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SYSTEMS AND METHODS FOR USE OF A DOSIMETRY APPLICATION SOFTWARE
TOOL TO CUSTOMIZE DOSIMETRY AND SPHERE SELECTION FOR
RADIOEMBOLIZATION PROCEDURE PLANNING

CROSS-REFERENCE TO RELATED APPLICATIONS

[0001] The present application claims the benefit of U.S. Provisional Pat. App. No. 62/673,628, entitled “DUAL-STAGE SYRINGES WITH LOCKING MECHANISM,” and filed on May 18, 2018, and U.S. Provisional Pat. App. No. 62/673,632, entitled “RADIOEMBOLIZATION DELIVERY DEVICE,” and filed on May 18, 2018, the entireties of which are incorporated by reference herein.

TECHNICAL FIELD

[0001] The present specification generally relates to procedure planning utilizing medical devices for treating cancer, and more particularly to procedure planning utilizing medical devices configured and operable to deliver radioactive compounds to a treatment area within a patient's body in procedures such as transarterial radioembolization and determination of customized dosimetry and sphere selection of the radioactive compounds for use in such radioembolization delivery devices.

BACKGROUND

[0002] In cancer treatments involving radiation therapy, inadvertent or excess exposure to radiation from radioactive therapeutic agents can be harmful and potentially lethal to patients or medical personnel. Accordingly, medical instruments for radiation therapies must be configured to localize the delivery of radioactive material to a particular area of the patient's body while shielding others from unnecessarily being exposed to radiation.

[0003] Transarterial radioembolization is a transcatheter intra-arterial procedure performed by interventional radiology and is commonly employed for the treatment of malignant tumors. During this medical procedure, a microcatheter is navigated into a patient's liver where radioembolizing microspheres loaded with a radioactive compound, such as yttrium-90 (⁹⁰Y), are delivered to the targeted tumors. The microspheres embolize blood vessels that supply the tumors while also delivering radiation to kill tumor cells.

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[0004] Generally, medical devices for performing radioembolization procedures require multiple syringes, external tubing, a vial containing the radioactive compound, and a bulky shield assembly for containing and shielding the radioactive vial. Such devices typically involve time consuming and labor-intensive setup procedures. The complex devices are commonly stationary and thereby limit a physician's mobility in an operating room to within a certain proximity of the device.

[0005] Routine manipulation of a product container storing radioactive material during radioembolization procedures generally requires a Nuclear Medicine Technician, who handles the material with forceps or tweezers. This process involves further potential of exposing additional medical personnel to radioactivity, and contaminating the operating room. Syringes for manually administering the radioactive compound as an administered fluid are prone to inconsistent flow rates and pressures. Insufficient injection rates result in decreased bead dispersion, which may impact efficacy of the treatment.

[0006] Accordingly, a need exists for a tool to determine efficient amounts of radioactive compounds to administer to a patient through a simplified medical device that is configured and operable to perform radioembolization.

SUMMARY

[0007] In one embodiment, a method that is computer-implemented for selection of dosimetry levels and sphere amounts of radioactive compounds for use in a radioembolization procedure for procedure planning may include inputting activity parameter information into a dosimetry portal of a dosimetry selection tool, determining, via a processor, a customized activity based on the activity parameter information and one or more customized activity algorithms, and generating one or more sphere amount and dosage recommendations based on the customized activity and one or more dosimetry selection algorithms. The method may further include selecting one of the one or more sphere amount and dosage recommendations as a selected sphere amount and dosage recommendation, and generating, via the processor, a radioactive compound order for the radioembolization procedure based on the customized activity and the selected sphere amount and dosage recommendation.

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[0008] In another embodiment, a system for selection of dosimetry levels and sphere amounts of radioactive compounds for use in a radioembolization procedure for procedure planning may include a dosimetry selection tool including a dosimetry portal and a graphical user interface, and a processor communicatively coupled to a dosimetry selection tool and a non-transitory computer storage medium. The non-transitory computer storage medium may store instructions that, when executed by the processor, cause the processor to: receive, via the graphical user interface, an input of activity parameter information into the dosimetry portal of the dosimetry selection tool, determine, via the processor, a customized activity based on the activity parameter information and one or more customized activity algorithms, and generate, via the processor, one or more sphere amount and dosage recommendations based on the customized activity and one or more dosimetry selection algorithms. The instructions may, when executed by the processor, further cause the processor to receive, via the graphical user interface, a selection of one of the one or more sphere amount and dosage recommendations as a selected sphere amount and dosage recommendation, and generate, via a processor, a radioactive compound order for the radioembolization procedure based on the customized activity and the selected sphere amount and dosage recommendation.

[0009] These and additional features provided by the embodiments described herein will be more fully understood in view of the following detailed description, in conjunction with the drawings.

BRIEF DESCRIPTION OF THE DRAWINGS

[0010] The embodiments set forth in the drawings are illustrative and exemplary in nature and not intended to limit the subject matter defined by the claims. The following detailed description of the illustrative embodiments can be understood when read in conjunction with the following drawings, where like structure is indicated with like reference numerals and in which:

[0011] FIG. 1 illustrates a home page screen view of a graphical user interface (GUI) of a dosimetry portal of a dosimetry selection tool for radioembolization procedure planning, according to one or more embodiments shown and described herein;

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[0012] FIG. 2 illustrates an order page screen view of the dosimetry portal of FIG. 1 to submit one or more dosimetry inputs and select order details based on dosimetry and sphere recommendations, according to one or more embodiments shown and described herein;

[0013] FIG. 3 illustrates a review order page screen view of the dosimetry portal of FIG. 1, according to one or more embodiments shown and described herein;

[0014] FIG. 4 illustrates a confirm order page screen view of the dosimetry portal of FIG. 1 to input procedure and shipping information, according to one or more embodiments shown and described herein;

[0015] FIG. 5 illustrates a confirm order page screen view of the dosimetry portal of FIG. 1 to assign shipping information input to appropriate review personnel, according to one or more embodiments shown and described herein;

[0016] FIG. 6 illustrates another, basic order page screen view of the dosimetry portal of FIG. 1 to submit one or more dosimetry inputs and select order details based on dosimetry and sphere recommendations on a basic screen including one activity customization algorithm, according to one or more embodiments shown and described herein;

