US010940332B2

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Zhang et al.

(10) **Patent No.: US 10,940,332 B2**
(45) **Date of Patent: Mar. 9, 2021**

(54) **CHERENKOV IMAGING SYSTEMS AND METHODS TO MONITOR BEAM PROFILES AND RADIATION DOSE WHILE AVOIDING INTERFERENCE FROM ROOM LIGHTING**

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(73) Assignee: **THE TRUSTEES OF DARTMOUTH COLLEGE**, Hanover, NH (US)

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 1134 days.

(21) Appl. No.: **15/160,576**

(22) Filed: **May 20, 2016**

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US 2016/0263402 A1 Sep. 15, 2016

Related U.S. Application Data

(63) Continuation-in-part of application No. PCT/US2016/029458, filed on Apr. 27, 2016, and a (Continued)

(51) **Int. Cl.**

A61B 5/05	(2006.01)
A61B 5/00	(2006.01)
A61N 5/10	(2006.01)

(52) **U.S. Cl.**
CPC ***A61N 5/1071*** (2013.01); ***A61N 5/1049*** (2013.01); ***A61N 5/1077*** (2013.01);
(Continued)

(58) **Field of Classification Search**
None
See application file for complete search history.

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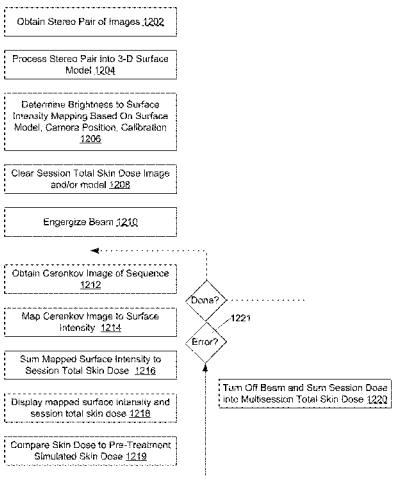
Primary Examiner — Patricia J Park
(74) *Attorney, Agent, or Firm* — Lathrop GPM LLP

(57) **ABSTRACT**

A monitor for pulsed high energy radiation therapy using a radiation beam passing through a treatment zone, the radiation of 0.2 MEV or greater; has a camera for imaging Cherenkov light from the treatment zone; apparatus for preventing interference by room lighting, the camera synchronized to pulses of the radiation beam; and an image processor adapted to determine extent of the beam area on the patient skin from the images. Additionally an image processor determines cumulative skin dose in the treatment zone from the images. In embodiments, the processor uses a three-dimensional model of a subject to determine map-

(Continued)



ping of image intensity in images of Cherenkov light to radiation intensity in skin, applies the mapping to images of Cherenkov light to verify skin dose delivered, and accumulates skin dose by summing the maps of skin dose.

24 Claims, 13 Drawing Sheets

Related U.S. Application Data

continuation-in-part of application No. PCT/US2014/066668, filed on Nov. 20, 2014, and a continuation-in-part of application No. 14/118,825, filed as application No. PCT/US2012/038609 on May 18, 2012, now Pat. No. 10,201,718.

(60) Provisional application No. 62/153,417, filed on Apr. 27, 2015, provisional application No. 61/906,805, filed on Nov. 20, 2013, provisional application No. 61/585,366, filed on Jan. 11, 2012, provisional application No. 61/488,129, filed on May 19, 2011.

(52) **U.S. Cl.**
CPC *A61N 5/1065* (2013.01); *A61N 2005/1054* (2013.01); *A61N 2005/1059* (2013.01)

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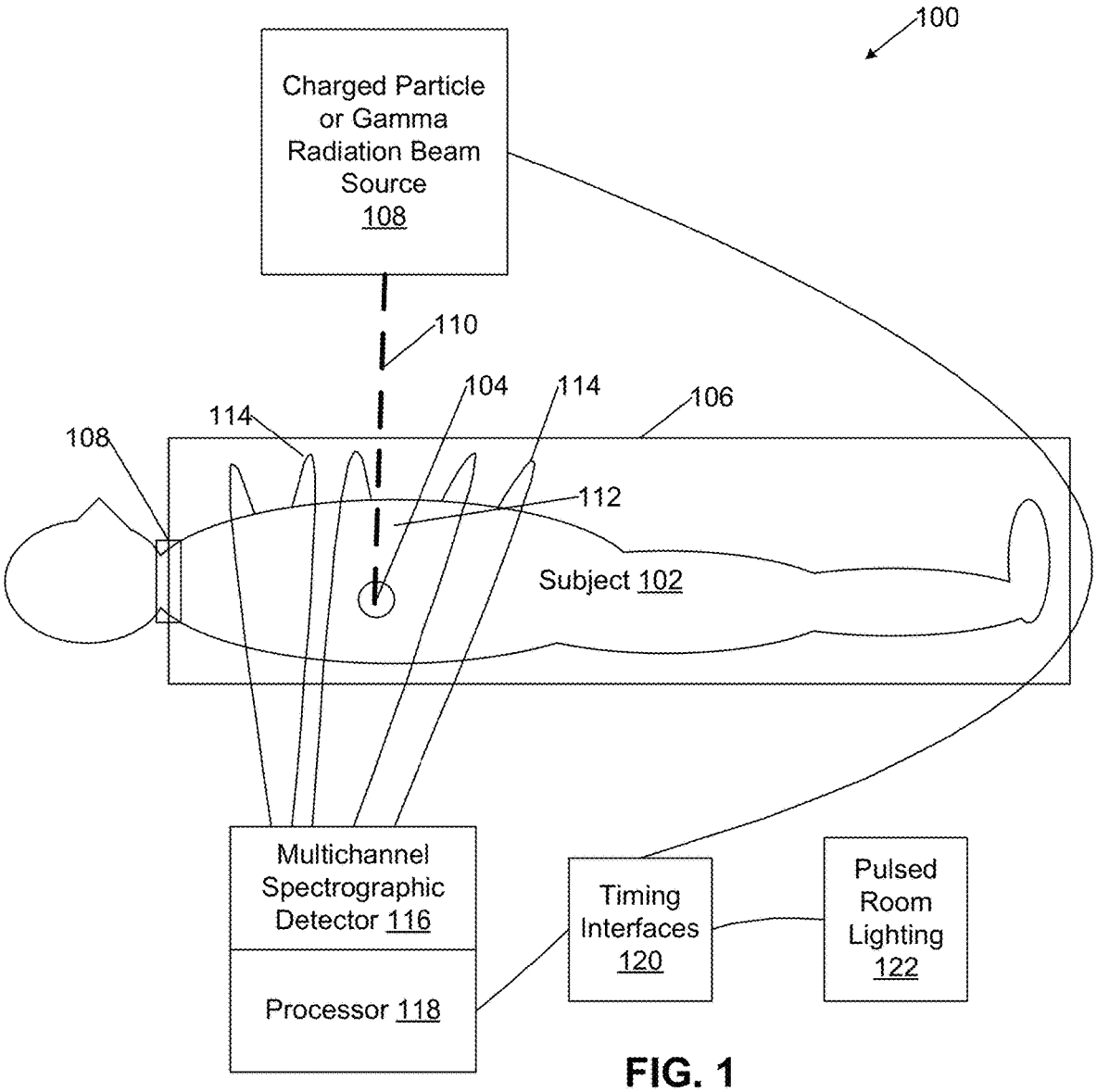
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Charged Particle or Gamma Radiation Beam Source 108
110
104
114
106
114
108
112
Subject 102
Multichannel Spectrographic Detector 116
Processor 118
Timing Interfaces 120
Pulsed Room Lighting 122

FIG. 1

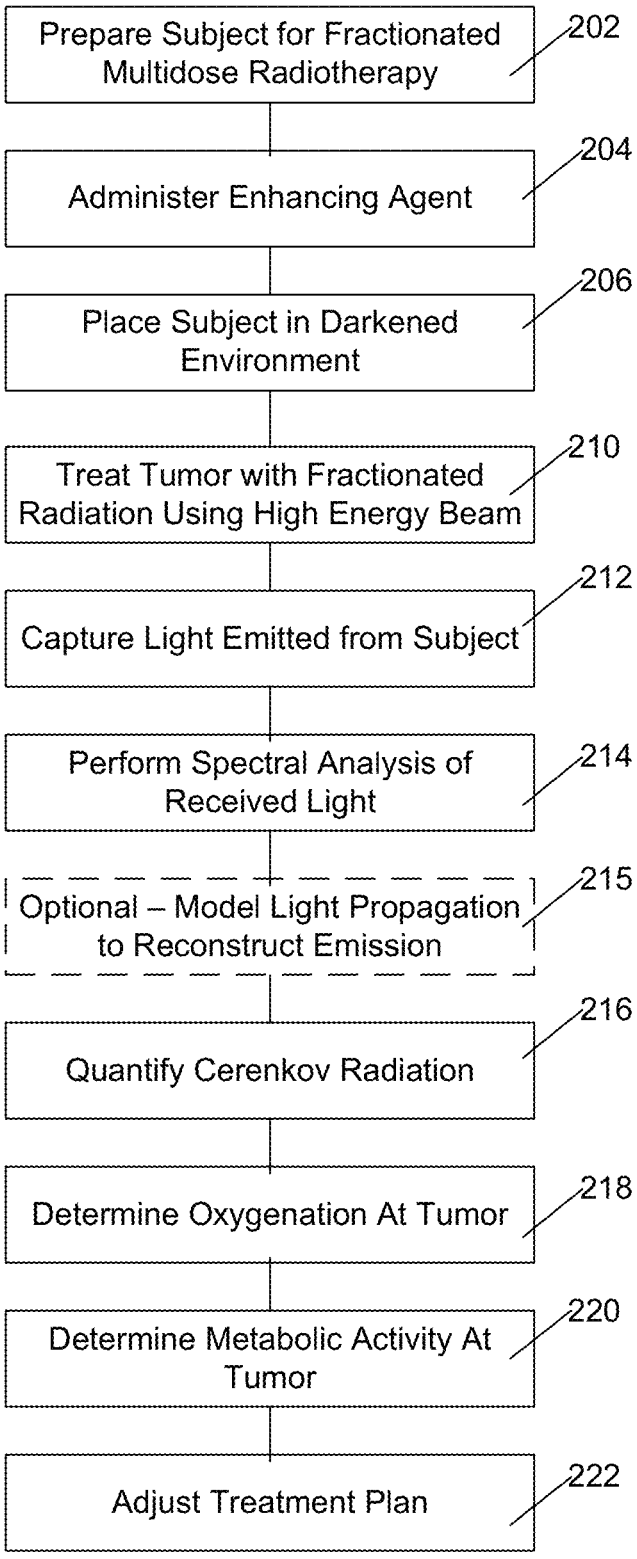

Prepare Subject for Fractionated Multidose Radiotherapy
202
Administer Enhancing Agent
204
Place Subject in Darkened Environment
206
Treat Tumor with Fractionated Radiation Using High Energy Beam
210
Capture Light Emitted from Subject
212
Perform Spectral Analysis of Received Light
214
Optional – Model Light Propagation to Reconstruct Emission
215
Quantify Cerenkov Radiation
216
Determine Oxygenation At Tumor
218
Determine Metabolic Activity At Tumor
220
Adjust Treatment Plan
222

FIG. 2

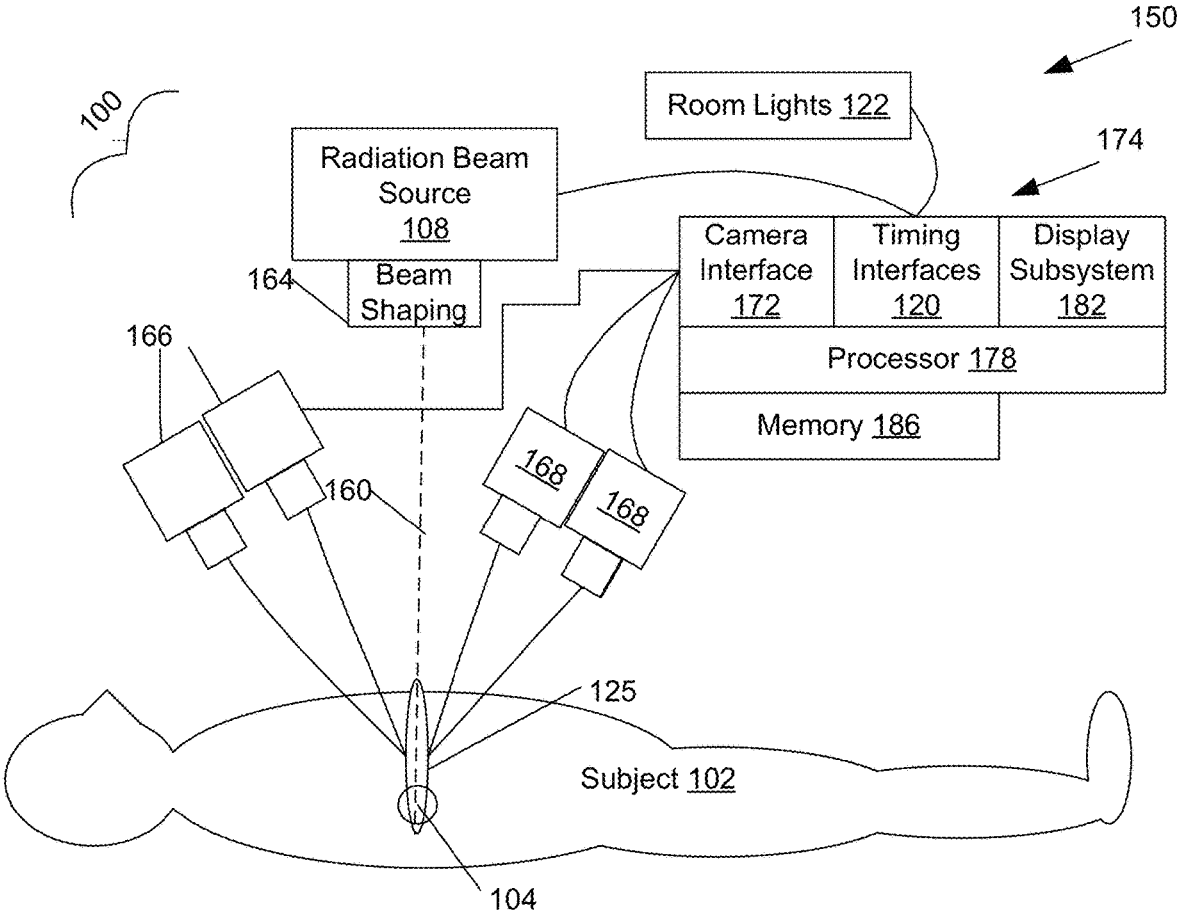

150
100
Room Lights 122
174
Radiation Beam Source 108
Camera Interface 172
Timing Interfaces 120
Display Subsystem 182
164
Beam Shaping
166
Processor 178
Memory 186
168
168
160
125
Subject 102
104

FIG. 3

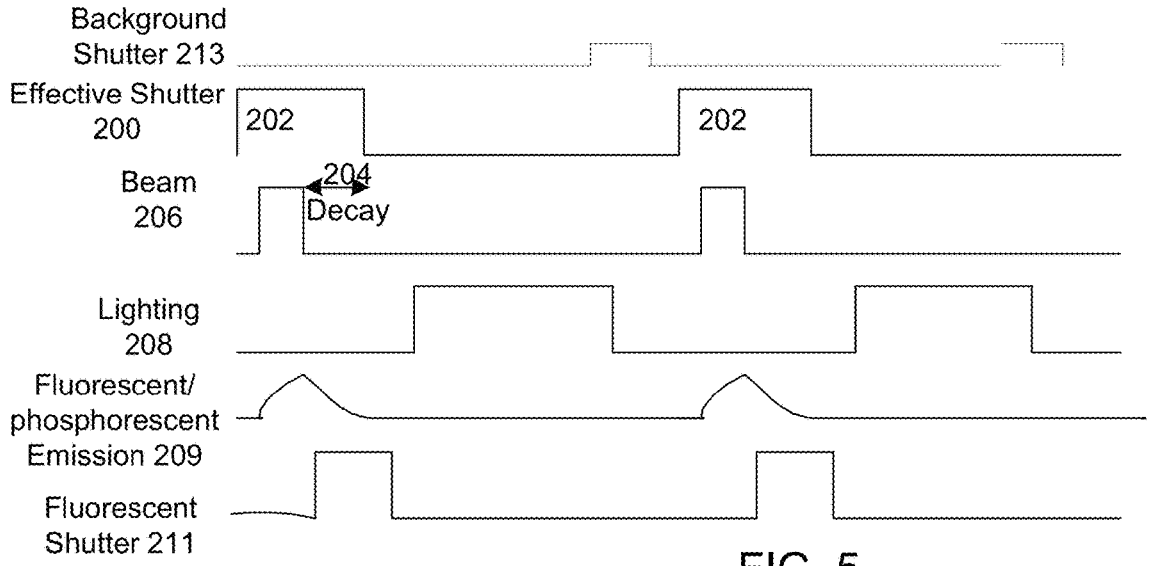

Background Shutter 213
Effective Shutter 200
202
202
Beam 206
204
Decay
Lighting 208
Fluorescent/ phosphorescent Emission 209
Fluorescent Shutter 211

FIG. 5

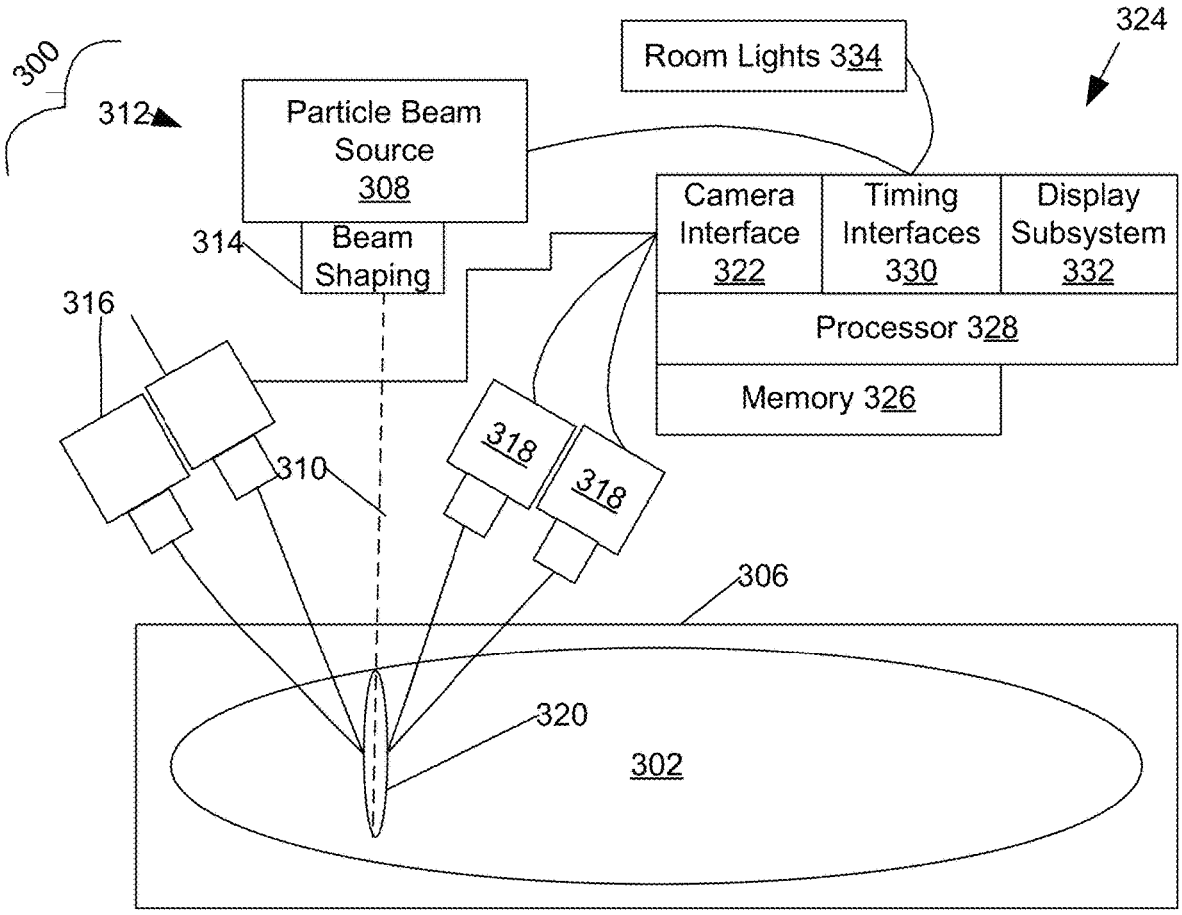

300
312
Particle Beam Source 308
Beam Shaping
314
316
310
318
318
Room Lights 334
324
Camera Interface 322
Timing Interfaces 330
Display Subsystem 332
Processor 328
Memory 326
306
320
302

