as cameras to quantitatively map and determine radiation dose received by patients exposed to radiation treatments. We also desire to monitor the inter-fraction change of these spectral correction factors to predict radiation toxicity.

Issues with Prior Systems

[00023] The accuracy of quantitative optical sensing is heavily dependent on the presence of confounding effects that alter the light transport from a target, such as tissue of a patient, under observation to the optical sensor. The disclosed device particularly applies to Cherenkov and scintillation imaging as used for dosimetry and beam shape mapping in radiotherapy, where clinically acceptable accuracies of detectors may lie in the range of 1%-5% of maximum allowed standard deviation.

[00024] Optical signals, such as light emitted from tissue of a patient exposed to a radiation beam, are susceptible to photon absorption and scattering, especially in complex targets such as human body, and in complex environments such as treatment rooms. In certain cases of optically-based radiation dosimetry (Cherenkov imaging, scintillation imaging), the detected optical photon fluence is linear with local dose. However, the confounding effects of photon absorption, scattering, reflection, and refraction induce inaccuracies in this optical fluence-dose linearity. Other confounding factors include spatially varying light source distributions due to, for example, radio-therapeutic beam depth-dose curves and varying beam energy. We address this unwanted optical alteration utilizing differences in magnitude of such optical alterations of light at different wavelengths and/or polarization states. Our system is capable of quantifying the extent of such alteration and correcting the detected optical signals in order to re-establish an optical fluence-dose linearity to better permit dose estimation.

[00025] We also monitor changes in both normal and tumor tissue over the course of radiation treatment to better assess treatment progress and to predict toxic effects of radiation on tissues. It is known that tissue biologic factors, such as melanin, deoxygenated hemoglobin and oxygenated

hemoglobin differentially absorb specific wavelengths of light and therefore emitted light spectra during Cherenkov imaging depends on the levels of each. Radiotherapy may induce both early and late toxicity, compromising quality of life of the patients. By example, fibrosis is an important late complication that can be detectable at the onset of radiotherapy. It was demonstrated that early grade 3 radiation dermatitis and increasing N stage assessed at the end of RT can be an accurate predictor of late toxicity, specifically fibrosis at 6 months. Radiation dermatitis is one of the most common side effects of radiotherapy for cancer, in which the skin changes include erythema, edema, pigmentation change, and others. While any of these dermatitis effects occur in over 90 percent of patients receiving radiotherapy, the rate at which the erythema and pigmentation change occurs is hypothesized to correlate with late toxicities such as fibrosis. As most of these dermatitis effects involve increased blood flow and change in oxygenation, it is hypothesized that change between treatment session in spectrally-resolved Cherenkov signals are a quantitative surrogate of acute radiation dermatitis, and that they correlate with late toxicities in patients.

Imaging System

[00026] FIG. 2 schematically depicts portions of an illustrative external-beam radiation therapy system 100. System 100 provides context relevant to various embodiments described herein. In particular, system 100 depicts high-sensitivity electronic cameras or groups of cameras 102, 104 used to image Cherenkov light and/or light emitted by fluorescent substances (fluorophores) excited by Cherenkov light and to localize locations on or in a human subject 106, or other diffuse media such as a phantom, positioned in a treatment zone and exposed to a radiation beam from where this light is emitted. In certain embodiments, the subject 106 is located in the treatment zone within an environment from which light from uncontrolled sources, such as the sun and incandescent lamps, is excluded or minimized. In the system 100 depicted in FIG. 1, the subject 106 is placed in the path of a radiation beam 108 so that the beam 108 irradiates a tumor 110. Beam 108 is provided by a radiation beam source 112, e.g., a particle accelerator or other device for providing high-energy radiation, and typically is cross-sectionally shaped by a beam-shaping apparatus such as a multi-leaf collimator.

[00027] In the illustrative system 100 of FIG. 2, the source 112 is an accelerator that provides a beam 108 of X-rays having energy spectrum corresponding to Bremsstrahlung emission spectrum generated by electrons of between 4 million electron volts (4 MeV) and 24 MeV, such as is used to deliver treatment energy to deep tumors as opposed to treatment of surface skin. Alternative embodiments may use an electron beam with energies of between 4 million electron volts (4 MeV) and 24 MeV or a high-energy proton beam source (with proton energies of 50 MeV to 250 MeV) instead of a radio-therapeutic x-ray source. In general, various embodiments are combined with

therapeutic radiation systems that produce beams capable of inducing Cherenkov radiation emission in human tissue, including but not limited to systems described explicitly herein.

[00028] In certain embodiments similar to system 100, cameras 102, 106 image the subject 106 from fewer or more points of view than are depicted in FIG. 2, or non-stereoscopic cameras are used, or a single camera is arranged to move to more than one position with respect to the subject, or the subject 106 is supported in a manner that permits their rotation with respect to one or more cameras, or some combination of one or more of these or other imaging arrangements is employed. Cherenkov and/or fluorescent radiation emission occurs where the tissues (or tissue equivalent) of the subject 106 are irradiated by the beam 108, a volume herein termed the emission volume 116. Fluorescent light emissions can be induced by Cherenkov-light excitation of fluorophores in tissue, where such fluorophores are present.

[00029] In some embodiments, either the subject or the radiation source is positioned in a rotating apparatus so that it can provide a beam to the subject (also known as a patient) from more than one angle, use of a rotator can spread out radiation dosage accrued by normal tissues while still providing adequate treatment dosages to a tumor.

[00030] In certain embodiments, the cameras 102, 104 are aimed to image at least part of the emission volume 116 and are coupled to a camera interface 118 of an image-processing system 120. Camera connections to the camera interface 118 may be wired or wireless and are not depicted in FIG. 2 for clarity. Herein, in certain embodiments, camera connections may serve both to transfer image data from a camera to the camera interface 118 and to convey commands (e.g., for setting shutter timing, exposure) from the camera interface 118 to the camera. In certain embodiments similar to system 100, light-modifying components such as optical filters and image intensifiers are aligned with cameras, or included in cameras, to intensify and/or selectively admit Cherenkov and/or fluorescence light; however, such light-modifying devices are omitted from FIG. 1 for simplicity. The camera interface 118 captures and stores digital images from the cameras 102, 104 in memory 122 for later retrieval and processing by at least one processor 124 of the image processing system 120. The processor 124 can exchange information not only with the camera interface 118 and memory 122 but with a timing interface 126, a display subsystem 128, and potentially other devices as well. The processor 124 can provide an interlock signal to the radiation source in order to halt the radiation emission in at least one of the cases of overdose and dose delivered to unplanned tissue is detected and evaluated by the camera system. The display subsystem 128 communicates with a user interface 130 through which a user 132 can interact with the imaging-processing system 120. In certain embodiments, timing interface 126 is adapted to communicate with a system interface 134 of the radiation therapy device 136 to determine timing of pulses of radiation from the source 112 and

to control pulsed room lighting 138 to mitigate interference from room lighting during imaging of Cherenkov emissions and/or fluorescence by synchronizing lighting with image capture by cameras 102, 104, as discussed below.

[00031] In certain embodiments of the system 100 of FIG. 2, the imaging system cameras 102, 104 are spectrally-sensitive cameras capable of providing spectral data permitting distinction between Cherenkov and fluorescent light. Emitted Cherenkov and fluorescent light is subject to attenuation by absorbance as it propagates through and emitted by tissue, and in some embodiments spectrally-sensitive cameras permit distinction between light absorbed by oxyhemoglobin and by deoxyhemoglobin by determining ratios of absorbance at two or more wavelength bands.; the two or more wavelength bands may include two or more bands between having wavelengths centers between 600 and 800 nanometers.

[00032] In certain embodiments of the systems, for example in the system 100 of FIG. 2, raw or de-noised images from the imaging system are recorded in one or more suitable digital memory systems (e.g., memory 122) as documentation of the radiation treatment.

[00033] In embodiments, ordinary color cameras are provided that can image a subject in addition to high sensitivity cameras that can image relatively dim Cherenkov light.

[00034] Figs 1A-1D are PRIOR ART as published in Alexander. Fig. 1A illustrates a patient subject to radiation treatments while being observed by a camera. Fig. 1B illustrates gated camera timing synchronized to radiation pulse timing through an intensifier gate as has been done with intensified cameras to reduce interference from background light. Fig. 1C is a photograph of a prototype tricolor, intensified, gated, camera capable of color imaging of Cherenkov radiation emissions. Fig. 1D is a block diagram of the gated, color, intensified camera of Fig. 1C showing image splitters that divert red light into a red intensified camera, blue light into a blue intensified camera, and allow green light into a green intensified camera. This imaging system is described in Alexander. The red, green, and blue intensified cameras provide a red, a green, and a blue color layer of a color image stack for image analysis.

[00035] The imaging system of Figs. 1A-1D can be modified by insertion of filters in the green path, and by replacement of the beam-splitting dichroic mirrors for the red and blue paths, with beam splitters and filters for other wavelengths; in principle the system can also be expanded with additional beam splitters, such as a third beamsplitter, and a fourth intensified, gated, camera to provide a fourth color layer, such as an infrared color layer of a color or hyperspectral image stack. Further, with appropriate filters and beam-splitting optics, imaging may provide four wavelength channels at four selected wavelengths anywhere in the near infrared through the visible spectrum as described below.

[00036] We anticipate alternative imaging systems as illustrated in Fig. 5 are possible that can also provide color or hyperspectral image stacks, although some imaging system types provide images of each color layer sequentially, rather than in parallel as is possible with the system of Figs. 1A-1D. For example, a filter-changer or filter-wheel imager 202 (Fig. 5A) provides a repeating sequence of images each associated with a color layer of the color or hyperspectral image stack but cannot continuously monitor treatment in all colors at once; similarly a system that replaces the filter-changer or filter-wheel with a tunable filter can prepare a color or hyperspectral image stack with excellent resolution of wavelengths, but cannot continuously monitor treatment in all colors at once. The system of Figs. 1A-1D is essentially a beam-splitter color or hyperspectral imager 212 as illustrated in Fig. 5B and can continuously monitor treatment in all colors for which a beam-splitter and imager are provided, as can a multiple-camera system 222 as illustrated in Fig. 5C. The multi-camera system 222, however, typically requires a parallax adjustment to provide full-color imaging. [00037] A prism-based system 232 (Fig. 5D), also illustrated in Fig. 6, with multiple filters 234, 236, that combines separate wavelength bands into different portions of a single camera 238 image sensor, may also continuously monitor treatment.

