



- (51) **International Patent Classification:**
A61N 5/10 (2006.01)
- (21) **International Application Number:**
PCT/US2017/020015
- (22) **International Filing Date:**
28 February 2017 (28.02.2017)
- (25) **Filing Language:** English
- (26) **Publication Language:** English
- (30) **Priority Data:**
62/302,761 2 March 2016 (02.03.2016) US
- (71) **Applicant:** VIEWRAY TECHNOLOGIES, INC.
[US/US]; 2 Thermo Fisher Way, Oakwood Village, OH 44146 (US).
- (72) **Inventors:** DEMPSEY, James, F.; 815 E Middlefield Rd., Mountain View, CA 94043 (US). SHVARTSMAN, Shmaryu, M.; 2 Thermo Fisher Way, Oakwood Village, OH 44146 (US). KAWRYKOW, Iwan; 2 Thermo Fisher Way, Oakwood Village, OH 44146 (US).
- (74) **Agents:** LATTA, Robert, T.S. et al.; Mintz Levin Cohn Ferris Glovsky and Popeo, P.C., 3580 Carmel Mountain Road, Suite 300, San Diego, CA 92130-6768 (US).
- (81) **Designated States** (*unless otherwise indicated, for every kind of national protection available*): AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DJ, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KH, KN, KP, KR, KW, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.
- (84) **Designated States** (*unless otherwise indicated, for every kind of regional protection available*): ARIPO (BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK,

[Continued on next page]

(54) **Title:** PARTICLE THERAPY WITH MAGNETIC RESONANCE IMAGING

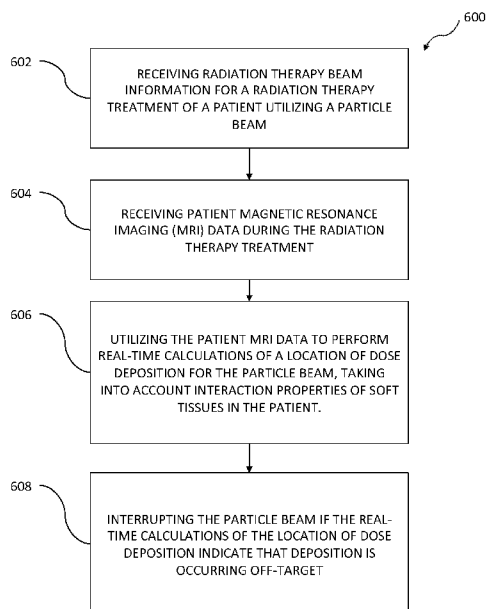


FIG. 6

(57) **Abstract:** Particle radiation therapy and planning utilizing magnetic resonance imaging (MRI) data. Radiation therapy prescription information and patient MRI data can be received and a radiation therapy treatment plan can be determined for use with a particle beam. The treatment plan can utilize the radiation therapy prescription information and the patient MRI data to account for interaction properties of soft tissues in the patient through which the particle beam passes. Patient MRI data may be received from a magnetic resonance imaging system integrated with the particle radiation therapy system. MRI data acquired during treatment may also be utilized to modify or optimize the particle radiation therapy treatment.



SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, —
GW, KM, ML, MR, NE, SN, TD, TG).

*before the expiration of the time limit for amending the
claims and to be republished in the event of receipt of
amendments (Rule 48.2(h))*

Published:

— *with international search report (Art. 21(3))*

PARTICLE THERAPY WITH MAGNETIC RESONANCE IMAGING

RELATED APPLICATION

[0001] This application claims the benefit of U.S. Provisional Application No. 62/302,761, filed March 2, 2016, which is hereby incorporated by reference.

TECHNICAL FIELD

[0002] The subject matter described herein relates to devices, systems and methods for particle radiotherapy treatment planning and administration.

BACKGROUND

[0003] Particle therapy uses beams of particles to kill cells to treat disease, typically proliferative tissue disorders such as cancer. Particle therapy can be used to treat targets in patients requiring a dose of ionizing radiation for curative effect, such as grossly observable tumors, anatomic regions containing microscopic disease or potential disease spread, or regions that include margins for motion and/or delivery uncertainties. The ionizing radiation delivered by particle therapy beams destroys the DNA and other important components of diseased cells and prevents the cells from replicating.

[0004] Typical particle therapy involves treatment planning to determine how to deliver the prescribed radiation dose to the target, while at the same time sparing healthy tissues in the vicinity by limiting doses below acceptable thresholds to prevent deadly or debilitating side effects. Treatment planning often uses X-Ray computed tomography (CT) data to determine the composition of the patient's body in conjunction with developing the particle therapy treatment plan.

SUMMARY

[0005] In one aspect, described is a non-transitory computer program product storing instructions that, when executed by at least one programmable processor forming part of at least one computing system, cause the at least one programmable processor to perform operations. The operations can include receiving patient radiation therapy prescription information, receiving patient magnetic resonance imaging (MRI) data, and determining a radiation therapy treatment plan for use with a particle beam utilizing the patient radiation therapy prescription information and utilizing the patient MRI data to account for interaction properties of soft tissues through which the particle beam passes. The patient magnetic resonance imaging data can be received from a magnetic resonance imaging device integrated with a particle radiation therapy system.

[0006] In some variations, the influence of a magnetic field produced by an MRI system on the particle beam can be accounted for.

[0007] Determining the radiation therapy plan can include a determination of a biological effectiveness of dose delivered to the soft tissues by the particle beam. The determination can be made through utilization of the patient magnetic resonance imaging data.

[0008] X-ray computed tomography data can be received. Determining a radiation therapy treatment plan can utilize the x-ray computed tomography data.

[0009] The operations can include receiving radiation therapy beam information for a radiation therapy treatment of a patient utilizing a particle beam, receiving patient magnetic resonance imaging (MRI) data during the radiation therapy treatment, and, utilizing the patient MRI data to perform real-time calculations of a location of dose deposition for the particle beam, taking into account interaction properties of soft tissues through which the particle beam passes. The influence of a magnetic field produced by an MRI system on the

particle beam can be taken into account in performing the real-time calculations of location of dose deposition. The operations can include interrupting the particle beam if the real-time calculations of the location of dose deposition indicate that dose deposition is occurring off-target. The operations can include adjusting the energy of the particle beam if the real-time calculations of the location of dose deposition indicate that dose deposition is occurring off-target.

[0010] The patient MRI data and the real-time calculations of the location of dose deposition can be utilized to modify a direction of the particle beam in order to track a target. In some variations modifying the direction of the particle beam can be performed through deflection magnets. In some variations, the patient MRI data and the radiation therapy beam information can be utilized to calculate accumulated dose deposition to the patient during the radiation therapy treatment.

[0011] The real-time calculations of a location of dose deposition can include a determination of a biological effectiveness of dose delivered to the soft tissues by the particle beam through utilization of the patient magnetic resonance imaging data. The radiation therapy treatment can be re-optimized based on the calculated dose deposition.

[0012] In one aspect a radiation therapy system is described. The radiation therapy system can include a particle therapy delivery system for delivery of radiation therapy to a patient via a particle beam. The radiation therapy system can include a magnetic resonance imaging system configured to obtain patient magnetic resonance imaging (MRI) data during radiation therapy. The radiation therapy system can include a controller configured to receive the patient MRI data during radiation therapy and utilize the patient MRI data to perform real-time calculations of a location of dose deposition for the particle beam, taking into account interaction properties of soft tissues through which the particle beam passes.

[0013] The controller can be configured to interrupt the particle beam if the real-time calculations of the location of dose deposition indicate that deposition is occurring off-target. The controller can be configured to determine influence of a magnetic field of the magnetic resonance imaging system on the particle beam in the calculations of the location of dose deposition. The controller can be configured to determine a biological effectiveness of dose delivered to the soft tissues by the particle beam through utilization of the patient magnetic resonance imaging data.

[0014] The controller can be configured to interrupt the particle beam if the real-time calculations of the location of dose deposition indicate that dose deposition is occurring off-target. The controller can be configured to adjust the energy of the particle beam if the real-time calculations of the location of dose deposition indicate that dose deposition is occurring off-target. The controller can be configured to utilize the patient MRI data and the real-time calculations of the location of dose deposition to modify a direction of the particle beam in order to track a target.

[0015] The radiation therapy system can comprise deflection magnets. The modification of the direction of the particle beam can be effectuated using the deflection magnets.

[0016] In some variations, the controller can be configured to utilize the patient MRI data and particle beam information to calculate dose deposition to the patient during the radiation therapy. The controller can be configured to re-optimize the radiation therapy based on the calculated dose deposition.

[0017] The radiation therapy system can include a dosimetry system. The dosimetry system can be used for monitoring the radiation therapy to the patient. The radiation therapy system can include a magnetic shielding structure surrounding at least a portion of the

dosimetry system. The magnetic shielding structure can include a plurality of shells. The plurality of shells can be separated by an annular disk.