FIG. 4

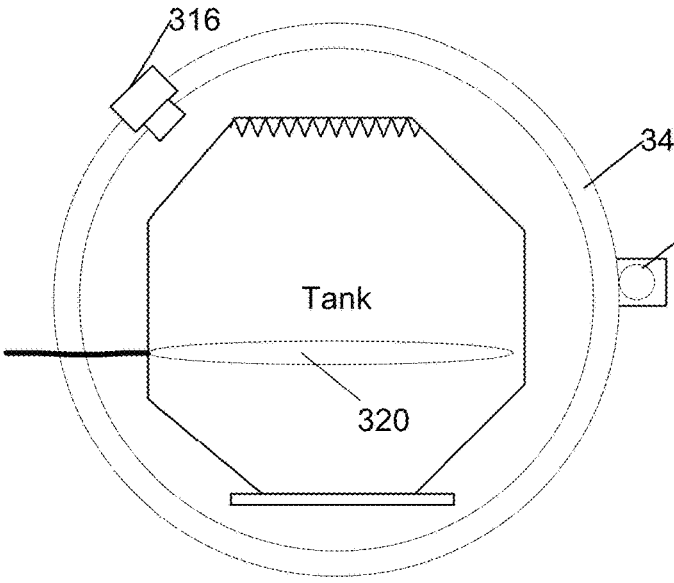


FIG. 6

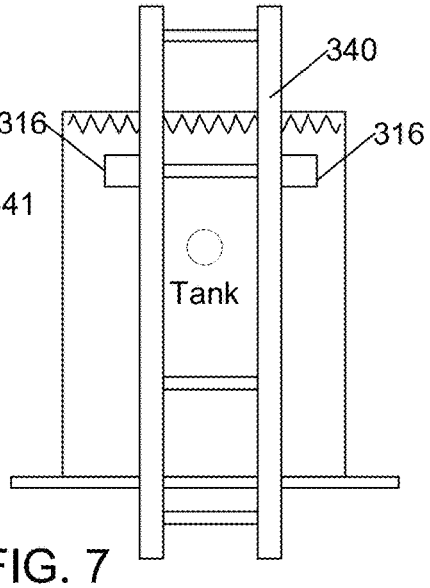


FIG. 7

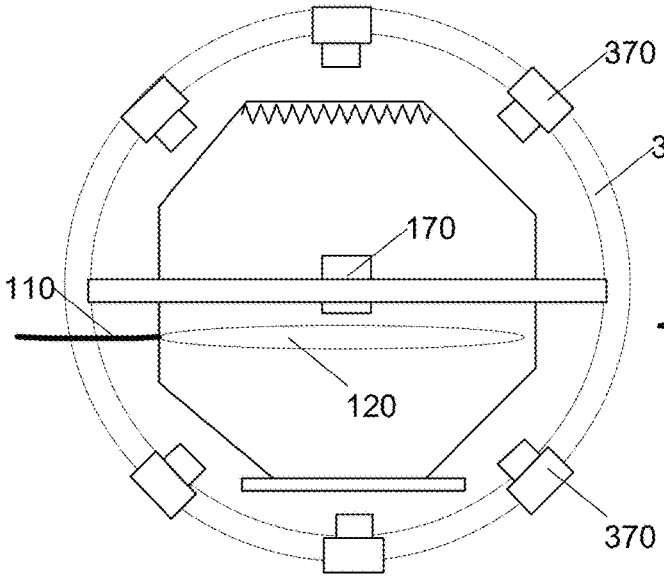


FIG. 8

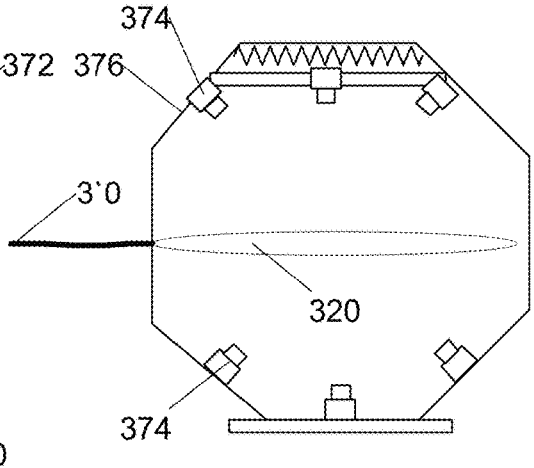


FIG. 9

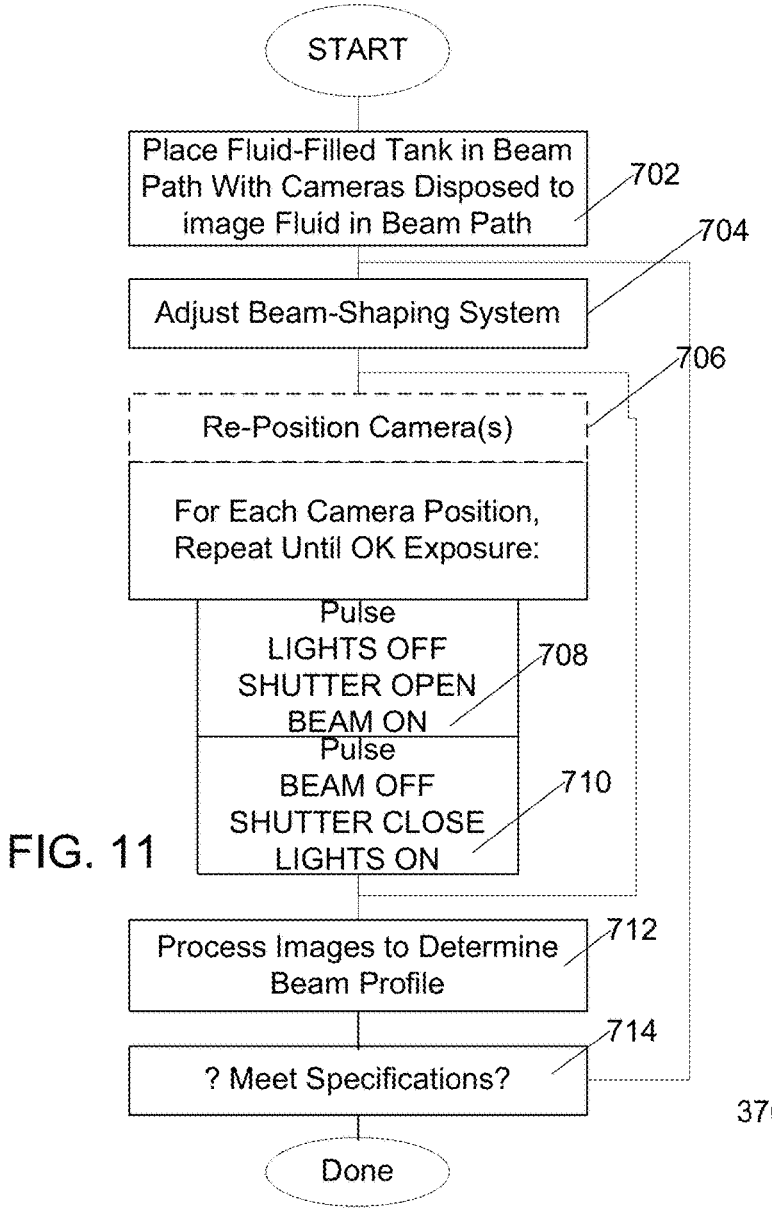


FIG. 11

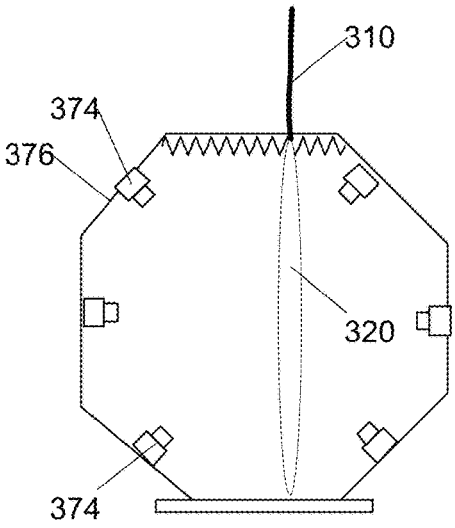


FIG. 10

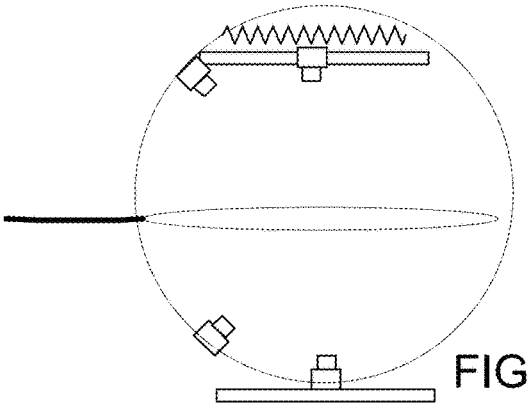
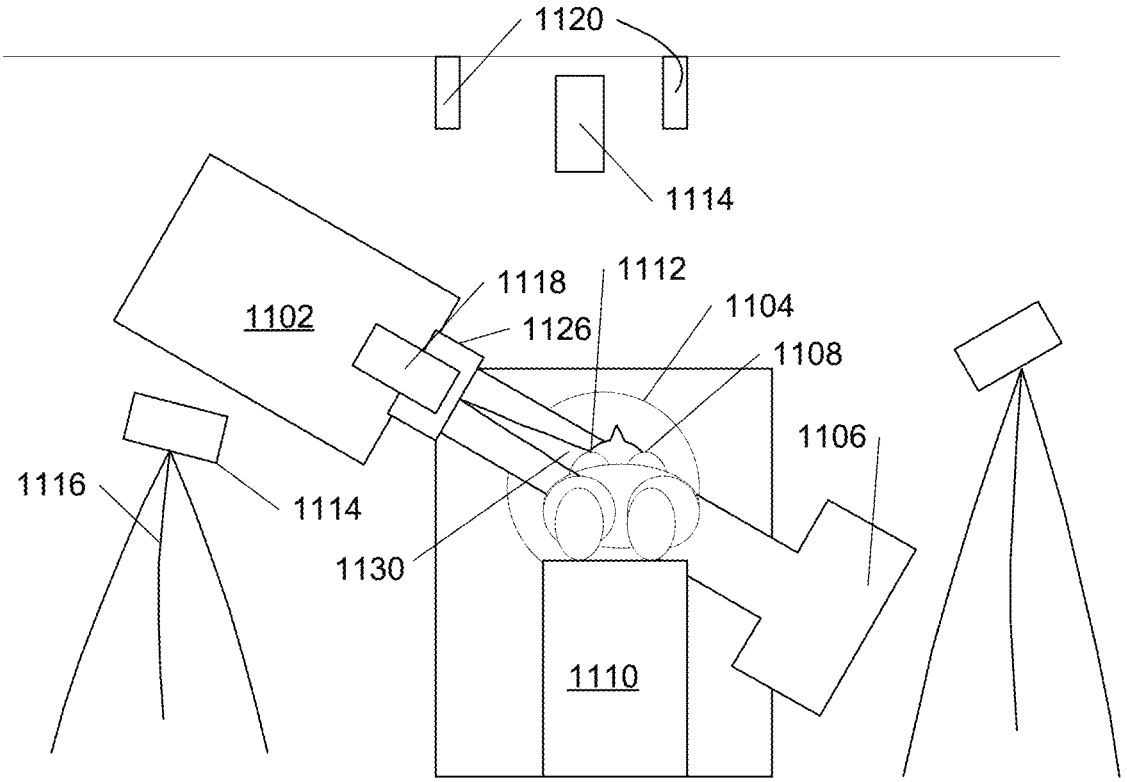


FIG. 12



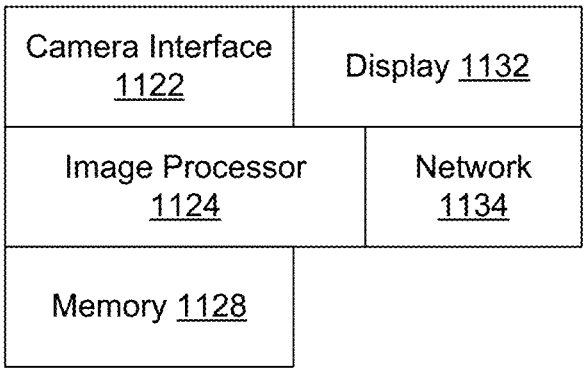


FIG. 13

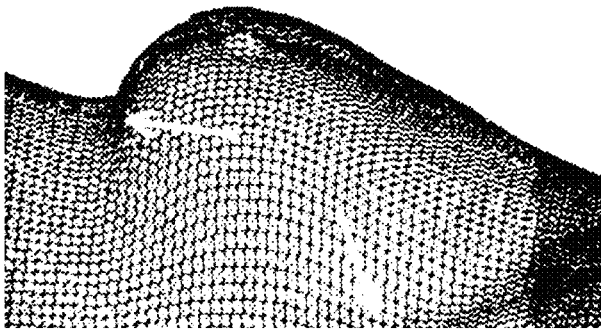


FIG. 14

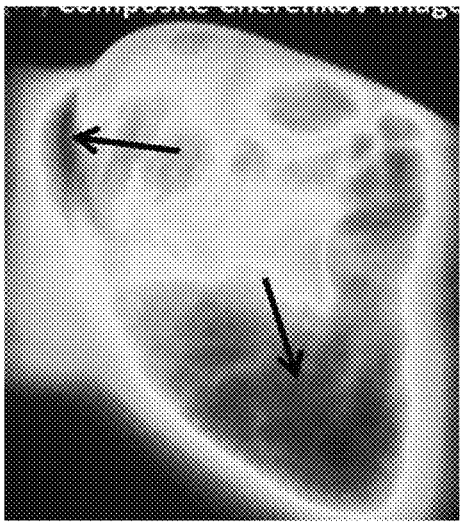


FIG. 16

Skin reaction

FIG. 17

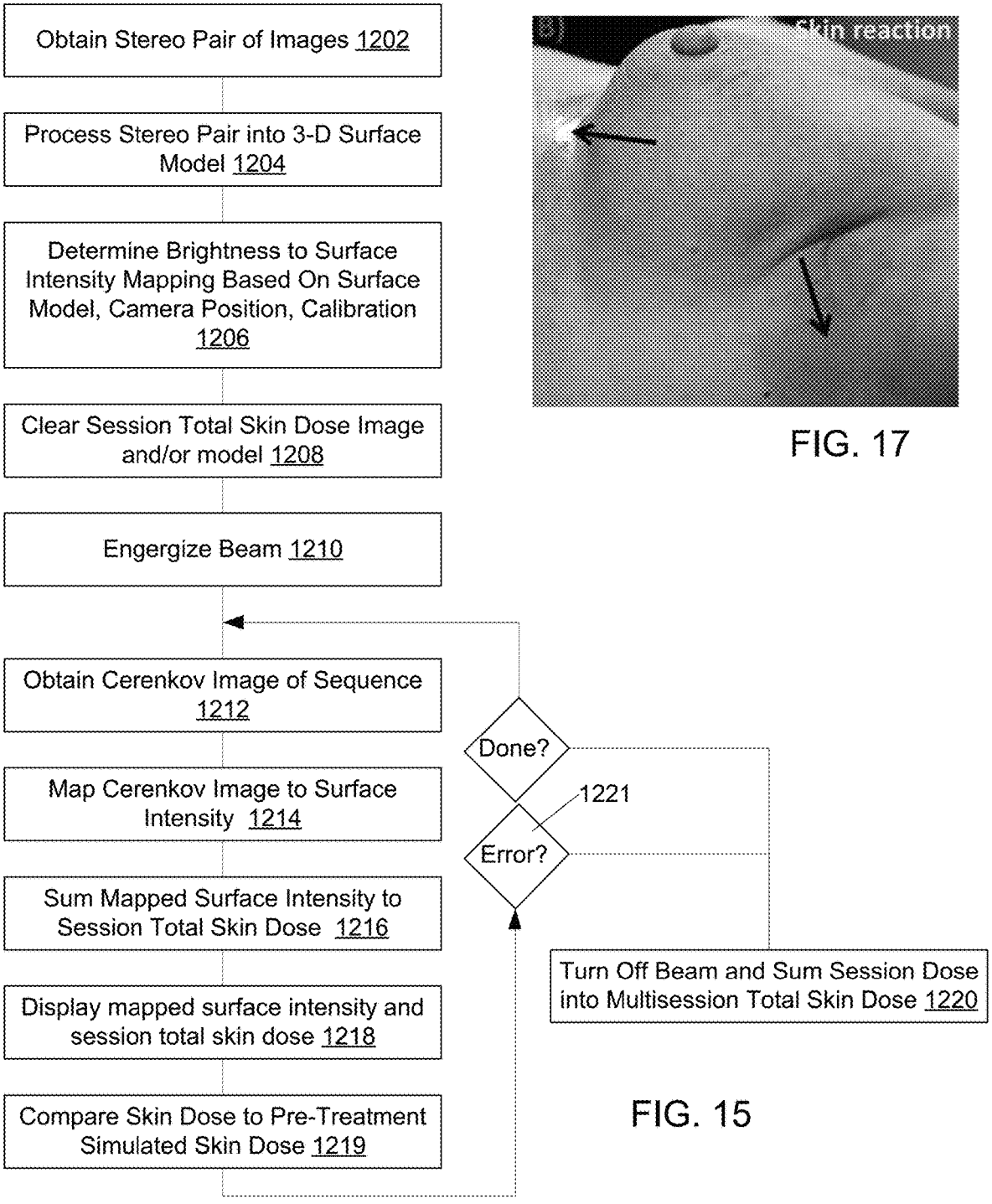

Obtain Stereo Pair of Images 1202
Process Stereo Pair into 3-D Surface Model 1204
Determine Brightness to Surface Intensity Mapping Based On Surface Model, Camera Position, Calibration 1206
Clear Session Total Skin Dose Image and/or model 1208
Engergize Beam 1210
Obtain Cerenkov Image of Sequence 1212
Map Cerenkov Image to Surface Intensity 1214
Sum Mapped Surface Intensity to Session Total Skin Dose 1216
Display mapped surface intensity and session total skin dose 1218
Compare Skin Dose to Pre-Treatment Simulated Skin Dose 1219
Done?
Error?
1221
Turn Off Beam and Sum Session Dose into Multisession Total Skin Dose 1220

FIG. 15

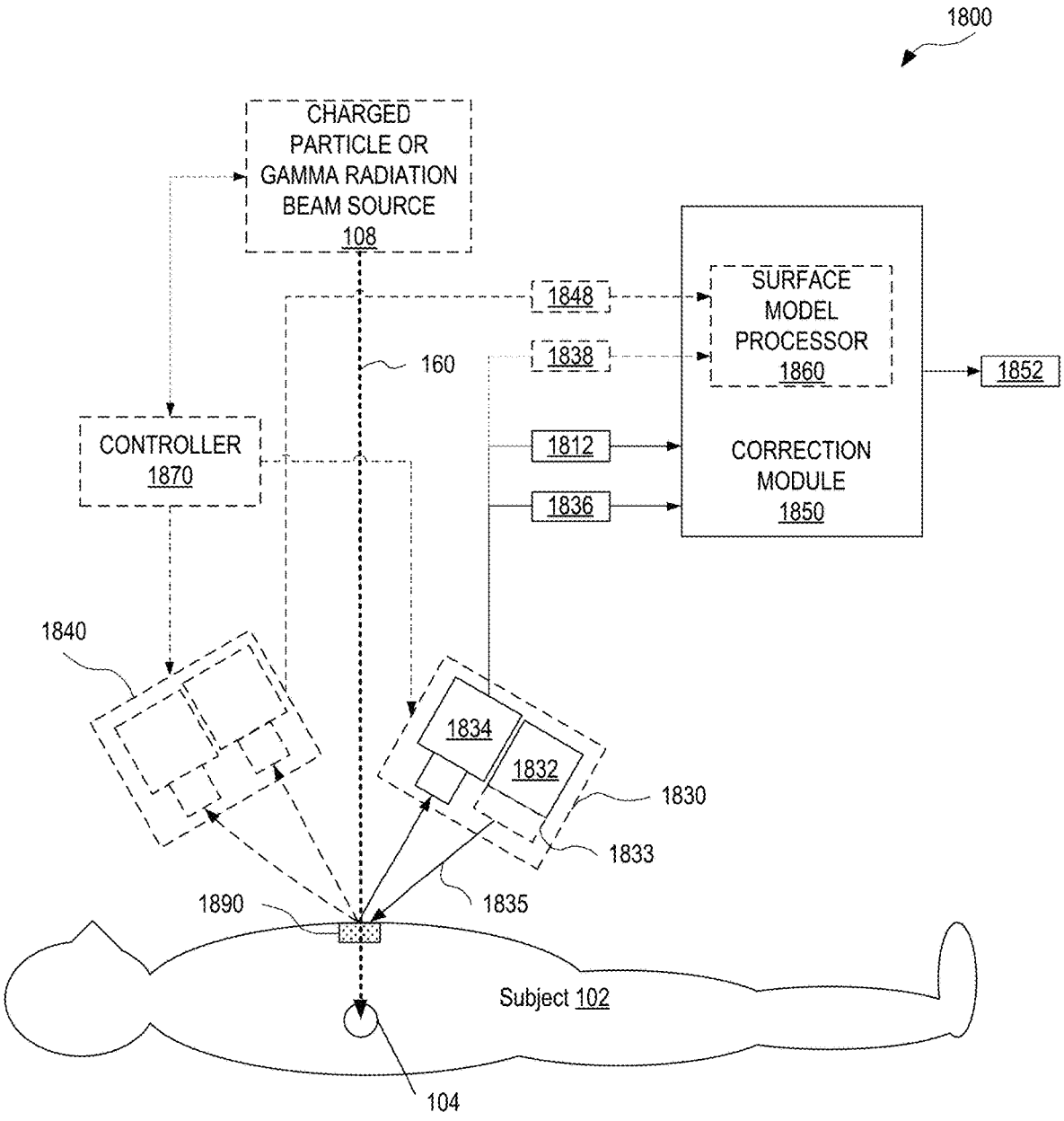
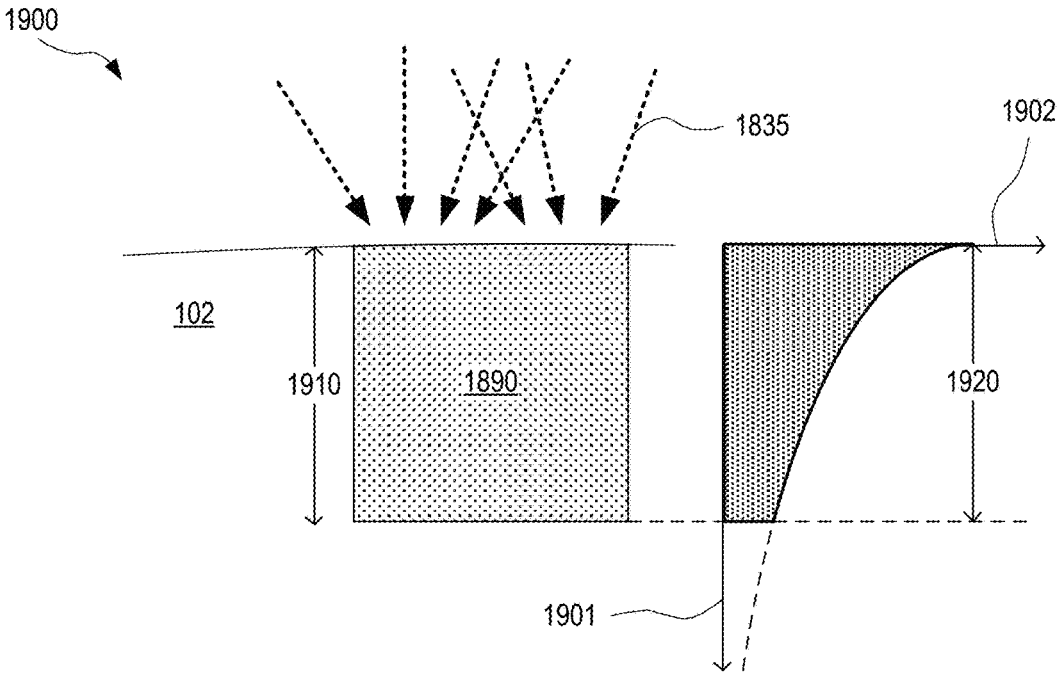