[00038] Camera embodiments 202, 212, 222, and 232 may be built with gated, intensified, cameras. In alternative systems, single-photon avalanche photodiode array (SPAD)-based time-gated cameras may be used in camera embodiments similar to 202, 212, 222, and 232, but may also be built with a Bayer-pattern-like tiling pattern of three, four, six, nine, or more filters of different wavelength characteristics deposited directly on a semiconductor array. Similarly, a high-sensitivity, multi-pulse-integrating, CMOS photosensor may be used in any of the herein-described embodiments including Bayer-pattern-like embodiments.

[00039] In all embodiments, the cameras have high photon sensitivity to resolve Cherenkov emissions because these emissions are fairly dim. The cameras are configured to record light intensity separately in each of a pre-defined plurality of spectral bands.

[00040] A subject is placed in the path of a high-energy radiation beam so that the beam irradiates a tumor. The beam is provided by a radiation beam source, such as a particle accelerator or other device for providing pulsed or continuous high-energy radiation, and typically is cross-sectionally shaped by a beam-shaping apparatus such as a multi-leaf collimator.

[00041] The optical imaging system or cameras captures image information of optical signals from targets, such as a phantom or tissue, which are subject to radiation dose deposition, for the purpose of evaluating the dose deposited to the target and determining physiological parameters of irradiated tissue. Some of these optical signals are incited by radiation dose deposition in targets – this can be Cherenkov emission and fluorescence from the subject, as well as scintillation emissions

from scintillators placed in the beam. These emissions are altered by propagation through overlying diffuse media such as phantom material, tissue and/or skin before reaching the cameras. The optical alteration of the image signals typically involves one or more of: photon absorption, scattering, reflection, refraction, spectrally distributed absorption and scattering, and polarization filtering, and vary with the types of diffuse media such as tissues or phantom material through which the light propagates, as illustrated in Fig. 4 and Fig. 9A. These effects alter “color,” or the wavelength distribution, at each pixel of the image from an original wavelength distribution expected of Cherenkov and fluorescent emissions.

[00042] In embodiments, these intensity differences are caused by local absorption and scattering of light generated within the target. In embodiments, this light is incited by Cherenkov effect in the target due to the presence of high-energy charged particles. In such embodiments, at a given beam energy, the generated light is proportional to radiation dose, but as this light (i.e., optical photons in the ultraviolet through short-wave or near infrared range) undergoes absorption and scattering events within the target, the light detected by the camera is no longer proportional to dose; instead, it is proportional to a combination of dose and local diffuse media or tissue optical properties. This method uses diffuse media or tissue optical properties to evaluate the extent this light absorption and scattering, such as local attenuation of the optical signal, in order to establish a correction parameter that can be applied to the detected light to correct for the effect of absorption and scattering, thereby enabling the observer to more accurately use the detected optical images to estimate radiation dose deposited in the target whether the target be a phantom or a patient.

[00043] In embodiments, the imaging system provides imaging at a plurality of wavelength bands in the range 600 to 900 nanometers wavelength, including in many embodiments at least one wavelength bands centered at a wavelength of at least 750 nanometers. In an alternative embodiment, at least two wavelength bands centered at wavelengths between 580 and 900 nanometers. In a low cost embodiment focused on observing radiation effects and likely less accurate for dose estimation than embodiments with three or more spectral bands, only two wavelength bands having centers between 580 and 900 nanometers are used.

[00044] The imaging at the plurality of wavelength bands is read from cameras 102, 104 through camera interface 118 and input to image processor 124. Image processor 124 executes firmware in memory 122 to execute the method of using this spectrally resolved optical information and target optical properties to calculate depth of the optical photon emissions. In an embodiment, the method allows for indirect optical signal-to-dose calibration by the means of a pre-established correction function. The method also can utilize this spectral information to estimate the dose deposited to the

target at certain depth within the target. This method also allows to estimate the energy of the radiation beam impinging on the target.

[00045] In embodiments, the method utilizes this spectrally resolved optical information to calculate target optical properties and depth of the optical photon propagation and determine a dose correction function therefrom. In other embodiments, the method allows for indirect optical signal-to-dose calibration by the means of a pre-established dose correction function. The method also can utilize this spectral information to estimate the dose deposited to the target at certain depth within the target. This method also allows estimating energy of the radiation beam impinging on the target.

[00046] In some embodiments, the method uses this spectrally resolved optical information to extract wavelength-dependent absorption coefficients in the target, and to use these absorption coefficients to map both oxygenated and deoxygenated hemoglobin concentrations in the target.

[00047] The image processor that receives images from the imaging system of Figs. 5A-5E totalizes Cherenkov images from each treatment session to produce a raw, totalized, Cherenkov image that can then be corrected to represent radiation dose at pixels using the dose correction function.

[00048] In embodiments, the presented system and method utilizes this tissue optical property correction function to correct the raw Cherenkov image and present a dosage map of the surface and sub-surface dose to clinical staff during radiotherapy treatment. The method also compares the optically estimated dose to the planned dose and presents deviation of actual versus planned dose at certain depths in tissue. The method also utilizes the spectral information to improve the spatial resolution of the images. In other embodiments, the spectral information takes form of red-green-blue information that is presented to the user in the form of a color image.

[00049] The system consists of a camera equipped with at least one optical sensor and at least one wavelength-selective filter (further "filters"), configured to allow wavelength discrimination of received light, and a signal processor. In embodiments, the filters are optical bandpass filters. In some embodiments the filters are in form of a Bayer-pattern filter array deposited on an image sensor integrated circuit within one or more of cameras 102, 104.

[00050] In some embodiments, the system has a plurality of sensors, each equipped with optical filters having different wavelength pass characteristics such as bandpass filters passing different wavelength bands.

[00051] In other embodiments, an image-splitting optical component such as a prism 602 (Fig. 6), a cross section 602A is shown, is used to project the same image field-of view through lens 604 and a single image intensifier 606 onto different regions of a single optical sensor 608. In such case, the optical filter is in multiple sections and designed in a way that it allows different spectral bands to be detected by these individual regions of image sensor.

[00052] In yet another embodiment, the filters are embedded in each pixel of the imaging sensor in a repeating pattern. Such pattern can be an RGB (red-green-blue) Bayer pattern, an RGBI (red-green-blue-infrared) pattern, a custom pattern where the pixels detect different spectral bands within the range of 550 nm – 900 nm; in particular embodiments at least one spectral band is used that is centered at a wavelength between 750 and 900 nanometers. In another embodiment, this filter is realized by at least one of the following: a filter wheel, or an electrically tunable optical filter.

[00053] The optical sensors used in this system are typically one of the following: gated CMOS such as 2-tap and 3-tap multi-pulse-integrating CMOS, gated intensified CMOS image sensors, single-photon avalanche photodetector (SPAD) image sensors, and quantitative CMOS (QCMOS) image sensors.

[00054] Fig. 7 illustrates the effect melanin in skin can have on Cherenkov emissions from a subject exposed to high energy radiation as viewed by a camera; it shows about a 14:1 difference in observed Cherenkov intensity from the palest skin to the darkest despite a constant radiation dose. The system typically also has at least one reflectance camera or sensor capable of capturing a target or subject's surface reflectance. Such surface reflectance is utilized as a surrogate quantity to melanin content and/or erythema in skin of a patient undergoing radiotherapy to make corrections for absorbance of Cherenkov light by melanin and hemoglobin. This reflectance is captured either at a specific wavelength band, or as spectrally resolved reflectance maps each at a different wavelength band. To image the reflectance, the system requires a controllable light source. This light source can be at least one of the following: room lights, additional light in the room, or a light projector that is a part of the presented system (further "projector"). The projector includes a light source (led, laser, bulb) whose emission spectrum overlaps at least one of the wavelengths used in at least one of the camera's sensors. In some embodiments, the imaging system is equipped with a controllable structured-light projector adapted to provide a sequence of at least three phases of each of a plurality of spatial wavelengths; the reflectance camera being configured to capture structured light images of the target or subject as illuminated by each phase of each spatial wavelength; the processor is then configured to map optical properties of the target in three dimensions from the structured light images in the manner known in the optical medical imaging art as structured light depth imaging (SFDI). In other embodiments, such SFDI projector is a single pattern projector wherein the spatial pattern is pseudo-random noise pattern containing a plurality of spatial frequencies and thus allows recovery of optical properties of the skin.

[00055] We have found that applying a correction factor derived from a linear fit of skin reflectance to received Cherenkov light intensity gives significantly more accurate radiation dose estimates than received Cherenkov light intensity alone.

[00056] The projector can be emitting constantly, or it can be pulsed (time-gated). In the time gated mode (pulsed source), the projector on-time can be timed prior or following the Cherenkov + scintillation + fluorescence signal, such that it does not interfere with the Cherenkov images from the target or patient. In embodiments, a polarizer is added to remove specular reflections. In embodiments, the camera and projector are synchronized, and such synchronization signal is used to mute room lights in systems that use gated room lighting.

Methods for estimating optical correction factors

[00057] The system and method use a plurality of spectrally-resolved images obtained by the imaging system. Further, it relies on the assumption that some optical properties of the target, including absorption and scattering coefficients, are different for respective spectral bands of each image. These images are geometrically aligned such that the pixels in each image record the light emanating from similar topological area of the target.