[0017] FIG. 7 illustrates a first part of another, advanced order page screen view of the dosimetry portal of FIG. 1 to submit one or more dosimetry inputs and select order details based on dosimetry and sphere recommendations on an advanced screen including three different activity customization algorithms, according to one or more embodiments shown and described herein;

[0018] FIG. 8 illustrates a second part of the advanced order page screen view of FIG. 7 to show treatment, dose, and sphere selection information, according to one or more embodiments shown and described herein;

[0019] FIG. 9 illustrates an order form screen view of the dosimetry portal of FIG. 1, according to one or more embodiments shown and described herein;

[0020] FIG. 10 illustrates an approve order screen view of the dosimetry portal of FIG. 1, according to one or more embodiments shown and described herein;

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[0021] FIG. 11 illustrates an order history screen view of the dosimetry portal of FIG. 1, according to one or more embodiments shown and described herein;

[0022] FIG. 12 is a flow chart of a process utilizing the dosimetry portal screens of FIGS. 1-11, according to one or more embodiments shown and described herein; and

[0023] FIG. 13 schematically illustrates a system for implementing computer and software based methods to apply the process of FIG. 12 with the dosimetry portal of FIG. 1, according to one or more embodiments shown and described herein.

DETAILED DESCRIPTION

[0024] Referring generally to the figures, embodiments of the present disclosure are directed to systems and methods for selection of dosimetry levels and sphere amounts of radioactive compounds for use in a radioembolization procedure for procedure planning as described herein. Various embodiments of such systems and methods are described in detail herein.

[0025] The present disclosure is directed to a centralized portal as a software application tool utilized across platforms, such as web-based to mobile applications, to determine a radioactivity and number of spheres to order for a Yttrium-90 (Y90) radioembolization procedure. A patient being planned for radioembolization will typically undergo several rounds of imaging to determine a location, size, shape, vascularity, uptake of the tumor, and/or shunting of particles (e.g., spheres) to other organs. The determined information is then used to calculate a required radioactive dose at the time of treatment. Current dosimetry models may include a MIRD, Body Surface Area (BSA) model, Partition model, or modified versions to make this determination, which may be used through mobile applications, online applications, and/or spreadsheets for model evaluation. However, this creates a disjointed process requiring extra physician steps decentralized from the model platforms and less ease of hospital coordinate logistics with respect to ordering based on the determined required radioactive dose. Further, market suppliers tend to control dosages based on a pre-set activity per sphere. In current dosimetry models, the model steps are performed separately and individually such that results are collated manually for comparison to the controlled dosage, which increases delays in procedure planning in contrast to one or more technical effect of the one or more models of this disclosure to vary dosage selections per patient and to reduce delays in procedure planning.

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[0026] As an example, SIRTeX spheres have an activity of 50-80 Bq/sphere and BTG spheres are approximately 2500 Bq/sphere. Becquerel (Bq) is a unit of radioactivity defined as the activity of a quantity of radioactive material in which a nucleus decays per second. Consequences of such pre-set activities per sphere may include suppliers having to increase the ordered doses more than a physician prescribes to allow the orders to age and decay down to a desired dose, which results in an extended delivery time and extraneous use of materials, and physicians are not presented with an option to prescribe a number of sphere and a dosage per sphere as increasing a number of spheres for pre-set activities per spheres would simply increase a total dose. Physicians instead tend to order even higher doses than needed to accommodate a desire for a number of spheres and further extend the radioactivity decay and delivery time.

[0027] A dosimetry selection software application tool as described herein is configured to act as a centralized platform that allows physicians and users to prescribe and select both a dosage and a number of spheres desired to deliver to a patient for a radioembolization procedure. Through the dosimetry selection software application tool, users may simultaneously evaluate multiple dosimetry models along with one or more dosimetry selection algorithms to determine an appropriate number of spheres to order with a selected dosage per sphere for a radioembolization procedure. The dosimetry selection software application tool may utilize one or more algorithms based on prior treatments and/or specific procedure strategies or procedure locations. Further, to aid with ease of hospital logistics and processing, the selected order information may be directly translated to an order form as well as other clinical documentation. The dosimetry selection software application tool may include a notification and/or tracking system to allow for internal and/or external personnel use, such as with respect to a hospital, of the systems and portals described herein.

[0028] Referring to FIG. 1, a home page screen **103** is shown of a dosimetry portal **100** of a dosimetry selection tool **1312** including a graphical user interface (GUI) **1326** (FIG. 13) for radioembolization procedure planning, which is described in greater detail further below. The dosimetry portal includes a navigation menu **101** to navigate to a desired screen of the dosimetry portal **100** through selection of a menu navigation option. The dosimetry portal further includes, for navigation to respective screens, a home tab **102**, a place an order tab **104**, an order history tab **106** such that a user may review the histories of one or more orders, and a review orders tab **108** such that a user may review, update, and/or approve one or more saved orders. The home

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page screen **103** illustrates a To Dos sub-screen **110**, including a list of items to accomplish for a user of the dosimetry portal **100**. By way of example, and not as a limitation, the To Dos sub-screen **110** of FIG. 1 includes a listing of tasks for the signed in user specific to the user of (1) review an order from Dr. Stevens and (2) add a procedure date and time to an order. The home page screen **103** further illustrates an Order Status sub-screen **114** including a listing of one or more order status to which the signed in user has access rights to view.

[0029] In embodiments, the dosimetry portal **100** may include a sign in (e.g., log in) for one or more users for user specified portal usage, data security, and/or data collaboration. The dosimetry portion **100** may thus include a security feature to permit one or more users to access one or more different levels of the dosimetry portal **100** based on user assigned access rights. A first user may have access to a specific set of GUI screens of the dosimetry portion **100** based on a basic security clearance level, while a second user may have access to another specific set of GUI screens of the dosimetry portion **100** including more screens than the first user has access to based on an advanced security clearance level. It is to be understood that different levels of security clearance assigning one or more users corresponding different levels of access rights to GUI screens and permissions with respect to the dosimetry portion **100** are contemplated and within the scope of this disclosure.