1800
CHARGED PARTICLE OR GAMMA RADIATION BEAM SOURCE 108
1848
1838
160
SURFACE MODEL PROCESSOR 1860
1852
CONTROLLER 1870
1812
1836
CORRECTION MODULE 1850
1840
1834
1832
1830
1833
1890
1835
Subject 102
104

FIG. 18


1900
1835
1902
102
1910
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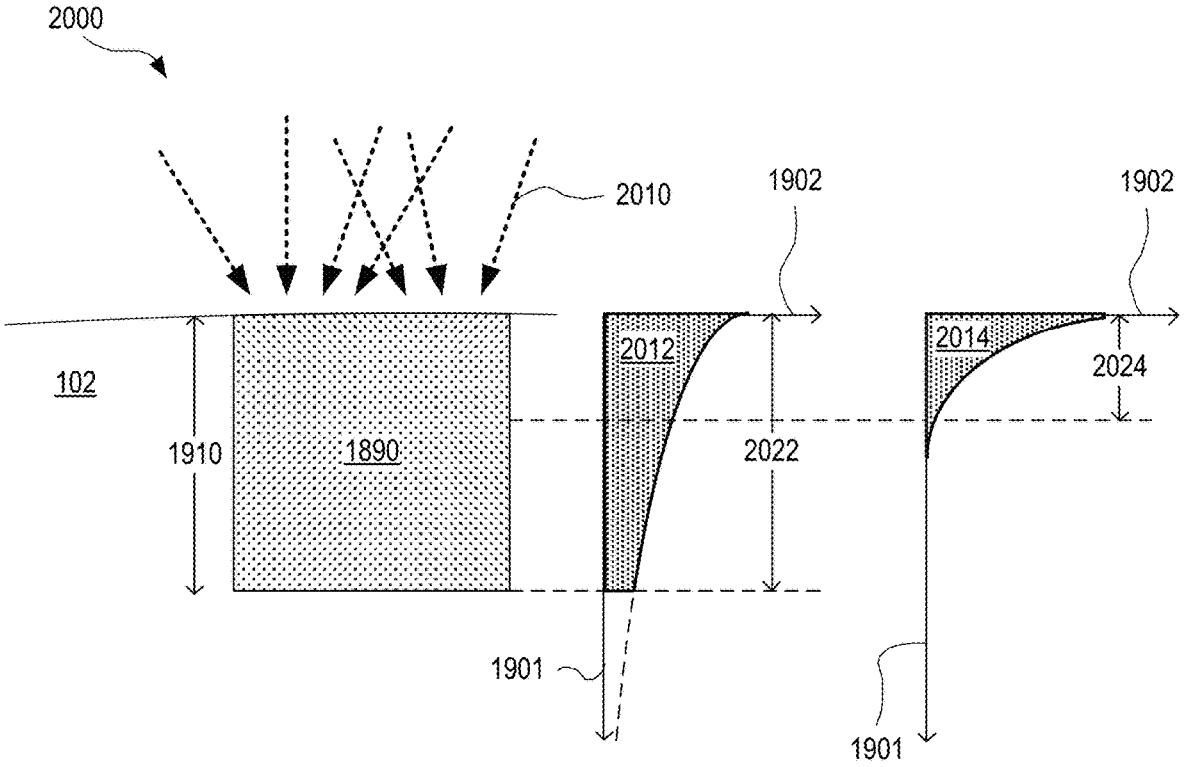
1920
1901

FIG. 19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2010
1902
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102
2012
2014
2024
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2022
1901
1901

FIG. 20

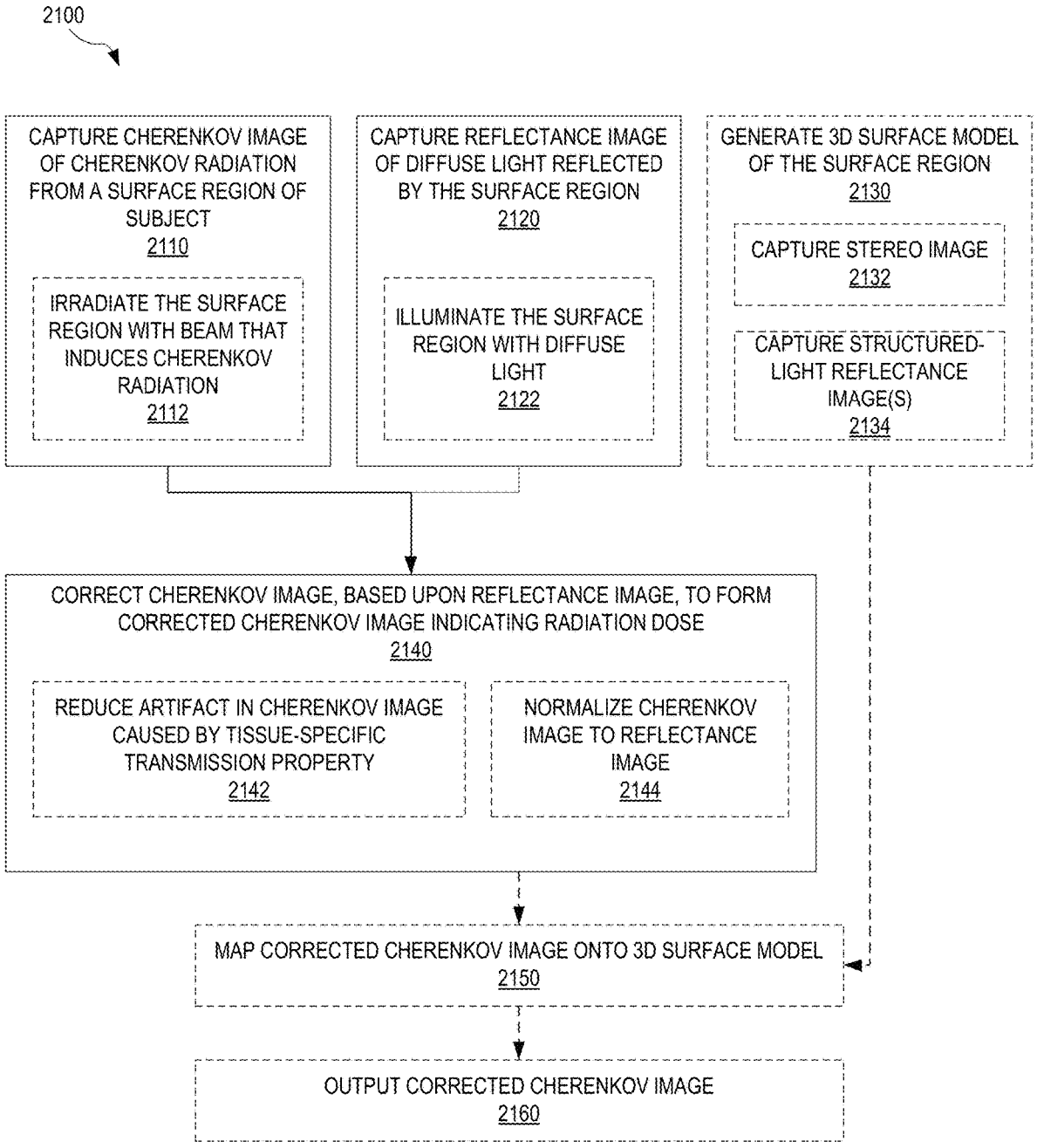
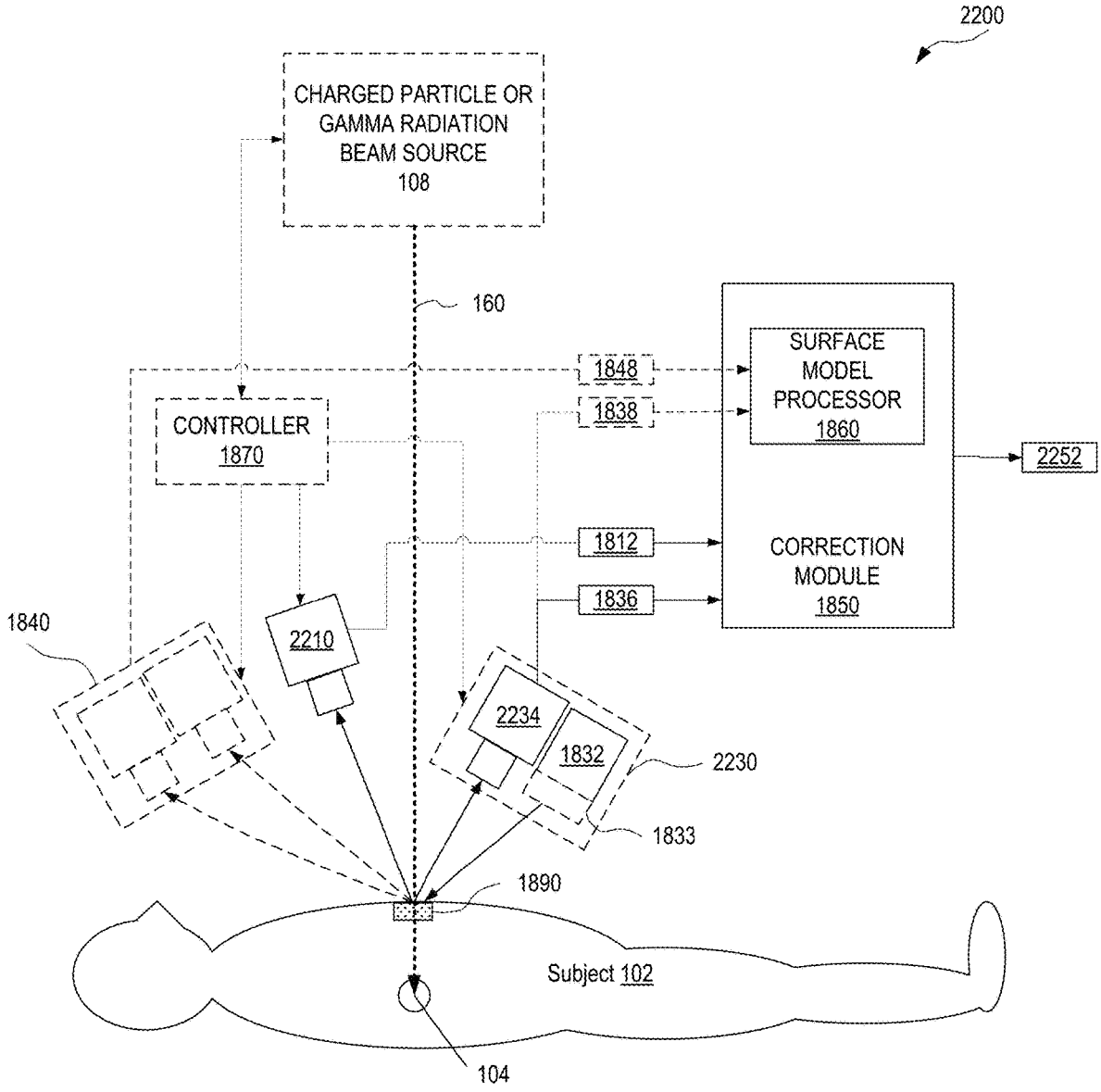

2100
CAPTURE CHERENKOV IMAGE OF CHERENKOV RADIATION FROM A SURFACE REGION OF SUBJECT
2110
IRRADIATE THE SURFACE REGION WITH BEAM THAT INDUCES CHERENKOV RADIATION
2112
CAPTURE REFLECTANCE IMAGE OF DIFFUSE LIGHT REFLECTED BY THE SURFACE REGION
2120
ILLUMINATE THE SURFACE REGION WITH DIFFUSE LIGHT
2122
GENERATE 3D SURFACE MODEL OF THE SURFACE REGION
2130
CAPTURE STEREO IMAGE
2132
CAPTURE STRUCTURED-LIGHT REFLECTANCE IMAGE(S)
2134
CORRECT CHERENKOV IMAGE, BASED UPON REFLECTANCE IMAGE, TO FORM CORRECTED CHERENKOV IMAGE INDICATING RADIATION DOSE
2140
REDUCE ARTIFACT IN CHERENKOV IMAGE CAUSED BY TISSUE-SPECIFIC TRANSMISSION PROPERTY
2142
NORMALIZE CHERENKOV IMAGE TO REFLECTANCE IMAGE
2144
MAP CORRECTED CHERENKOV IMAGE ONTO 3D SURFACE MODEL
2150
OUTPUT CORRECTED CHERENKOV IMAGE
2160

FIG. 21


2200
CHARGED PARTICLE OR GAMMA RADIATION BEAM SOURCE 108
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1848
1838
SURFACE MODEL PROCESSOR 1860
2252
CONTROLLER 1870
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Subject 102
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FIG. 22

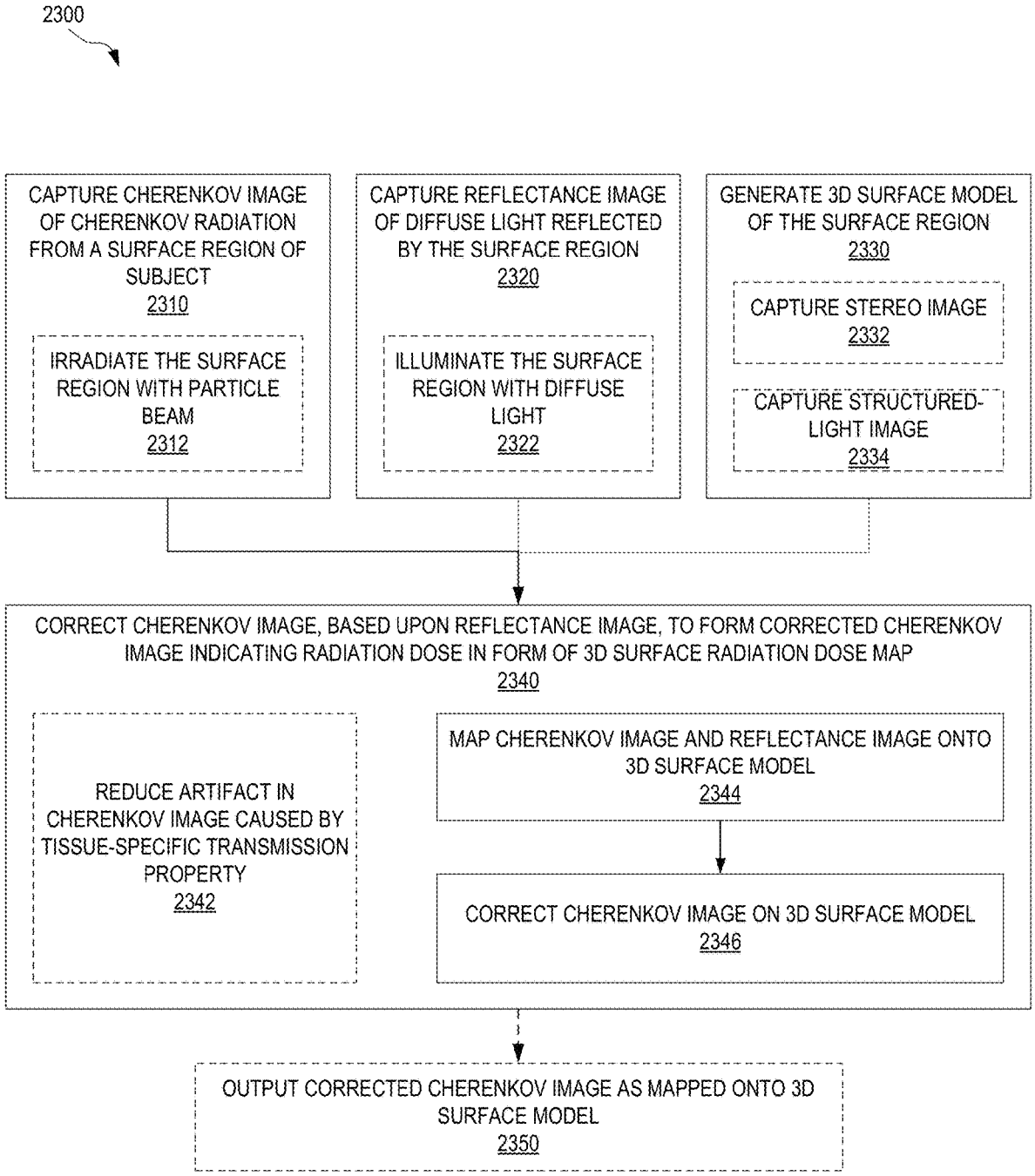
2300
CAPTURE CHERENKOV IMAGE OF CHERENKOV RADIATION FROM A SURFACE REGION OF SUBJECT
2310
IRRADIATE THE SURFACE REGION WITH PARTICLE BEAM
2312
CAPTURE REFLECTANCE IMAGE OF DIFFUSE LIGHT REFLECTED BY THE SURFACE REGION
2320
ILLUMINATE THE SURFACE REGION WITH DIFFUSE LIGHT
2322
GENERATE 3D SURFACE MODEL OF THE SURFACE REGION
2330
CAPTURE STEREO IMAGE
2332
CAPTURE STRUCTURED-LIGHT IMAGE
2334
CORRECT CHERENKOV IMAGE, BASED UPON REFLECTANCE IMAGE, TO FORM CORRECTED CHERENKOV IMAGE INDICATING RADIATION DOSE IN FORM OF 3D SURFACE RADIATION DOSE MAP
2340
REDUCE ARTIFACT IN CHERENKOV IMAGE CAUSED BY TISSUE-SPECIFIC TRANSMISSION PROPERTY
2342
MAP CHERENKOV IMAGE AND REFLECTANCE IMAGE ONTO 3D SURFACE MODEL
2344
CORRECT CHERENKOV IMAGE ON 3D SURFACE MODEL
2346
OUTPUT CORRECTED CHERENKOV IMAGE AS MAPPED ONTO 3D SURFACE MODEL
2350

FIG. 23

CHERENKOV IMAGING SYSTEMS AND METHODS TO MONITOR BEAM PROFILES AND RADIATION DOSE WHILE AVOIDING INTERFERENCE FROM ROOM LIGHTING

RELATED APPLICATIONS

This application is a continuation-in-part of PCT/US16/29458, filed Apr. 27, 2016, which claims priority to U.S. Provisional Patent Application No. 62/153,417 filed Apr. 27, 2015. This application is also a continuation-in-part of International Application No. PCT/US14/66668, filed Nov. 20, 2014, which claims priority to U.S. Provisional Patent Application 61/906,805, filed Nov. 20, 2013, and this application is a continuation-in-part of U.S. patent application Ser. No. 14/118,825, with a filing date of May 18, 2012 and § 371(c) date of Nov. 19, 2013, which is a § 371 National Phase Application of PCT Patent Application Serial No. PCT/US12/38609 filed May 18, 2012, which claims priority to U.S. Provisional Patent Application 61/488,129, filed May 19, 2011 and to U.S. Provisional Patent Application 61/585,366, filed Jan. 11, 2012. The disclosures of all these prior applications are incorporated herein by reference in their entireties.

GOVERNMENT INTEREST

This invention was made with Government support under NIH Grant Nos. R01CA109558 and R21EB017559, both awarded by the National Institutes of Health. The Government has certain rights to the inventions.

FIELD

The present document describes apparatus and methods for imaging and monitoring radiation treatments such as are frequently administered in malignant diseases.