[0018] In some variations, the radiation therapy system can include a gantry. The gantry can be configured to allow delivery of the particle beam from different angles around the patient.

[0019] In some variations, the magnetic resonance imaging system can comprise two split main magnets. The radiation therapy system can include an isocenter. The two split main magnets can be separated by a plurality of buttresses located no further from the isocenter than an outer boundary of the two split main magnets.

[0020] The details of one or more variations of the subject matter described herein are set forth in the accompanying drawings and the description below. Other features and advantages of the subject matter described herein will be apparent from the description and drawings, and from the claims. While certain features of the currently disclosed subject matter are described for illustrative purposes, it should be readily understood that such features are not intended to be limiting. The claims that follow this disclosure are intended to define the scope of the protected subject matter.

DESCRIPTION OF DRAWINGS

[0021] The accompanying drawings, which are incorporated in and constitute a part of this specification, show certain aspects of the subject matter disclosed herein and, together with the description, help explain some of the principles associated with the disclosed implementations. In the drawings,

[0022] FIG. 1 is a graph showing the penetrative depth of various exemplary forms of radiation therapy into human tissue;

[0023] FIG. 2 is a flowchart for a method of radiation therapy treatment planning for particle radiation therapy, utilizing MRI data, that can be implemented by software;

[0024] FIG. 3 is an illustration of a radiation therapy system having one or more features consistent with the present description;

[0025] FIG. 4 is an illustration of a radiation therapy system having one or more features consistent with the present description;

[0026] FIGS. 5A-5B illustrate a magnetic shielding system for shielding, for example, a portion of a dosimetry system of a particle therapy system, having one or more features consistent with the current description; and,

[0027] FIG. 6 is a flowchart for a method of particle radiation therapy treatment having one or more elements consistent with the present description.

DETAILED DESCRIPTION

[0028] Particle therapy is a form of radiotherapy using beams of energetic particles for the treatment of disease, for example, cancer. Particle beams can be aimed at a target within a patient and can cause damage to the DNA and other important cellular components of the target cells, eventually causing the death of the cells. Cancerous cells have less ability than non-cancerous cells to repair radiation damage and are therefore particularly susceptible to particle therapy. Depending on the context, “particle therapy” is sometimes used to refer to therapy with hadrons, such as protons, neutrons, antiprotons, mesons, etc., while it may also refer to therapy utilizing ions or nuclei, such as lithium ions, helium ions, carbon ions, etc. Often, therapy with ions such as carbon ions is said to be “heavy ion therapy,” although the line between “light ions” and “heavy ions” is not precisely defined. As used herein, the terms particle therapy, particle radiation therapy, particle beam and the like, refer to therapy

utilizing hadrons as well as nuclei (or ions). This terminology specifically excludes therapies such as photon therapy or electron-beam therapy.

[0029] FIG. 1 is a graph 100 showing the penetrative depth of various forms of radiation therapy into human tissue. For a given energy, electron beams have a low penetrative depth into human tissue (as shown by trace 102) compared to other radiation therapy forms. X-ray beams penetrate human tissue to a greater depth than electrons, but the dose absorbed by tissue falls off with the penetrative depth of the X-rays as shown by trace 104. Particle therapy beams deposit more of their energy at a particular depth into the tissue of the patient at the end of their range, as shown by trace 108. This depth near the end of their range may be referred to as the Bragg Peak, shown as 108. A benefit provided by particle therapy is that less energy is deposited into healthy tissue outside of the target, thereby reducing the potential for damage to the healthy tissue. Additionally, beyond the Bragg peak there is very little dose deposited compared to X-Ray beams.

[0030] Before particle radiation therapy can take place, a treatment plan must be generated. The present disclosure contemplates the use of magnetic resonance imaging (MRI) data in a particular fashion in generating a treatment plan, which will have a predicted dose deposition closely matching the actual dose delivered to the patient and closely matching the desired dose. X-ray computed tomography (CT) imaging data may also be employed to determine, for example, the mass density of the patient's tissues and regions of the patient that contain low and high density tissues or regions such as lung, air, and bone. The analysis can be performed for all particle beam paths.

[0031] A magnetic resonance imaging system can be employed to obtain MRI data that, when analyzed, can more accurately determine the types of soft tissues along beam paths to and through the target. Particle interaction properties can then be determined from the MRI data, allowing for a more accurate determination of the dose delivered to the patient's tissues

and to the target. In addition, the MRI data can enable more accurate determination of the biological effectiveness of the particle beam therapy.

[0032] The present disclosure contemplates that the MRI data may be combined with X-Ray CT data (for example, by using deformable image registration) to improve the accuracy of chemical composition and mass density determination and thus improve the determination of particle therapy doses. If X-Ray CT data is not available, regions containing bone may be determined by ultra-short echo time (TE) MR imaging, while lung and air may be determined from proton density weighted MR imaging.

[0033] X-Ray CT is well suited to produce a map of electron densities in the human body and is useful in determining dose delivered by photon beam radiation therapy because photons' dominant interaction probabilities are proportional to electron density. Electron densities are also well correlated to mass density due to the fact that, for human tissues, the atomic numbers are low where nuclei have a fairly constant ratio of neutrons to protons. CT Hounsfield numbers reflect the attenuation coefficient of human tissues to X-rays. Thus, the Hounsfield number may be identical for a variety of combinations of elemental compositions, elemental weights and mass densities, not to mention that the measured Hounsfield number may be inaccurate due to image beam hardening effects and other artifacts. The uncertainty of elemental composition introduced when defining tissues using X-Ray CTs and Hounsfield numbers can cause the determined range of a particle beam to err significantly. This error can lead directly to dose computation errors, for example, because particle stopping powers are required to accurately model dose deposition along an energetic particle's path and to determine where the particles reach the end of their range. Uncertainties in stopping power directly translate into uncertainties in the location of the Bragg peak 108, as illustrated in FIG. 1, which can move large dose regions off of targets and tumors, failing to deliver an

effective dose to the treatment target and, instead, delivering particle radiation therapy dose to healthy tissues that should be shielded from receiving high doses of particle radiation.

[0034] Soft tissues have better contrast and definition when imaged with MRI systems over X-Ray CT. As noted, X-Ray CT is excellent at determining the mass density of tissues with very different densities and the definition of regions containing air or cortical bone, due to its low or high contrast and low or high Hounsfield numbers. But, many soft tissues will have very similar densities, with very different elemental compositions. For example, tissues can have a fat-like (or adipose-like) nature or a water-like (or muscle-like) nature while having a very similar mass density, and hence such are hard to distinguish with X-Ray CT data. Image noise, artifacts, and low contrast in X-Ray CT data conspire to often misidentify tissue types with current methods. In terms of stopping powers, removing any density dependence, the difference in stopping power between fat-like tissue (CH₂) or water-like tissue (OH₂) is dominated by the difference in atomic number between O and C. For energies above tens of MeV/nucleon, as used in particle therapy, the ratio of stopping powers is significant.

[0035] Acquiring MRI data with pulse sequences that are sensitive to only water or only fat, allows for the water-to-fat ratio of tissues to be determined through, for example, Dixon methods or sandwich echoes. The determined water-to-fat ratios in the vicinity of the treatment target can then be employed to improve the knowledge of the elemental compositions of the soft tissues. An MRI can obtain different “contrasts” by reading the signal of the excited protons at different times and/or in different ways (the signal decays differently depending on what type of molecule the hydrogen is attached to). It is therefore possible to better differentiate different tissue types and deduce chemical compositions utilizing an MRI.

[0036] The interactions (frequency and type of interaction) of a particle beam with the tissues it is passing through depends on a number of factors including beam particle type, particle energy, and the mass density and chemical composition of the tissue. Particle interactions, at least for charged particles, include Coulomb interactions (i.e., electromagnetic interactions). Coulomb interactions almost always lead to a small energy loss of the incident particle and/or a small deflection in direction. Deflections, which cause the beam to spread out, are referred to as Coulombic scattering. The amount of energy lost per unit length may be referred to as stopping power. The small energy losses that particles experience in Coulomb interactions are due to ionizations and excitations of the atoms and molecules of the tissue. The frequency of such interactions determines the ionization density along the path of a particle. The higher the ionization density, the higher the probability for cell damage. This is often measured with a quantity termed linear energy transfer (LET).

[0037] Particle interactions also include nuclear interactions, which are less frequent than Coulomb interactions but are much more catastrophic. They tend to result in the nucleus having been hit disintegrating into fragments (e.g., individual protons and neutrons, deuterons, tritons, lithiums, alphas, etc.). The type and number of such fragments depend on the incident particle type and energy, and the nucleus that has been hit. Nuclear interactions also leave behind radioactive nuclei, which decay and deposit additional dose.