[00058] Then, at least one spectral quantity such as intensity ratio between two spectrally-different images is calculated for each pixel group of size of at least one pixel in the image, to form a spectral quantity map. Next, the spectral quantity map is used as an input to a dose evaluation algorithm.

[00059] In certain embodiments, the image analysis workflow includes the following order: image acquisition -> image digitization -> darkfield correction -> spatial pixel-to-pixel alignment -> spectral quantity map evaluation -> estimation of dose correction factor from an existing look-up table -> intensity-to-dose correction. In embodiments, the darkfield correction is followed by a flat-field correction. The following analysis workflow can be utilized to convert multispectral image to dose:

- 1) Cherenkov emission during irradiation is imaged using an array of pre-determined number i of spectral filters (central wavelength denoted by $I(\lambda)$ and spectral bandwidth of 10 to 100 nm). In particular embodiments the spectral bandwidth is 50 nm.
- 2) Image data corresponding to each filter is isolated into individual grayscale images (denoted by $I(\lambda_i)$); number of filters (thus images with different wavelength sensitivity bands) must be one more than the number of components corrected for;
- 3) At least one spectral image is selected as a normalization factor to remove influence of relative dose (denoted by $I(\lambda_j)$, $j = i-1$), and at least one image is selected as a pre-correction map that is to be converted into dose (denoted by $I(\lambda_{ref})$, further reference image);
- 4) For each component (j), an input image $I(\lambda_i)$ is divided by the normalization wavelength image $I(\lambda_j)$ yielding the ratio image $I(\lambda_i)/I(\lambda_j)$

- 5) The ratio image is converted to a correction factor image (K) using a pre-defined correction function $K = f(I(\lambda_i), I(\lambda_j))$ acting on each pixel in images $I(\lambda_j)$
- 6) The initial reference image $I(\lambda_i)$ is scaled by the correction factor image (K) to get the corrected intensity image $I_{corr} = I(\lambda_i) * K$
- 7) The corrected intensity image I_{corr} is directly related to dose using a known intensity-dose translation factor for a given beam energy;
- 8) The dose image D is calculated by scaling the corrected image I_{corr} by intensity-to-dose correction factor.

[00060] In particular embodiments, filters from the following table of central wavelength and bandwidth are used:

Central (nm)	Bandwidth (nm)
550	90
600	40
650	80
695	50
710	40
800	50

Table 1

[00061] In certain other embodiments, filters from the following table of central wavelength and bandwidth are used:

Central (nm)	Bandwidth (nm)
625	50
675	50
725	50
800	50

Table 2

[00062] In yet another embodiment, filters from the following table of central wavelength and bandwidth were used:

Central (nm)	Bandwidth (nm)
600	50
650	50
700	50
750	50
800	50

Table 3

[00063] Certain algorithms perform first step of converting optically affected Cherenkov image to optically unaffected Cherenkov image by employing correction function f. This correction function

must be evaluated prior the intended use by the means of calibration, i.e. by using one of the following: phantom measurement, numerical simulation, tissue measurement. Function f is found in embodiments by fitting an arbitrary smooth function to the set of sparsely acquired data using minimization algorithm; such function can be a higher order polynomial function. The dimensionality of such function depends on the number of wavelength bands utilized. In addition, certain algorithms will perform the conversion of optically unaffected Cherenkov image to dose map by utilizing intensity-to-dose conversion factor, which is found in similar manner prior the intended use by employing calibration of the test Cherenkov images against a dosimetric reference, which may be one of ionization chambers, radiochromic film, semiconductor dosimeter, and simulation using dose calculation algorithm. In some embodiments, the dose evaluation algorithm utilizes at least one of the spectral quantity maps as an input to a machine-learning based dose correction algorithm, which was trained with multiple sets of training data in the form of spectral quantity – dose correction factor data pairs.

[00064] In other embodiments, where the target is a scintillating object, the camera detects scintillation signals from different spectral bands. Once the spectral quantity is evaluated from the images of these scintillators, the spectral quantity is used to evaluate the coefficient of local scintillation signal change due to one of the following effects: exciton-exciton quenching, concentration quenching, loss due to optical transfer, specular reflection, and diffuse reflection.

[00065] To counteract the additional effect due to the light absorption due to absorbers whose distribution is preferentially located at the target's surface, such as melanin molecules due to specific skin color, in some embodiments an additional method of reflectance quantity of the target is acquired by the system and utilized in the image analysis as part of the dose correction algorithm.

[00066] In embodiments, the reflectance quantity is used by the image processor to scale the intensity of recorded light to counteract the effect of such light absorption, following the image analysis workflow:

- 1) the darkfield value is subtracted from each color channel.
- 2) color images are flatfield corrected by division from a previously acquired flatfield image.
- 3) color images are color graded based on a standardized color palette with known color values to account for variations in room lighting and camera response.
- 4) corrections may be made to the color images based on reflectance images obtained in visible light to account for uneven illumination across the patient surface.
- 5) color images are spatially co-registered to the corresponding Cherenkov images.

6) pixel by pixel color values in one or more color spaces, such as SRGB, CIELAB, CIEXYZ are obtained across the patient surface.

7) one or more color metrics, such as luminance, individual topology angle, or color channel ratios, are compared to the corresponding Cherenkov value within the image.

8) a map between color metric and Cherenkov intensity is generated for calibration

9) each Cherenkov pixel is normalized by the calibration factor for the corresponding pixel's color metric based on the map generated.

10) each color-corrected Cherenkov pixel is then scaled by a pre-determined correlation ratio to convert pixel intensity to absolute surface dose.

[00067] In summary: we: a) collect color or multispectral Cherenkov images of the subject or target, and use this multispectral information to determine a dose correction factor at pixels of the images for scattering and absorption between sources of Cherenkov emissions in the subject or target and the camera; b) we may optionally also collect color reflectance images, and use them to extract additional correction factors for light absorption in at least the melanin in skin of the subject or target; c) we may obtain reflectance images at multiple phases of multiple spatial frequencies of multiple wavelengths of structured light, and use those images to extract additional correction factors for scattering and absorbance between sources of Cherenkov emissions in the subject or target and the camera. We use all these correction factors to derive corrected Cherenkov images.

[00068] The image processor is configured by at least one of firmware and software to use the color or multispectral Cherenkov images, and the color reflectance images if available, as inputs to a multi-spectral two dimensional Cherenkov intensity map of tissue of skin and near-skin tissue. In embodiments, the two-dimensional Cherenkov-corrected dose map is compared against a planned surface or sub-surface dose map generated from a treatment planning data, that include a at least a Computer Tomography (CT) scan and a treatment dose volume, as viewed from the same point of view as the Cherenkov camera. For such purpose, the Cherenkov camera(s) are localized spatially in relation to treatment device coordinate space, and the imaging transformation matrix is quantified using intrinsic optical calibration. We also save images from one or more timepoints in each radiation treatment session of a particular subject in a treatment database and perform such comparison at these timepoints. In embodiments, such comparison is performed in real time. In other image processor embodiments, the Cherenkov images are ray-traced onto a known patient's or target's three-dimensional surface profile. This textured surface profile then contains actual 3D surface dose map, and the comparison against planned dose is done in three-dimensional space. In embodiments,

the 3D planned dose volume as calculated on a static CT scan is spatially deformed to match the actual 3D surface, and the planned dose is recalculated within this spatially registered CT volume.

[00069] In other embodiments, it is intended that the map of quantified tissue optical properties and spectral components of the Cherenkov image is used to monitor progress of the radiation treatment and assist treatment personnel in avoiding excessive damage to normal tissues of the subject or patient. In embodiments this at least two -dimensional map of quantified tissue damage is generated from an initial saved set of Cherenkov, color reflectance images if available, and mapped optical properties from structured light imaging if available, compared to a current, coregistered, set Cherenkov, color reflectance images if available, and mapped optical properties from structured light imaging if available; in a particular embodiment this comparison is performed by a trained classifier or algorithm executing in the image processor, the classifier or algorithm being trained on training sets of images where a physician has classified initial and later image sets according to tissue damage types, extents, and likely development of complications.

[00070] In embodiments, the image processor is configured by at least one of firmware and software to use the corrected Cherenkov image to determine a radiation dosage map of the subject as treatment progresses and use that radiation dosage map both as feedback to treating personnel and to automatically abort treatment when the radiation dose map deviates from any planned dose map or when maximum treatment thresholds are exceeded.

[00071] Monitoring changes in Cherenkov emission over fractionated radiation treatments may be a predictor for radiation-induced tissue toxicity, which may hypothetically be used by clinical staff to evaluate treatment effectiveness or to alter the treatment towards a less toxic treatment plan.

The Method

[00072] In operation, the method 800 may be summarized as in Fig. 8. Diffuse media, which in some embodiments is a subject or patient, in other embodiments a phantom, and in other embodiments another object, is positioned 802 for treatment. Skin or surface coloration is determined 804, in embodiments by obtaining color images with a color camera and processing those images. When fractionated radiation treatment is being performed, the skin or surface coloration is determined for each session separately to account for changes that may occur over the course of radiation treatment. Subsurface optical parameters, including scattering and absorption coefficients, of the diffuse media are also determined 806, in some embodiments by processing images obtained in “structured light” (patterned light) in multiple phases and spatial frequencies, and in some other embodiments by use of estimated parameters. The radiation beam is then applied 808 to the diffuse media, and color or hyperspectral Cherenkov images are obtained 810 of the diffuse media with a high-sensitivity camera and color bands each 10 to 100 nanometers wide.

[00073] In some embodiments, an estimated beam energy is determined 813 from the color Cherenkov images and compared to a planned beam energy.

[00074] Meanwhile, using the skin or surface coloration and subsurface optical parameters of the diffuse media, dose correction functions are determined 812. Further, as frames of the color Cherenkov images are obtained 810, a running totalized color Cherenkov image is prepared 814.