A portion of the material disclosed herein resembles that in the published paper article entitled Cherenkov Video Imaging allows for the first visualization of radiation therapy in real time by Lesley A Jarvis, Rongxiao Zhang, David J. Gladstone, Shudong Jiang, Whitney Hitchcock, Oscar D. Friedman, Adam K. Glaser, Michael Jermyn, and Brian W. Pogue, reported in the International Journal of Radiation Oncology, Biology and Physics Volume 89, Issue 3, pp. 615-622, on Jul. 1, 2014 (Epub Mar. 28, 2014). The entire contents of this article are incorporated herein by reference.

This document relates to the detection and use of Cherenkov radiation (sometimes spelled Cerenkov radiation or Cerenkov radiation) emitted as a radiation beam strikes tissue to observe, verify accuracy in delivery and then also potentially control radiation treatment machines, to ensure that medical radiation prescription protocols are properly followed

BACKGROUND

It is desirable when treating cancers with radiation to have a high ratio of energy deposited in the tumor, relative to energy deposited in normal tissues surrounding the tumor, resulting in a high therapeutic ratio of tumor to normal dose. Radiation treatments using high energy electron particle beams or high energy photon beams are used in the treatment of many cancers. Such beams are typically provided by a linear accelerator, a cyclotron, or related apparatus.

Charged particles, such us electrons, positrons, protons, or alpha particles, moving at greater than the effective speed of light in a medium tend to slow down while releasing Cherenkov radiation. Mammalian tissue, including human tissue, is a medium where the speed of light is reduced relative to air or vacuum due to its refractive index being greater than unity. Therefore fast-moving charged particles release Cherenkov radiation after entering such tissue. Water is also a medium where the speed of light is reduced relative to air or vacuum, fast-moving charged particles in water also release Cherenkov radiation after entering such water. Cherenkov emission has been detected with incident radiation in the range of 6 to 24 MeV energies for both x-ray photons as well as electrons. It is expected that Cherenkov radiation will also be released from beams of very-high-energy protons and other charged particles.

When this Cherenkov light is induced in tissue, it is predominantly blue in color, but with a broad spectrum which tapers off into the green, red, and near-infrared (NIR) with an inverse square wavelength dependence given by the Frank-Tamm formula. This light emitted in tissue is attenuated by absorbers in the tissue, and can also excite other molecular species in tissue, inducing their photo-luminescence (fluorescence or phosphorescence).

Prior to treating patients with high energy beams, it is desirable to know the shape of the beam, and to verify that the beam shape is as planned. Additionally, when beams enter tissue it is important to accurately predict how radiation beam shape varies with depth in tissue, to ensure adequate dosage to tumor while minimizing dosage to surrounding normal tissues. If beam shape and position is adjusted by positioning deflection magnets or shielding devices, it can be important to confirm that the resulting beam shape and dosage profile are as desired prior to exposing patients to the beam; radiation treatment centers may therefore desire to confirm beam shape and dose profile for complex beam shaping procedures for each patient, or as part of routine calibration and maintenance.

Manufacturers of radiation treatment devices often prepare documentation of beam shapes and dosage profiles produced by common configurations of their devices for training users and guiding operators in using their machines to treat patients. Further, they must seek regulatory approvals of their machines, and as part of the regulatory approvals process they are expected to provide documentation of beam shapes and dosage profiles achievable by their machines. Manufacturers may therefore also need to accurately verify and document beam profiles for this regulatory approval process.

It is also desirable to monitor treatment in real-time, both to ensure treatment protocols are met and prevent accidental overdosing, and to image an intersection of the beam with skin to ensure that beam profiles are as expected for treatment protocols.

SUMMARY

In an embodiment, a system for providing monitored radiation therapy has a source of pulsed high energy radiation disposed to provide a radiation beam to a treatment zone, the high energy radiation of 200 keV or greater; a camera for imaging Cherenkov light from the treatment zone; apparatus for preventing interference by room lighting by synchronizing the camera to pulses of the radiation beam and blanking room lighting during pulses of radiation; and an image processor adapted to determine cumulative skin dose in the treatment zone from the images.

In an alternative embodiment, a system for providing and monitoring delivery and accuracy of radiation therapy has a

source of pulsed high energy radiation disposed to provide a radiation beam to a treatment zone, at least one imaging system camera configured to obtain observations images of light emitted from the treatment zone, the camera is synchronized to pulses of the pulsed high energy radiation. The system also has an image processor.

In a particular embodiment, the image processor has firmware adapted to subtract images acquired when the pulsed high energy radiation is off from images acquired when the pulsed high energy radiation is on to generate images of Cherenkov light.

In a particular embodiment, the processor uses a three-dimensional model of a subject to determine a mapping of image intensity in the images of Cherenkov light to radiation intensity in skin of the subject, to acquire multiple images of Cherenkov light, to apply the mapping to the images of Cherenkov light to map skin dose, and to accumulate skin dose by summing the maps of skin dose.

In another particular embodiment, biological features apparent in the tissue which appear in the Cherenkov emission image can be used as landmarks or fiducials for verification of the beam delivery accuracy. In particular the major blood vessels have high Cherenkov absorption and appear as dark lines in the image, and are therefore apparent in the images and useful for soft tissue fiducials. These are apparent in successive days in fractionated therapy, so that they could be used for patient alignment verification on a day to day basis. The images can be recorded and saved in the patient record for a permanent verification of the delivered radiation treatment.

In another embodiment, a method of determining surface dose during radiation treatment of a first object beneath a surface of a second object to limit dose at the surface includes obtaining stereo images of the surface, and extracting a three-dimensional computer model of the surface; determining a mapping of image brightness at the surface in Cherenkov light images obtained by a digital camera to radiation intensity; recording surface brightness at the surface in a plurality of Cherenkov light images; and a summing step including using the mapping of image brightness at the surface to translate each Cherenkov light image into a surface dose image, or summing the surface dose images to provide a total session surface dose image. The method continues with summing the image brightness in each Cherenkov light image into a total session surface Cherenkov light image and using the mapping of image brightness at the surface to translate the total session surface Cherenkov light image into a total session surface dose image. The method concludes with displaying the total session surface dose image.

In an embodiment, a Cherenkov imaging system for determining surface radiation dose for a subject undergoing radiation therapy includes (a) a first camera for capturing a Cherenkov image of Cherenkov radiation from a surface region of the subject undergoing Cherenkov-radiation-inducing radiation therapy, (b) a second camera for capturing a reflectance image of reflectance of optical illumination off the surface region, and (c) a correction module for correcting the Cherenkov image based upon the reflectance image to form a corrected Cherenkov image that indicates radiation dose for the surface region.

In an embodiment, a Cherenkov imaging method for determining surface radiation dose for a subject undergoing radiation therapy includes correcting a Cherenkov image, of Cherenkov radiation from a surface region of the subject undergoing Cherenkov-radiation-inducing radiation therapy, using a reflectance image, of optical illumination reflected by the surface region, to form a corrected Cherenkov image that indicates radiation dose for the surface region.

BRIEF DESCRIPTION OF THE DRAWINGS

FIG. **1** is an illustration of a system for performing monitored radiotherapy.

FIG. **2** is an approximate flowchart of a method of monitoring radiotherapy.

FIG. **3** is an illustration of an alternative embodiment of a system for performing monitored radiotherapy with time-controlled room lighting and camera sensing of light emissions from a subject.

FIG. **4** is a block diagram of apparatus for determining beam profiles of high energy radiation for use in radiotherapy.

FIG. **5** is an approximate timing diagram of time windows showing relationships of room lighting, beam pulses, and camera shutter windows.

FIG. **6** illustrates a system utilizing a single camera, or camera pair, on a rotating mount for determining profiles of high energy radiation for use in radiotherapy.

FIG. **7** illustrates the system of FIG. **3** from a different angle.

FIG. **8** illustrates a system having multiple cameras on a fixed mount outside the tank.

FIG. **9** illustrates a system having multiple cameras mounted inside the tank.

FIG. **10** illustrates a system having the beam enter the tank from above the tank.

FIG. **11** is a flowchart of a method of determining beam profiles of high energy radiation for use in radiotherapy.

FIG. **12** is an illustration having a spherical or cylindrical tank with internal cameras, with the tank mounted on a rotary mount.

FIG. **13** is an illustration of a radiation treatment system having realtime observation of skin dose using Cherenkov radiation emitted by the interaction of beam and skin.

FIG. **14** is an illustration of a three-dimensional model of tissue, such as a breast, derived by stereovision surface extraction and used in mapping image intensity to skin dose.

FIG. **15** is a flowchart of operation of the system of FIG. **13**

FIG. **16** is an illustration of skin dose intensity as imaged by the system of FIG. **13**.

FIG. **17** is a photograph of a subject indicating areas of skin damage correlated to areas of high dose in FIG. **16**.

FIG. **18** illustrates one Cherenkov imaging system for determining radiation dose for a surface region of a subject undergoing radiation therapy, according to an embodiment.

FIG. **19** is a diagram showing exemplary illumination of a surface region of a subject by optical illumination.

FIG. **20** is a diagram showing exemplary illumination of a surface region of a subject by multi-colored optical illumination.

FIG. **21** illustrates one Cherenkov imaging method for determining radiation dose for a surface region of a subject undergoing radiation therapy, according to an embodiment.

FIG. **22** illustrates another Cherenkov imaging system for determining radiation dose for a surface region of a subject undergoing radiation therapy, according to an embodiment.

FIG. **23** illustrates another Cherenkov imaging method for determining radiation dose for a surface region of a subject undergoing radiation therapy, according to an embodiment.

DETAILED DESCRIPTION OF THE EMBODIMENTS

A system **100** for providing radiotherapy and monitoring factors known to affect the effectiveness of radiotherapy, and monitoring effects of radiotherapy on tissue, is illustrated in FIG. **1**.

Portions of a subject **102** containing a tumor **104** requiring radiotherapy are placed within an enclosure **106** for excluding light. The enclosure **106** may be made of black plastic or cloth, and has a sealing portion **108** drawn tight by an elastomeric band such that a subject's eyes may be permitted access to ambient light and thereby prevent claustrophobia while still excluding room light from optical fibers **114**. It is anticipated that a variety of enclosures **106** may be provided to exclude light from various portions of a subject in various embodiments, in some embodiments light may be excluded from a subject's cranium, in others from a subject's chest or abdomen, according to location of tumor **104** within subject **102** and desired beam angles.

In an alternative embodiment, enclosure **106** is an entire room containing the subject **102**. In order to improve subject comfort, and taking advantage of visual persistence of the human eye and the pulsed nature of many radiation sources such as linear and cyclotron accelerators, a rapidly pulsed light source **107** is used that appears steady to the human eye. Pulses of light source **107** are timed, and appropriate gating of the detector **116** or camera **117** used, such that imaging or sensing of Cherenkov radiation is done at intervals where light source **107** is off, and radiation beam **110** is on. Acquisition of Cherenkov images is thereby done in synchronized room light conditions.

An accelerator **108**, or other device for providing high energy radiation, is aimed to provide a beam **110** of radiation through normal tissue **112** to tumor **104**. In all embodiments, the system herein described uses incident radiation from accelerator **108** at beam energies of at least 200 keV because, at beam energies of less than 200 keV (0.2 MeV), Cherenkov radiation is typically of insufficient intensity for imaging. In a particular embodiment, the accelerator **108** provides a beam of electrons having energy of 6 million electron volts (6 MeV) or greater, in a particular embodiment the beam energy lies between 6 and 24 MeV. In an alternative embodiment, the device for providing high energy radiation provides a beam of high energy photons, the photons interact with tissue or tumor to produce charged particles that in turn produce Cherenkov radiation. In an alternative embodiment, the accelerator **108** provides a high-energy proton beam. In an alternative embodiment, the radiation source is implanted in the body, inducing Cherenkov emission light directly as charged particles are emitted during radiation decay. The subject **102** and enclosure **106** is positioned within a room having subdued lighting.

Since high radiation doses are desired in tumors, while high doses are not desired in surrounding normal tissue or on skin because those tissues can be damaged by radiation, provisions are typically made for varying arriving beam delivery angles by, for example, rotating the subject and enclosure in the beam, rotating the radiation source about the subject and enclosure, or periodically interrupting treatment to reposition the subject and enclosure. Additionally the beam is shaped either in a static beam, or in other embodiments the beam shape is dynamically changed while rotation is performed, to allow customized dose delivery to the shape of the tumor to be treated, at each delivered beam angles.

At least one, and in an embodiment an array of many, optical fibers **114** are provided and positioned, such as in contact with or close to, subject **102** in enclosure **106**, for collecting any light that may be emitted from subject **102**. In an alternative embodiment, a camera system **117**, having a lens system adapted to collecting light from the subject and an array photosensor for detecting the collected light, positioned some distance from the subject is used to image light emitted from the tissue.

Optical fibers **114** provide light to multichannel spectrographic detector **116**. For each channel of the multichannel spectrographic detector **116** there is a wavelength-dependent dispersive device such as a prism or diffraction grating for separating light according to wavelength, and an array of photosensors such as a CCD or CMOS sensor, an array of PIN diodes, or an array of photomultiplier tubes. In another embodiment, optical filters are inserted in the detection channel before the spectrograph to reduce ambient light and Cherenkov emission above or below a specified wavelength range, thus reducing the required dynamic range of the detector.

For convenience in this document, the array of optical fibers **114** and detector **116**, or camera **117**, are forms of an imaging system adapted to imaging light from subject **102**, such as Cherenkov light generated by interactions of the beam of high energy radiation with tissue of the subject.

Detector **116** provides information indicative of received light amplitude at each of many wavelengths to processor **118**. Processor **118** analyzes this information to provide indications of heme concentration in tumor, oxygen concentration in tumor, and other parameters (such as metabolic activity and oxygenation) provided by photo-luminescent emission

In an alternative embodiment, detector **116** is a spectrally sensitive detector constructed of a filter wheel and photodetector, providing spectral information on captured light from fiber **114** by alternately interposing an assortment of filters each having a passband at a wavelength of interest. In an alternative embodiment, a tunable filter is used in place of a filter wheel. In another alternative embodiment, a filter wheel or tunable filter is placed in front of a camera positioned some distance from the subject. This embodiment allows collection of a series of images, each image of the series imaging light from the subject at a different wavelength band, to allow spectral analysis on the series of images.

In an alternative embodiment, detector **116** is timed to be enabled in a temporal relationship after each radiation pulse, such that the emissions from Cerenkov excited luminescence, such as phosphorescence or fluorescence, are captured, allowing a capture of images of light emitted from a secondarily-emitting chemical or indicating agent, such as a fluorescent or phosphorescent chemical, in or on the tissue and as stimulated by Cherenkov radiation emitted as radiation interacts with the tissue. This time sequenced signal is generated from the Cherenkov radiation, but can provide information regarding the bio-molecular environment of the tissue being irradiated. The secondarily-emitting chemical in some embodiments is a chemical intrinsic to the body, and in some embodiments is a drug, or a metabolite of a prodrug, that is administered to the subject.

In an alternative embodiment, detector **116** is replaced with a camera **117** having similar timing characteristics and spectral sensitivity. The imager, whether including detector **116** and/or camera **117**, in embodiments using secondarily-emitting substances may be sensitive to light in infrared as well as some visible wavelengths.

In a particular embodiment, the imager is a hyperspectral camera. For purposes of this document, a hyperspectral

camera is a camera having spectral response that extends beyond the visible light spectrum, such as a camera able to respond to at least some near-infrared light. Further, a hyperspectral camera is a camera that is adapted to resolve wavelengths of received light into more, and narrower, bins than the three (red, green, and blue) wavelength bins of a typical color electronic camera. Hyperspectral cameras are known in the electronic camera art that are capable of resolving received light into dozens of wavelength bands, including one or more infrared bands; such cameras may operate by using patterned filters on photosensor arrays that have more than the usual three colors of filters, or by using line-scanning spectrographic techniques.

The system **100** is operated according to a method illustrated in FIG. **2**. The subject is prepared **202** for multidose radiotherapy as known in the art of radiotherapy; tumor **104** is localized and imaged, alignment marks may be applied by tattoo or in other ways, and aiming and positioning masks or frames may be made. A desired dose of radiation for each session is prescribed.

Prior to each session for which monitoring is desired, in an embodiment an enhancing and indicating agent is administered **204**. In an embodiment, the enhancing and indicating agent is a dose of 20 milligrams per kilogram body weight of 5-delta-aminolevulinic acid (5-ALA), the dose being administered an incubation time of approximately four hours before each divided radiotherapy session begins.

In metabolically active tumor **104**, some of the 5-ALA is metabolized to Protoporphyrin IX (PpIX). In alternative embodiments, it is expected that other enhancing agents may be developed or utilized. PpIX production in normal tissue **112** and tumor **104** is due to metabolic processes in those tissues and a quantity of PpIX produced in those tissues is dependent on an amount of metabolic activity in those tissues.

The subject **102** is then placed **206** in a darkened environment, which in an embodiment includes placing those parts of the subject to be subjected to radiotherapy within enclosure **106**, and positioning light collecting fibers **114** to collect light from the subject **102**, as heretofore described with reference to the enclosure.

The tumor is then treated **210** by having accelerator **108** then provide a beam of high energy charged particles aimed along a beam path at tumor **104** to perform radiotherapy of the tumor. In an embodiment, the subject **102** may be rotated during the session to distribute radiation absorbed by normal tissues **112** while maintaining beam targeting at tumor **104**.

As charged particles of beam **110** decelerate in both normal tissue **112** and tumor **104**, these particles generate light by Cherenkov radiation, with broadband spectral constituents decreasing with wavelength to the inverse square power.

Some of the light generated by Cherenkov radiation propagates to light collecting fibers **114**, and some may be absorbed by fluorophores (or phosphors) within subject **102**, including fluorophores (or phosphors) within normal tissue **112** and tumor **104**. Among fluorophores within subject **102** are any PpIX produced from metabolic activity in tissue **112** and tumor **104**. Light from Cherenkov radiation that is absorbed by fluorophores (or phosphors) in tissue and tumor may stimulate photo-luminescent emission by those tissues and tumor.

Light from both Cherenkov radiation and photo-luminescent emission propagates from the beam path to a surface of the subject **102**, intersecting any tissue between the tumor and the surface, and being attenuated by absorption from molecular absorbers such as deoxyhemoglobin, oxyhemoglobin, proteins, lipids and water before being emitted from the subject.

The dominant absorption is from deoxyhemoglobin and oxyhemoglobin, which differ in their spectral absorption, and so changes in spectral characteristics of the attenuated light emitted from the subject are a reasonable measure of oxygen saturation of the blood in the region.

Protoporphyrin IX (PpIX), formed in tissue from 5-ALA as part of the heme synthesis pathway that is upregulated in many tumors, absorbs across the visible spectrum, with a large absorption in the blue Soret band. This absorption leads to fluorescence emission from PpIX in the 640-720 nm wavelength range. In an embodiment, incident radiation stimulates emission of blue Cherenkov radiation within the subject, which in turn stimulates fluorescent light emission by PpIX; some of the fluorescent light from the PpIX is then emitted from the subject and imaged.

Light emitted from the subject **102**, both of Cherenkov origin as modulated by absorption in tissue and tumor, and of fluorescent (or phosphorescent) origin, and attenuated by molecular absorbers in the subject, is captured **212** by fibers **114** or camera **117**. This light is directed to multichannel spectrographic detector **116**, which performs a spectral analysis of received light. Electronic spectrographic signals indicative of light amplitude at each of several wavelengths of interest are provided from spectrographic detector **116** to processor **118** for processing.

In an embodiment, processor **118** utilizes a model of light propagation from the beam path through a model of subject **102** to determine a spatial model of light emitted within, and light attenuation within, subject **102** and tumor **104**. It is expected that such an embodiment could offer enhanced accuracy over an uncorrected system. In an embodiment, a Monte-Carlo photon propagation model is used.

In an alternative embodiment, beam **110** is directed at tumor **104** from multiple angles through tissue **112** within each treatment session. In such an embodiment, processor **118** uses information regarding beam angle to correlate measurements such that tumor oxygenation and tumor metabolic activity determined during one session is compared with tumor oxygenation and metabolic activity determined along a similar beam angle in other sessions.

Processor **118** quantifies Cherenkov emission **216** in tumor and total hemoglobin from an amount of light measured at one or more wavelengths to which oxyhemoglobin and deoxyhemoglobin are isosbestic.

Processor **118** quantifies percent oxygenation **218** of hemoglobin in tumor from light quantity received at 2 specific wavelength bands such as bands centered at 750 nm and 580 nm wavelengths. Alternatively the measured spectral characteristics of light captured by fibers **114** are curve-fit to pre-measured Cherenkov emissions spectra and transmission attenuation data obtained from samples of liquid with blood and water that have been oxygenated and deoxygenated.

Processor **118** quantifies metabolic activity **220** of tumor by quantifying fluorescent emission from PpIX by quantifying received light from fibers **114** in the 640-720 nanometer wavelength band, and applying any corrections provided in the embodiment. In alternative embodiments, these corrections may include corrections from a Monte-Carlo or diffusing photon propagation model of the tissue.

The stimulation of fluorescence emission by protoporphyrin IX can be taken as a signal which is proportional to the amount of PpIX produced, and this is indicative of metabolic activity in the tumor. Destruction of cellular mitochondrial

function through radiation damage due to the applied radiotherapy would appear in some embodiments as a reduction of PpIX production, and hence a decrease in light emitted at PpIX fluorescent wavelengths versus light emitted at Cherenkov wavelengths in the detected spectrographic signals.