[0030] Further, a first user may select another user to review and approve an order in the dosimetry portion **100**, or the dosimetry portion **100** may be configured to automatically assign the order for review and approval by another user after the first user has generated a first order draft. As a non-limiting example, the first user with the basic security clearance level may be permitted to input an order and generate the first order draft as described herein. The first user may assign the first order draft to a second user with the advanced security clearance level for review and approval, or the dosimetry portion **100** may be configured to place the first order draft into an review order approvals GUI listing one or more orders for approval by the second user and/or notify the second user that the first order draft is ready for review and approval by the second user.

[0031] In embodiments, the dosimetry portion **100** is configured to provide a data collaboration platform such that one or more orders may be created, edited, viewed, approved, and/or placed by a plurality of users have one or more levels of security clearance and user

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specific access rights to the one or more orders as described herein. Thus, multiple users may be able to view and/or review an order as well as historical data of a plurality of orders to aid with, for example, ease of hospital logistics in sharing, reviewing, and submitting such orders in a centralized platform.

[0032] Referring to FIG. 2, an order page screen **200A** is shown. The order page screen **200A** is accessible through the place an order tab **104** of FIG. 1, for example. The order page screen **200A** includes a Dosimetry Inputs sub-screen **202**, a customized activity algorithm sub-screen **206**, and an Order Details sub-screen **208**. Activity parameter information may be input into the dosimetry portal **100** in embodiments described herein, where such activity parameter information may include information used to estimate a dosage activity using one or more models and/or algorithms as described herein. As a non-limiting example, the Dosimetry Inputs sub-screen **202** includes fields to input one or more of the following activity parameter information inputs: (1) lung shunt fraction (LSF) as a percentage value, (2) anticipated residual waste as a percentage value, previous dose to the lungs in units of Gray (Gy), which is a derived unit of ionizing radiation defined as the absorption of one joule of radiation energy per kilogram of matter, (3) desired dose to liver in units of Gy, and (4) target liver volume as tissue volume in units of cubic centimeter (cc). As a non-limiting example, the Dosimetry Inputs sub-screen **202** of FIG. 2 includes a %LSF of 2%, an anticipated residual waste of 1%, a previous dose to the lungs of 0 Gy, a desired dose to liver of 200 Gy, and target liver volume of 300 cc. The activity parameter inputs may further include a time zone, a treatment date, a treatment time, patient specific parameters, prior treatment information, and/or the like. The Dosimetry Inputs sub-screen **202** further includes a calculate button **204** to calculate a customized activity based on the activity parameter information inputs and a customized activity algorithm. As described herein, the customized activity is an amount of radioactivity for spheres that may be variable such that different amount of spheres options may each include respective radioactivity per sphere levels to each obtain a total customized activity level, which different amount of sphere options are generated based on associated customized activity algorithms as described herein.

[0033] As a non-limiting example, the customized activity algorithm sub-screen **206** includes a MIRD dosimetry calculation algorithm to determine a customized activity based on the inputs from the Dosimetry Inputs sub-screen **202**. As a non-limiting example, based on the inputs in the Dosimetry Inputs sub-screen **202** of FIG. 2, the MIRD dosimetry calculation of the customized

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activity algorithm sub-screen **206** includes a target liver mass of 0.31 kg, an activity at administration value of 1.27 GBq (e.g. as a customized activity), a calculated dose to lungs of 1.26 Gy, a dose limit to lungs of 30 Gy, a cumulative dose to lungs of 1.26 Gy, and a cumulative dose limit to lungs of 50 Gy. It is to be understood that any dosimetry calculation algorithms as known or as yet-to-be developed may be used by the dosimetry portal **100** and within the scope of the disclosure. The dosimetry calculation algorithms as customized activity algorithms described herein may include a MIRD dosimetry calculation algorithm, a BSA dosimetry calculation algorithm, or a Partition dosimetry calculation algorithm as known to one of ordinary skill in the art.

[0034] The Order Details sub-screen **208** includes one or more sphere amount and dosage recommendations based on the customized activity and a utilized dosimetry selection algorithm, such as the MIRD dosimetry calculation algorithm of FIG. 2. Displaying of different recommendations from different models allows the compared different recommendations to be directly compared by a user, and further displaying of results in a same format assists a user when deciding between recommendations from one or more models to select. In embodiments, one or more dosimetry selection algorithms to generate the one or more sphere amount and dosage recommendations may include an activity-per-sphere algorithm, an activity based on embolic load algorithm, or combinations thereof. The activity-per-sphere algorithm may include a division of the customized activity with a predetermined amount of spheres per activity unit, such as 300 Bq/sphere. As a non-limiting example, a customized activity of 3 gigabecquerel (GBq) divided by 300 Bq/sphere results in 10,000,000 spheres at 300 Bq/sphere. In embodiments, outputting model results in a format of number of spheres with number of Bq/sphere provides immediate, real-time clarity to a user as to what the possible order options are in contrast to current dosimetry models in which model results are converted in an order manually by a user by comparing model outputs to a fixed activity of supplier spheres.

[0035] Alternatively, the activity based on embolic load algorithm may include use of a tissue volume input and a predetermined embolic load determination per cubic centimeter of tissue such that the spheres and dosage amount determination is a function of embolic load. A non-limiting embolic load example of how many spheres one cubic centimeter of tissue may handle may be, for example, 20,000 spheres/cc. Thus, a tissue volume of 300 cc would yield a calculation of 6,000,000 spheres. A user may adjust an amount of spheres achieving a customized activity,

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such as to reduce the amount of spheres such that each sphere includes a greater amount of radioactivity to achieve the total customized activity level, or to increase the amount of spheres such that each sphere includes a lower amount of radioactivity to achieve the total customized activity level. In embodiments, a user may select 3 million spheres to achieve a total customized activity level of 1.27 from the Order Details sub-screen **208** at 425 Bq/sphere, or the user may select a greater amount of 5 million spheres to achieve the total customized activity level of 1.27 from the Order Details sub-screen **208** at a reduced dosage per sphere of 255 Bq/sphere. The user may select from a drop down sphere selection amount between 1 million spheres to 40 million spheres to achieve the total customized activity level (e.g., of 1.27 in FIG. 2). In embodiments, the user may be presented with up to thirteen options ranging from between and including 1 million spheres to 40 million spheres.