[00075] The determined 812 dose correction function is applied 818 to the totalized color Cherenkov images to give corrected dose images. Further, the surface coloration and subsurface optical parameters are optionally applied to the totalized color Cherenkov images to derive a three-dimensional dose distribution within the diffuse media target.

[00076] The corrected dose images may in some embodiments be compared 820 to planned dosages and to limit dosages, both for a current treatment session and for a total treatment plan, and treatment automatically aborted if a significant deviation from plan is occurring.

[00077] In an alternative embodiment, termed by us an "Iterative Composition Fitting" approach, uses pre-defined absorption and scatter characteristics (obtained from literature or prior experiment) of expected tissue components such as oxygenated or deoxygenated hemoglobin, fat, water, and melanin are used; exemplary absorption spectra of oxygenated hemoglobin, deoxygenated hemoglobin, fat, and water are shown in Fig. 9A. Light emitted by the diffuse media, which in a particular embodiment may be a phantom and in another embodiment a mammalian tissue, is imaged in multiple spectral bands as heretofore described, in a particular embodiment 5 spectral bands Band A, Band B, Band C, Band D, and Band E, each of width 50 nanometers and centered at 600, 650, 700, 750, and 800 nanometers are used. A pristine expected Cherenkov emissions spectra is shown in Fig. 9B along with an exemplary emitted spectra from the diffuse media. The pristine expected Cherenkov emissions are used in a voxel-based light propagation model with parameters for concentration of each of several tissue components, in the example of Fig. 9A and Fig. 9B tissue components for which concentration parameters are used include oxygenated and deoxygenated hemoglobin, water, and fat, and a fit is performed of the concentration parameters to the pristine expected Cherenkov emissions and observed light emitted by the diffuse media. In embodiments, absorption loss of melanin is included. In this way, diffuse media or tissue composition can be mapped using the color images.

Combinations

[00078] A radiation treatment system designated A include a radiation source configured to provide radiation to a subject in a treatment zone, a first optical camera system configured to image Cherenkov light emissions from the treatment zone to generate Cherenkov images, the first optical camera system being configured to record light intensity separately in each of a pre-defined plurality

of spectral bands including at least one spectral band having a center wavelength between 750 and 900 nanometers, and an image processor. The image processor is configured to determine Cherenkov spectral correction parameters at pixels of the Cherenkov images based on differences between imaged intensity of Cherenkov light in the spectral bands at pixels of the Cherenkov images, and determine a corrected dosage map of the subject based upon at least the Cherenkov images and the Cherenkov spectral correction parameters.

[00079] A radiation treatment system designated AA including the radiation treatment system designated A further including a second optical camera system comprising color reflectance imaging cameras configured to provide color reflectance images of the subject in the treatment zone. In this embodiment, the image processor is configured to: determine color reflectance correction parameters at pixels of the color reflectance images, and the corrected dosage map of the subject is based upon at least the Cherenkov images, the Cherenkov spectral correction parameters, and the reflectance correction parameters.

[00080] A radiation treatment system designated AB including the radiation treatment system designated A or AA further including a structured light projector. In this embodiment, the color reflectance images comprise color reflectance images captured at at least two spatial wavelengths of structured light; and the image processor is configured to construct an optical properties map from the color reflectance images; and the corrected dosage map of the subject is based upon at least the Cherenkov images, the color Cherenkov correction parameters, the reflectance correction parameters, and the optical properties map.

[00081] A radiation treatment system designated AC including the radiation treatment system designated A, AA, or AB where spectral Cherenkov images from an initial treatment session are stored in a database as initial spectral Cherenkov images, and the image processor is configured to compare current spectral Cherenkov images to the initial spectral Cherenkov images to determine tissue response images.

[00082] A radiation treatment system designated AD including the radiation treatment system designated A, AA, AB, or AC further comprising color reflectance imaging cameras configured to provide color reflectance images of the subject in the treatment zone. In this embodiment, the image processor is configured to: save color reflectance images from an initial treatment session are stored in a database as initial color reflectance images, and the image processor is configured to at least compare current color reflectance images to the initial color reflectance images to determine tissue response images.

[00083] A radiation treatment system designated AE including the radiation treatment system designated A, AB, AC, or AD where color Cherenkov images from an initial treatment session are

stored in the database as initial color Cherenkov images, and the image processor is configured to compare current color Cherenkov images to the initial color Cherenkov images while determining tissue response images.

[00084] A radiation treatment system designated AF including the radiation treatment system designated A, AB, AC, AD, or AE where the first optical camera system comprises an optical system that receives light from the subject through a plurality of filters each passing a different wavelength band, and light from each of the plurality of filters is combined onto a separate region of a common image sensor.

[00085] A radiation treatment system designated AFA including the radiation treatment system designated AF where each of the plurality of filters has bandpass between 10 and 100 nanometers wide.

[00086] A radiation treatment system designated AG including the radiation treatment system designated A, AB, AC, AD, AE, AF, or AFA wherein the second optical camera system comprises polarizing filters.

[00087] A radiation treatment system designated AH including the radiation treatment system designated A, AB, AC, AD, AE, AF, AFA, or AG wherein the image processor is configured to compare the corrected dosage map to a planned radiation dosage map.

[00088] A radiation treatment system designated AI including the radiation treatment system designated A, AB, AC, AD, AE, AF, AFA, AG, or AH wherein the plurality of spectral bands includes at least two spectral bands having center wavelengths between 580 and 900 nanometers.

[00089] A radiation treatment system designated B includes a radiation source configured to provide radiation to a subject in a treatment zone; a first optical camera system configured to image Cherenkov light emissions from the treatment zone to generate Cherenkov images, the first optical camera system configured to record light intensity separately in each of a pre-defined plurality of spectral bands, the plurality of spectral bands including at least one spectral band having a center wavelength between 750 and 900 nanometers, and where spectral Cherenkov images from an initial treatment session are stored in a database as initial spectral Cherenkov images, and the image processor is configured to compare current spectral Cherenkov images to the initial spectral Cherenkov images to determine tissue response images.

[00090] A radiation treatment observation system designated BA including radiation treatment system designated B wherein the image processor is further configured to determine Cherenkov-spectral correction parameters at pixels of the Cherenkov images based on differences between imaged intensity of Cherenkov light in the spectral bands at pixels of the Cherenkov images, and

determine a corrected dosage map of the subject based upon at least the Cherenkov images and the Cherenkov spectral correction parameters.

[00091] A radiation treatment observation system designated BB including radiation treatment system designated B or BA wherein the plurality of spectral bands includes at least two spectral bands having center wavelengths between 580 and 900 nanometers.

[00092] A radiation treatment observation system designated BC including radiation treatment system designated BB wherein the plurality of spectral bands includes only two spectral bands having center wavelengths between 580 and 900 nanometers.

[00093] A method of monitoring radiation treatment of diffuse media designated C includes determining skin or surface coloration by processing color images; determining subsurface optical parameters of the diffuse media; obtaining color or hyperspectral Cherenkov images of the diffuse media with a high-sensitivity camera; using the determined skin or surface coloration and determined subsurface optical parameters of the diffuse media, determine dose correction functions; totalizing the color Cherenkov images to prepare a totalized color Cherenkov image; and applying the determined dose correction function to the totalized color Cherenkov images to give corrected dose images.

[00094] A method designated CA including the method designated C further including determining an estimated beam energy is from the color Cherenkov images.

[00095] A method designated CB including the method designated C or CA further including using the surface coloration and subsurface optical parameters and the totalized color Cherenkov images to derive a three-dimensional dose distribution within the diffuse media.

[00096] A method designated CC including the method designated C, CA, or CB further including comparing the corrected dose images to planned dosages and to limit dosages.

[00097] Changes may be made in the above methods and systems without departing from the scope hereof. It should thus be noted that the matter contained in the above description or shown in the accompanying drawings should be interpreted as illustrative and not in a limiting sense. The following claims are intended to cover all generic and specific features described herein, as well as all statements of the scope of the present method and system, which, as a matter of language, might be said to fall therebetween.

Claims

What is claimed is:

1. A radiation treatment system comprising:
 - a radiation source configured to provide radiation to a subject in a treatment zone;
 - a first optical camera system configured to image Cherenkov light emissions from the treatment zone to generate Cherenkov images,
 - the first optical camera system configured to record light intensity separately in each of a pre-defined plurality of spectral bands,
 - the plurality of spectral bands including at least one spectral band having a center wavelength between 750 and 900 nanometers, and
 - an image processor configured to:
 - determine Cherenkov spectral correction parameters at pixels of the Cherenkov images based on differences between imaged intensity of Cherenkov light in the spectral bands at pixels of the Cherenkov images, and determine a corrected dosage map of the subject based upon at least the Cherenkov images and the Cherenkov spectral correction parameters.
2. The radiation treatment system of claim 1 further comprising a second optical camera system comprising color reflectance imaging cameras configured to provide color reflectance images of the subject in the treatment zone, wherein the image processor is configured to:
 - determine color reflectance correction parameters at pixels of the color reflectance images, and
 - where the corrected dosage map of the subject is based upon at least the Cherenkov images, the Cherenkov spectral correction parameters, and the reflectance correction parameters.
3. The radiation treatment system of claim 2 further comprising:
 - a structured light projector;
 - where the color reflectance images comprise color reflectance images captured at at least two spatial wavelengths of structured light;
 - the image processor is configured to construct an optical properties map from the color reflectance images; and
 - the corrected dosage map of the subject is based upon at least the Cherenkov images, the color Cherenkov correction parameters, the reflectance correction parameters, and the optical properties map.