In an alternative embodiment, fluorescent emissions from another metabolite are used as a fluorophore for tracking metabolic activity of tumor **104**, the fluorophore being excited by the Cherenkov radiation. In alternative embodiments, the fluorescent emission could be used to track the activity of an alternative enhancement agent, such as antibodies or antibody fragments to cell surface receptors tagged with a fluorescent (or phosphorescent) dye. In yet other alternative embodiments, fluorescent emissions from NADH or NAD excited by the Cherenkov radiation are used as indicators of metabolic activity within tumor **104**.

Since radiation damage to tumor cells during radiotherapy involves free radical reactions, it is expected that treatment effectiveness will depend somewhat on the relative oxygenation of heme at the tumor **104** as monitored by processor **118**. Further, changes in metabolic activity in tumor **104** from a first treatment session to a later second treatment session as measured by PpIX or other fluorescent emissions measured by processor **118** are also expected to be indicative of treatment effectiveness. In fractionated radiotherapy subjects may receive as many as 30 to 40 fractions of a total radiation dose, each fraction being administered on a separate day as part of a total treatment series. During the treatment series, changes in tumor metabolic activity are expected if the tumor is responsive to therapy. It is expected that metabolic signal changes would occur as a decrease in the fluorescent signal over time if the patient is responding to therapy.

These measures of treatment effectiveness are presented to a physician and used to adjust **222** the treatment plan, both of the radiotherapy and following adjunct therapies such as chemotherapy.

In an embodiment, multiple spectrographic analyzers are provided, each coupled to receive Cherenkov and fluorescent emissions from a different point on the subject through separate pickup fibers. In this embodiment, diffuse optical modeling or Monte Carlo modeling software executing on processor **118** allowing reconstruction of a shape and spectral characteristics of an emissions zone within the subject, and for determining spectral characteristics of light emitted within the tumor as opposed to light emitted elsewhere (such as in normal tissues) in the subject by compensating for changes due to light transport in surrounding tissues. The diffuse optical modeling software provides for more accurate estimation of the fluorescent emissions thereby refining the measurements to more directly inform about pertinent areas of tissue.

In an alternative embodiment, light emissions from the subject are sampled only from certain predetermined beam locations or from certain predetermined locations within the subject, with the goal of maximizing information from non-tumor tissues. Also, in an alternative embodiment, comparison of measurements of emitted light spectra from tumor and non-tumor regions is performed to accurately calibrate data to the individual subject, making interpretation of changes over different days more reliable.

In an alternative embodiment, in addition to collecting fibers **114** placed at a surface of subject **102**, there are additional optical collecting fibers (not shown) placed within body cavities or, in some alternative embodiments, even directly implanted in tumor **104**. Light from such fibers is processed by spectrographic detector **116** and processor **118** in a manner similar to that stated herein for light from fibers **114**. Such additional collecting fibers may permit improved accuracy by enabling the system to track light signals which do not propagate well in tissue, or minimizing the spectral distortion of light passing through tissue to the detector. In an alternative embodiment, implantation of fibers onto surfaces or in cavities is incorporated as part of radiation therapy preparation.

Measurement of emission stimulated by radiation emitted from implanted radio-isotope sources, such as brachytherapy seeds is feasible, and can allow direct measurement at the tissue site where the radiation is imparting maximal energy. Implanting fiber optic measurements at these sites is feasible via fiber optics or small photodiode arrays. Following the same procedures as above, the tissue function or blood oxygen saturation could be probed during the prolonged delivery of radiation during brachytherapy radiation delivery.

Many sources of high energy charged-particle beams, including cyclotrons and some other particle accelerators, including some linear accelerators, provide pulsed beams. Further, the human visual system is known to integrate received light, so that black intervals that are short enough, and repeated rapidly enough, may not be noticed by a human subject. In an alternative embodiment, therefore, the enclosure **106** is omitted. The treatment room is sealed to exclude all natural and uncontrolled artificial light. Timing interfaces **120** are provided for determining intervals of beam transmission, and for controlling pulsed room lighting **122**.

In operation, the timing interfaces **120** controls an effective shutter (FIG. **5**) interval **200** of the spectrographic detector **116** to effectively consider only light received by the cameras in an interval **202** during and/or surrounding pulses of, and including a fluorescent decay interval **204** after, pulses **206** of the beam. Timing interfaces **120** also controls and pulses room lighting such that the shutter interval does not overlap pulses **208** of the room lighting. Light received at the spectrographic detector **116** during multiple shutter intervals is totalized, in an embodiment at the camera, and in an alternative embodiment multiple images are captured and per-channel spectrographic light totals are totalized by processor **118**.

In an alternative embodiment **150** (FIG. **3**), as an alternative to optical fibers **114** and multichannel spectrographic detector **116**, high-sensitivity electronic cameras **166**, **168**, are used to image Cherenkov light and localize locations on the subject where this light is emitted. In another alternative embodiment, some optical fibers **114** and multichannel spectrographic detectors **116** are provided, with the fibers placed in particular tumor locations, and electronic cameras **166** are provided for imaging light escaping from the subject.

A subject **102** is placed in the path of a radiation beam **160** such that the beam intersects tumor **104**. Beam **160** is provided by an accelerator **108**, or other device for providing high energy radiation, and is typically shaped by beam-shaping apparatus **164**.

The subject **102** is located within an environment that excludes daylight, and light from uncontrolled sources, such as incandescent lamps, is also excluded.

In an embodiment, a drape or paint of a light-absorbing material is provided so that stray light emitted from the subject **102** and not absorbed by a camera **166**, **168** is absorbed.

In an embodiment, the accelerator **108** provides a beam of electrons having energy of 6 million electron volts (6 MeV)

or greater, as used to provide treatment energy to deep tumors as opposed to treatment of surface skin. In a particular embodiment the beam energy lies between 6 and 24 MeV. In an alternative embodiment, the accelerator **108** produces a photon beam of 6 MeV or greater. In another alternative embodiment, the accelerator **108** provides a high-energy proton beam. In an alternative embodiment, an electron beam having electron energy of 0.5 MeV or greater is used.

At least one camera **166** is used to capture the images, and in an embodiment a second or more cameras **168**, are positioned to provide multiple images of Cherenkov and fluorescent radiation emission from subject **102**. In an embodiment, multiple cameras with a defined linear and angular spacing between them at each camera location are provided.

The cameras **166**, **168** are coupled to camera interface **172** of image processing system **174**; camera interface **172** captures and stores digital images from the cameras **166**, **168**, in memory **176** for processing by at least one processor **178** of the image processing system **174**. In addition to interfaces to the camera interface **172** and memory **176**, processor **178** interfaces with a timing interface **120** and a display subsystem **182**. Timing interface **120** is adapted to determine timing of pulses of radiation from the radiation beam source **108**, to control pulsed room lighting **122** to avoid interference from room lighting in the way discussed with reference to FIG. **5**, and to synchronize light or image capture by spectrographic detector **116** or cameras **166**, **168** at shutter intervals discussed with reference to FIG. **5**.

In an alternative embodiment, instead of blanking room lighting during pulses of the radiation beam, room lighting is left on, but subdued. The image processor is configured by machine readable instructions to operate the camera twice for each Cherenkov-light image. The camera is operated to obtain a first image during the time the radiation beam is ON; this image is exposed by both room lighting and by Cherenkov light. A second image is then obtained during a nearby time, and for an equivalent shutter period, when the radiation beam is OFF, and therefore is exposed by room lighting alone. The Cherenkov-light image used for further processing is determined by the image processor by subtracting the second image from the first image, leaving an image corresponding to an image taken under Cherenkov light alone.

In yet another alternative embodiment, during a radiation treatment the room lighting is replaced by a subdued, monochromatic, light at a first wavelength or first wavelength band. This may, for example, be light provided by light-emitting diodes. The Cherenkov-light images are obtained at wavelengths other than the first wavelength by use of a notch filter that blocks light of the first wavelength or wavelength band. Since Cherenkov emissions are typically broadband, albeit more intense toward the blue end of the spectrum, a Cherenkov-light image that excludes light of the first wavelength, but includes other wavelengths, is adequate for determining beam shape and intensity of skin irradiation. For example, the first wavelength may be a green wavelength. Cherenkov light emitted at the skin surface can be visualized by imaging at blue wavelengths, and, since heme in tissue blocks many short wavelengths of light, Cherenkov light emitted at deeper levels in tissue may be visualized by imaging at wavelengths in red wavelengths. Cherenkov-stimulated fluorescent and phosphorescent emissions may also be visualized by imaging at wavelengths in the infrared and red visible wavelengths.

As the beam penetrates subject **102**, Cherenkov light is emitted within an emissions zone **125**, including the tumor **104**.

In an embodiment, the imaging system cameras **166**, **168** are spectrally-sensitive cameras capable of providing spectral data permitting distinction between Cherenkov and fluorescent light, and in a particular embodiment permitting distinction between oxyhemoglobin and deoxyhemoglobin. Spectrally-sensitive cameras suitable for this application may be implemented as black and white cameras equipped with apparatus for positioning and changing filters in front of each camera, such as rotatable multiple-filter disks; by deposition of custom filter elements in a pattern on pixel sensors of a photosensor array as is common for color cameras; or in other ways.

In embodiments, raw or de-noised images from the imaging system are recorded in a suitable digital memory system as documentation of the radiation treatment.

While Cherenkov radiation is emitted during beam pulses **206** (FIG. **5**), light emitted **209** from naturally occurring, artificially administered, and drug metabolite fluorescent materials within a subject, including PpIX, lags the beam and decays exponentially after each pulse of the beam turns off as illustrated. In an embodiment therefore, an effective shutter interval during beam pulse **206** is used to image light primarily emitted by Cherenkov mechanisms, and an effective fluorescent-emissions shutter interval **211** is used to capture light emitted from the subject or phantom by fluorescent and phosphorescent mechanisms. In this embodiment, light arriving in fibers **114** or light imaged by cameras **166**, **168**, is recorded as image pairs, with a first image of each pair indicative of light emitted during beam pulse **206** and a second image of each pair indicative of light emitted during the fluorescent shutter interval **211**. Processor **118** or **178** executes machine-readable instructions in associated memory, such as memory **186** to reconstruct first tomographic image sets of the subject from the first images of all image pairs captured, to reconstruct second tomographic image sets of the subject from the second images of all image pairs captured, and the ratios or otherwise processes the first and second tomographic image sets to determine a tomographic image set of fluorophore distribution in the subject.

In embodiments, such as those where 5-ALA is administered, where fluorophore distribution is related to metabolic activity in the subject, the tomographic image set of fluorophore distribution in the subject is also indicative of metabolic activity in the subject. The processor **118** or **178** further executes machine readable instructions in memory to compare the tomographic image set of fluorophore distribution in the subject against a tomographic image set of fluorophore distribution obtained during a prior radiation treatment session to produce a tomographic image set indicative of treatment effectiveness.

Since both an enclosure **106** surrounding and excluding ambient light from the subject, and the combination of timing interfaces **120** and pulsed room lighting **122** serve to prevent interference of room lighting from interfering with measurement of Cherenkov radiation and fluorescent radiation emitted from an emissions zone in the subject, the term "apparatus for preventing interference by room lighting" as used herein shall mean either or both of an enclosure **106** surrounding and excluding ambient light from the subject, and the combination of timing interfaces **120** and pulsed room lighting **122**.

Cherenkov radiation and associated fluorescent emissions are useful for beam profiling and calibration as well as for monitoring treatment.

A system **300** for providing radiotherapy equipped with a subsystem for determining beam profiles is illustrated in FIG. **4**.

A beam-calibration phantom **302** is placed in a zone where it is desired to measure a profile of a radiation beam **310** provided by a radiation treatment machine **312**. The zone may be a volume above or beside a treatment table **306**. In many embodiments, the phantom is a fluid-filled tank, the fluid in the tank being a transparent fluid having an index of refraction greater than that of air; in a particular embodiment the transparent fluid is water. In an embodiment, the tank has transparent top and sides such as glass or transparent plastic. In a particular embodiment the tank has sides constructed of acrylic sheets; another particular embodiment has sides constructed of polycarbonate panels. In an embodiment, a small amount of scattering agent is added to the liquid in the tank to enhance scatter of Cherenkov light but not affect propagation of the radiation beam, overcoming directionality of Cherenkov light and allowing more light to be detected laterally around the tank. The treatment room may be blacked out to prevent interference of ambient light with measurements of the Cherenkov radiation because a phantom is not subject to claustrophobia like live subjects.

In an alternative embodiment, the tank is filled with a transparent fluid having an index of refraction greater than that of water, such as silicone oil. In yet another embodiment, the phantom is formed from a high-index, transparent, material, such as a cast high-index plastic, and may have both fluorophores and light-scattering additives embedded within it.

The treatment table **306** and phantom **302** are located within an environment that excludes daylight, and light from uncontrolled sources, such as incandescent and fluorescent lamps, and LED indicator lights, is also excluded. In another embodiment, the phantom walls are coated on their interior surface with a light-absorbing coating except for camera viewing windows positioned in front of each camera, the coating is provided to absorb both stray light originating from outside the phantom and to prevent Cherenkov light from being reflected from the phantom wall into a camera to give a false indication of beam profile.

In an embodiment, a drape of a light-absorbing material is provided so that stray light emitted from Cherenkov radiation zone **320** and not absorbed by a camera is absorbed without being scattered back to the treatment zone. The light-absorbing drape improves contrast in Cherenkov images by reducing stray light.

An accelerator **308**, or other device for providing high energy radiation, is aimed to provide a beam **310** of radiation through beam-shaping apparatus **314** to phantom **302**. In an embodiment, the accelerator **308** provides a beam of electrons having energy of 6 million electron volts (6 MeV) or greater, in a particular embodiment the beam energy lies between 6 and 24 MeV. In an alternatively embodiment, the accelerator **308** produces a photon beam of 6 MeV or greater. In an alternative embodiment, the accelerator **308** provides a proton beam. In an alternative embodiment, the accelerator **308** produces a beam of electrons or photons having a substantial percentage of electrons or photons having energy of 1 MeV or greater.

At least one camera **316** is used to capture the images, and in an embodiment a second or more cameras **318**, are positioned to provide multiple images of the Cherenkov radiation emission zone **320** where beam **310** intersects the transparent fluid of phantom **302**. In an embodiment, as illustrated in FIG. **4**, a pair of cameras is used by providing two cameras **316** with a defined spacing between them at each camera location, allowing imaging of the beam with or without tomographic recovery. In an alternative embodiment as illustrated in FIG. **6**, a single camera **316**; or in a variation as illustrated in FIG. **7**, a single camera pair **316** is provided; the embodiments of FIGS. **6** and **7** mount the camera or camera pair on a rotary, movable, mount **340** such that single images, or stereo pairs of images, can be made of the Cherenkov emissions zone from several camera positions, In the interest of simplicity, structure and bearings for supporting the rotary mount **340** and motor **341** has not been shown. The embodiment of FIG. **7** illustrates the beam entering the tank from out of the page.

While the embodiments of FIGS. **6**, **7**, **8**, and **9** illustrate the beam entering the tank from a side of the tank, the method is applicable to beams entering the tank from any angle, including by way of example a beam as illustrated in FIG. **10**. where the beam comes from above the tank.

The cameras **316**, **318** are coupled to camera interface **322** of image processing system **324**; camera interface **322** captures and stores digital images from the cameras **316**, **318**, in memory **326** for processing by at least one processor **328** of the image processing system **324**. In addition to interfaces to the camera interface **322** and memory **326**, processor **328** interfaces with a timing interfaces **330** and a display subsystem **332**.

In an alternative embodiment, as illustrated in FIG. **8**, a plurality of cameras **370** are disposed on a fixed frame **372** outside the volume of the phantom but configured to provide images of the emissions zone **320** from several angles.

In an alternative embodiment, as illustrated in FIG. **9**, a plurality of submersible cameras **374** are disposed within the volume of the phantom and configured to provide images of the emissions zone **320** from several angles. In a particular embodiment, submersible cameras **374** are cemented to a wall of phantom **376**.

In a particular embodiment, a camera is disposed to image the emissions zone from approximately every 60 degrees in the horizontal plane, into which the radiation beam is being sent. The camera field of view is designed to capture the relevant depth of the beam into the tank from above, and the depth of focus of the cameras is designed to capture light from the entire cross section of the beam. The angular arrangement is chosen to allow capture of the beam profile data in a time which matches with the temporal requirements of characterizing the beam. For example, fast beam profile changes or complex beam cross section shapes require more cameras and less mobile cameras, for fast profile imaging.

Camera numbers and viewing angles may in some embodiments be determined according to the expected beam profile; for example standard square beam cross sections may only require one or two cameras to characterize the beam, and may not even require tomographic recovery to characterize the beam. Where imaging time is unconstrained, beams may be imaged with a rotation stage or rotating frame for sequential imaging of the beam from multiple angles. A standard square beam may be adequately profiled by only two camera positions at 90 degrees from each other, whereas a non-square or non-circular beam would require more camera positions for tomographic recovery of the profile. If adaptive delivery of radiation such as arc therapy or intensity modulated radiation therapy are imaged, then multiple parallel cameras would be desirable to allow imaging of the complex beam cross sections in reasonable or in real time during delivery to the tank. The

time constraints and complexity of the beam therefore determine the exact number of cameras and degree of sequential or parallel acquisition.

In each embodiment, as illustrated in FIG. **11**, the tank is positioned **702** in the beam, and beam adjustment devices, if any, are adjusted **704** to provide a particular beam profile. The cameras **316**, **318**, **370**, **374** in all embodiments are disposed to provide images of the Cherenkov radiation emissions zone **320**, where beam **310** intersects fluid of phantom **302**, and may be repositioned **706** if movable camera mounts are used. It should be noted that, because cameras are likely to be damaged if the beam directly impinges on the camera, movable mount **340** is configured, and the cameras are located, to avoid direct impingement of the beam on any camera.

In each embodiment, images and/or stereo pairs of images each are taken by sequentially **708** turning OFF room lighting, opening effective or physical camera shutters, pulsing the beam, then sequentially **710** turning off the beam, closing shutters, and turning ON room lighting. This process results in multiple images taken from multiple angles of Cherenkov radiation zone **320** by cameras **316**, **318**, **370**, **374**. Once sufficient images are captured, they are processed **712** by processor **328** to generate a fully three dimensional image of the Cherenkov emission. These images are then used to tomographically reconstruct the beam profile.

Prior to reconstruction of the beam profile from the images, the images obtained by any cameras located outside the phantom volume (such as those of FIGS. **4**, **6**, and **8**) are corrected for distortions caused by refraction as light passes from the emissions zone **320** through known surfaces of the phantom.

A combination of rotation angles both vertical and lateral around the beam may be used.

The multiple camera image formation by tomography would use a filtered backprojection computational algorithm for recovery of the emissions zone **320**.

It is known that Cherenkov emissions from beams of intensities used during radiotherapy are somewhat dim, hence sensitive cameras with long, integrated, exposures are required, and it is also advisable to avoid interference from extraneous lighting sources. In an alternative embodiment, sensitive cameras take multiple short exposures, the multiple exposures being summed to provide an overall integrated exposure.

Timing interfaces **330** are arranged to sense a timing of beam pulses provided by particle beam source **308** and to control room lighting **334** such that room lighting is pulsed and does not overlap pulses of beam **310**. Similarly, timing interface **330** is arranged to control capture of images at camera interface **322** from stereo camera pairs **316**, **318** to capture images of light emitted at emission zone **320** during pulses of beam **310**, and to ignore light received by camera pairs **316**, **318**, during pulses of room lighting. It is anticipated that room lighting **334** may be provided by fast-responding light-emitting diode arrays.

In operation, the timing interfaces **330** controls an effective shutter (FIG. **5**) interval of the cameras or stereo camera pairs **316**, **318**, **370**, **374** to effectively consider only light received by the cameras in an interval **202** surrounding pulses of the beam. The timing interfaces **330** also controls and pulses room lighting such that the shutter interval does not overlap pulses of the room lighting. Light received at the cameras **316**, **318**, **370**, **374** during multiple camera intervals is totalized, in an embodiment at the camera, and in an alternative embodiment multiple images are captured and pixel light totals are totalized by processor **328**.

Once sufficient light is received at cameras **316**, **318**, **370**, **374** during the shutter intervals and totalized images prepared in or read through camera interface **322** into memory **326**, the beam is shut off. Then at least one processor **328** then processes the images in memory **326**, to construct a three-dimensional model of light emissions in the emission zone **320**. Since the light emissions in the emissions zone are from Cherenkov radiation emitted as charged particles of beam **310** decelerate in the fluid of the phantom, with broadband spectral constituents decreasing with wavelength to the inverse square power, these light emissions relate directly to radiation dose from beam **310** passing into and absorbed in the emissions zone **320**. Further, since Cherenkov radiation is emitted from where the beam intersects fluid of the phantom in emissions zone **320**, and not from surrounding un-irradiated fluid, the reconstructed three dimensional model of light emissions in emissions zone **320** provides an indication of beam shape.

The processor **328** then uses display subsystem **332** to provide displayable images illustrating cross section, overall surface, and tomographic images representing radiation dose profile in the emissions zone **320**. In a particular embodiment, processor **328** has at least one processor as known in the art of computing coupled to execute instructions from a memory system; in an embodiment the memory contains machine readable instructions for processing multiple sets of images to construct the three-dimensional models of light emissions in the emission zone **320**, and to prepare displayable images representing radiation dose profile in the emissions zone; the memory containing machine readable instructions may be the same or a different memory than the memory **326** in which images are stored.

In an embodiment, processor **328** has calibration information in its memory system, and translates the determined three dimensional models of Cherenkov light emission in the emissions zone into three dimensional models of radiation intensity and/or dose.