[0036] As a non-limiting example, the dosimetry selection algorithm may provide for the values of FIG. 2 a recommendation of a dosage of 3 million spheres with a radioactive activity of 425 Bq/Sphere along with an alternative recommendation of 5 million spheres with activity of 255 Bq/Sphere such that more spheres with a reduced amount of activity are used in the alternative recommendation. It is to be understood that the physical size of the spheres, also referenced as microspheres, do not change though different amounts of spheres at different dosage levels may be ordered to meet a customized activity value and to vary amount of radioactivity across the ordered spheres per sphere. In embodiments, however, the dosimetry portal **100** may include provide a GUI providing size and/or size distribution information as generated by a size determination algorithm. Manufacturers may use such information to manufacture the ordered spheres of varying size, distribution, activity, and/or amount based on manufacturer sphere production processes.

[0037] The user may further use the Order Details sub-screen **208** to modify the dosage, such as to increase by +10% or to decrease by -10%. In embodiments, the modification may be input as a fractional amount rather than a percentage amount. Additionally or alternatively, the user may split the dose across vials, such as up to a maximum of three vials to achieve a total 100% dosage amount. Thus, the dosage amounts may be varies across up to three tissue areas of different radioactive sensitivities, or across three blood vessels feeding a tumor requiring up to three different radioactive dosing levels to achieve the total customized activity value to treat the

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tumor during the radioembolization procedure. A review order button **210** allows a user to review an order on a review order page **212** of FIG. 3.

[0038] Referring to FIG. 3, the review order page **212** includes an Order Details sub-screen **214**, a Dosimetry Inputs sub-screen **216**, and a customized activity algorithm sub-screen **218** from which a user may review inputted and generated values to confirm correctness of the order to be place. In embodiments, model outputs on the review order page **212** may include target liver mass, activity at administration, calculated dose to the lungs, dose limit to the lungs, cumulative dose to the lungs, cumulative dose limit to the lungs, and/or a recommended number of radioactive compound microspheres for Y90 radioembolization (e.g., spheres). The user may utilize a Back button **220** to return to the previous order page screen **200A** of FIG. 2 to edit an order input and/or selection. Alternatively, the user may select a Confirm Order Details button **222** to advance through the dosimetry portal **100** to a confirm order page screen **230** of FIG. 4 to confirm and place an order.

[0039] Referring to the confirm order page screen **230** of FIG. 4, a user may determine through selection of a Yes button **232** that the user is ready to enter the procedure date and shipping information to prepare for order placement. The user may enter procedure information into a Procedure Information sub-screen **234**, such as procedure date, time, and time zone, and/or other pertinent procedure information such as a patient identifier and the like. The user may further enter shipping information in a Shipping Information sub-screen **236**, such as a shipment address and shipment receiver information. In embodiments, the shipping information may be auto-populated or selected from a pre-configured drop-down menu.

[0040] Referring to the confirm order page screen **230** of FIG. 5, a user may determine through selection of a No button **238** that the user is to assign shipping information input to another assigned user, selected from a drop down menu. In additional or alternative embodiments, the use of the No button **238** or through another assignment interface, the user may indicate that the user is not yet ready to enter the procedure date and shipping information to prepare for order placement and rather wishes to assign the order to appropriate review personnel for review and approval. In embodiments, the appropriate review personnel may approve the order and send the order back to the user for order placement, may place the order, may edit the order, and/or may send the order back to the user for editing. For one or more of such

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embodiments set forth above, the user may select the appropriate review personnel from a prepopulated personal name listing menu **240**. The user may select a Back button **242** to return to a previous order screen as described above or select a Save and Next button **244** to send the order to the selected appropriate review personnel for review.

[0041] Referring to FIG. 6, a basic order page screen **200B** as an alternative order page screen of the dosimetry portal **100** is shown. The user may use the order page screen **200B** to submit one or more dosimetry inputs and select order details based on dosimetry and sphere recommendations as described herein on the order page screen **200B** as a basic screen including one customized activity algorithm, such as the MIRD dosimetry calculation algorithm. The basic order page screen **200B** may be used for a radioembolization procedure with a simply analysis. Alternatively, the user may select an Advanced Dosimetry button **250** to advance to an advanced order page screen **200C** of FIG. 7. The advanced order page screen **200C** may be used to evaluate the dosimetry models and sphere algorithms as described herein against one or more customized activity algorithms to view differences of end sphere amount and dosage recommendations per dosimetry selection algorithm and respective customized activity algorithm. The basic order page screen **200B** and the advanced order page screen **200C** may be linked for navigation and data transfer therebetween and with respect to a placed order.

[0042] Referring to FIG. 7, a first portion of the advanced order page screen **200C** is shown. The first portion includes one or more dosimetry inputs for a respective plurality of customized activity algorithms, including for input into a MIRD Dosimetry Info sub-screen **252**, a BSA Dosimetry Info sub-screen **254**, and a Partition Dosimetry Info sub-screen **256**. The inputs of the MIRD Dosimetry Info sub-screen **252**, the BSA Dosimetry Info sub-screen **254**, and the Partition Dosimetry Info sub-screen **256** are provided into respective customized activity algorithms to provide the calculated values in the respective customized activity sub-screens of, for example, a MIRD Calculate sub-screen **262**, a BSA Calculate sub-screen **264**, and a Partition Calculate sub-screen **266**.

[0043] FIG. 8 shows a second portion of the advanced order page screen **200C** in, for example, a scrolled down view, and including the MIRD Calculate sub-screen **262**, the BSA Calculate sub-screen **264**, and the Partition Calculate sub-screen **266**, along with a Select Treatment Type option **270** to select as a non-limiting example a number of Bq per radioactive

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microsphere and a Recommendation Number of Spheres Selection Option **272** and may select between a set amount of recommendations of sphere amounts and dosages. Further included is a modification sub-screen **274** allowing for a user to select a desired amount of spheres values of millions, select an activity selection from a drop down list as may be calculated from the models of sub-screens 262, 264, and 266, input a dose modification as a percentage, and or insert as calculated based on the modified value (e.g., through a percentage or fractional value) a required activity value in units of gigabecquerel (GBq), which is a unit of radioactivity defined as the activity of a quantity of radioactive material in which a nucleus decays per second. An advanced button the advanced order page screen **200C** may be used to show one or more different sphere selection algorithms.

[0044] The second portion of the advanced order page screen **200C** of FIG. 8 further shows a Final Order Details sub-screen **276** including patient target dose in Gy units, Required Activity at Treatment in GBq units, Number of Spheres in Millions of units, GBq per sphere as a reference value, and a Date of expected Delivery. Once the Final Order Details of the Final Order Details sub-screen **276** are confirmed, the user may select an Order button **278** to continue with placing an order.