4. The radiation treatment system of claim 1 where spectral Cherenkov images from an initial treatment session are stored in a database as initial spectral Cherenkov images, and the image processor is configured to compare current spectral Cherenkov images to the initial spectral Cherenkov images to determine tissue response images.
5. The radiation treatment system of claim 2 further comprising color reflectance imaging cameras configured to provide color reflectance images of the subject in the treatment zone, wherein the image processor is configured to:
 - save color reflectance images from an initial treatment session are stored in a database as initial color reflectance images, and
 - the image processor is configured to at least compare current color reflectance images to the initial color reflectance images to determine tissue response images.
6. The radiation treatment system of claim 5 where color Cherenkov images from an initial treatment session are stored in the database as initial color Cherenkov images, and the image processor is configured to compare current color Cherenkov images to the initial color Cherenkov images while determining tissue response images.
7. The radiation treatment system of claim 1 where the first optical camera system comprises an optical system that receives light from the subject through a plurality of filters each passing a different wavelength band, and light from each of the plurality of filters is combined onto a separate region of a common image sensor.
8. The radiation treatment system of claim 7 where each of the plurality of filters has bandpass between 10 and 100 nanometers wide.
9. The radiation treatment system of claim 2 wherein the second optical camera system comprises polarizing filters.
10. The radiation treatment system of claim 1, 2, 3, 4, 5, 6, 7, 8, or 9 wherein the image processor is configured to compare the corrected dosage map to a planned radiation dosage map.
11. The radiation treatment system of claim 1, 2, or 3 wherein the plurality of spectral bands includes at least two spectral bands having center wavelengths between 580 and 900 nanometers.
12. A radiation treatment observation system comprising:
 - a first optical camera system configured to image Cherenkov light emissions from a treatment zone to generate Cherenkov images,
 - the first optical camera system configured to record light intensity separately in each of a pre-defined plurality of spectral bands,
 - the plurality of spectral bands including at least one spectral band having a center wavelength between 750 and 900 nanometers, and

where spectral Cherenkov images from an initial treatment session are stored in a database as initial spectral Cherenkov images, and the image processor is configured to compare current spectral Cherenkov images to the initial spectral Cherenkov images to determine tissue response images.

13. The radiation treatment observation system of claim 12 wherein the image processor is further configured to:

determine Cherenkov-spectral correction parameters at pixels of the Cherenkov images based on differences between imaged intensity of Cherenkov light in the spectral bands at pixels of the Cherenkov images, and

determine a corrected dosage map of the subject based upon at least the Cherenkov images and the Cherenkov spectral correction parameters.

14. The radiation treatment observation system of claim 12 or 13 wherein the plurality of spectral bands includes at least two spectral bands having center wavelengths between 580 and 900 nanometers.

15. The radiation treatment observation system of claim 12 or 13 wherein the plurality of spectral bands includes only two spectral bands having center wavelengths between 580 and 900 nanometers.

16. A method of monitoring radiation treatment of diffuse media comprises:

determining skin or surface coloration by processing color images;

determining subsurface optical parameters of the diffuse media;

obtaining color or hyperspectral Cherenkov images of the diffuse media with a high-sensitivity camera;

using the determined skin or surface coloration and determined subsurface optical parameters of the diffuse media, determine dose correction functions;

totalizing the color Cherenkov images to prepare a totalized color Cherenkov image; and

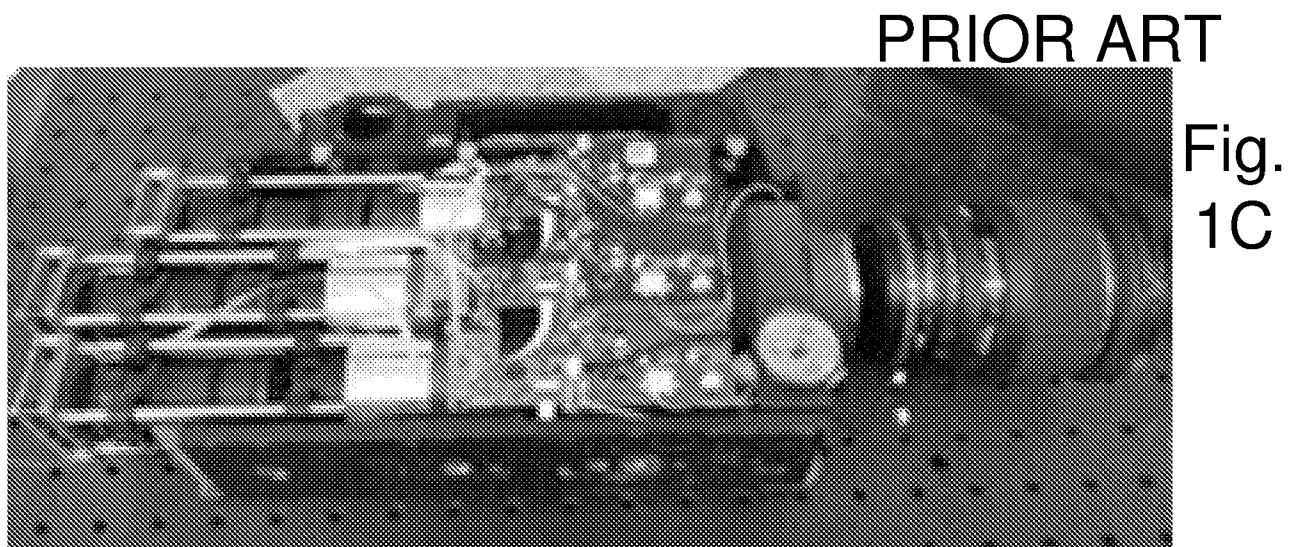
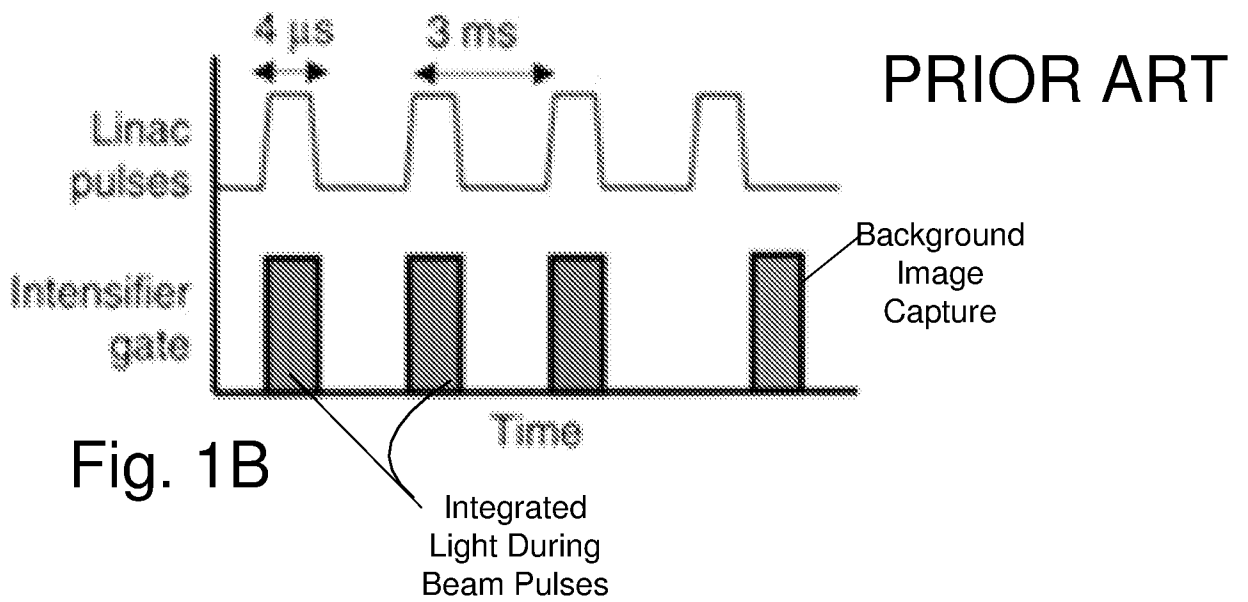
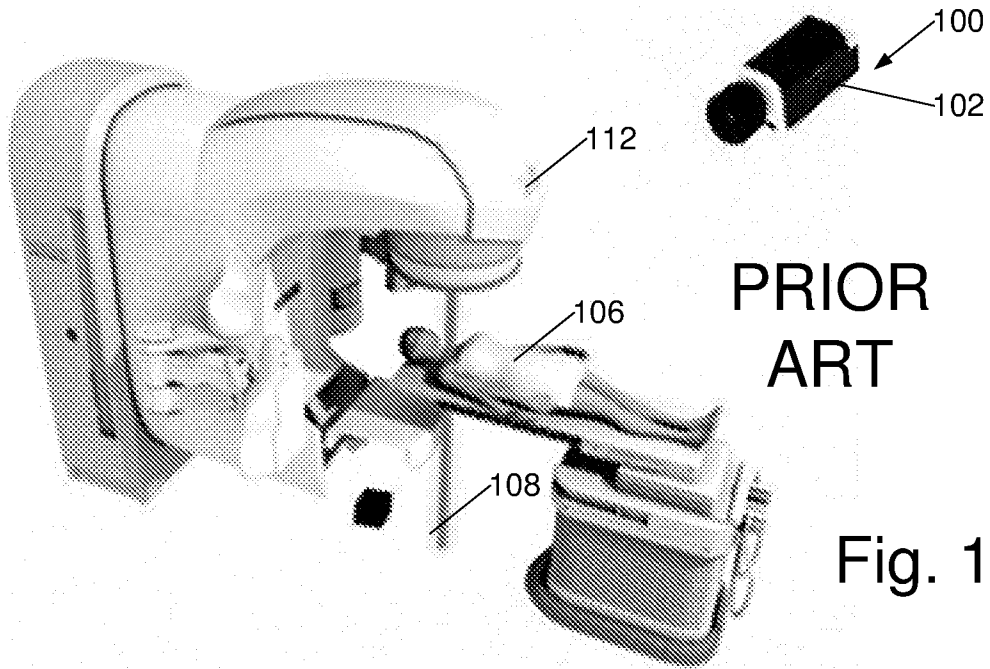
applying the determined dose correction function to the totalized color Cherenkov images to give corrected dose images.