Monte Carlo simulations are used to study the complex directionality of Cherenkov radiation at each spatial location within the irradiated tank. Due to the finite field of view of the cameras, the intrinsic proportionality between the imparted dose and emitted Cherenkov radiation may be distorted. Therefore necessary calibration factors may be sought through analysis of the system and its camera placements. Additional correction factors may be necessary to correct for inherent differences between the emitted Cherenkov light and imparted dose, specifically spatial locations where the relative fluence of low keV energy electrons is high.

Because fluorescent emissions are omnidirectional, a fluorophore or fluorescent dye in a phantom helps overcome distortions that may otherwise result due to the directionality of emitted Cherenkov radiation, whether the charged particles are part of a charged-particle radiation beam or induced by high-energy photons of a gamma-ray photon beam.

Since high index materials may absorb radiation differently than does tissue, in an embodiment processor **328** has calibration information in its memory system for adjustment for beam attenuation in the phantom, and translates determined three dimensional models of light emission in the emissions zone into three dimensional models of radiation dose in tissue using that calibration information.

While Cherenkov radiation is emitted during beam pulses **206** (FIG. **5**), light emitted **209** from fluorophores lags the

beam and decays exponentially after each pulse of the beam turns off as illustrated. In an embodiment therefore, an effective shutter interval during beam pulse **206** is used to image light primarily emitted by Cherenkov mechanisms, and an effective fluorescent shutter interval **211** is used to capture light emitted from the phantom by fluorescent and phosphorescent mechanisms. In this embodiment, light imaged by cameras **316**, **318** is recorded as image pairs, with a first image of each pair indicative of light emitted during beam pulse **206** and a second image of each pair indicative of light emitted during the fluorescent shutter interval **211**. Processor **328** therefore executes machine-readable instructions in associated memory, such as memory **326** to reconstruct beam shape and beam energy distribution profiles from the captured image pairs.

In an alternative embodiment, in order to increase sensitivity and improve contrast, images obtained during and after **211** multiple pulses **206** of the beam are summed and/or averaged.

In an embodiment, an operator may turn on the beam, and have the system construct a model of emissions zone **320**, then turn off the beam and view the images provided on display subsystem **332**. If the beam fails to meet specifications **714** for a particular treatment, the operator may then use the images provided on display subsystem **332** to determine a different setting of beam-shaping apparatus **314** that should provide a beam that more closely resembles a beam desired for treatment of a patient. The operator may then adjust beam shaping apparatus **314**, following which the beam is turned back on while new images of Cherenkov radiation in emissions zone **320** are captured by the cameras **316**, **318**, **370**, **374**, the beam then being turned off and a new three-dimensional model of the emissions zone and displayable images prepared. Once beam profile meets a desired beam profile, the phantom is removed and replaced by a patient, and the system may then be used to provide radiation of the desired profile for treating the patient.

In an embodiment, parameters of the three dimensional model of the emissions zone and the displayable images are recorded in a machine-readable memory system, such that the model and images may be used to document treatment, for periodic quality assurance and calibration, or to seek regulatory approvals. In another embodiment, the parameters of the three dimensional model are used to satisfy monthly quality assurances checks on the clinical electron and x-ray photon beam qualities.

In an embodiment, the system is utilized with optically translucent anthropomorphic tissue phantoms, or complex tissue phantoms to capture images of the beam shape in more complex geometries and tissue compositions than is possible in homogeneous water phantoms.

Motion Systems for Skin Dose and Beam-Skin Intersection Tracking

As is known in the art of radiotherapy, the relative positions of subject and beam source is often altered during treatment. For example, a subject may be rotated in a radiation beam, or more commonly the radiation source is rotated about the subject, to irradiate a tumor within the patient from multiple angles, and thereby spread out radiation dose received by normal tissues of the subject. In an embodiment, surface images of Cherenkov emission from tissue are repetitively captured during standard courses of fractionated radiotherapy, and these images provide real time video of beam delivery on the subject's tissue, both for relatively stationary and relatively moving beam and subject. Further, the images can be used as real time video or integrated to provide an estimate for total skin dose. The images can be acquired from gated cameras set up inside or alongside the linear accelerator to image skin illuminated by the accelerator or at fixed positions within the treatment room. In embodiments utilizing fiducial markers placed on or in tissue, the images have both information about the delivered dose map on the tissue as well as biological fiducial information, and both can be used in treatment verification.

In an embodiment, as illustrated in FIG. **13**, a movable particle accelerator **1102** on rotary mount **1104** and counterweight **1106** with a subject **1108** positioned on a table **1110**, such that the accelerator **1102** may rotate about subject **1108** to provide radiation treatment to a breast **1112** of subject **1108**. One or more intensified CCD (ICCD) cameras **1114** are positioned on tripods **1116**, suspended from ceiling of a room enclosing the accelerator, or attached **1118** to the accelerator **1102**. At least two optical cameras, such as a stereo pair of cameras **1120**, are also provided. Accelerator **1102** may be equipped with a multi-leaf collimator **1126**. All cameras, including ICCD cameras **1114** and stereo optical cameras **1120** are interfaced (connections are not shown for simplicity) through a camera interface **1122** to an image processor **1124** that has memory **1128** having recorded therein machine readable code for performing the steps referenced below with reference to FIG. **15**. In alternative embodiments, high-sensitivity CMOS or other electronic cameras are used in place of ICCD cameras **1114**.

An embodiment is used to provide skin dose totals over multiple sessions of treatment; a particular variation of this embodiment has positioning devices or camera mounts suitable for mounting ICCD cameras **1114** in the same position and angle from treatment session to treatment session such that images are comparable from session to session.

In operation, as illustrated by the flowchart of FIG. **15**, a stereo pair of images under white light is captured **1202** by stereo cameras **1120**, and a three-dimensional computer model (FIG. **14**), is generated **1204** of skin of breast **1112** of subject **1108** in the area to be treated. In alternative embodiments, the skin is skin of other parts of human or other mammal anatomy, such as skin of a head. A translation or mapping of image intensity at the skin surface in Cherenkov light images, as obtained by one or more ICCD cameras **1114**, to surface radiation intensity is determined **1206**. The mapping is based in part on ray tracing from skin as modeled in the three dimensional model into the ICCD camera or cameras, and a scale factor determined by calibration. A total session-dose image and model is then cleared **1208**.

Once the beam is energized **1210** and treatment begins, a sequence of images of Cherenkov light emitted from skin illuminated by a radiation beam **1130** from accelerator **1102** is obtained **1212** by at least one camera of ICCD cameras **1114** during beam-on intervals while ambient illumination is blanked as previously described. Each image is then processed by applying **1214** the mapping of image intensity in Cherenkov light images as obtained by the ICCD cameras **1114** to surface radiation intensity. The mapped surface intensity is then summed into the session total skin dose **1216** image or model. The mapped surface intensity, the session total skin dose image, and a multisession total skin dose image obtained by summing a current session total skin dose image with prior session skin dose images, are provided **1218** in real time on display **1132**. In an alternative embodiment, the Cherenkov light images are summed, then the mapping of image intensity to surface radiation intensity is applied to provide a session total skin dose image. At the end of the session, the session total skin dose and multises-

sion total skin dose are stored over a network **1134** in the subject's electronic health record (not shown), and the session total skin dose is summed into a multisession total skin dose.

The system permits direct observation of the effect altered multileaf collimator **1126** settings, and/or accelerator **1102** rotation about subject **1108**, on the areas of skin illuminated by beam **1130**. Further, the system permits determination of both session total and treatment total skin dose.

In an embodiment, a pre-treatment simulation of predicted skin radiation dose versus time is copied into memory **1128**. During a treatment session, image processor **1124** compares **1219** an image of skin dose derived from surface radiation intensity maps derived from Cherenkov light images to the pre-treatment simulation of skin radiation dose. If the skin dose determined from Cherenkov light images differs by more than a preset, configurable, limit from the pre-treatment simulation, an error **1221** is declared, the beam is turned off, and the session is aborted. This embodiment makes use of the Cherenkov emitted light to prevent subject harm due to overdose, whether from failed equipment or improper system operation.

In an embodiment, the processor **328** is provided with machine-readable instructions in memory **326** for determining if skin and organ dose as administered differs from planned dosage, or from prior dosage, by more than a limit in order to generate an error flag. Such an error flag may be generated if a subject has shed weight, is miss-positioned, or otherwise needs treatment replanning.

In this embodiment, in order to identify differences from prior dosage, during each treatment session a cumulative Cherenkov-light image is stored. During each treatment session other than the first treatment session, processor **328** executed machine readable instructions in memory **326** to retrieve a first or prior Cherenkov image from storage for comparison with current Cherenkov images, and the processor performs edge detection on this first or prior image, and feature extraction on the edge-detected prior image to provide prior features. The processor then performs edge detection and feature extraction on a current Cherenkov image, and the current image features are mapped to prior image features.to determine correspondence points between the images. A displacement between the features of the current image and the prior image is computed, and compared to limits. If the displacement exceeds the limits, the processor then generates an alarm to notify an operator.

In this embodiment, in order to detect differences from plan, a predicted skin-dosage map for dosage of, and simulated cumulative dosage through, a particular treatment session is generated from pre-treatment simulations and saved in memory **326**. A do-not-exceed-without-warning dosage is determined and set as a limit in memory **326**. A maximum difference percentage is also determined and set as a limit in memory **326**. After each fractionated treatment session a totalized skin dosage image for all treatment sessions of this subject is determined, and pixels of the totalized skin dose are compared to the "do not exceed" skin dose and an alarm is provided to a treatment operator if this limit has been exceeded for any pixels. Further, the totalized skin dose is compared to the simulated cumulative skin dose, and if any pixels of the totalized skin dose differ from the simulated skin dose by more than the maximum difference percentage, an alarm is generated. In order to compensate for subject weight loss and precise positioning, the comparison of simulated to totalized dose is performed by processor **328** performing edge detection in simulated skin dose at this treatment stage, performing edge detection in totalized skin dose as determined from Cherenkov radiation, determining a warping of totalized actual skin dose to simulated skin dose, performing image warping, and then comparing totalized actual skin dose to warped simulation skin dose. The images are then compared and if any pixels differ by more than a limit, an alarm is generated.

In an embodiment, in order to compensate for subject weight changes (cancer patients are often ill, have often been subjected to toxic chemotherapies, and may suffer additional effects due to treatment radiation) and minor differences in subject positioning, when totalizing skin dose across sessions, the processor executes machine readable instructions to determine edges and features in both the current image, and in the totalized image. The processor then determines edge offsets between corresponding features and a warping function to correctly superimpose the images. The processor then uses the warping function to warp the current session total image to fit the prior images before adding it to the totalized image in order to compensate for weight loss or subject position.

In another embodiment, the shape of the beam can be readily detected in the Cherenkov image, and if the multileaf collimators or the gantry angle are in error due to computer or human set up error, then the beam delivery can be halted manually (after display of the image to an operator) or automatically in order to avoid erroneous or excessive radiation dose.

In another embodiment, significant biological features of the tissue such as blood vessels, moles and skin variations in absorption appear in the Cherenkov images as variations in detected intensity, and can be used to match the position of the subject each day while administering daily portions of fractionated radiation treatments. Changes in subject position which could occur from day to day can be detected by changes or offsets in locations of these biological features in the images, indicating changes in relative position of beam and subject. These changes may result from subject weight changes, or differences in subject positioning. If these changes are found and exceed limits they can be used to alter the treatment plan or halt therapy until a cause is determined, and changes in subject positioning and/or multileaf collimator settings can be made to compensate.

Experiments with a system of the type illustrated in FIG. **13**, operated according to the method of FIG. **15**, have produced a map of multisession total skin dose as illustrated in FIG. **16**, where high total skin dose correlates with areas of maximal skin damage on a human subject, as indicated in photograph FIG. **17**. The system has been demonstrated as operable with beam energies of 6 MEV and 10 MEV.

As previously described, internal and surface biological features which absorb radiation and emit Cherenkov and fluorescent light, such as blood in blood vessels and tissue, provide information about the oxygenation of the tissue being treated. Further, images obtained from Cherenkov emissions may be co-registered with prior image data such as the contrast CT scans and MRI scans previously used for simulation and/or planning of treatment. These features provide an internal biological fiducial for treatment verification.

Cherenkov images in visible light, with infrared fluorescent light excluded, may show regions of high and low emission, corresponding to areas of high and low skin dose to a depth of up to a centimeter in tissue.

Correction of Cherenkov Images to Determine Surface Radiation Dose

Cherenkov images of a surface region of subject **102** may be used as a tool to determine surface radiation dose during

radiation therapy. However, the signal intensities in raw (as-captured) Cherenkov images are frequently affected by tissue-specific properties that produce artifacts in the Cherenkov images such that the Cherenkov images do not provide an accurate representation of the delivered radiation dose. These tissue-specific features include tissue curvature and heterogeneities in optical properties of the tissue such as tanned skin versus normal skin, moles, tattoos, blood vessels, tumor resection cavities, and optical property changes caused by skin reactions to prior sessions of radiation treatment. In the following, systems and methods are disclosed, which use a reflectance image to correct a Cherenkov image to eliminate or at least reduce artifacts caused by tissue-specific properties so as to generate a corrected Cherenkov image that provides an improved determination of surface radiation dose.

Each of the systems and methods disclosed in FIGS. **2-13** and **15** may be extended to implement the correction methods and/or systems discussed in the following.

FIG. **18** illustrates one exemplary Cherenkov imaging system **1800** for determining radiation dose for a surface region **1890** of subject **102** undergoing radiation therapy. Radiation beam **160**, generated by charged particle or gamma radiation beam source **108**, is aimed at tumor **104** and generates Cherenkov radiation in the tissue of subject **102**. Cherenkov radiation from a surface region **1890**, located at and near the surface of subject **102** exposed to radiation beam **160**, is imaged from outside subject **102**. Depending on the location of tumor **104** within subject **102**, surface region **1890** may or may not include at least a portion of tumor **104**.

Cherenkov imaging system **1800** includes a camera system **1830** and a correction module **1850**. Camera system **1830** includes an electronic camera **1834** and a light source **1832**. Camera **1834** captures a Cherenkov image **1812** of Cherenkov radiation emitted from surface region **1890** when subject **102** is exposed to radiation beam **160**. Light source **1832** illuminates surface region **1890** with optical illumination **1835**. Camera **1834** captures a reflectance image **1836** of optical illumination **1835** as reflected from surface region **1890** when light source **1832** illuminates surface region **1890** with optical illumination **1835**. Correction module **1850** corrects Cherenkov image **1812**, based upon reflectance image **1836**, to produce a corrected Cherenkov image **1852**.

Light source **1832** may be monochromatic, broadband, or multi-colored. Without departing from the scope hereof, light source **1832** may omitted from system **1800** and optical illumination **1835** instead be provided through ambient illumination such as room lights **122**.

In one embodiment, optical illumination **1835** generated by light source **1832** is diffuse, for example to reduce or avoid glare in reflectance image **1836**. In another embodiment, optical illumination **1835** generated by light source **1832** is polarized and camera **1834** is configured to, at least when capturing reflectance image **1836**, filter the polarization of optical illumination **1835** reflected by surface region **1890** to deselect the polarization direction of optical illumination **1835** as generated by light source **1832**. In one such example, light source **1832** and camera **1834** are equipped with polarizers that are mutually crossed such that only polarization components orthogonal to the polarization direction of optical illumination **1835**, as generated by light source **1832**, contribute to reflectance image **1836**. The polarizer associated with camera **1834** may be mounted on a filter wheel, or similar device, such that Cherenkov image **1812** in some embodiments is captured by the same camera without use of the polarizer.

Surface region **1890** scatters optical illumination **1835** in a manner similar to scattering of the Cherenkov radiation generated in surface region **1890**. Hence, the signal intensities in reflectance image **1836** provide a measure of the tissue-specific properties of surface region **1890**. Correction module **1850** utilizes reflectance image **1836** to at least partly correct artifacts caused by the tissue-specific properties of surface region **1890** such that corrected Cherenkov image **1852** is free of, or at least less affected by, these artifacts. Thus, corrected Cherenkov image **1852** provides a determination of surface radiation dose for surface region **1890**, which is more accurate than that provided by Cherenkov image **1812**.

Since Cherenkov image **1812** and reflectance image **1836** are captured by the same camera **1834**, Cherenkov image **1812** and reflectance image **1836** are inherently spatially co-registered. In addition, Cherenkov image **1812** and reflectance image **1836** are subject to the same camera properties. As a result, the correction performed by correction module **1850** may further eliminate or reduce artifacts inherent to camera **1834**, such as optical aberrations and fixed-pattern electronic noise.

In an embodiment, camera **1834** is a spectrally-sensitive camera capable of providing spectral data permitting distinction between Cherenkov radiation and optical illumination **1835**. Camera **1834** may further be able to distinguish between Cherenkov radiation, optical illumination **1835**, and fluorescent light, and in a particular embodiment permitting distinction between oxyhemoglobin and deoxyhemoglobin, as discussed above in reference to FIG. **3**. A spectrally-sensitive camera suitable for this application may be implemented as a black and white camera equipped with a filter-changer in front of the camera, or a hyperspectral camera, as discussed above in reference to FIG. **3**.

In certain embodiments, system **1800** is configured to generate corrected Cherenkov image **1852** in the form of a three-dimensional (3D) surface map, and correction module **1850** includes a surface model processor **1860** that processes 3D surface models and 3D surface maps. In one such embodiment, camera system **1830** further includes a light-structure encoder **1833** that encodes patterns of light and dark, known as structure, onto optical illumination **1835** emitted by light source **1832** while camera **1834** captures at least one structured-light reflectance image **1838**. In this embodiment, surface model processor **1860** uses the at least one structured-light reflectance image **1838** to generate a 3D surface model of surface region **1890**. In another such embodiment, system **1800** includes a stereo camera **1840** that captures a stereo image **1848**. In this embodiment, surface model processor **1860** processes stereo image **1848** to generate the 3D surface model of surface region **1890**, as discussed above in reference to FIGS. **3**, **14**, and **15**, for example. Whether the 3D surface model is based upon stereo image **1848** or the at least one structured light reflectance image **1838**, correction module **1850** may map corrected Cherenkov image **1852** onto the 3D surface model to output corrected Cherenkov image **1852** in the form of a 3D surface map. In a particular embodiment, one camera of the stereo camera does double-duty as a Cherenkov-light imaging camera and/or as a reflectance-imaging camera.

In an embodiment, system **1800** further includes a controller **1870** that controls timing of capture of Cherenkov image **1812** and reflectance image **1836**, and also, if applicable, stereo image **1848** or the at least one structured

reflectance image **1838**. In one example, controller **1870** pulses on light source **1832** and triggers capture of reflectance image **1836** by camera **1834** while light source **1832** is on. Controller **1870** may trigger capture of Cherenkov image **1812** with timing as discussed above in reference to FIG. **5**, while also ensuring that light source **1832** is off when camera **1834** captures Cherenkov image **1812**. In embodiments that include stereo camera **1840**, controller **1870** may trigger capture of stereo image **1848** by stereo camera **1640**. In embodiments that include light-structure encoder **1833**, controller **1870** trigger may configure light-structure encoder **1833** and trigger image capture by camera **1834** such that (a) light-structure encoder **1833**, which may be a projection cathode-ray tube, a multimirror display device, a liquid-crystal display device, or a slide projector, encodes structure of one or more sequential patterns onto optical illumination **1835** during capture of the at least one structured reflectance image **1838** and (b) light-structure encoder **1833** does not encode structure onto optical illumination **1835** during capture of reflectance image **1812**.

FIG. **19** is a diagram **1900** showing exemplary illumination of surface region **1890** by optical illumination **1835** as performed by system **1800**. Surface region **1890** is the region of subject **102** from which Cherenkov radiation is captured in Cherenkov image **1812**. Surface region **1890** has a characteristic depth **1910** below the surface of subject **102**. Typically, characteristic depth **1910** is in the range between two and six millimeters. Surface region **1890** may have shape different from that shown in FIG. **19**, without departing from the scope hereof. It is preferred that reflectance image **1836** samples the same region of subject **102** as Cherenkov image **1812**. Hence, it is preferred that the penetration depth **1920** of optical illumination **1835** substantially matches characteristic depth **1910**. Penetration depth **1920** may refer to the distance **1901** into subject **102**, at which the intensity **1902** of optical illumination **1835** has been attenuated to approximately 10%, 30%, or 37% (1/e) of the intensity of optical illumination **1835** at the surface of subject **102**. Typically, optical illumination **1835** is in the red to near-infrared spectrum to sample typical values of characteristic depth **1910**.

FIG. **20** is a diagram **2000** showing exemplary illumination of surface region **1890** by multi-colored optical illumination **2010** generated by a multi-colored embodiment of light source **1832**. Multi-colored optical illumination **2010** is an example of optical illumination **1835**. In the example shown in FIG. **20**, multi-colored optical illumination **2010** includes two different spectral components **2012** and **2014**. Without departing from the scope hereof, multi-colored optical illumination **2010** may include three or more spectral components. Since Cherenkov radiation is spectrally broadband, multi-colored optical illumination **2010** may be better suited, as compared to monochromatic optical illumination, for sampling surface region **1890** in the same manner as the Cherenkov radiation captured in Cherenkov image **112**. Furthermore, multi-colored optical illumination **2010** may be, or include, a spectrally broad component, for example with spectral width of a hundred or hundreds of nanometers. Spectral components **2012** and **2014** have respective penetration depths **2022** and **2024**, wherein penetration depth **2022** is different from penetration depth **2024**. It is clear from diagram **2000** that spectral components **2012** and **2014**, and optionally additional other spectral components, may be combined to better match the sampling intensity profile of Cherenkov radiation from surface region **1890**, as compared to the match that may be achieved using only a single spectral component.