[0045] The user may advance to an Order Form screen **280** of FIG. 9, for example, that may be pre-populated with the calculated values and ready to be printed and/or further editing for submission to a manufacturer to generate the order. The Order Form screen **280** may further include an optional vial split section **282** such that a user may determine a percentage of split of the selected sphere amount and dosage among up to three different vials. The manufacturer may be able to receive the Order Form generated from the Order Form screen **280** to generate a printed bill of order based on the Order Form.

[0046] In embodiments, FIG. 10 illustrates an Approve Order screen **300** for appropriate review personnel selected to review an inputted order prior to submission of the order to the manufacturer to generate the order. The appropriate review use a Save button **302** to save information on the Approve Order screen **300**.

[0047] FIG. 11 illustrates an Order History screen **400** in which a user may review a status of all orders, whether requiring approval, fulfilled, or in transit. A navigation sub-screen **402** on the Order History screen **400** may be utilized to navigate between screens to create, update, and

approve orders and well as to see Order Status and History Information or to Fulfill Orders. In embodiments, the dosimetry portal **100** is configured to save, store, analyze, and/or report such as through the Order History screen **400** or another reporting interface information based on Order Status and History Information of one or more orders as described herein.

[0048] Referring to FIG. 12, a flow chart is shown of a process **1200** that utilizes the dosimetry portal screens of FIGS. 1-11 of the dosimetry portal **100** to generate an order as described herein, which may include the shipping and/or reviewer process embodiments as described herein. The process **1200** of FIG. 12 includes control scheme blocks for selection of dosimetry levels and sphere amounts of radioactive compounds for use in a radioembolization procedure for procedure planning. A user may sign into the dosimetry portal **100** with a user assigned security clearance level as described herein. In a block **1202**, activity parameter information is input into the dosimetry portal **100** of a dosimetry selection tool **1312** (FIG. 13), which is described in greater detail further below. In embodiments, the activity parameter information may include a lung shunt fraction percentage value, an anticipated residual waste percentage value, a previous dose to lungs value, a desired dose to liver value and a target liver volume, such as shown in order page screen **200A**, **200B**, and **200C** described herein.

[0049] In a block **1204**, a customized activity is determined based on the activity parameter information of the block **1202** and one or more customized activity algorithms as described herein. The one or more customized activity algorithms may include at least one of a MIRD dosimetry calculation algorithm, a BSA dosimetry calculation algorithm, or a Partition dosimetry calculation algorithm, such as shown in order page screen **200A**, **200B**, and **200C** described herein. In embodiments, the one or more customized activity algorithms may generate customized activity information include a target liver mass, activity at administration, a calculated dose to lungs, a dose limit to lungs, a cumulative dose to lungs, and a cumulative dose limit to lungs, and the customized activity may be based on the customized activity information.

[0050] In a block **1206**, one or more sphere amount and dosage recommendations are generated based on the customized activity and one or more dosimetry selection algorithms as described herein. In embodiments, the one or more dosimetry selection algorithms to generate the one or more sphere amount and dosage recommendations may include at least one of an activity-per-sphere algorithm or an activity based on embolic load algorithm. The activity-per-

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sphere algorithm comprises division of the customized activity with a predetermined amount of spheres per activity unit as described herein. The activity based on embolic load algorithm may include use of a tissue volume input and a predetermined embolic load determination per cubic centimeter of tissue as described herein. For example, the predetermined embodiment load may include 20,000 spheres per cubic centimeter of tissue.

[0051] One of the one or more sphere amount and dosage recommendations is selected as a selected sphere amount and dosage recommendation. In embodiments, selecting the selected sphere amount and dosage recommendation may include selecting a desired radioactivity level per sphere and/or may include inputting a dose modification as a positive or negative percentage value, such as shown in the Order Details sub-screen **208** of FIG. 2. Further, also as shown in the Order Details sub-screen of FIG. 2, selecting the selected sphere amount and dosage recommendation may include splitting the selected sphere amount and dosage recommendation across a plurality of vials based on a percent differentiation per vial, the percent differentiation in total summing to 100% of the selected sphere amount and dosage recommendation. In embodiments, the plurality of vials may include a maximum of up to three vials.

[0052] In block **1208**, a radioactive compound order for the radioembolization procedure is generated based on the customized activity and the selected sphere amount and dosage recommendation and placed such that the order is submitted to a manufacturer to fulfill. The process **200** may further include transmitting the radioactive compound order to a radioactive compound manufacturer for processing and order fulfillment. As a non-limiting example, this may occur through the confirm order page screen **230** of FIG. 4 when the Yes button **232** is selected and the user enters and submits procedure and shipping information. Alternatively, the process **200** may include assigning the radioactive compound order for review by an assigned personnel such that the radioactive compound order is transmitted to a radioactive compound manufacturer for processing and order fulfillment after approval by the assigned personnel. In embodiments, this may occur through the confirm order page screen **230** of FIG. 5 when the No button **238** is selected and a user assigns the order for review by a colleague as assigned personnel.

[0053] Referring to FIG. 13, a system **1300** for implementing a computer and software-based method to utilize the dosimetry selection software application tool embodiments described herein

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to determine one or more dosimetry and sphere selection recommendations for radioactive compounds for use with administered fluid to delivery through radioembolization delivery devices in a procedure is illustrated as being implemented along with using a graphical user interface (GUI) **1326** communicatively coupled to a computing device **1324**, for example. The system **1300** includes a communication path **1302**, one or more processors **1304**, a memory component **1306**, a dosimetry selection tool **1312**, a storage or database **1314**, a dosimetry selection algorithm **1316** configured to provide one or more dosimetry recommendations to the dosimetry selection tool **1312** as described herein, a network interface hardware **1318**, a network **1322**, a server **1320** that may include a cloud-based server, and the computing device **1224**. The various components of the system **1300** and the interaction thereof will be described in detail below. In embodiments, the dosimetry selection tool **1312** may be directed to a flow software application tool, and the dosimetry selection algorithm **1316** may be directed to an optimization algorithm for flow rate determination for a radioembolization procedure for procedure planning as described in greater detail further below.