17. The method of claim 16 further comprising determining an estimated beam energy is from the color Cherenkov images.

18. The method of claim 17 further comprising using the surface coloration and subsurface optical parameters and the totalized color Cherenkov images to derive a three-dimensional dose distribution within the diffuse media.

19. The method of claim 17 or 18 further comprising comparing the corrected dose images to planned dosages and to limit dosages.

20. The radiation treatment system of claim 8 where the plurality of filters each have bandwidth of 50 nanometers.



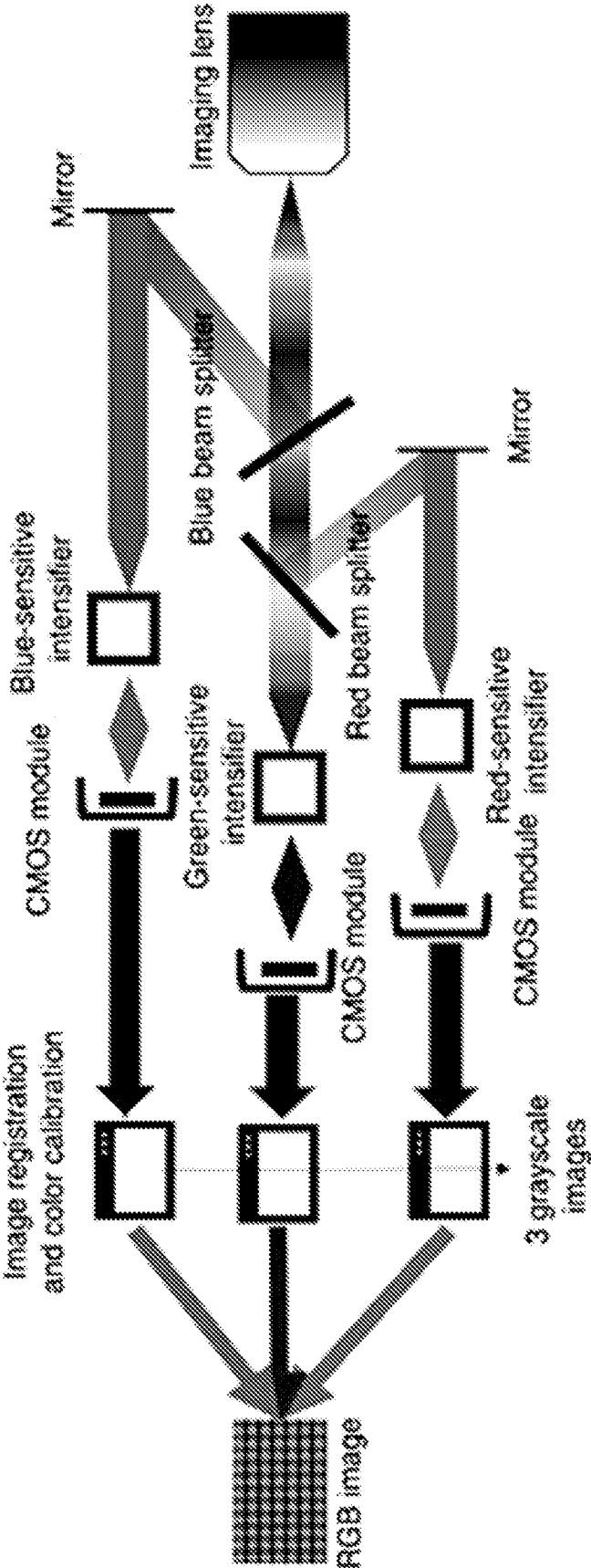


Fig. 1D

PRIOR ART

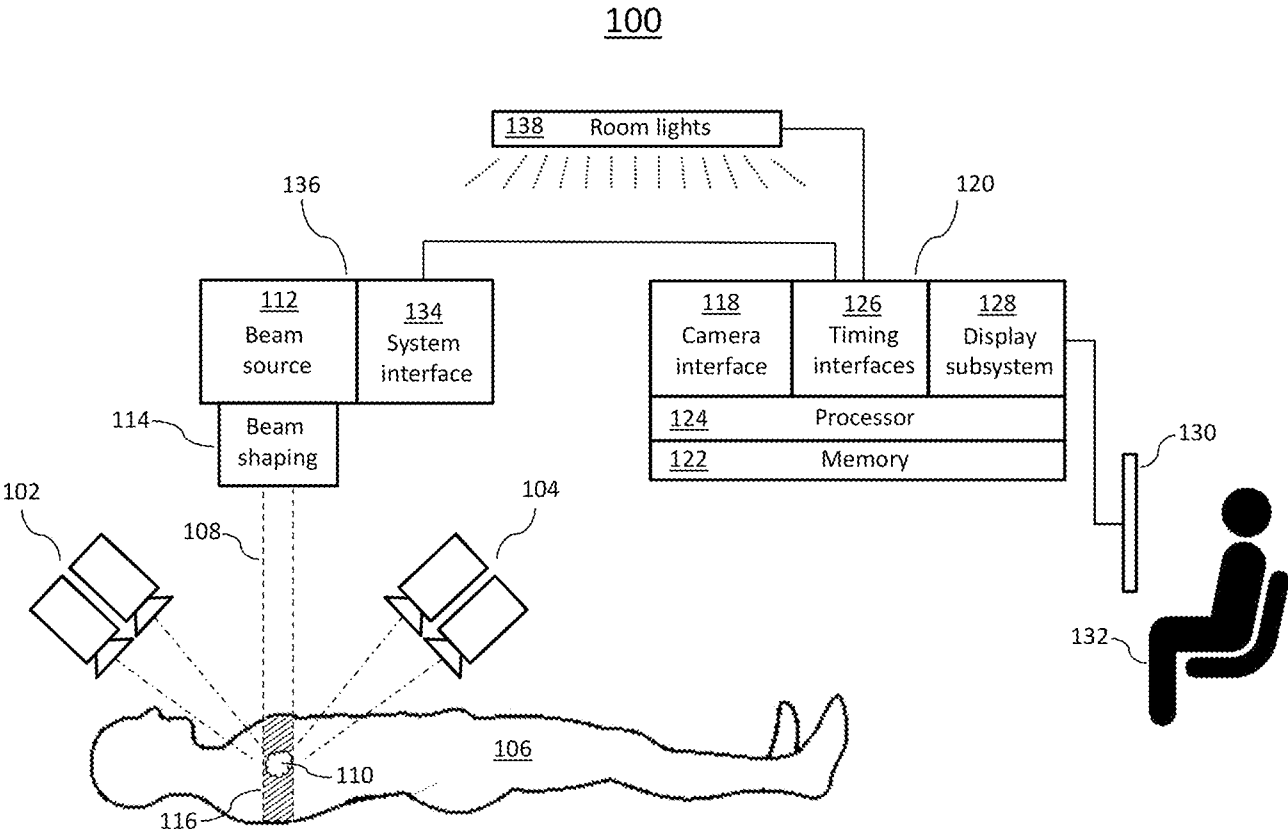


Fig. 2

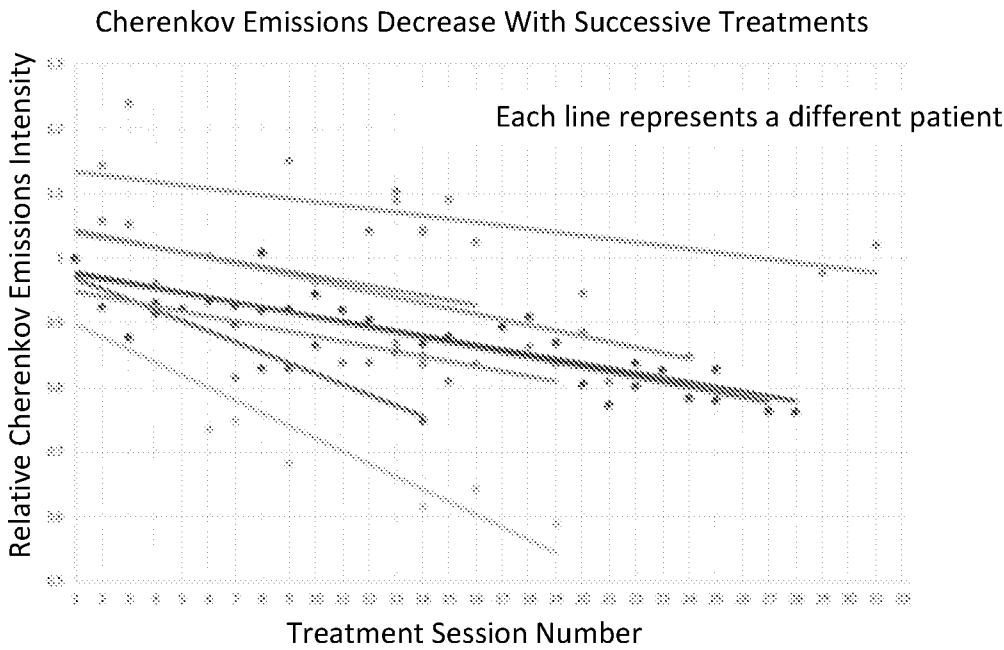


Fig. 3

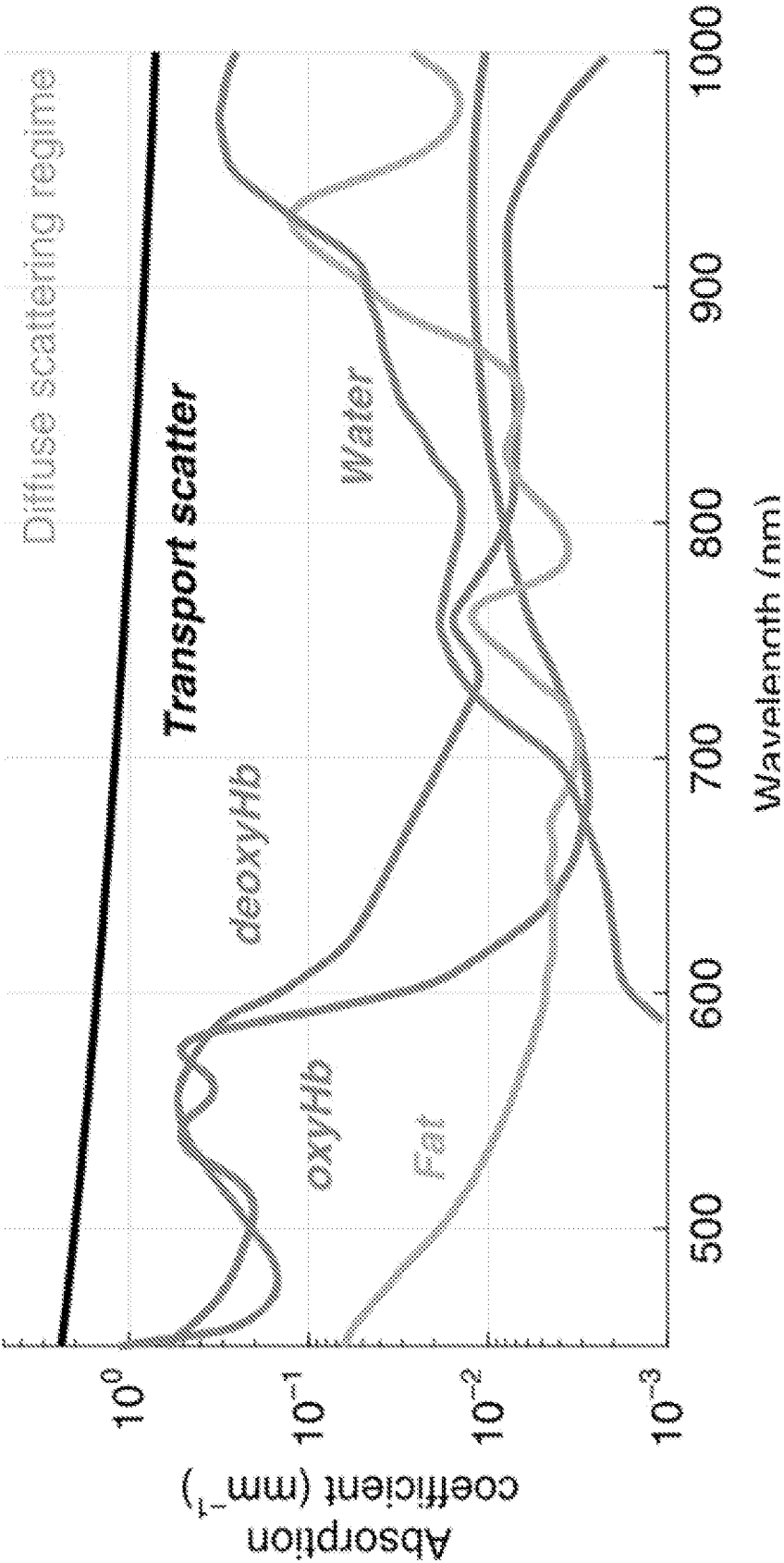


Fig. 4

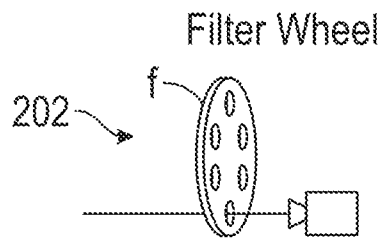


Fig. 5A

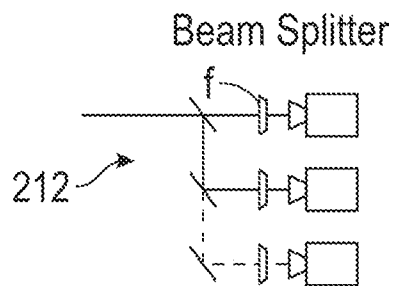


Fig. 5B

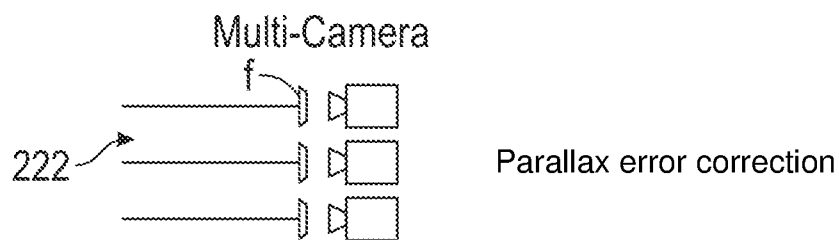


Fig. 5C

Prism Beam Splitter with Single Image Detector

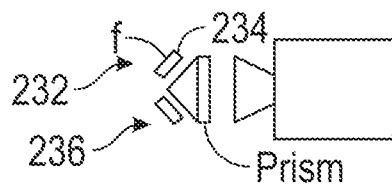


Fig. 5D

Optical Parameter Extraction using Structured Light or Pulsed Illuminator SFDI

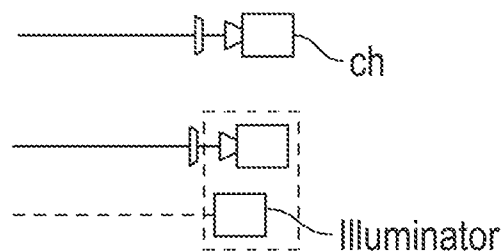


Fig. 5E

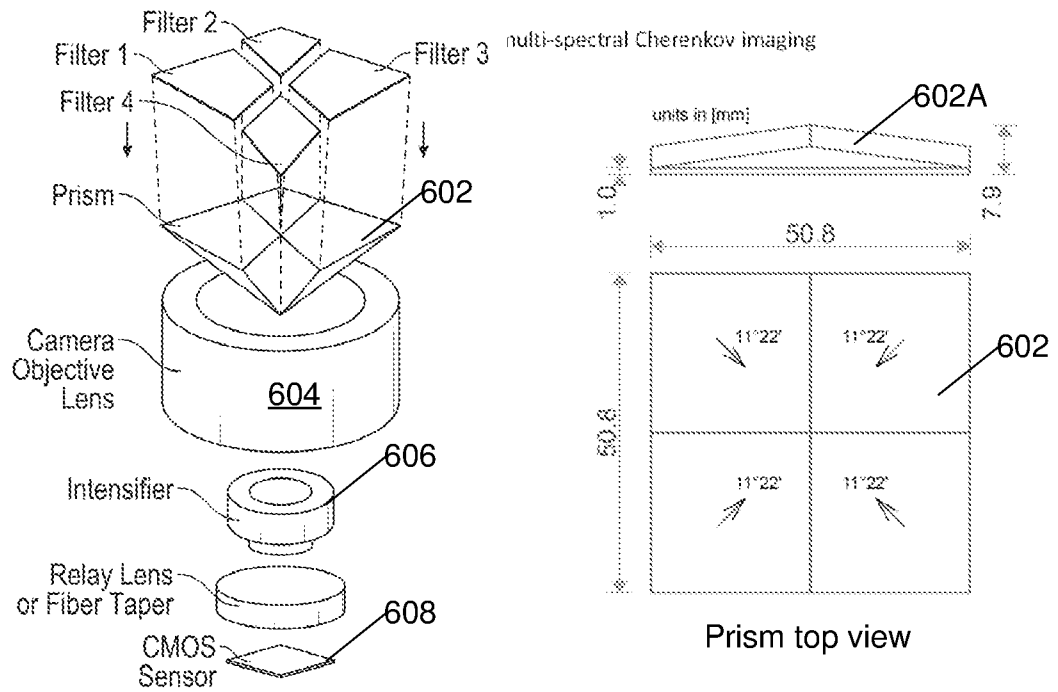


Fig. 6

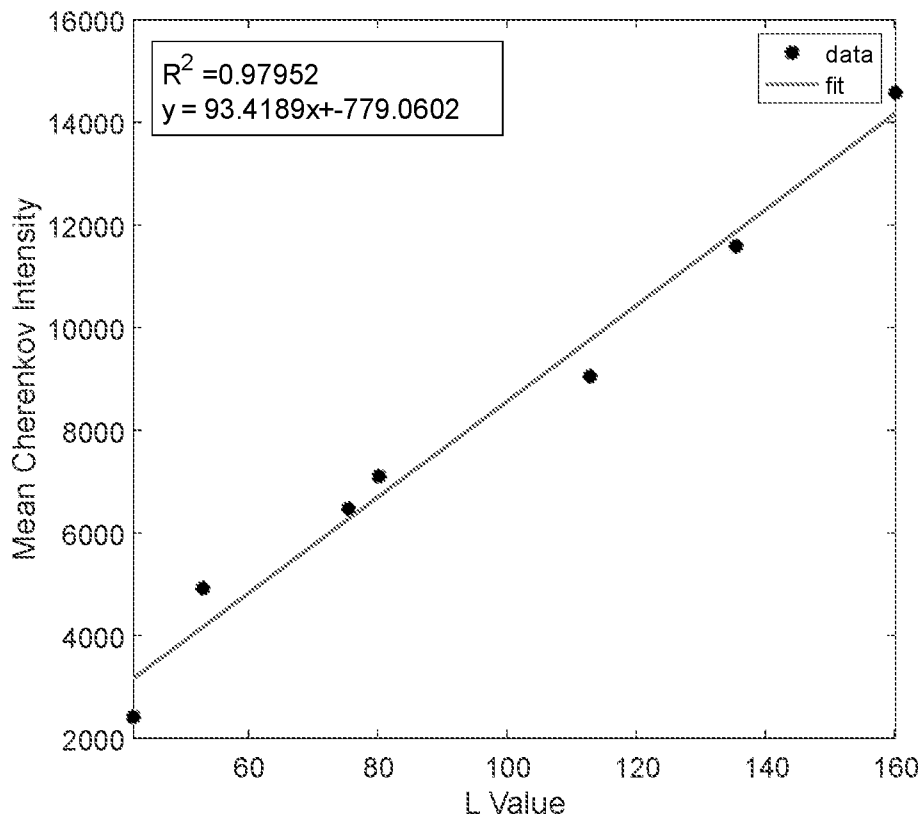


Fig. 7

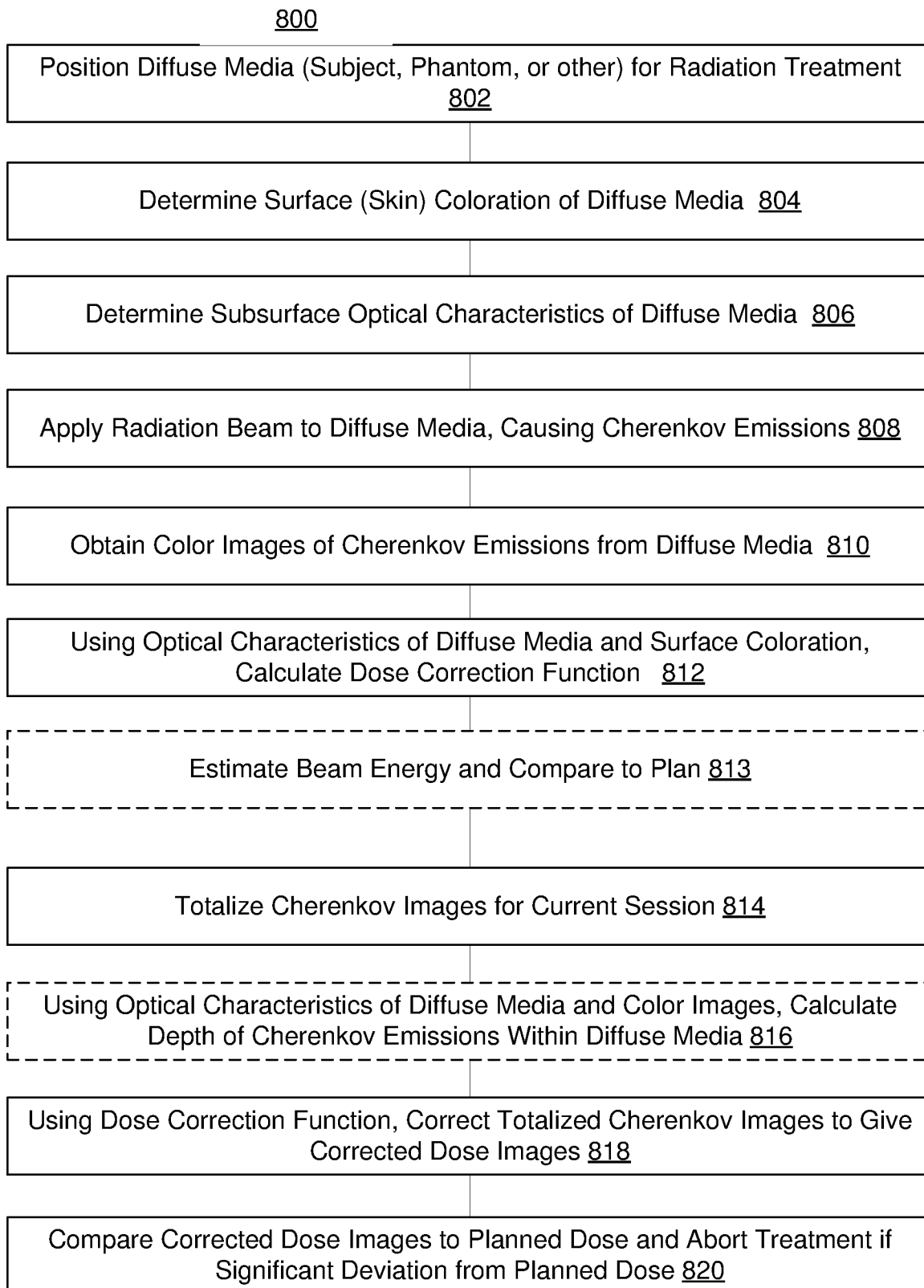


Fig. 8

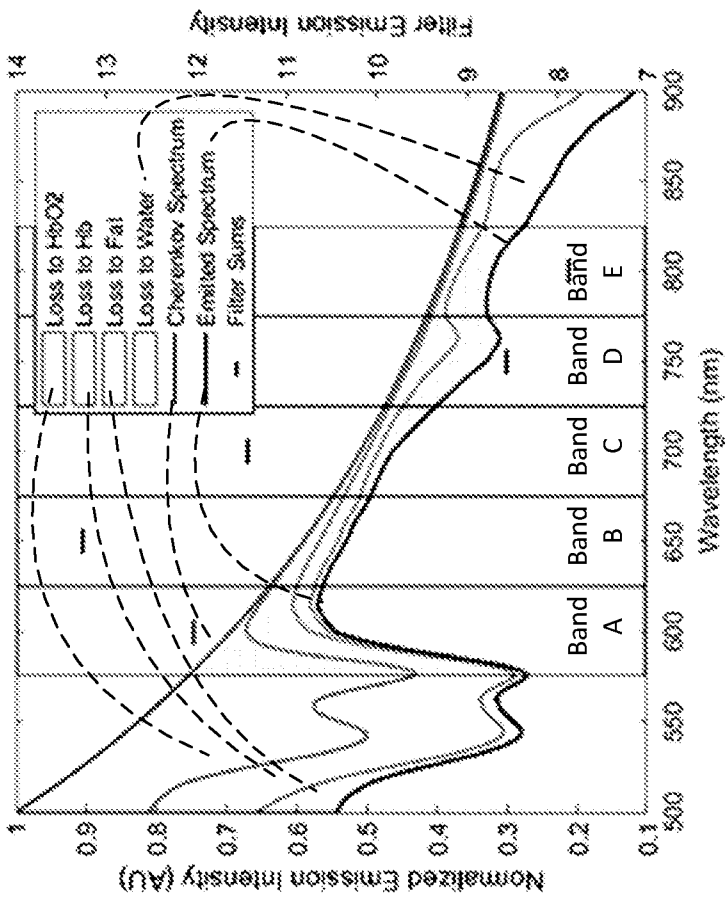


Fig. 9A

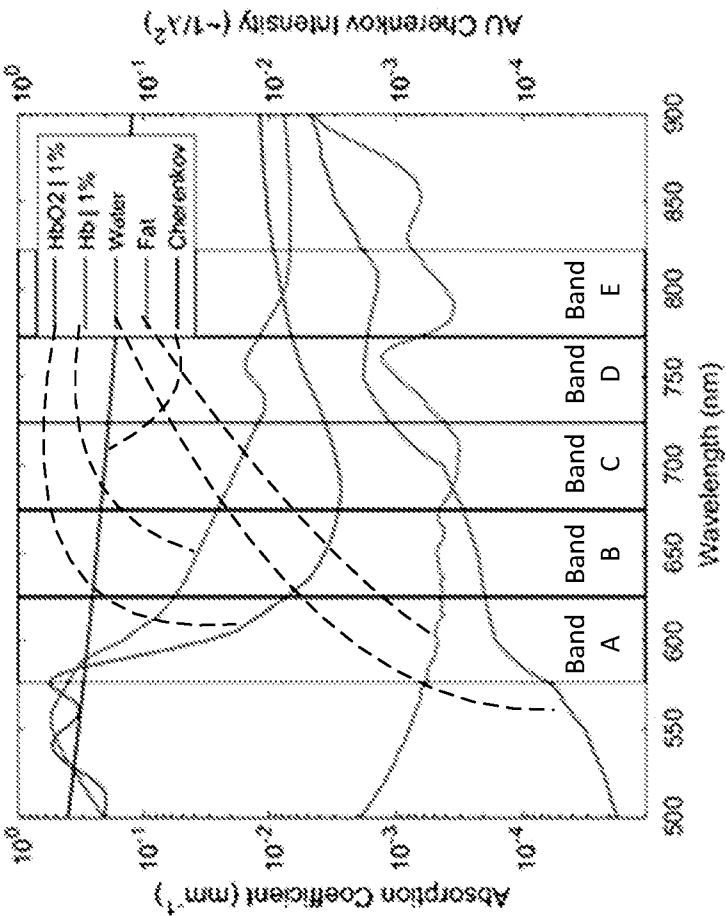


Fig. 9B

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US2024/035968

A. CLASSIFICATION OF SUBJECT MATTER

IPC: **A61N 5/10** (2024.01); **G01T 1/22** (2024.01); **G01T 1/36** (2024.01); **G02F 1/37** (2024.01); **A61B 6/42** (2024.01); **A61B 6/58** (2024.01); **A61N 5/06** (2024.01)

CPC: **A61N 5/1067**; **A61N 5/06**; **A61N 5/1071**; **G01T 1/22**; **G01T 1/363**; **G02F 1/374**; **A61B 6/582**; **A61B 6/4266**; **A61B 6/4208**; **A61N 5/1048**; **A61N 2005/0628**; **A61N 2005/1074**

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

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

See Search History Document

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

See Search History Document

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

See Search History Document

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 10,940,332 B2 (THE TRUSTEES OF DARTMOUTH COLLEGE) 09 March 2021 (09.03.2021) entire document	12, 16-19
Y	entire document	1-11, 13-15, 20
Y	US 9,731,150 B2 (VISION RT LIMITED) 15 August 2017 (15.08.2017) entire document	1-11, 13-15, 20
Y	CN 114949630 A (NUAA - NANJING UNIVERSITY OF AERONAUTICS & ASTRONAUTICS) 30 August 2022 (30.08.2022) entire document	8, 20
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Date of the actual completion of the international search

19 September 2024 (19.09.2024)

Date of mailing of the international search report

25 September 2024 (25.09.2024)

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