FIG. **21** illustrates one exemplary Cherenkov imaging method **2100** for determining radiation dose for surface region **1890** of subject **102** undergoing radiation therapy. Method **2100** is performed, for example, by Cherenkov imaging system **1800**.

In a step **2110**, method **2100** captures a Cherenkov image of Cherenkov radiation from surface region **1890** of subject **102**. In one example of step **2110**, camera **1834** captures Cherenkov image **1812**. Step **2110** may include a step **2112** of irradiating surface region **1890** with a radiation beam that induces the Cherenkov radiation. In one example of step **2112**, charged particle or gamma radiation beam source **108** irradiates surface region **1890** with radiation beam **160**.

In a step **2120**, method **2100** captures a reflectance image of optical illumination reflected by surface region **1890**. In one example of step **2120**, camera **1834** captures reflectance image **1836**. Step **2120** may include a step **2122** of illuminating surface region **1890** with the optical illumination that produces the reflected light imaged in the reflectance image. In one example of step **2122**, light source **1832** illuminates surface region **1890** with optical illumination **1835**, such as discussed in reference to FIG. **19** or in reference to FIG. **20**. In another example of step **2122**, ambient light illuminates surface region **1890** with optical illumination **1835**.

In one embodiment, step **2122** illuminates surface region **1890** with diffuse optical illumination. Such diffuse optical illumination may help reduce glare in the reflectance image and also better resemble the sampling of surface region **1890** by the Cherenkov radiation imaged in step **2110**.

In another embodiment, step **2122** illuminates surface region **1890** with polarized optical illumination, and step **2120** further includes filtering the reflected optical illumination to produce the reflectance image based upon only randomly polarized reflected light. In one example, step **2120** may image reflected optical illumination only of polarization orthogonal to the polarization of the incident polarized optical illumination. Deselection of the incident polarization ensures that substantially all photons contributing to the reflectance image (or at least the majority of such photons) have undergone a sufficient number of scattering processes within surface region **1890** to be diffusely scattered by surface region **1890**, the resulting reflectance image being a scattered-light image with a reduced surface specular reflection component.

In a step **2140**, the Cherenkov image captured in step **2110** is corrected, based upon the reflectance image captured in step **2120**, to form a corrected Cherenkov image that indicates the radiation dose for surface region **1890**, at least with improved accuracy over the Cherenkov image captured in step **2110**. In one example of step **2140**, correction module **1850** corrects Cherenkov image **1812** based upon reflectance image **1836** to produce corrected Cherenkov image **1852**. In an embodiment, step **2140** includes a step **2142** of reducing an artifact in the Cherenkov image captured in step **2110**, wherein the artifact is caused by a tissue-specific light-transmission property, as discussed above in reference to FIG. **18**. In an embodiment, step **2140** includes a step **2144** of normalizing the Cherenkov image captured in step **2110** to the reflectance image captured in step **2120**. In one example of step **2144**, correction module **1850** normalizes Cherenkov image **1812** to reflectance image **1836**. This example of step **2144** benefits from Cherenkov image **1812** and reflectance image **1836** being spatially co-registered and subject to the same inherent camera properties. In certain embodiments, corrected Cherenkov image **1852** is Cherenkov image **1812** normalized to reflectance image **1836**.

Although not shown in FIG. **21**, step **2140** may use a model, such as a Monte Carlo simulation, that describes transport of both Cherenkov radiation (and optionally radiation beam **160**) and optical illumination within surface region **1890**, so as to account for differences in propagation through and sampling of surface region **1890** by the Cherenkov radiation and optical illumination. This model is formed by independently simulating the propagation of each of (a) Cherenkov radiation and (b) the optical illumination for a plurality of different conditions, such as different tissue conditions of subject **101** and different configurations both for the radiation beam that induces the Cherenkov radiation and for the optical illumination. Step **2140** may use modification parameters, according to this model, to compensate for the difference of propagation between the Cherenkov radiation and the optical illumination. The model may be implemented as a looking up database with modification parameters for typical combinations of optical illumination properties (e.g., intensity, beam profile, and spectral composition), radiation beam properties (e.g., beam energy and beam type), geometries (e.g., curvature of surface of subject **101** and incident angles of the radiation beam and the optical illumination). Optionally, the modification parameters for a specific case encountered in real radiation therapy are determined by interpolations within existing modification parameters in the database.

In an optional step **2160**, method **2100** outputs the corrected Cherenkov image generated in step **2140**. In one example of step **2160**, correction module **1850** outputs corrected Cherenkov image **1852**.

In certain embodiments, method **2100** includes a step **2150** of mapping the corrected Cherenkov image onto a 3D surface model of surface region **1890**. In one example of step **2150**, surface model processor **1860** maps corrected Cherenkov image **1852** onto a 3D surface model of surface region **1890** to form a 3D surface radiation dose map. Optionally, such embodiments of method **2100** further include outputting, in step **2160**, the corrected Cherenkov image in the form of the 3D surface radiation dose map. These surface model based embodiments of method **2100** may further include a step **2130** of generating the 3D surface model. In one such embodiment, step **2130** includes a step **2132** of capturing a stereo image, which is then processed to generate the 3D model. In another such embodiment, step **2130** includes a step **2134** of capturing at least one structured-light reflectance image, which is then processed to generate the 3D model. In one example of step **2130** implemented with step **2132**, stereo camera **1840** captures stereo image **1848**, and surface model processor **1860** processes stereo image **1848** to produce the 3D surface model. In one example of step **2130** implemented with step **2134**, camera **1834** captures at least one structured-light reflectance image **1838**, and surface model processor **1860** processes the at least one structured-light reflectance image **1838** to produce the 3D surface model.

Without departing from the scope hereof, step **2140** may be a stand-alone method, for example suitable for implementation as machine-readable instructions, on non-transitory media, wherein these machine-readable instructions may be executed by a processor to perform step **2140**.

FIG. **22** illustrates one exemplary Cherenkov imaging system **2200** for determining radiation dose for a surface region **1890** of subject **102** undergoing radiation therapy. Cherenkov imaging system **2200** is similar to Cherenkov imaging system **1800** except that Cherenkov imaging system **2200** includes two separate cameras **2210** and **2234** that capture Cherenkov image **1812** and reflectance image **1836**, respectively. Since Cherenkov imaging system **2200** uses two different cameras, Cherenkov image **1812** and reflectance image **1836** are not spatially co-registered. Therefore, correction module **1850** includes surface model processor **1860**. Surface model processor **1860** maps each of Cherenkov image **1812** and reflectance image **1836** onto a 3D surface model of surface region **1890** to generate respective 3D surface maps of Cherenkov image **1812** and reflectance image **1836**. Correction module **1850** then corrects the 3D surface map of Cherenkov image **1812** based upon the 3D surface map of reflectance image **1836** to produce a 3D surface radiation dose map **2252**. Camera **2234** is implemented with light source **1832** in a camera system **2230**. Each of cameras **2210** and **2234** are electronic cameras and may be similar to camera **1834**. In addition, controller **1870** (if included) may trigger operation of each of cameras **2210** and **2234**. As discussed in reference to FIGS. **18-20**, optical illumination **1835** may be monochromatic, multi-colored, or broadband, and light source **1821** may emit optical illumination **1835** as diffuse light or as polarized light. Accordingly, camera **2234** may be equipped with a polarizer that deselects the polarization of polarized optical illumination **1835** to generate images emphasizing scattered light over specular reflected light.

FIG. **23** illustrates one exemplary Cherenkov imaging method **2300** for determining radiation dose for surface region **1890** of subject **102** undergoing radiation therapy. Method **2300** is performed, for example, by Cherenkov imaging system **2200**.

In a step **2310**, method **2300** captures a Cherenkov image of Cherenkov radiation from surface region **1890** of subject **102**. In one example of step **2310**, camera **2210** captures Cherenkov image **1812**. Step **2310** may include a step **2312** of irradiating surface region **1890** with a radiation beam that induces the Cherenkov radiation. In one example of step **2312**, charged particle or gamma radiation beam source **108** irradiates surface region **1890** with radiation beam **160**.

In a step **2320**, method **2300** captures a reflectance image of optical illumination reflected by surface region **1890**. In one example of step **2320**, camera **2234** captures reflectance image **1836**. Step **2320** may include a step **2322** of illuminating surface region **1890** with the optical illumination that produces the reflected light imaged in the reflectance image. In one example of step **2322**, light source **1832** illuminates surface region **1890** with optical illumination **1835**, such as discussed in reference to FIG. **19** or in reference to FIG. **20**. In another example of step **2322**, ambient light illuminates surface region **1890** with optical illumination **1835**. As discussed above in reference to step **2120** of method **2100**, step **2320** may use diffuse or polarized optical illumination.

In a step **2330**, method **2300** generates a 3D surface model. In one embodiment, step **2330** includes a step **2332** of capturing a stereo image, which is then processed to generate the 3D model. In another embodiment, step **2330** includes a step **2334** of capturing at least one structured-light reflectance image, which is then processed to generate the 3D model. In one example of step **2330** implemented with step **2332**, stereo camera **1840** captures stereo image **1848**, and surface model processor **1860** processes stereo image **1848** to produce the 3D surface model. In one example of step **2330** implemented with step **2334**, camera **2234** captures at least one structured-light reflectance image **1838**, and surface model processor **1860** processes the at least one structured-light reflectance image **1838** to produce the 3D surface model.

In a step **2340**, the Cherenkov image captured in step **2310** is corrected, based upon the reflectance image captured

in step **2320**, to form a corrected Cherenkov image that indicates the radiation dose for surface region **1890**, at least with improved accuracy over the Cherenkov image captured in step **2310**. Step **2340** forms the corrected Cherenkov image in the form of a 3D surface radiation dose map. In an embodiment, step **2340** includes a step **2342** of reducing an artifact in the Cherenkov image captured in step **2310**, wherein the artifact is caused by a tissue-specific light-transmission property, as discussed above in reference to FIG. **18**.

Step **2340** includes a step **2344** of (a) mapping the Cherenkov image captured in step **2310** onto the 3D surface model generated in step **2330** to produce a 3D surface map of the Cherenkov radiation, and (b) mapping the Cherenkov image captured in step **2310** onto the 3D surface model generated in step **2330** to produce a 3D surface map of the optical illumination reflected by surface region **1890**. In one example of step **2344**, surface model processor **1860** maps each of Cherenkov image **1812** and reflectance image **1836** onto the 3D surface model generated in step **2330**. Step **2340** further includes a step **2346** of correcting the 3D surface map of the Cherenkov radiation, based upon the 3D surface map of the optical illumination reflected by surface region **1890**, to form the 3D surface radiation dose map. In one example of step **2346**, correction module **1850** corrects the 3D surface map of the Cherenkov radiation, based upon the 3D surface map of the optical illumination reflected by surface region **1890**, to form 3D surface radiation dose map **2252**. Step **2345** may include, or consist of, normalizing the 3D surface map of the Cherenkov radiation to the 3D surface map of the optical illumination reflected by surface region **1890**.

Although not shown in FIG. **23**, step **2340** may use a model, such as a Monte Carlo simulation model, that describes transport of both Cherenkov radiation (and optionally radiation beam **160**) and optical illumination within surface region **1890**, so as to account for differences in propagation through and sampling of surface region **1890** by the Cherenkov radiation and optical illumination, as discussed in reference to step **2140**.

In an optional step **2350**, method **2300** outputs the 3D surface radiation dose map generated in step **2340**. In one example of step **2350**, correction module **1850** outputs 3D surface radiation dose map **2252**.

Without departing from the scope hereof, step **2340** may be a stand-alone method, for example suitable for implementation as machine-readable instructions, on non-transitory media, wherein these machine-readable instructions may be executed by a processor to perform step **2340**.

In particular embodiments discussed herein with respect to FIGS. **18**, **19**, **20**, **21**, **22**, and **23**, the correction module makes use of a voxel-based light propagation model having scattering parameters and absorbance parameters at each voxel of the model. In these embodiments, the optical parameters extracted by using the optical illumination include the scattering parameter and an absorbance parameter at each voxel of the model. In particular embodiments where the optical illumination is performed at multiple wavelengths, the model may have multiple absorbance parameters at each voxel with each absorbance parameter modeling light absorbance at a particular wavelength of the multiple wavelengths. In embodiments where a three-dimensional model of the subject is determined such as by surface extraction from stereo images, the voxel-based light-propagation model is adjusted to conform to the three-dimensional model by assuming primary absorbance and scattering occurs within the subject. In particular embodiments, the correction module operates by adding a Cherenkov emissions parameter to each voxel of the light propagation model, applying the scattering and absorbance parameters as determined under optical illumination at each voxel of the mode to modeled Cherenkov light, and fitting the Cherenkov emissions parameters to provide a best-fit to observed intensities at pixels of the Cherenkov images.

Each of system **1800**, method **2100**, system **2200**, and method **2300** may be extended to correction of fluorescence images of fluorescence induced by Cherenkov radiation, such as PpIX images discussed above. For example, Cherenkov image **1812** may be replaced by a fluorescence image of Cherenkov-radiation-induced fluorescence, without departing from the scope hereof.

Combinations

The treatment recording and measuring system herein described can be implemented with various combinations of features, some combinations are listed below and some are claimed. These combinations include:

A system designated A for providing and monitoring delivery and accuracy of radiation therapy includes a source of pulsed high energy radiation disposed to provide a radiation beam to a treatment zone, the high energy radiation of at least 0.2 MeV or greater; at least one camera configured to obtain images of Cherenkov light from the treatment zone; and apparatus for adapted to prevent interference by room lighting with the images of Cherenkov light by synchronizing the camera to pulses of the radiation beam, and blanking room lighting during pulses of the radiation beam. The system also has an image processor adapted with machine readable code in a memory to determine an accuracy of actual delivered dose relative to a planned treatment from the images of Cherenkov light.

A system designated AA including the system designated A where the image processor is adapted with machine readable code to estimate cumulative skin dose in the treatment zone from the images of Cherenkov light.

A system designated AB including the system designated A or AA, where the image processor is adapted with machine readable code to resolve patient position relative to the treatment beam from by using vascular and skin structures which appearing in the emitted Cherenkov images as biological alignment features.

A system designated AC including the system designated A, AA, or AB, where a radiation beam extent is determined from the Cherenkov images, and in a system the determined radiation beam extent is used for estimation of accuracy of delivery of the radiation.

A system designated AD including the system designated A, AA, AB, or AC further comprising a positioning device configured to hold the camera in the same angle and position in a first fractionated radiation treatment session and a second fractionated radiation treatment session.

A system designated AE including the system designated A, AA, AB, AC, or AD wherein the memory is configured with machine readable instructions for using a three-dimensional model of a subject to determine a mapping of image intensity in the images of Cherenkov light to the radiation dose deposited in skin of the subject.

A system designated AF including the system designated A, AA, AB, AC, AD, or AE wherein the image processor is configured to acquire multiple images of Cherenkov light during a treatment session.

A system designated AG including the system designated A, AA, AB, AC, AD, AE, or AF, wherein the image processor is configured with machine readable instructions to compare a skin dose determined from pre-treatment

simulations to a skin dose determined from imaged Cherenkov light and to interrupt the delivery of radiation if the imaged Cherenkov signal disagrees with the pre-treatment simulations by more than a limit.

A system designated AH including the system designated A, AA, AB, AC, AD, AE, AF, or AG configured with machine readable code to apply the mapping of image intensity from the multiple images of Cherenkov light to determine maps of skin dose, and to determine if changes in position have occurred and to warn an operator if the treatment beam design is providing excessive skin dose or excessive changes in position have occurred.

A system designated AK including the system designated A, AA, AB, AC, AD, AE, AG, or AH wherein the processor is configured with machine readable instructions to indicate on a display when the Cherenkov images show significant differences in the daily images.

A system designated AL including the system designated A, AA, AB, AC, AD, AE, AG, AH, or AK wherein the image processor is configured to sum dosage maps from a first treatment session and a second treatment session to provide a map of total multisession dose.

A method designated B of determining surface dose during radiation treatment of a first object beneath a surface of a second object to limit dose at the surface includes obtaining stereo images of the surface, and extracting a three-dimensional computer model of the surface; determining a mapping of image brightness at the surface in Cherenkov light images obtained by a digital camera to radiation intensity; recording surface brightness at the surface in a plurality of Cherenkov light images; and summing step including using the mapping of image brightness at the surface to translate each Cherenkov light image into a surface dose image, or summing the surface dose images to provide a total session surface dose image; and summing the image brightness in each Cherenkov light image into a total session surface Cherenkov light image and using the mapping of image brightness at the surface to translate the total session surface Cherenkov light image into a total session surface dose image. The method concludes with displaying the total session surface dose image.

A method designated BA including the method designated B and further including summing the total session surface dose image with at least one prior session surface dose image to provide a total treatment surface dose image; and displaying the total treatment surface dose image.

A method designated BB including the method designated B or BA and further including blanking room lighting during acquisition of the Cherenkov light images.

A method designated BC including the method designated B, BA, or BB wherein the second object is a subject and the first object is a tumor.

A method designated BD including the method designated B, BA, BB, or BC and further comprising using an image selected from the group consisting of the total session surface dose image and the total treatment surface dose image to modify a radiation treatment plan for at least one radiation treatment session.

A system designated C for providing and monitoring delivery and accuracy of radiation therapy includes a source of pulsed high energy radiation disposed to provide a radiation beam to a treatment zone, with high energy radiation of at least 0.2 MeV; at least one imaging system configured to obtain observations of light emitted from the treatment zone, the imaging system selected from the group consisting of cameras disposed to image the treatment zone, and photodetectors coupled through optical fibers to gather and detect light from the treatment zone; apparatus adapted to minimize interference by room lighting with the observations; and apparatus adapted to record the observations; wherein the imaging system is synchronized to pulses of the pulsed high energy radiation.

A system designated CA including the system designated C wherein the imaging system comprises at least one camera, and the observations of light are images, and the system further comprises an image processor.

A system designated CB including the system designated CA or C wherein the apparatus adapted to prevent interference by room lighting with the imaging system comprises apparatus adapted to synchronize pulsed room lighting to allow image capture without ambient lighting.

A system designated CC including the system designated C, or CA, wherein the apparatus adapted to prevent interference by room lighting operates through the image processor being adapted with machine readable instructions configured to obtain a first image of the treatment zone during a pulse of the high energy radiation source, and a second image of the treatment zone at a time other than during a pulse of the high energy radiation source; and with machine readable instructions configured to subtract the second image from the first image to provide an image of Cherenkov emissions from the treatment zone.

A system designated CCA including the system designated C, or CA, wherein the apparatus adapted to prevent interference by room lighting operates through a method comprising providing narrowband room lighting at a first wavelength, and wherein images of Cherenkov light exclude light at the first wavelength.

A system designated CD including the system designated CA, CB, or CC wherein the image processor is adapted with machine readable code to estimate a beam shape from the images of Cherenkov light.

A system designated CE including the system designated CD wherein the image processor is adapted with machine readable code to estimate a radiation dose map of the high energy radiation beam on a subject's skin from the images.

A system designated CF including the system designated CA, CB, CC, CCA, CD or CE, where the image processor is further adapted with machine readable code to resolve patient position relative to the treatment beam by using vascular and skin structures appearing in the emitted Cherenkov images as biological alignment features.

A system designated CG including the system designated CA, CB, CC, CCA, CD, CE, or CF where the image processor is further adapted with machine readable code to compare intensity patterns from the images with images from at least one prior treatment session to determine if changes have occurred between sessions.

A system designated CH including the system designated CA, CB, CC, CCA, CD, CE, CF, or CG **10** wherein the image processor is adapted with machine readable code to estimate a radiation dose map of the high energy radiation beam on a subject's skin from the images for a treatment session.

A system designated CI including the system designated CA, CB, CC, CCA, CD, CE, CF, or CG wherein the image processor is adapted with machine readable code to estimate cumulative skin dose across a plurality of a treatment sessions in the treatment zone.

A system designated CK including the system designated CA, CB, CC, CCA, CD, CE, CF, CG, CH, or CI wherein the image processor is configured with machine readable code adapted to using a three-dimensional model of a subject to

determine a mapping of image intensity in the images of Cherenkov light to the radiation dose deposited in skin of the subject.

A system designated CL including the system designated CA, CB, CC, CCA, CD, CE, CF, CG, CH, CI, or CK further comprising a positioning device configured to hold the camera in a same location, angle and position in a first fractionated radiation treatment session and all subsequent fractionated radiation treatment session.

A system designated CM including the system designated CA, CB, CC, CCA, CD, CE, CF, CG, CH, CI, CK, or CL wherein the image processor is configured to acquire multiple images of Cherenkov light during a treatment session.

A system designated CN, including the system designated CM, wherein the image data is used to verify delivery as planned by comparison to the prescribed radiation dose.

A system designated CO including the system designated CA, CB, CC, CCA, CD, CE, CF, CG, CH, CI, CK, CL, or CN wherein the image processor is configured with machine readable instructions to compare a skin dose determined from pre-treatment simulations to a skin dose determined from imaged Cherenkov light and to interrupt the delivery of radiation if the imaged Cherenkov signal disagrees with the pre-treatment simulations by more than a limit.

A system designated CP including the system designated C, CA, CB, CC, CCA, CD, CE, CF, CG, CH, CI, CK, CL, CN, or CO wherein the imaging system is spectrally selective such that the imaging system is adapted to capture Cherenkov-stimulated light emissions from tissue and to distinguish this light from Cherenkov light.