[0054] In some embodiments, the system **1300** is implemented using a wide area network (WAN) or network **1322**, such as an intranet or the Internet. The computing device **1324** may include digital systems and other devices permitting connection to and navigation of the network. The computing device **1324** may be a laptop or desk computer or a smart mobile device such as a smartphone, a tablet, or a like portable handheld smart device. As a non-limiting example, the computing device **1324** may be a smartphone such as the iPhone® or a tablet such as the iPad®, both of which are commercially available from Apple, Inc. of Cupertino, CA. The lines depicted in FIG. 13 indicate communication rather than physical connections between the various components.

[0055] As noted above, the system **1300** includes the communication path **1302**. The communication path **1302** may be formed from any medium that is capable of transmitting a signal such as, for example, conductive wires, conductive traces, optical waveguides, or the like, or from a combination of mediums capable of transmitting signals. The communication path **1302** communicatively couples the various components of the system **1300**. As used herein, the term “communicatively coupled” means that coupled components are capable of exchanging data signals with one another such as, for example, electrical signals via conductive medium, electromagnetic signals via air, optical signals via optical waveguides, and the like.

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[0056] As noted above, the system **1300** includes the processor **1304**. The processor **1304** can be any device capable of executing machine readable instructions. One or more algorithms described herein may be integrated directly into hardware, such as the processor **1304**. The processor **1304** in embodiments may retrieve the algorithms and/or algorithm parameters from a database that may be local and/or stored in a cloud-server. Accordingly, the processor **1304** may be a controller, an integrated circuit, a microchip, a computer, or any other computing device. The processor **1304** is communicatively coupled to the other components of the system **1300** by the communication path **1302**. Accordingly, the communication path **1302** may communicatively couple any number of processors with one another, and allow the modules coupled to the communication path **1302** to operate in a distributed computing environment. Specifically, each of the modules can operate as a node that may send and/or receive data.

[0057] As noted above, the system **1300** includes the memory component **1306** which is coupled to the communication path **1302** and communicatively coupled to the processor **1304**. The memory component **1306** may be a non-transitory computer readable medium or non-transitory computer readable memory and may be configured as a nonvolatile computer readable medium. The memory component **1306** may comprise RAM, ROM, flash memories, hard drives, or any device capable of storing machine readable instructions such that the machine readable instructions can be accessed and executed by the processor **1304**.

[0058] The machine readable instructions may comprise logic or algorithm(s) written in any programming language such as, for example, machine language that may be directly executed by the processor, or assembly language, object-oriented programming (OOP), scripting languages, microcode, etc., that may be compiled or assembled into machine readable instructions and stored on the memory component **1306**. Alternatively, the machine readable instructions may be written in a hardware description language (HDL), such as logic implemented via either a field-programmable gate array (FPGA) configuration or an application-specific integrated circuit (ASIC), or their equivalents. Accordingly, the methods described herein may be implemented in any conventional computer programming language, as pre-programmed hardware elements, or as a combination of hardware and software components.

[0059] Still referring to FIG. 13, as noted above, the system **1300** comprises the display such as a GUI **1326** on a screen of the computing device **1324** for providing visual output such as, for

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example, information, graphical reports, messages, or a combination thereof. The display on the screen of the computing device **1324** is coupled to the communication path **1302** and communicatively coupled to the processor **1304**. Accordingly, the communication path **1302** communicatively couples the display to other modules of the system **1300**. The display can include any medium capable of transmitting an optical output such as, for example, a cathode ray tube, light emitting diodes, a liquid crystal display, a plasma display, or the like. Additionally, it is noted that the display or the computing device **1324** can include at least one of the processor **1304** and the memory component **1306**. While the system **1300** is illustrated as a single, integrated system in FIG. 13, in other embodiments, the systems can be independent systems.

[0060] The system **1300** may comprise the dosimetry selection algorithm **1316** to compute and provide one or more dosimetry and sphere selection recommendations to the dosimetry selection tool **1312**, as per one or more of the embodiments described herein. As will be described in further detail below, the processor **1304** may process the input signals received from the system modules and/or extract information from such signals. For example, in embodiments, the processor **1304** may execute instructions stored in the memory component **1306** to implement the processes described herein.

[0061] The system **1300** includes the network interface hardware **1318** for communicatively coupling the system **1300** with a computer network such as network **1322**. The network interface hardware **1318** is coupled to the communication path **1302** such that the communication path **1302** communicatively couples the network interface hardware **1318** to other modules of the system **1300**. The network interface hardware **1318** can be any device capable of transmitting and/or receiving data via a wireless network. Accordingly, the network interface hardware **1318** can include a communication transceiver for sending and/or receiving data according to any wireless communication standard. For example, the network interface hardware **1318** can include a chipset (e.g., antenna, processors, machine readable instructions, etc.) to communicate over wired and/or wireless computer networks such as, for example, wireless fidelity (Wi-Fi), WiMax, Bluetooth®, IrDA, Wireless USB, Z-Wave, ZigBee, or the like.

[0062] Still referring to FIG. 13, data from various applications running on the dosimetry selection tool **1312** can be provided from the computing device **1324** to the system **1300** via the network interface hardware **1318**. The computing device **1324** can be any device having

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hardware (e.g., chipsets, processors, memory, etc.) for communicatively coupling with the network interface hardware **1318** and a network **1322**.

[0063] The network **1322** can include any wired and/or wireless network such as, for example, wide area networks, metropolitan area networks, the Internet, an Intranet, satellite networks, or the like. Accordingly, the network **1322** can be utilized as a wireless access point to access one or more servers (e.g., a server **1320**). The server **1320** and any additional servers generally include processors, memory, and chipset for delivering resources via the network **1322**. Resources can include providing, for example, processing, storage, software, and information from the server **1320** to the system **1300** via the network **1322**. Additionally, it is noted that the server **1320** and any additional servers can share resources with one another over the network **1322** such as, for example, via the wired portion of the network, the wireless portion of the network, or combinations thereof.

[0064] The embodiments of the dosimetry selection tool **1312** described herein through the dosimetry portal **100** permit users to calculate a required customized radioactivity as a customized activity for a Y90 radioembolization procedure for a particular patient set for a planned procedure as well as a desired amount of spheres and a dosage per sphere to obtain the customized activity. Furthermore, the selection of the desired amount of spheres may be split among separate vials for separate delivery to tissue and/or blood vessels.