[0038] Nuclear interactions and Coulombic scattering are highly dependent on atomic numbers of the nuclei. They both lead to broadening of a Bragg peak. For ions, nuclear interactions are also responsible for the tail of dose deposited beyond the Bragg peak. When there are heterogeneities in the beam path (e.g., air cavities, bones), Coulombic scattering leads to a complex dose deposition structure behind the heterogeneity.

[0039] When the term interaction properties is utilized herein, it refers to any combination of interaction properties such as the Coulombic interactions and nuclear interactions

described above. Preferred embodiments of the present disclosure for, e.g., treatment planning or real-time MRI guidance of radiation therapy, will utilize as many interaction properties as necessary in determining the location and quantity of dose deposition in patient tissues.

[0040] “Heavy ions” such as Carbon ions tend to have a much more devastating effect on cells than protons. Their nuclear interaction fragments have high LETs and tend to deposit their energy locally around the interaction site. This is the main mechanism responsible for Carbon ions having a much higher “biological effectiveness” than protons. This leads to both more cells being killed (or damaged) per unit energy deposited in the tissue for ions compared to photons, electrons and even protons. The energy deposited in tissue is referred to as absorbed dose, measured in Gray (Gy). One Gy of absorbed dose from a Carbon ion beam will kill 3-12 times more cells than one Gy of absorbed dose from a photon or electron-beam, due to the differences in biological effectiveness.

[0041] With particle beam therapy, determination of the biological effectiveness is beneficial or even required for proper treatment. There are a number of different ways to determine biological effectiveness. For example, the determination of a biologically effective dose (BED) aims to indicate quantitatively the biological effect of a particular radiotherapy treatment, taking into account numerous factors such as the type of therapy, dose per fraction, dose rate, etc. In addition, relative biological effectiveness (RBE) is a ratio comparing the absorbed dose for a particular mode of therapy to an absorbed dose for photon therapy, where each dose leads to the same biological effect.

[0042] For protons, it has been assumed for years that RBE is constant at around 1.1, but some have opined that this leads to suboptimal planning results. Because the RBE for protons is so close to 1.0, neglecting to perform such a biological effectiveness calculation

may not have too significant an effect on therapy but for neutrons, ions, mesons, etc., RBE is much higher and can have a very significant effect on therapy if not taken into account.

[0043] To determine biological effectiveness, one needs to know the energy spectrum of the incident beam as well as the interaction properties of the materials or tissues that the beam passes through. Thus, precise knowledge of the chemical composition of the tissues is absolutely essential for accurate determinations of biological effectiveness. It is also important to determine where the incident particle beam has lost the majority of its energy (i.e., the Bragg peak). In addition, contributions to the dose distribution due to nuclear reactions, activation of tissues, time dose fractionation and cell damage vs. recovery can be incorporated into determination of biological effectiveness. For these reasons, patient MRI data is important in the determination of biological effectiveness measures, similar to its importance in dose calculation and treatment planning.

[0044] MRI data can similarly be employed to allow evaluation of tissue elemental composition and accurate dose computation for the evaluation of the quality of a delivery plan before delivery. If the quality of the dose to be delivered is insufficient, the data collected at setup can be employed to re-optimize a particle therapy treatment plan before delivery. This can be performed immediately prior to delivery of the therapy, while the patient is on the treatment couch, or prior to the patient's arrival for the actual treatment.

[0045] FIG. 2 is a flowchart for a method 200 of radiation therapy treatment planning for particle radiation therapy, utilizing MRI data, that can be implemented by software, the method having one or more features consistent with the present description. The software can be implemented using one or more data processors that may be part of a system controller. The software can include machine-readable instructions, which, when executed by the one or more data processors, can cause the one or more data processors to perform one or more operations.

[0046] In FIG. 2, at 202, patient radiation therapy prescription information can be received. Patient radiation therapy prescription information may include data such as minimum dose required to a target tumor, maximum dose allowed to nearby organs of interest, or the like. The patient radiation therapy prescription information described herein is not intended to be limiting. The patient radiation therapy prescription information received at the radiation therapy treatment planning system can include prescription information typical for radiation therapy treatment planning.

[0047] At 204, patient MRI data can be received. In some variations, the patient MRI data can be received from a magnetic resonance imaging device integrated with a particle therapy system. Patient MRI data may encompass the region of interest for treatment, including, for example, a target treatment area of the patient and surrounding tissue that radiation therapy beams may pass through and for which radiation dose should be monitored. The MRI data may be taken before treatment at a different location from the treatment itself, or the MRI data may be acquired on the treatment table where an MRI is integrated with the particle radiation therapy system.

[0048] At 206, a radiation therapy treatment plan can be determined for use with a particle beam. The radiation therapy treatment plan can utilize the patient radiation therapy prescription information and utilize the patient MRI data to account for interaction properties of soft tissues in the patient through which the particle beam passes. The radiation therapy treatment plan can include, for example, the number of beams to be utilized, the direction from which the beam(s) will be delivered, the energy of the beam(s), collimator configurations, and the like.

[0049] Determination of the radiation therapy treatment plan can also account for the influence of the magnetic field of an MRI on the particle beam. This involves including the influence of the strong magnetic field of the MRI on transport of the ionizing radiation

depositing dose in the patient. The interaction cross sections are not strongly influenced by polarization of spins as they compete with thermal effects (e.g., at body temperatures only about four parts per million of spins are aligned within a 1 Tesla magnetic field), but the magnetic field exerts an external Lorentz force on moving charged particles that can be accounted for to produce a more accurate dose computation.

[0050] Determination of the radiation therapy treatment plan can also include determination of a biological effectiveness of the dose delivered to the soft tissues of the patient by the particle beam, through utilization of the patient magnetic resonance imaging data.

[0051] FIG. 3 is an illustration of a particle therapy system 300 having one or more features consistent with the present description. To energize particles, the particles are first accelerated by a particle accelerator 302. The particle accelerator can be a synchrotron, cyclotron, linear accelerator, or the like. A synchrotron may be fed by either a low-energy cyclotron or a low-energy linear accelerator. The energy of the particle beam 304, prior to any downstream adjustment, determines the penetrative depth of the energized particles into the patient 306. Particle accelerators typically produce an energized particle beam having a defined energy. In some variations, the energy of the particles can be reduced, for example, by running the beam through an attenuating medium. It is preferable for such to be done away from the patient due to secondary neutrons that can increase unnecessary dose to the patient. The attenuating medium may be a wedge of material on a wheel or linear drive that can be rotated to increase or decrease the energy. The maximum energy is obtained by not applying any attenuating material in the beam. The minimum is obtained by applying the thickest amount of attenuating material in the beam. For a known material, a thickness can be determined that would halt all energized particles from reaching the patient to stop or interrupt the beam without deactivating the system.

[0052] Synchrotrons may also be configured to control beam energy by increasing or decreasing the number of passes through the accelerating elements in the synchrotron ring. In principle, a linear accelerator can also change the number of accelerating units, to a few fixed energies, over a limited range. Pulse to pulse energy changes are possible with the proper equipment.

[0053] In some variations, a particle therapy gantry 312 can be used to direct the energized particle beam 304 to the patient 306. The patient 306 can be positioned on a couch 314 within the center of the particle therapy gantry 312. The particle therapy gantry 312 can include gantry electro-magnets 316 configured to direct the beam toward the patient 306, through a dosimetry system 318.

[0054] The particle therapy gantry 312 can be configured to rotate to facilitate delivery of particle therapy at different angles. In some variations, the particle therapy gantry 312 can be configured to rotate 360 degrees. One or more slip rings can be employed to facilitate the delivery of electrical power to the electro-magnets other components disposed on the particle therapy gantry 312. In some variations, the particle therapy gantry 312 can be configured to rotate with a field of rotation of approximately 360 degrees. In such variations, the particle therapy gantry 312 may rotate in one direction as far as it will go and then rotate back in the other direction as far as it will go. Rotating the particle therapy gantry 312 around the patient 306 can facilitate delivery of the energized particle beam 304 to the target at different angles improving the sparing of healthy tissue and treatment plan quality.

[0055] The particle therapy gantry 312 may include scanning beam magnets 320. The scanning beam magnets 320 can include, for example, pairs of electro-magnets. The pairs of electro-magnets can be arranged to have their magnetic fields in orthogonal planes to one another. The scanning beam magnets 320 can be configured to manipulate the direction of the energized particle beam 304. In some variations, scanning beam magnets 320 can be

configured to direct the energized particle beam in a scanning motion back and forth across the treatment target of the patient.

[0056] In some variations, the system can include a fixed beamline 322. The fixed beamline 322 can be configured to deliver the energized particles directly to a patient through a dosimetry system 318, without a gantry. The system may also include one or more scanning beam electro-magnets 320 configured to modify the direction of the energized particles of the fixed-line beam.