A method designated D of determining surface dose during radiation treatment of a first object beneath a surface of a second object to limit dose at the surface includes obtaining at least two images of the surface, and extracting a three-dimensional computer model of the surface therefrom; determining a mapping of image brightness at the surface in Cherenkov light images obtained by a digital camera to radiation intensity; recording surface brightness at the surface in a plurality of Cherenkov light images; and a summing step of either using the mapping of image brightness at the surface to translate each Cherenkov light image into a surface dose image and summing the surface dose images to provide a total session surface dose image, or summing the image brightness in each Cherenkov light image into a total session surface Cherenkov light image and using the mapping of image brightness at the surface to translate the total session surface Cherenkov light image into a total session surface dose image; and displaying the total session surface dose image.

A method designated E of determining surface dose during radiation treatment from imaging of a fractionated radiation therapy includes obtaining multiple images of a surface, and extracting a three-dimensional computer model of the surface therefrom; synchronizing imaging to beam pulses, and obtaining Cherenkov light images; determining a mapping of image brightness at the surface in Cherenkov light images obtained by a digital camera to radiation intensity; recording surface brightness at the surface in a plurality of Cherenkov light images; a summing step selected from the group of using the mapping of image brightness at the surface to translate each Cherenkov light image into a surface dose image and summing the surface dose images, or summing the image brightness in each Cherenkov light image into a total session surface Cherenkov light image, and using the mapping of image brightness at the surface to translate the total session surface Cherenkov light image into a total session surface dose image; and displaying the total session surface dose image.

A method designated EA including the method designated D or E and further including blanking room lighting during acquisition of the Cherenkov light images.

A method designated EB including the method designated D or E further including correcting Cherenkov light images for ambient light by subtracting an ambient light image from an image obtained during a pulse of the beam.

A method designated EC including the method designated D, E, EA, or EB and further including summing the total session surface dose image with at least one prior session surface dose image to provide a total treatment surface dose image; and displaying the total treatment surface dose image.

A method designated ED including the method designated D, E, EA, EB, or EC wherein the surface is normal tissue and a deeper region is a tumor.

A method designated EE including the method designated D, E, EA, EB, EC, or ED wherein the radiation treatment is a fractionated radiation treatment and further comprising using an image selected from the group consisting of the total session surface dose image and the total treatment surface dose image to modify a radiation treatment plan for at least one radiation treatment session.

A Cherenkov imaging system designated F for determining surface radiation dose for a subject undergoing radiation therapy, comprising: a camera system comprising at least one digital camera, the camera system adapted to capture a Cherenkov image of Cherenkov radiation from a surface region of the subject undergoing Cherenkov-radiation-inducing radiation therapy, and to capture a reflectance image of reflectance of optical illumination off the surface region; a light source adapted to generate the optical illumination, and a correction module for correcting the Cherenkov image based upon the reflectance image to form a corrected Cherenkov image that indicates radiation dose for the surface region.

A Cherenkov imaging system designated FA including the Cherenkov imaging system designated F, further comprising a controller for controlling (a) timing of image capture by the first camera to capture the Cherenkov image to minimize room light interference and (b) timing of image capture by the second camera to capture the reflectance image when the surface region is exposed to the optical illumination.

A Cherenkov imaging system designated FB including the Cherenkov imaging system designated F or FA, the light source being configured to generate the optical illumination as diffuse optical illumination.

A Cherenkov imaging system designated FC including the Cherenkov imaging system designated F, FA, or FB, the light source being configured to generate the optical illumination as polarized optical illumination, the camera system including a filter for deselecting a polarization component of the polarized optical illumination to ensure that substantially all photons contributing to the reflectance image have been diffusely scattered by the surface region.

A Cherenkov imaging system designated FC including the Cherenkov imaging system designated F, FA, or FB, the optical illumination having wavelength such that penetration depth of the optical illumination into the subject substantially matches maximum depth of the Cherenkov radiation imaged by the first imaging module.

A Cherenkov imaging system designated FD including the Cherenkov imaging system designated F, FA, FB, or FC, the optical illumination having wavelength such that the penetration depth is between two and six millimeters.

A Cherenkov imaging system designated FE including the Cherenkov imaging system designated F, FA, FC, or FD, the light source being a multi-colored light source for generating the optical illumination at a plurality of different wavelengths to sample a respectively plurality of different depths of the subject so as to match depth-sampling properties of the Cherenkov radiation.

A Cherenkov imaging system designated FF including the Cherenkov imaging system designated FE, the reflectance image being a composite image based upon a plurality of wavelength-specific reflectance images, the Cherenkov imaging system further comprising: a controller for controlling the second camera to capture a plurality of wavelength-specific reflectance images using the plurality of different wavelengths, respectively.

A Cherenkov imaging system designated FG including the Cherenkov imaging system designated F, wherein the camera system is adapted to use a single camera for capturing the Cherenkov image and the reflectance image.

A Cherenkov imaging system designated FH including the Cherenkov imaging system designated F, FA, FC, or FD, the correction module being configured to generate the corrected Cherenkov image by normalizing the Cherenkov image to the reflectance image.

A Cherenkov imaging system designated FJ including the Cherenkov imaging system designated F, FA, FC, FD, or FE wherein the camera system is further adapted to capture a stereo image of the surface region under optical illumination, and further comprising a surface model processor adapted to (a) process the stereo image to produce a three-dimensional surface model of the surface region and (b) map the corrected Cherenkov image onto the three-dimensional surface model to generate a three-dimensional surface radiation dose map.

A Cherenkov imaging system designated FK including the Cherenkov imaging system designated F, FA, FC, FD, FE, or FH further comprising: a light-structure encoder for encoding structure onto the optical illumination to produce structured light to be used by the camera system to capture at least one structured-light reflectance image; and a surface model processor adapted to (a) process the at least one structured-light reflectance image to produce a three-dimensional surface model of the surface region and (b) map the corrected Cherenkov image onto the three-dimensional surface model to generate a three-dimensional surface radiation dose map.

A Cherenkov imaging system designated FL including the Cherenkov imaging system designated F, FA, FC, FD, FE, or FH, the correction module being configured to generate the corrected Cherenkov image in form of a three-dimensional surface radiation dose map by correcting a three-dimensional surface map of the Cherenkov radiation based upon a three-dimensional surface map of the reflectance of the optical illumination; the camera system being further configured to capture a stereo image of the surface region; and further comprising: a surface model processor for (a) processing the stereo image to produce a three-dimensional surface model of the surface region, (b) mapping the Cherenkov image onto the three-dimensional surface model to generate the three-dimensional surface map of the Cherenkov radiation, and (c) mapping the reflectance image onto the three-dimensional surface model to generate the three-dimensional surface map of the reflectance of the optical illumination.

A Cherenkov imaging system designated FM including the Cherenkov imaging system designated F, FA, FB, FC, FD, FE, or FH, the correction module being configured to further take into account discrepancies between light transport properties of the Cherenkov radiation and the optical illumination within the subject when correcting the Cherenkov image.

A Cherenkov imaging system designated FN including the Cherenkov imaging system designated F, FA, FB, FC, FD, FE, FG, FH, FJ, FK, FL, or FM, wherein, the correction module is configured to use a voxel-based light propagation model having scattering parameters and absorbance parameters at each voxel of the model; the optical parameters extracted by using the optical illumination including the scattering parameter and an absorbance parameter at each voxel of the model.

A Cherenkov imaging system designated FO including versions of the Cherenkov imaging system designated FN where the optical illumination is performed at multiple wavelengths, the voxel-based light propagation model having multiple absorbance parameters at each voxel with each absorbance parameter modeling light absorbance at a particular wavelength of the multiple wavelengths.

A Cherenkov imaging system designated FP including versions of the Cherenkov imaging system designated FN or FO wherein the correction module operates by adding a Cherenkov emissions parameter to each voxel of the light propagation model, applying the scattering and absorbance parameters as determined under optical illumination at each voxel of the mode to modeled Cherenkov light, and fitting the Cherenkov emissions parameters to provide a best-fit to observed intensities at pixels of the Cherenkov images.

A Cherenkov imaging method designated G for determining surface radiation dose for a subject undergoing radiation therapy, comprising: correcting a Cherenkov image, the Cherenkov image being an image of Cherenkov radiation emitted from a surface region of the subject undergoing Cherenkov-radiation-inducing radiation therapy, the correcting comprising using a reflectance image, the reflectance image being an image of optical illumination reflected by the surface region, to form a corrected Cherenkov image that indicates radiation dose for the surface region.

A Cherenkov imaging method designated GA including the Cherenkov imaging method designated G, the step of correcting comprising reducing artifact in the Cherenkov image caused by tissue-specific light transmission properties.

A Cherenkov imaging method designated GB including the Cherenkov imaging method designated G or GA, further comprising: capturing the Cherenkov image; illuminating the surface region with the optical illumination; and capturing the reflectance image.

A Cherenkov imaging method designated GC including the Cherenkov imaging method designated G, GA, or GB, in the step of illuminating, the optical illumination being diffuse.

A Cherenkov imaging method designated GD including the Cherenkov imaging method designated G, GA, GB, or GC wherein: in the step of illuminating, illuminating the surface region is done with polarized illumination; and in the step of capturing the reflectance image, a polarization component of the polarized illumination is deselected in the camera system to ensure that substantially all photons contributing to the reflectance image have been diffusely scattered by the surface region.

A Cherenkov imaging method designated GE including the Cherenkov imaging method designated G, GA, GB, GC, or GD further comprising irradiating the surface region with a beam that induces the Cherenkov radiation.

A Cherenkov imaging method designated GF including the Cherenkov imaging method designated G, GA, GB, GC, GD, or GE comprising: in the step of capturing the reflectance image, capturing the reflectance image using same camera as used to capture the Cherenkov image in the step of capturing the Cherenkov image, such that the reflectance image and the Cherenkov image are spatially co-registered; and in the step of correcting, normalizing the Cherenkov image to the reflectance image.

A Cherenkov imaging method designated GG including the Cherenkov imaging method designated G, GA, GB, GC, GD, GE, or GF further comprising: generating a three-dimensional surface model of the surface region; and in the step of correcting: (a) mapping the Cherenkov image onto the three-dimensional surface model to produce a three-dimensional surface map of the Cherenkov radiation, (b) mapping the reflectance image onto the three-dimensional surface model to produce a three-dimensional surface map of the reflectance, and (c) generating the corrected Cherenkov image in form of a three-dimensional surface radiation dose map by correcting the three-dimensional surface map of the Cherenkov radiation based upon the three-dimensional surface map of the reflectance of the optical illumination.

A Cherenkov imaging method designated GH including the Cherenkov imaging method designated G, GA, GB, GC, GD, GE, GF, or GG, the step of generating comprising: capturing a stereo image of the surface region; and processing the stereo image to determine the three-dimensional surface model.

A Cherenkov imaging method designated GJ including the Cherenkov imaging method designated G, GA, GB, GC, GD, GE, GF, GG, or GH the step of generating comprising: capturing a second reflectance image of structured light incident upon the surface region; and processing the second reflectance image to determine the three-dimensional surface model.

A Cherenkov imaging method designated GK including the Cherenkov imaging method designated G, GA, GB, GC, GD, GE, GF, GG, GH or GK further comprising generating the reflectance light image by: (a) illuminating the surface region with the optical illumination, and (b) capturing the reflectance image using a camera; and the step of capturing the second reflectance image comprising: (a) encoding structure onto the optical illumination to produce the structured light, and (b) capturing the second reflectance image using the camera.

A Cherenkov imaging method designated GL including the Cherenkov imaging method designated G, GA, GB, GC, GD, GE, GF, GG, GH or GK, in the step of illuminating, the optical illumination having wavelength such that penetration depth of the optical illumination into the subject substantially matches a maximum depth of the Cherenkov radiation of the Cherenkov image.

The Cherenkov imaging method designated GL, wherein, in the step of illuminating, the optical illumination having wavelength such that the penetration depth is between two and six millimeters.

A Cherenkov imaging method designated GM including the Cherenkov imaging method designated G, GA, GB, GC, GD, GE, GF, GG, GH, GK, GH, or GL, wherein in the step of illuminating, the optical illumination including a plurality of different wavelengths such that the optical illumination samples a respectively plurality of different depths of the subject to match depth-sampling properties of the Cherenkov radiation.

The Cherenkov imaging method designated GM, comprising: in the step of illuminating, illuminating the surface region with optical illumination of a plurality of wavelengths; and in the step of capturing the reflectance image: (a) capturing a respective plurality of wavelength-specific reflectance images, and (b) composing the reflectance image from the plurality of wavelength-specific reflectance images.

While the invention has been particularly shown and described with reference to a preferred embodiment thereof, it will be understood by those skilled in the art that various other changes in the form and details may be made without departing from the spirit and scope of the invention. It is to be understood that various changes may be made in adapting the invention to different embodiments without departing from the broader inventive concepts disclosed herein and comprehended by the claims that follow.

What is claimed is:

1. A system for providing, and monitoring delivery and accuracy of, a radiation therapy comprising:

a source of pulsed high energy radiation disposed to provide a radiation beam to a treatment zone, with high energy radiation of at least 0.2 MeV;

at least one camera configured to obtain images of light emitted from the treatment zone, the cameras disposed to image the treatment zone;

apparatus adapted to minimize interference by room lighting with the obtained images comprising apparatus adapted to synchronize pulsed room lighting to between pulses of the pulsed high energy radiation to allow obtaining images of Cherenkov light at times without ambient lighting; and

an image processor;

wherein the camera is synchronized to obtain the images during pulses of the pulsed high energy radiation;

wherein the image processor is configured with machine readable code adapted to using a three-dimensional model of a subject to determine a mapping of image intensity in the obtained images of Cherenkov light to a radiation dose deposited in skin of the subject provided by the radiation therapy.

2. The system of claim **1**, wherein the image processor is adapted with machine readable code to estimate a beam shape from the obtained images of Cherenkov light.

3. The system of claim **2**, wherein the image processor is adapted with machine readable code to estimate the radiation dose of the high energy radiation beam on the subject's skin from the obtained images-of Cherenkov light.

4. The system of claim **2**, where the image processor is further adapted with machine readable code to resolve patient position relative to the treatment beam by using vascular and skin structures appearing in the emitted Cherenkov images as biological alignment features.

5. The system of claim **2** where the image processor is further adapted with machine readable code to extract a shape of the beam, and code adapted to compare intensity patterns from the images with images from at least one prior treatment session to determine if changes have occurred and thereby to verify daily accuracy in delivery.

6. The system of claim **1**, further comprising a positioning device configured to hold the camera in a same location, angle and position in a first fractionated radiation treatment session and all subsequent fractionated radiation treatment sessions.

7. The system of claim **1**, wherein the image processor is configured to acquire multiple images of Cherenkov light during a treatment session.

8. The system of claim 7, wherein the image data is used to verify delivery as planned by comparison to a prescribed radiation dose.

9. A system for providing and monitoring delivery and accuracy of radiation therapy comprising:

a source of pulsed high energy radiation disposed to provide a radiation beam to a treatment zone, with high energy radiation of at least 0.2 MeV;

at least one camera configured to obtain images of light emitted from the treatment zone, the camera s disposed to image the treatment zone;

apparatus adapted to minimize interference by room lighting with the obtained images comprising apparatus adapted to synchronize pulsed room lighting to allow image capture of Cherenkov light at times without ambient lighting; and

an image processor;

wherein the camera is synchronized to obtain the images during pulses of the pulsed high energy radiation;

wherein the apparatus adapted to minimize interference by room lighting includes the image processor being adapted with machine readable instructions configured to obtain a first image of the treatment zone during at least one pulse of the high energy radiation source, and a second image of the treatment zone at a time other than during a pulse of the high energy radiation source; and with machine readable instructions configured to subtract the second image from the first image to provide an image of Cherenkov light from the treatment zone, the first and second images of the treatment zone being obtained while the treatment zone is illuminated with room lighting;

wherein the image processor is adapted with machine readable code to estimate a radiation dose of the high energy radiation beam on a subject's skin from the images.

10. The system of claim 9, wherein the machine readable code to estimate a radiation dose of the high energy radiation beam on the subject's skin from the images uses a three-dimensional model of the subject to determine a mapping of image intensity in the images of Cherenkov light to the radiation dose deposited in skin of the subject.

11. The system of claim 10, wherein the image processor is adapted with machine readable code to estimate cumulative radiation dose deposited in skin across a plurality of a treatment sessions in the treatment zone.

12. The system of claim 9, the image processor further configured with machine readable code to apply the mapping of image intensity from the multiple images of Cherenkov emissions from the treatment zone, the first and second images of the treatment zone being obtained while the treatment zone is illuminated with room lighting to determine maps of radiation dose to skin, and to determine if changes in position have occurred and to warn an operator if the treatment beam design is providing excessive radiation dose to skin or excessive changes in tissue position have occurred between successive sessions of treatment.

13. A system for providing, and monitoring delivery and accuracy of, a radiation therapy comprising:

a source of pulsed high energy radiation disposed to provide a radiation beam to a treatment zone, with high energy radiation of at least 0.2 MeV;

at least one camera configured to obtain images of light emitted from the treatment zone, the camera s disposed to image the treatment zone;

apparatus adapted to minimize interference by room lighting with the obtained images comprising apparatus adapted to synchronize pulsed room lighting to allow image capture of Cherenkov light at times without ambient lighting; and

an image processor;

wherein the camera is synchronized to obtain the obtained images during pulses of the pulsed high energy radiation;

where the image processor is further adapted with machine readable code to resolve patient position relative to the radiation beam by using vascular and skin structures appearing in the obtained images as biological alignment features.

14. The system of claim 13, where the image processor is further adapted with machine readable code to compare intensity patterns from the obtained images with obtained images from at least one prior treatment session to determine if changes have occurred between sessions.

15. The system of claim 14, wherein the image processor is adapted with machine readable code to estimate a cumulative radiation dose to skin across a plurality of a treatment sessions in the treatment zone.

16. The system of claim 15, wherein the image processor is configured with machine readable instructions to compare a skin determined from pre-treatment simulations to the cumulative radiation dose to skin and to interrupt the delivery of radiation if the cumulative radiation dose to skin disagrees with the pre-treatment simulations by more than a limit.

17. A system for providing, and monitoring delivery and accuracy of, a radiation therapy comprising:

a source of pulsed high energy radiation disposed to provide a radiation beam to a treatment zone, with high energy radiation of at least 0.2 MeV;

at least one camera configured to obtain images of light emitted from the treatment zone, the camera s disposed to image the treatment zone;

apparatus adapted to minimize interference by room lighting with the obtained images comprising apparatus adapted to synchronize pulsed room lighting to allow image capture of Cherenkov light at times without ambient lighting; and

an image processor;

wherein the camera is synchronized to obtain the images during pulses of the pulsed high energy radiation to form the obtained images;

wherein the image processor is configured with machine readable instructions to compare a radiation dose to skin determined from pre-treatment simulations to a radiation dose to skin determined from the obtained images of Cherenkov light and to interrupt the delivery of radiation if the radiation dose to skin determined from the obtained images disagrees with the radiation dose to skin determined from pre-treatment simulations by more than a limit.

18. A method of determining surface dose during radiation treatment of a first object beneath a surface of a second object to limit dose at the surface comprising:

obtaining at least two images of the surface, and extracting a three-dimensional computer model of the surface therefrom;

determining a mapping of image brightness at the surface in Cherenkov light images obtained by a digital camera to radiation intensity;

recording surface brightness at the surface in a plurality of Cherenkov light images;

a summing step selected from the group consisting of:

using the mapping of image brightness at the surface to translate each Cherenkov light image into a surface dose image, and summing the surface dose images to provide a total session surface dose image; and

summing the image brightness in each Cherenkov light image into a total session surface Cherenkov light image, and using the mapping of image brightness at the surface to translate the total session surface Cherenkov light image into a total session surface dose image; and

displaying the total session surface dose image.

19. The method of claim **18** further comprising blanking room lighting during obtaining of the Cherenkov light images.

20. The method of claim **18** further comprising correcting Cherenkov light images for ambient light by subtracting an ambient light image from an image obtained during a pulse of the beam.

21. The method of claim **20** further comprising:

summing the total session surface dose image with at least one prior session surface dose image to provide a total treatment surface dose image; and

displaying the total treatment surface dose image.

22. The method of claim **18** wherein the surface is normal tissue and a deeper region is a tumor.

23. A method of determining surface dose during radiation treatment from imaging of a fractionated radiation therapy comprising:

obtaining multiple images of a surface, and extracting a three-dimensional computer model of the surface therefrom;

obtaining Cherenkov light images synchronized to beam pulses, the Cherenkov light images obtained during beam pulses;

determining a mapping of image brightness at the surface in Cherenkov light images obtained by a digital camera to radiation intensity;

recording surface brightness at the surface in a plurality of Cherenkov light images;

a summing step selected from the group consisting of:

using the mapping of image brightness at the surface to translate each Cherenkov light image into a surface dose image, and summing the surface dose images to provide a total session surface dose image; and

summing the image brightness in each Cherenkov light image into a total session surface Cherenkov light image, and using the mapping of image brightness at the surface to translate the total session surface Cherenkov light image into a total session surface dose image; and

displaying the total session surface dose image.

24. The method of claim **23**, wherein the radiation treatment is a fractionated radiation treatment and further comprising using an image selected from the group consisting of the total session surface dose image and the total treatment surface dose image to modify a radiation treatment plan for at least one radiation treatment session.

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