[0065] The dosimetry platforms described herein offer a medium for physician and users to customize dosage per patient. Characteristics such as tumor vascularity, anatomy, cancer type, patient age, patient performance status, and the like, may be considered as factors in the selection of a desired amount of spheres with an selected activity per sphere to achieve a total customized activity based on dosimetry inputs and one or more algorithms as described herein. Users may input appropriate dosimetry information to view, evaluate, and compare several algorithms to determine an appropriate number of spheres or to use a predetermined activity per sphere value. After selection of an appropriate dosage and number of spheres for a patient, advanced dosimetry data may be imported into an ordering form to be sent to other personnel for review and/or approval or to a manufacturer for order processing and fulfillment.

[0066] It is contemplated and within the scope of this disclosure that the dosimetry selection tool **1312** may further be used for other radioactive materials and isolates, may include and be

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used for other embolics such as bland, scout dosing, chemo, and the like (e.g., chemoembolization), may be tailored to other sphere materials and delivery systems, may be directly integrated with imaging viewing and/or analysis software, and/or may be utilized across mobile to website platforms.

[0067] Further, and as a non-limiting example, during a radioembolization procedure, a determination of a flow rate of injection of the administered fluid including the spheres (e.g., particles) may affect a dispersion and the spheres themselves. The software application tools described herein may alternatively or additionally including algorithms directed to, based on input information, determine a recommended flow rate and probability of reflux with the recommended flow rate for a user that may be provided prior to and/or during a procedure in real-time. The software application tools may be provided in a separate application based platform, such as a mobile application (“app”) or a web-based app, and/or may be an integrated part of a delivery device and/or system for a radioembolization procedure such that a display communicatively coupled to the delivery device may display the output information generated by the software application tools.

[0068] In embodiments, computational fluid dynamics analysis (CFD) may be used to determine the effect of flow rate on dispersion and particles during a radioembolization procedure. Further, travel of injected inappropriate particles may travel in retrograde as a reflux against the flow of blood and into adjoining vasculature and organs, which may negatively affect healthy tissue. The software application tools are configured to receipt one or more inputs to generate an output including a recommended flow rate based on the inputs and/or a probability of reflux based on the inputs and/or the recommended flow rate. Inputs may include particle characteristics such as geometry, size, density, and/or the like. Inputs may additionally or alternatively include clinical procedure planning inputs for the radioembolization procedure such as fluid type, catheter tip angle, blood flow rate, and/or the like. A flow software application tool may output an injection flow rate in milliliters/minute and/or a probability of reflux based on the one or more inputs and a calculating algorithm within the tool.

[0069] In an embodiment, during a scout dose procedure in preparation of the radioembolization procedure, a clinician may inject Technetium-99 (99Tc or Tc-99) into a vascular system to assess particle flow and delivery and may monitor and record clinically

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relevant information for use as the one or more inputs in the flow software application tool. Such information may be, for example, a catheter tip angle, a blood flow rate, and the like. The clinician may input the one or more inputs into the flow software application tool. The flow software application tool is configured to apply one or more algorithms as described herein to optimize flow rate and minimize reflux and, based on the one or more inputs, output one or more recommended flow rates and/or probability of reflux based on a recommended flow rate as selected by a clinician.

[0070] During the radioembolization procedure, a clinician may confirm via the flow software application tool a match between the procedure and prior clinician inputs, such as catheter tip angle, blood flow rate, and/or the like. Alternatively, the clinician may enter new one or more inputs into the flow software application tool to generate one or more updated flow rate recommendations and/or corresponding probabilities of reflux. The delivery device may then be configured to automatically, partially automatically, or manually inject particles at the selected flow rate recommendation into a patient.

[0071] Thus, the flow software application tool be configured to generate one or more flow rate recommendations for an optimal injection flow rate for radioembolization beads (e.g., spheres or particles) and to evaluate an associated probability of reflux based on one or more inputs and an optimization algorithm to optimize flow rate and minimize reflux. The optimization algorithm may be based on parameters and factors such as information, data, and/or other stored sub-algorithms directs to engineering fluid mechanics calculations, integrated clinical data, and/or advanced computational fluid dynamics simulations that leverage physics-based partial differential equations to describe a transport of Y90 radioembolization spheres through hepatic arteries of a patient. Such parameters and factors may be available to the optimization algorithm through data lookup tables, regression models, transfer functions, neural networks, and/or the like. The one or more inputs may be entered for pre-treatment planning or to provide a near real-time insight for adjustments to be made during the radioembolization procedure. The flow software application tool may be used in a technical setting in which a radioactivity and number for spheres for Y90 radioembolization, as described herein, is determined.

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[0072] The systems described herein may be used for other radioactive materials and isotopes than those described herein, be used for other sphere materials and delivery systems as described herein, be configured to print out input and/or output or other clinical information for clinical documentation, be directly integrated with imaging viewing and/or analysis software, may be utilized across application platforms such as a mobile app or web-based app, and/or be converted into a mechanical system.

[0073] Items Listing

[0074] Item 1. A method that is computer-implemented for selection of dosimetry levels and sphere amounts of radioactive compounds for use in a radioembolization procedure for procedure planning may include inputting activity parameter information into a dosimetry portal of a dosimetry selection tool; determining, via a processor, a customized activity based on the activity parameter information and one or more customized activity algorithms; generating one or more sphere amount and dosage recommendations based on the customized activity and one or more dosimetry selection algorithms; selecting one of the one or more sphere amount and dosage recommendations as a selected sphere amount and dosage recommendation; and generating, via the processor, a radioactive compound order for the radioembolization procedure based on the customized activity and the selected sphere amount and dosage recommendation.

[0075] Item 2. The method of item 1, further including transmitting the radioactive compound order to a radioactive compound manufacturer for processing and order fulfillment.

[0076] Item 3. The method of items 1 or 2, further including assigning the radioactive compound order for review by an assigned personnel such that the radioactive compound order is transmitted to a radioactive compound manufacturer for processing and order fulfillment after approval by the assigned personnel.

[0077] Item 4. The method of any of items 1 to 3, wherein the activity parameter information includes a lung shunt fraction percentage value, an anticipated residual waste percentage value, a previous dose to lungs value, a desired dose to liver value and a target liver volume.