[0057] The particle therapy system may also include a scatterer. The scatterer can be configured to cause the energized particle beam 304 to scatter outward. The system can also contain a beam wobbler or raster scanning mechanism to spread out the beam. The system can also include a collimator. The collimator can be a multi-leaf collimator comprising a plurality of thin metallic blades. The thin metallic blades can be moveable, the position of which can be controlled by a computer. The thin metallic blades can be configured to absorb the energetic particles. The thin metallic blades can be arranged, by a controller, such that the shape of an aperture they form is complementary to the target within the patient. In this manner, the collimator can facilitate shielding of healthy tissue surrounding the target while permitting the energized particles to penetrate to the target. In some variations, a collimator carved into a permanent shape may be used. Similarly, a bolus can be positioned in the path of the energized particle beam 304, which may be formed from a material semi-permeable to the energized particles, and may be carved to compliment the shape of the tumor.

[0058] FIG. 4 is an illustration of a radiation therapy delivery system 400 having one or more features consistent with the present disclosure. The particle therapy delivery system 400 can have one or more elements similar to the elements of the system 300, illustrated in FIG. 3. The radiation therapy system 400, according to the present disclosure, may include a particle therapy delivery system for delivery of radiation therapy to a patient via a particle

beam, a magnetic resonance imaging system 402 configured to obtain patient magnetic resonance imaging (MRI) data during radiation therapy; and, a controller 424 configured to receive patient MRI data during radiation therapy and utilize the patient MRI data to perform real-time calculations of the location of dose deposition for the particle beam(s), taking into account interaction properties of the soft tissues in the patient through which the particle beam passes.

[0059] The particle therapy delivery system 400 may have a split magnet MRI 402. The split magnet MRI 402 can include two split main magnets 404 and 406. The radiation therapy system can include an isocenter 407. The two split main magnets 404 and 406 can be separated by a plurality of buttresses 408. The plurality of buttresses 408 can be located no further from the isocenter 407 than the outer boundary of the two split main magnets 404 and 406. While the two split main magnets 404 and 406 are each referred to as a single magnet, this terminology is not intended to be limiting. The two split main magnets 404 and 406 can each include a plurality of magnets for the purpose of obtaining MRI data of the patient.

[0060] A split MRI system is illustrated in FIG. 4 for illustrative purposes only. The MRI system used can be any type of MRI system. For example, the main magnets can include vertical open magnets, short bore magnets, magnets with a portal or thin section, or the like.

[0061] A couch 410 can be disposed within the split MRI system 402. The split MRI system 402 can be configured to receive a patient 412, on the couch 410, through the internal apertures of the two split main magnets 404 and 406.

[0062] The split magnet MRI system 402, couch 410 and patient 412 can all be disposed within a particle therapy gantry, such as gantry 312 illustrated in FIG. 3. The particle therapy gantry may be configured to rotate about the patient 412 delivering particle therapy to the patient from a multitude of angles.

[0063] The plurality of buttresses 408 can be disposed between the two main MRI magnets 404 and 406 and positioned within the outer periphery of the two main MRI magnets 404 and 406 so as not to further increase the overall diameter of the MRI system. The system may include, as an example, three buttresses 408 spaced at equal angles around the two main MRI magnets 404 and 406. The system can be operated such that the particle beam is directed toward the patient between the split magnets and in a manner such that it will not travel through any of the buttresses 408.

[0064] The system can be configured to facilitate delivery of energized particles to the patient such that the energized particles are directed into a gap 419 between the two main MRI magnets 404 and 406.

[0065] Particle therapy delivery system 400 can include a dosimetry system 416 for monitoring the radiation therapy to the patient. The dosimetry system 416 can also include one or more components to facilitate the delivery of particle therapy to the patient, for example, by providing feedback to a controller.

[0066] The particle therapy delivery system 400 can include one or more magnetic shielding structures 420 that may, for example, surround at least a portion of the dosimetry system. Magnetic shielding structures 420 can be configured to house electronic equipment that would otherwise be adversely affected by the magnetic fields produced by main MRI magnets 404 and 406.

[0067] FIGs. 5A-5B illustrate an exemplary magnetic shielding structure 500 for shielding at least a portion of a dosimetry system 502 of a particle therapy delivery system, having one or more features consistent with the present disclosure. The magnetic shielding structure 500 may comprise a plurality of shells. The plurality of shells can be formed from a series of concentric shields configured to shield magnetic fields produced by the split magnet MRI

system 402 illustrated in FIG. 4. The concentric shields may be configured to surround at least a portion of a dosimetry system 502.

[0068] The magnetic shielding structure 500 can include a first shield container 504. The first shield container 504 can comprise a cylindrical body portion 506 and an annular disk 508 disposed across one end of the cylindrical body portion. The annular disk 508 can include an aperture 510 to allow the particle particles to pass through unhindered. In some variations, the first shield container 504 can have a diameter of approximately seventeen inches. The diameter of the first shield container 504 can be selected to sufficiently house at least a portion of the components of the dosimetry system 502.

[0069] The magnetic shielding structure 500 can comprise a plurality of shells. For example 504, 512 and 514 in FIG. 5B, or the like. The plurality of shells 504, 512, 514 can be nested together. At least one of the plurality of shells preferably includes an annular disk 516, 518, or the like.

[0070] The magnetic shielding structure 500 may be positioned in a fixed location with respect to split magnet MRI system 402, or may be configured to rotate with a gantry, such as gantry 312 illustrated in FIG. 3. One or more structures can be disposed opposite or around the split magnet MRI system 402 and configured to mimic the magnetic properties of magnetic shielding structure 500 in order to minimize interference with the homogeneity of the MRI's magnetic fields.

[0071] The particle therapy delivery system 400, illustrated in FIG. 4, can include a controller 424. The controller 424 can be configured to electronically communicate with the particle therapy delivery system 300, as illustrated in FIG. 3, and to receive data from and control the system 400, as illustrated in FIG. 4. Controller 424 can also be configured to

receive patient MRI data from the split magnet MRI system 402 and to control the split magnet MRI system 402.

[0072] The controller 424 may be configured to utilize patient MRI data and particle beam information to calculate dose deposition to the patient during radiation therapy. The patient MRI data, along with information about the particle beam(s), can be used to calculate where, and to what extent, dose is deposited into patient tissues over time. The actual dose depositions can be accumulated so that a total dose may be known following a particular fraction of treatment. This information can be used to re-optimize the treatment plan prior to a subsequent fraction of treatment.

[0073] Furthermore, the calculated real-time dose deposition information may be utilized to improve or re-optimize the radiation therapy treatment plan during treatment delivery. Controller 424 may be configured to utilize software to perform the real-time calculations of the location of dose deposition. The software may include machine-readable instructions. The controller 424 may include one or more data processors configured to execute the machine-readable instructions. Execution of machine-readable instructions, by the data processor, may cause data processor to perform one or more operations, such as one or more of the operations described in the present disclosure.

[0074] Controller 424 can be configured to calculate Bragg peaks for particle beams relative to the location of a treatment target, utilizing the received MRI data. Controller 424 can be further configured to modify the therapy beams in instances where it is determined that the Bragg peak(s) of the beams are not properly located with respect to the treatment target.

[0075] As discussed with regard to treatment planning, real-time MRI data can be used to determine the location of fat-like tissue and water-like tissue within the patient due to the

MRI's ability to differentiate between the two. A water tissue-to-fat tissue ratio for the beam path through the patient can be determined to determine the interaction properties of the patient's tissues in real time while the patient is undergoing treatment.

[0076] A particle interaction property map may be generated in real time to increase the accuracy of the dose and range calculations. Determination of the interaction properties of patient tissues with the energetic particles in real time as the patient is being treated can facilitate greater accuracy and effectiveness in the delivery of particle therapy. Having a more accurate picture of the Bragg peak location relative to the treatment target can allow positioning of the Bragg peak more accurately. This lends itself to increasing the radiation therapy dosage to the target, without an increased risk in radiating healthy surrounding tissue.

[0077] Controller 424 may also be configured to determine the influence of a magnetic field of the magnetic resonance imaging system on the particle beam in calculating the location of dose deposition, as discussed above.

[0078] Controller 424 may further be configured to determine the biological effectiveness of the dose delivered to soft tissues by the particle beam through utilization of the patient magnetic resonance imaging data.

[0079] The MRI data provided in real-time can also facilitate determination of the precise location and/or velocity of tissues along with prediction of tissue trajectories. This information can also be used to provide a prediction of where the treatment target will be so that the controller 424 can cause the system 400 to deliver the particle beam to that location.

[0080] Controller 424 may be configured to interrupt the particle beam if the real-time calculations of the location of dose deposition indicate that dose deposition is occurring off-target. The location of the treatment target can be determined from MRI data obtained during the planning stages of the treatment. At the time of treatment, the location of the target may

have changed due to changes in the patient's anatomy. For example, weight loss, a full stomach, gas, or the like, can cause a relative change in the location of the treatment target between imaging the patient and delivering therapy to the patient. This increases the risk that the therapy will be less effective due to at least a portion of the treatment target not being irradiated and/or healthy tissue being damaged by the particle beam. Furthermore, a patient's voluntary or involuntary movements such as fidgeting, breathing, gas movement, and the like can cause the location of the treatment area to move during delivery of the particle therapy to the patient. Real-time calculations of the location of dose deposition can be used to cause controller 424 to determine whether the dose is being deposited at its intended target or whether the dose is off-target. If the dose is off-target, the controller 424 may interrupt the particle beam to avoid radiation dose to healthy tissues. The controller 424 may maintain the beam interruption until the calculated location of dose deposition again coincides with the target.

[0081] The controller 424 may be configured to adjust the energy of the particle beam if the real-time calculations of the location of dose deposition indicate that deposition is occurring off-target. If the real-time calculations of the location of dose deposition indicate the dose is off target, especially if the dose is simply being deposited short of the target or beyond the target, the controller may be configured to increase or decrease the energy of the particle beam so that the location of the dose deposition will again coincide with the target. The energy of the particle beam may be modified at the source or downstream from the source.

[0082] Controller 424 may be configured to utilize the patient MRI data and the real-time calculations of the location of dose deposition to modify a direction of the particle beam in order to track a target. If the real-time calculations of the location of dose deposition indicate that the dose is off target, especially if the aim of the beam is off target laterally (rather than

the depth), the controller may be configured to modify the direction of the particle beam so that the location of dose deposition will again coincide with the target. For example, the radiation therapy system 400 can include deflection magnets 426, sometime called bending magnets or scanning beam magnets. The direction of the particle beam can be modified through the deflection magnets to deflect the trajectory of the beam using magnetic forces. The deflection magnets are typically electromagnets where the strength of the magnetic force generated by the electromagnets can be modified by applying varying amounts of electric current across the electromagnets.

[0083] FIG. 6 is a flowchart for a method 600 of radiation therapy treatment for particle radiation therapy, utilizing MRI data, that may be implemented by software, the method having one or more features consistent with the present description. The software can be implemented using one or more data processors. The software can include machine-readable instructions, which, when executed by the one or more data processors, can cause the one or more data processors to perform one or more operations. Method 600 is an example of the operations that can be performed by controller 424, as discussed herein.

[0084] At 602, radiation therapy beam information for radiation therapy treatment of a patient utilizing a particle beam can be received. The radiation therapy beam information can include one or more characteristics of a particle beam. The one or more characteristics can include an indication of penetrative abilities of the particle beam, the spread characteristics of the particle beam, the number of particle beams, or the like.

[0085] At 604, patient magnetic resonance imaging (MRI) data can be received during the radiation therapy treatment.

[0086] At 606, the patient MRI data can be utilized to perform real-time calculations of a location of dose deposition for the particle beam, taking into account interaction properties of

soft tissues in the patient through which the particle beam passes, as discussed herein. The influence of a magnetic field produced by an MRI system on the particle beam may also be accounted for in performing the real-time calculations of location of dose deposition, as discussed above. And, a determination of the biological effectiveness of dose delivered to the soft tissues by the particle beam, through utilization of the patient magnetic resonance imaging data, may also be performed in conjunction with the real-time dose calculations.

[0087] At 608, the particle beam can be interrupted if real-time calculations of the location of dose deposition indicate that deposition is occurring off-target.

[0088] In some variations, the energy of the particle beam can be adjusted if the real-time calculations of the location of dose deposition indicate that deposition is occurring off-target. In other variations, the patient MRI data can be utilized and the real-time calculations of the location of dose deposition to modify a direction of the particle beam in order to track a target.

[0089] While components have been described herein in their individual capacities, it will be readily appreciated the functionality of individually described components can be attributed to one or more other components or can be split into separate components. This disclosure is not intended to be limiting to the exact variations described herein, but is intended to encompass all implementations of the presently described subject matter.

[0090] In the descriptions above and in the claims, phrases such as “at least one of” or “one or more of” may occur followed by a conjunctive list of elements or features. The term “and/or” may also occur in a list of two or more elements or features. Unless otherwise implicitly or explicitly contradicted by the context in which it used, such a phrase is intended to mean any of the listed elements or features individually or any of the recited elements or features in combination with any of the other recited elements or features. For example, the

phrases “at least one of A and B;” “one or more of A and B;” and “A and/or B” are each intended to mean “A alone, B alone, or A and B together.” A similar interpretation is also intended for lists including three or more items. For example, the phrases “at least one of A, B, and C;” “one or more of A, B, and C;” and “A, B, and/or C” are each intended to mean “A alone, B alone, C alone, A and B together, A and C together, B and C together, or A and B and C together.” Use of the term “based on,” above and in the claims is intended to mean, “based at least in part on,” such that an unrecited feature or element is also permissible.

[0091] The subject matter described herein can be embodied in systems, apparatus, methods, and/or articles depending on the desired configuration. The implementations set forth in the foregoing description do not represent all implementations consistent with the subject matter described herein. Instead, they are merely some examples consistent with aspects related to the described subject matter. Although a few variations have been described in detail above, other modifications or additions are possible. In particular, further features and/or variations can be provided in addition to those set forth herein. For example, the implementations described above can be directed to various combinations and subcombinations of the disclosed features and/or combinations and subcombinations of several further features disclosed above. In addition, the logic flows depicted in the accompanying figures and/or described herein do not necessarily require the particular order shown, or sequential order, to achieve desirable results. Other implementations may be within the scope of the following claims.

CLAIMS

What is claimed is:

1. A non-transitory computer program product storing instructions that, when executed by at least one programmable processor forming part of at least one computing system, cause the at least one programmable processor to perform operations comprising:
receiving patient radiation therapy prescription information;
receiving patient magnetic resonance imaging (MRI) data; and,
determining a radiation therapy treatment plan for use with a particle beam utilizing the patient radiation therapy prescription information and utilizing the patient MRI data to account for interaction properties of soft tissues through which the particle beam passes.
2. The computer program product of claim 1 further comprising accounting for influence of a magnetic field produced by an MRI system on the particle beam.
3. The computer program product of claim 1 wherein determining the radiation therapy plan further includes a determination of a biological effectiveness of dose delivered to the soft tissues by the particle beam through utilization of the patient magnetic resonance imaging data.
4. The computer program product of claim 1 further including receiving x-ray computed tomography data, and wherein determining a radiation therapy treatment plan further utilizes the x-ray computed tomography data.
5. The computer program product of claim 1 wherein the patient magnetic resonance imaging data is received from a magnetic resonance imaging device integrated with a particle radiation therapy system.

6. A non-transitory computer program product storing instructions that, when executed by at least one programmable processor forming part of at least one computing system, cause the at least one programmable processor to perform operations comprising:

receiving radiation therapy beam information for a radiation therapy treatment of a patient utilizing a particle beam;

receiving patient magnetic resonance imaging (MRI) data during the radiation therapy treatment; and,

utilizing the patient MRI data to perform real-time calculations of a location of dose deposition for the particle beam, taking into account interaction properties of soft tissues through which the particle beam passes.

7. The computer program product of claim 6 further comprising taking into account influence of a magnetic field produced by an MRI system on the particle beam in performing the real-time calculations of location of dose deposition.

8. The computer program product of claim 6 further comprising:
interrupting the particle beam if the real-time calculations of the location of dose deposition indicate that dose deposition is occurring off-target.

9. The computer program product of claim 6 further comprising:
adjusting the energy of the particle beam if the real-time calculations of the location of dose deposition indicate that dose deposition is occurring off-target.

10. The computer program product of claim 6 further comprising:
utilizing the patient MRI data and the real-time calculations of the location of dose deposition to modify a direction of the particle beam in order to track a target.

11. The computer program product of claim 10 further comprising:

modifying the direction of the particle beam through deflection magnets.

12. The computer program product of claim 6 further comprising:

utilizing the patient MRI data and the radiation therapy beam information to calculate accumulated dose deposition to the patient during the radiation therapy treatment.

13. The computer program product of claim 6 wherein the real-time calculations of a location of dose deposition include a determination of a biological effectiveness of dose delivered to the soft tissues by the particle beam through utilization of the patient magnetic resonance imaging data.

14. The computer program product of claim 12 further comprising:

re-optimizing the radiation therapy treatment based on the calculated dose deposition.

15. A radiation therapy system comprising:

a particle therapy delivery system for delivery of radiation therapy to a patient via a particle beam;

a magnetic resonance imaging system configured to obtain patient magnetic resonance imaging (MRI) data during radiation therapy; and,

a controller configured to receive the patient MRI data during radiation therapy and utilize the patient MRI data to perform real-time calculations of a location of dose deposition for the particle beam, taking into account interaction properties of soft tissues through which the particle beam passes.

16. The radiation therapy system of claim 15, wherein the controller is further configured to interrupt the particle beam if the real-time calculations of the location of dose deposition indicate that deposition is occurring off-target.

17. The radiation therapy system of claim 15 wherein the controller is further configured to determine influence of a magnetic field of the magnetic resonance imaging system on the particle beam in the calculations of the location of dose deposition.

18. The radiation therapy system of claim 15 wherein the controller is further configured to determine a biological effectiveness of dose delivered to the soft tissues by the particle beam through utilization of the patient magnetic resonance imaging data.

19. The radiation therapy system of claim 15, wherein the controller is further configured to interrupt the particle beam if the real-time calculations of the location of dose deposition indicate that dose deposition is occurring off-target.

20. The radiation therapy system of claim 15, wherein the controller is further configured to adjust the energy of the particle beam if the real-time calculations of the location of dose deposition indicate that dose deposition is occurring off-target.

21. The radiation therapy system of claim 15, wherein the controller is further configured to utilize the patient MRI data and the real-time calculations of the location of dose deposition to modify a direction of the particle beam in order to track a target.

22. The radiation therapy system of claim 21 further comprising deflection magnets and wherein the modification of the direction of the particle beam is effectuated through the deflection magnets.

23. The radiation therapy system of claim 15, wherein the controller is further configured to utilize the patient MRI data and particle beam information to calculate dose deposition to the patient during the radiation therapy.

24. The radiation therapy system of claim 23, wherein the controller is further configured to re-optimize the radiation therapy based on the calculated dose deposition.

25. The radiation therapy system of claim 15 further comprising:
a dosimetry system for monitoring the radiation therapy to the patient; and,
a magnetic shielding structure surrounding at least a portion of the dosimetry system.

26. The radiation therapy system of claim 25 wherein the magnetic shielding structure comprises a plurality of shells.

27. The radiation therapy system of claim 25 wherein at least one of the plurality of shells are separated by an annular disk.

28. The radiation therapy system of claim 15 further comprising:
a gantry configured to allow delivery of the particle beam from different angles around the patient.

29. The radiation therapy system of claim 28 wherein the magnetic resonance imaging system comprises two split main magnets, and the radiation therapy system includes an isocenter, and wherein the two split main magnets are separated by a plurality of buttresses located no further from the isocenter than an outer boundary of the two split main magnets.

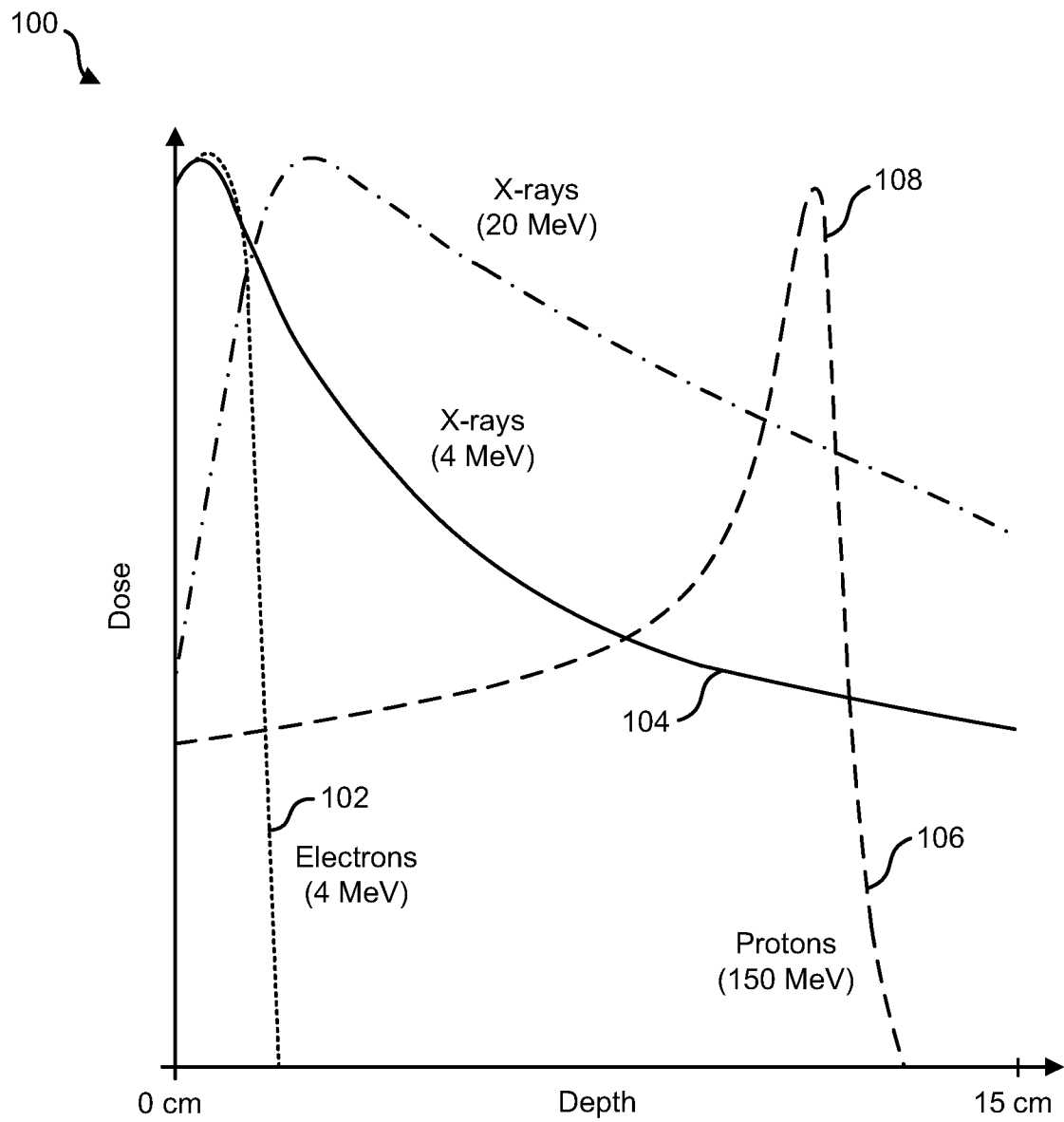


FIG. 1

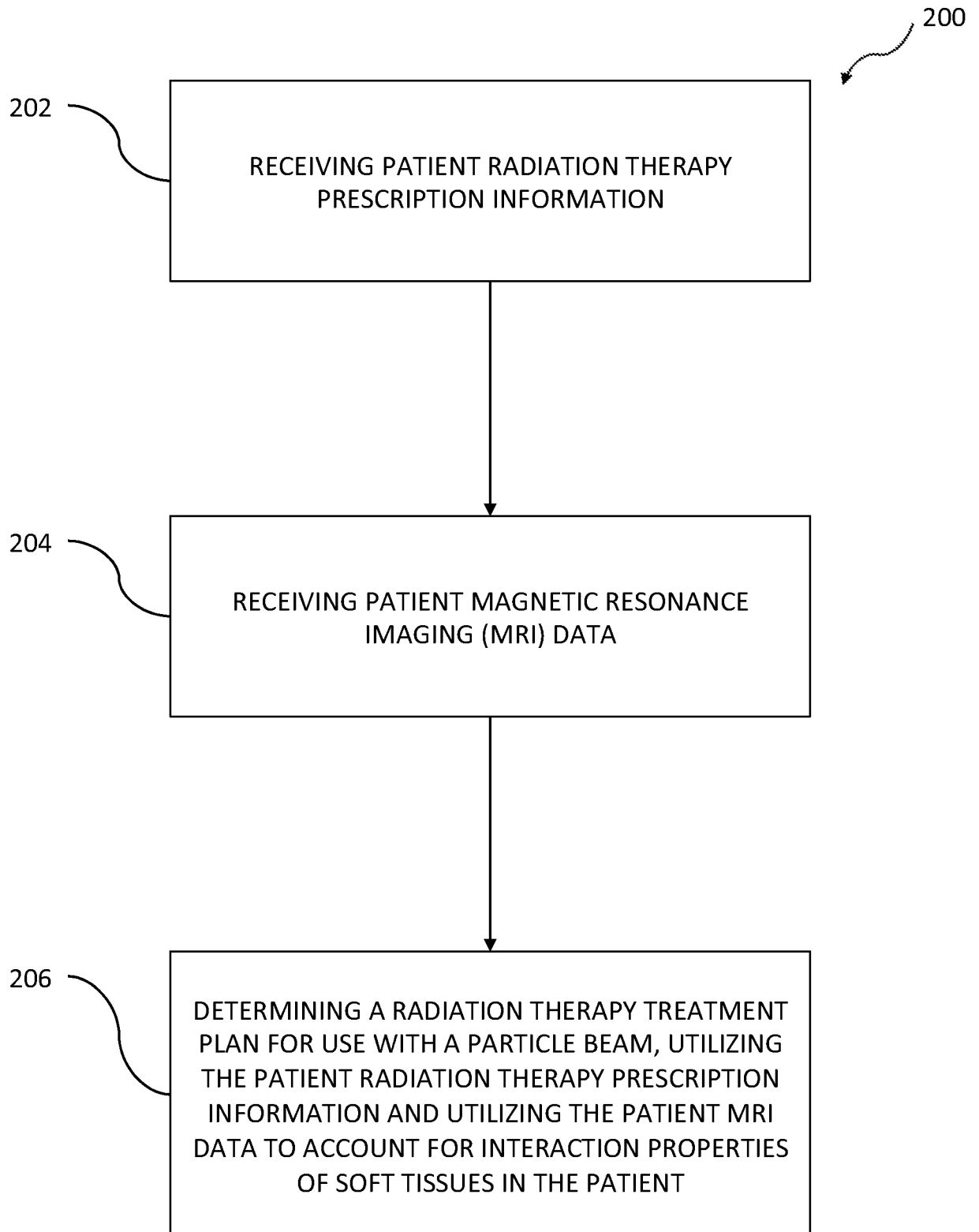


FIG. 2

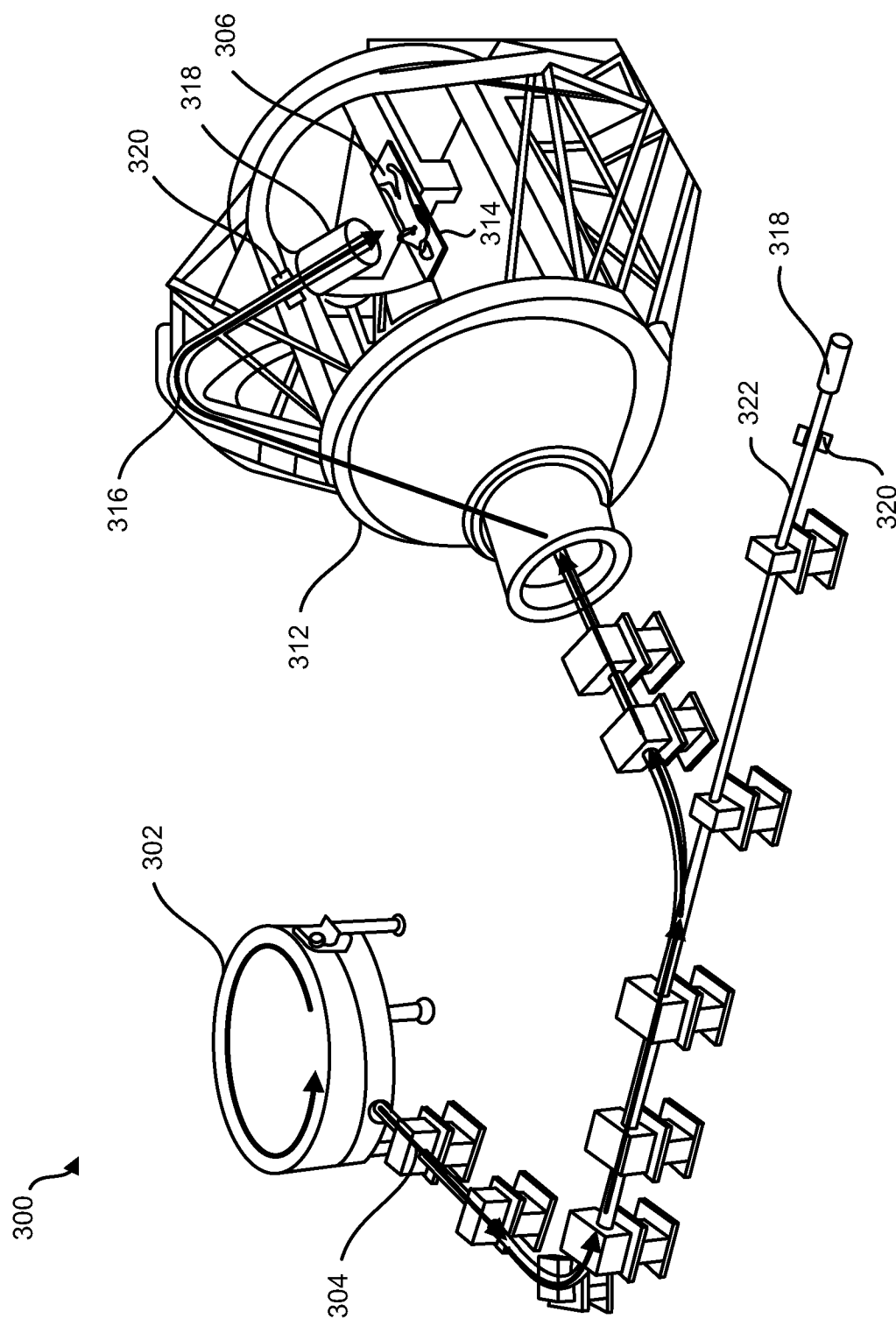


FIG. 3

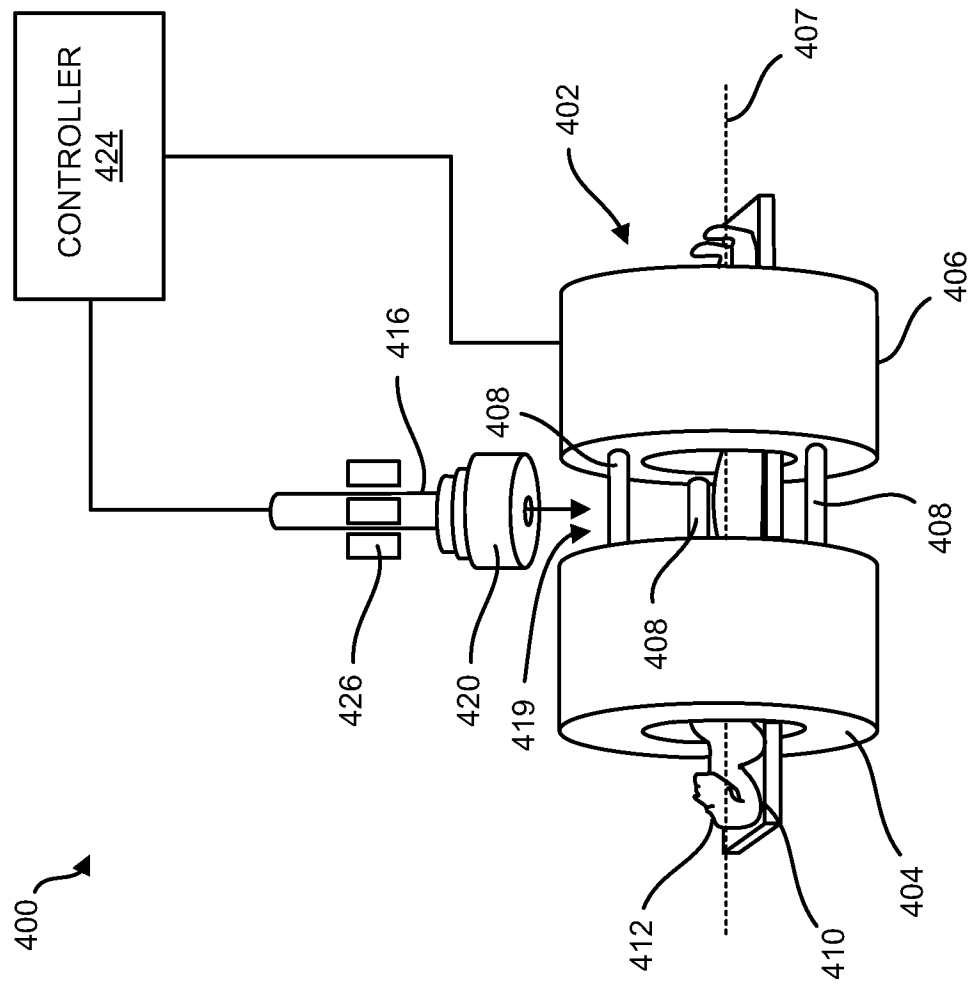
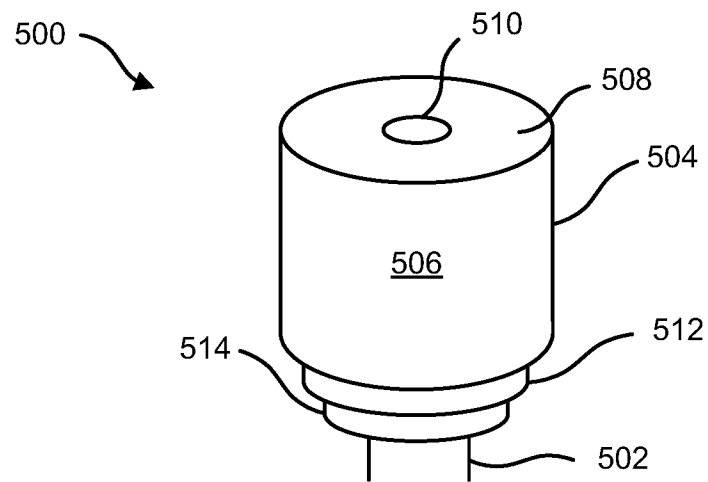
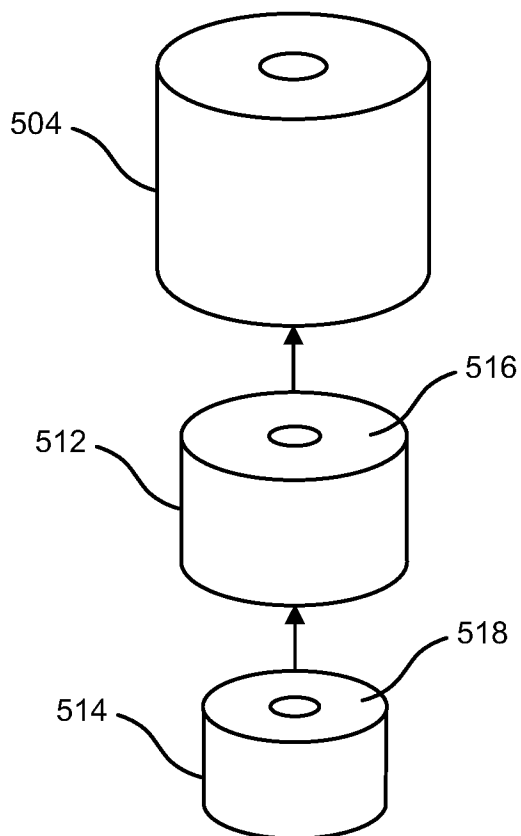


FIG. 4

**FIG. 5A****FIG. 5B**

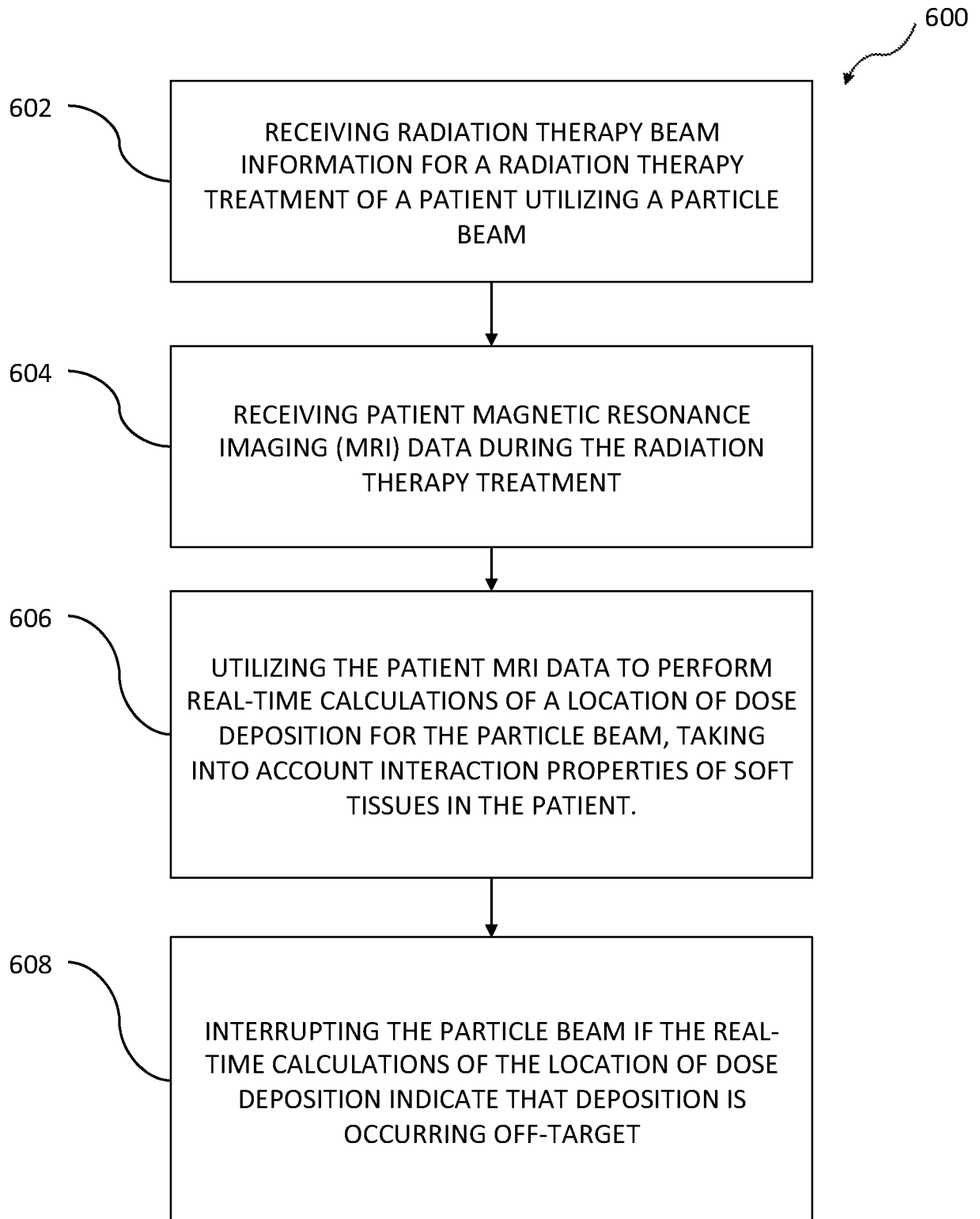


FIG. 6

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2017/020015

A. CLASSIFICATION OF SUBJECT MATTER
INV. A61N5/10
ADD.

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

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
A61N

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

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

EPO-Internal, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 2011/237859 A1 (KUHN MICHAEL HARALD [DE] ET AL) 29 September 2011 (2011-09-29)	1,2,4,5
Y	figures 1-4 paragraph [0010] paragraph [0011] paragraph [0073] paragraph [0076] paragraph [0077] paragraph [0080] paragraph [0082] paragraph [0088] paragraph [0089] paragraph [0138] paragraph [0026] ----- -/-	3



Further documents are listed in the continuation of Box C.



See patent family annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search

8 May 2017

Date of mailing of the international search report

26/07/2017

Name and mailing address of the ISA/

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040,
Fax: (+31-70) 340-3016

Authorized officer

Rodríguez Cosío, J

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2017/020015

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fees, this Authority did not invite payment of additional fees.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

1-5

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.
- ☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.
- ☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2017/020015

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 2013/090549 A1 (MELTSNER MICHAEL [US] ET AL) 11 April 2013 (2013-04-11)	1
Y	figure 1 paragraph [0026] paragraph [0030] paragraph [0042]; claims 9,12,14,15,19 -----	3
Y	US 2014/336442 A1 (KEPPEL CYNTHIA E [US] ET AL) 13 November 2014 (2014-11-13) the whole document -----	3
Y	US 2009/060130 A1 (WILKENS JAN [DE] ET AL) 5 March 2009 (2009-03-05) the whole document -----	3

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/US2017/020015

Patent document cited in search report		Publication date	Patent family member(s)		Publication date
US 2011237859	A1	29-09-2011	CN	102245265 A	16-11-2011
			EP	2196240 A1	16-06-2010
			EP	2379172 A1	26-10-2011
			JP	5469675 B2	16-04-2014
			JP	2012511382 A	24-05-2012
			US	2011237859 A1	29-09-2011
			WO	2010067287 A1	17-06-2010

US 2013090549	A1	11-04-2013	CN	102939607 A	20-02-2013
			EP	2580698 A1	17-04-2013
			RU	2012157808 A	20-07-2014
			US	2013090549 A1	11-04-2013
			WO	2011154853 A1	15-12-2011

US 2014336442	A1	13-11-2014	DE	112007000801 T5	12-02-2009
			JP	5174005 B2	03-04-2013
			JP	5462340 B2	02-04-2014
			JP	2009531138 A	03-09-2009
			JP	2013063273 A	11-04-2013
			US	2007228305 A1	04-10-2007
			US	2009224183 A1	10-09-2009
			US	2012001096 A1	05-01-2012
			US	2014012062 A1	09-01-2014
			US	2014107395 A1	17-04-2014
			US	2014225010 A1	14-08-2014
			US	2014336442 A1	13-11-2014
			US	2015073200 A1	12-03-2015
			WO	2007126782 A2	08-11-2007

US 2009060130	A1	05-03-2009	EP	1818078 A1	15-08-2007
			EP	1988969 A1	12-11-2008
			JP	2009525797 A	16-07-2009
			US	2009060130 A1	05-03-2009
			WO	2007090798 A1	16-08-2007

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-5

Determining a radiation therapy treatment plan for use with a particle beam utilizing patient radiation therapy prescription information and patient MRI data to account for interaction properties of soft tissues through which the particle beam passes.

2. claims: 6-29

Performing real-time calculations of a location of dose deposition for a particle beam by utilizing patient MRI data received during the particle therapy treatment taking into account interaction properties of soft tissues through which the particle beam passes.