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[0078] Item 5. The method of any of items 1 to 4, wherein the one or more customized activity algorithms includes at least one of a MIRD dosimetry calculation algorithm, a BSA dosimetry calculation algorithm, or a Partition dosimetry calculation algorithm.

[0079] Item 6. The method of any of items 1 to 5, wherein: the one or more customized activity algorithms generate customized activity information comprising a target liver mass, activity at administration, a calculated dose to lungs, a dose limit to lungs, a cumulative dose to lungs, and a cumulative dose limit to lungs; and the customized activity is based on the customized activity information.

[0080] Item 7. The method of items 1 to 6, wherein the one or more dosimetry selection algorithms to generate the one or more sphere amount and dosage recommendations include at least one of an activity-per-sphere algorithm or an activity based on embolic load algorithm.

[0081] Item 8. The method of item 7, wherein the activity-per-sphere algorithm comprises division of the customized activity with a predetermined amount of spheres per activity unit.

[0082] Item 9. The method of item 7, wherein the activity based on embolic load algorithm comprises use of a tissue volume input and a predetermined embolic load determination per cubic centimeter of tissue.

[0083] Item 10. The method of item 9, wherein the predetermined embodiment load comprises 20,000 spheres per cubic centimeter of tissue.

[0084] Item 11. The method of any of items 1 to 10, wherein selecting the selected sphere amount and dosage recommendation further includes selecting a desired radioactivity level per sphere.

[0085] Item 12. The method of any of items 1 to 11, wherein selecting the selected sphere amount and dosage recommendation further includes inputting a dose modification as a positive or negative percentage value.

[0086] Item 13. The method of any of items 1 to 12, wherein selecting the selected sphere amount and dosage recommendation further includes splitting the selected sphere amount and dosage recommendation across a plurality of vials based on a percent differentiation per vial, the

percent differentiation in total comprising 100% of the selected sphere amount and dosage recommendation.

[0087] Item 14. The method of item 13, wherein the plurality of vials includes a maximum of three vials.

[0088] Item 15. The method of any of items 1 to 14, wherein the dosimetry portal is configured to provide for data collaboration among a plurality of users such that the plurality of users are granted access rights to view at least one of a first draft order or one or more radioactive compound orders, a user is assigned one of a plurality of security clearance levels, and the plurality of security clearance levels include at least one of a basic security clearance level or an advanced security clearance level providing a user with a greater amount of access rights than the basic security clearance level.

[0089] Item 16. The method of item 15, wherein the basic security clearance level is configured to allow a first user to create the first draft order, and the advanced security clearance level is configured to permit a second user to review and approve the first draft order.

[0090] Item 17. A system for selection of dosimetry levels and sphere amounts of radioactive compounds for use in a radioembolization procedure for procedure planning may include a dosimetry selection tool including a dosimetry portal and a graphical user interface, and a processor communicatively coupled to a dosimetry selection tool and a non-transitory computer storage medium, wherein the non-transitory computer storage medium stores instructions that, when executed by the processor, cause the processor to: receive, via the graphical user interface, an input of activity parameter information into the dosimetry portal of the dosimetry selection tool; determine, via the processor, a customized activity based on the activity parameter information and one or more customized activity algorithms; generate, via the processor, one or more sphere amount and dosage recommendations based on the customized activity and one or more dosimetry selection algorithms; receive, via the graphical user interface, a selection of one of the one or more sphere amount and dosage recommendations as a selected sphere amount and dosage recommendation; and generate, via a processor, a radioactive compound order for the radioembolization procedure based on the customized activity and the selected sphere amount and dosage recommendation.

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[0091] Item 18. The system of item 17, further including instructions that, when executed by the processor, cause the processor to transmit the radioactive compound order to a radioactive compound manufacturer for processing and order fulfillment.

[0092] Item 19. The system of items 17 or 18, further including instructions that, when executed by the processor, cause the processor to assign the radioactive compound order for review by an assigned personnel such that the radioactive compound order is transmitted to a radioactive compound manufacturer for processing and order fulfillment after approval by the assigned personnel.

[0093] Item 20. The system of any of items 17 to 19, wherein the one or more customized activity algorithms includes at least one of a MIRD dosimetry calculation algorithm, a BSA dosimetry calculation algorithm, or a Partition dosimetry calculation algorithm.

[0094] Item 21. The system of any of items 17 to 20, wherein the one or more dosimetry selection algorithms to generate the one or more sphere amount recommendations includes at least one of an activity-per-sphere algorithm or an activity based on embolic load algorithm.

[0095] Item 22. The system of any of items 17 to 21, further including instructions that, when executed by the processor, cause the processor to receive, via the graphical user interface, a percentage split of the selected sphere amount and dosage recommendation across a plurality of vials.

[0096] Item 23. A system for flow rate determination for a radioembolization procedure for procedure planning may include a delivery device, a flow software application tool including a graphical user interface to receive one or more inputs related to the radioembolization procedure, and a processor communicatively coupled to the delivery device, the flow software application tool, and a non-transitory computer storage medium, wherein the non-transitory computer storage medium stores instructions that, when executed by the processor, cause the processor to: receive, via the graphical user interface, the one or more inputs related to the radioembolization procedure; determine, via the processor, one or more flow rate recommendations based on the one or more inputs and one or more optimization algorithms; generate, via the processor, one or more corresponding probabilities of reflux based on the one or more flow rate recommendations; receive, via the graphical user interface, a selection of one of the one or more flow rate

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recommendations as a selected flow rate recommendation; and use the delivery device to deliver Y90 radioembolization spheres for the radioembolization procedure based on the selected flow rate recommendation.

[0097] It is noted that the terms "substantially" and "about" and "approximately" may be utilized herein to represent the inherent degree of uncertainty that may be attributed to any quantitative comparison, value, measurement, or other representation. These terms are also utilized herein to represent the degree by which a quantitative representation may vary from a stated reference without resulting in a change in the basic function of the subject matter at issue.

[0098] While particular embodiments have been illustrated and described herein, it should be understood that various other changes and modifications may be made without departing from the spirit and scope of the claimed subject matter. Moreover, although various aspects of the claimed subject matter have been described herein, such aspects need not be utilized in combination. It is therefore intended that the appended claims cover all such changes and modifications that are within the scope of the claimed subject matter.

[0099] What is claimed is: