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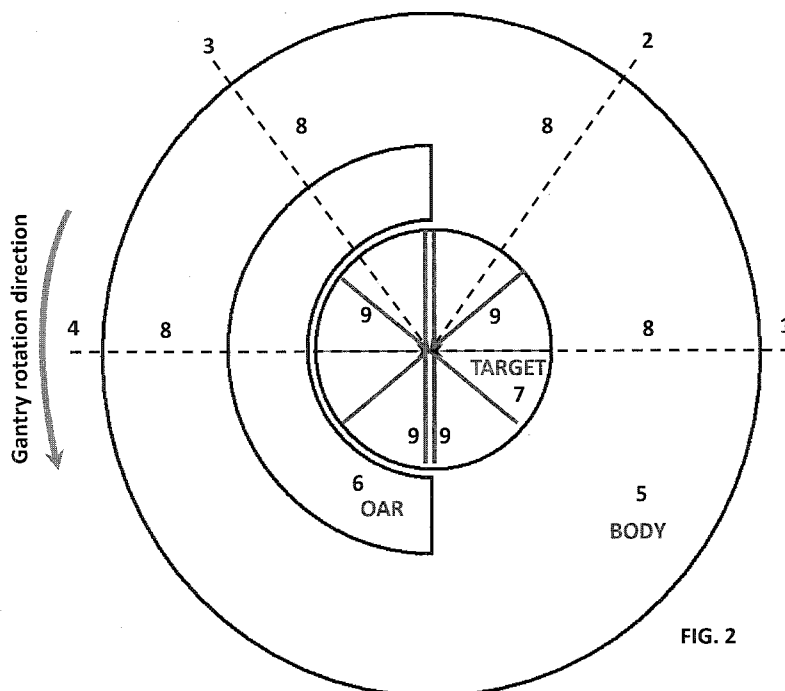
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(54) Title: CHARGED PARTICLE SYSTEM AND METHODS FOR IRRADIATING A PLANNING TARGET VOLUME



(57) Abstract: A method for irradiating a planning target volume with charged particles includes delivering the charged particles to the planning target volume with a charged particle therapy system including a charged particle beam path and a gantry configured to rotate about the planning target volume and to direct the charged particle beam path; rotating the gantry, during an irradiation session, to a plurality of positions; during the rotation, irradiating the planning target volume with the charged particles at a first energy level at one or more of the plurality of positions.

CHARGED PARTICLE SYSTEM AND METHODS FOR IRRADIATING A PLANNING TARGET VOLUME

CROSS-REFERENCE TO RELATED APPLICATIONS

This application claims priority to U.S. Provisional application serial no. 62/026,832 entitled CHARGED PARTICLE SYSTEM AND METHODS FOR IRRADIATING A PLANNING TARGET VOLUME filed on July 21, 2014 and U.S. Provisional application serial no. 62/078,197 entitled CHARGED PARTICLE SYSTEM AND METHODS FOR IRRADIATING A PLANNING TARGET VOLUME filed on November 11, 2014, the contents of which are incorporated fully herein by reference.

FIELD OF THE INVENTION

This invention relates to the field of charged particle therapy systems.

BACKGROUND OF THE INVENTION

Charged particle therapy systems have proven applications in the treatment of cancerous cells. Conventional radiation therapy uses X-rays which pass through the target volume and deliver an undesirable exit dose to healthy tissue. A charged particle beam path can be terminated at a precise location, minimizing damage to healthy tissue surrounding the target volume.

Current methods of delivering charged particles in pencil beam scanning (PBS) mode require the target volume be treated in layers, with each layer corresponding to a different charged particle beam energy level. Inter-layer switching time, which includes changing the energy level of the charged particle beam, can vary between several microseconds to several seconds and leads extended treatment times. Thus, if the dose was to be delivered while the particle gantry or patient positioning device (PPS) rotates, the radiation dose cannot be delivered fast enough to all the layers at a given gantry or PPS angle.

SUMMARY OF THE INVENTION

Aspects of the invention relate to methods for irradiating a planning target volume with charged particles, as well as charged particle therapy systems.

In one aspect of the invention, a method for irradiating a planning target volume with charged particles is provided. The method includes the steps of delivering the charged particles to the planning target volume with a charged particle therapy system including a charged particle beam path and one or more charged particle beam path direction including either or both of a gantry configured to rotate about the planning target volume and a patient positioning device configured to rotate the planning target volume; rotating the charged particle beam path direction devices, during an irradiation session, to a plurality of positions, and during the rotation, irradiating the planning target volume with the charged particles at a first energy level at one or more of the

- 2 -

plurality of positions. At each of the one or more plurality of positions, the charged particle beam path terminates within the planning target volume to produce a Bragg peak within the planning target volume.

In another aspect of the invention, a method for irradiating a planning target
5 volume with charged particles is provided. The method includes the steps of delivering the charged particles to the planning target volume with a charged particle therapy system including a charged particle beam path and one or more charged particle beam path direction devices including either or both of a gantry configured to rotate about the planning target volume and a patient positioning device configured to rotate the planning
10 target volume, which directs the charged particle beam path; rotating the one or more charged particle beam path direction devices, during an irradiation session, to a plurality of positions, and during the rotation, irradiating the planning target volume with the charged particles at a first energy level at one or more of the plurality of positions.

In yet another aspect of the invention, a charged particle therapy system is
15 provided. The system includes a charged particle beam path and one or more charged particle beam path direction devices including either or both of a gantry configured to rotate about a planning target volume and to deliver charged particles while rotating and a patient positioning device configured to rotate the planning target volume such that the charged particle beam path terminates within the planning target volume to produce
20 a Bragg peak within the planning target volume.

It is to be understood that both the foregoing general description and the following detailed description are exemplary, but are not restrictive, of the invention.

BRIEF DESCRIPTION OF THE DRAWINGS

The invention is best understood from the following detailed description
25 when read in connection with the accompanying drawings, with like elements having the same reference numerals. When a plurality of similar elements are present, a single reference numeral may be assigned to the plurality of similar elements with a small letter designation referring to specific elements. When referring to the elements collectively or to a non-specific one or more of the elements, the small letter designation
30 may be dropped. This emphasizes that according to common practice, the various features of the drawings are not drawn to scale unless otherwise indicated. On the contrary, the dimensions of the various features may be expanded or reduced for clarity. Included in the drawings are the following figures:

FIG. 1 is a block diagram of a method for irradiating a planning target
35 volume with charged particles according to aspects of the present invention;

- 3 -

FIG. 2 is a schematic illustration of an irradiation session involving irradiating a symmetrical planning target volume with charged particles according to aspects of the present invention;

FIG. 3 is a schematic illustration of an irradiation session involving
5 irradiating a non-symmetrical planning target volume with charged particles according to aspects of the present invention;

FIG. 4 is a schematic illustration of an irradiation session involving irradiating a non-symmetrical planning target volume with charged particles according to aspects of the present invention;

10 FIG. 5 is a schematic illustration of an irradiation session involving irradiating an irregular phantom with a non-symmetrical planning target volume with charged particles according to aspects of the present invention;

FIG. 6 is an image of a circular uniform phantom containing a defined symmetrical planning target volume that has been irradiated with charged particles
15 according to aspects of the present invention;

FIG. 7 is an image of a circular uniform phantom containing a defined non-symmetrical planning target volume that has been irradiated with charged particles according to aspects of the present invention;

FIG. 8 is an image of an elliptical non-uniform phantom containing a
20 defined non-symmetrical planning target volume that has been irradiated with charged particles according to aspects of the present invention;

FIG. 9 is an image of a brain astrocytoma that has been simulated for the delivery of charged particles according to aspects of the present invention;

FIG. 10 is an image of the linear energy transfer (LET) distribution in a
25 circular uniform phantom containing a defined symmetrical planning target volume that has been irradiated with charged particles according to aspects of the present invention;

FIG. 11 is an image of an elliptical non-uniform phantom containing a defined annular target that has been irradiated with charged particles according to aspects of the present invention;

30 FIG. 12 is a schematic of the beam range for treatment of a real patient's brain with one mono-energetic arc according to aspects of the present invention;

FIG. 13 is a schematic of the beam ranges for treatment of a real patient's brain with two mono-energetic arcs according to aspects of the present invention;

FIG. 14 is a schematic of the beam ranges for treatment of a real patient's
35 brain with three mono-energetic arcs according to aspects of the present invention;

FIG. 15 is a schematic of the beam range for treatment of a uniform elliptical phantom with one mono-energetic arc according to aspects of the present invention;

FIG. 16 is a schematic of the beam ranges for treatment of a uniform elliptical phantom with two mono-energetic arcs according to aspects of the present invention;

FIG. 17 is a schematic of the beam ranges for treatment of a uniform elliptical phantom with three mono-energetic arcs according to aspects of the present invention;

FIG. 18 is a schematic depicting an irradiation process in accordance with aspects of the present invention;

FIG. 19 is a schematic depicting an irradiation process for non-uniform elliptical phantom according to aspects of the present invention;

FIG. 20 is an image of the dose distribution when a single mono-energetic arc is planned according to the data presented in FIGs. 18 and 19;

FIG. 21 is a schematic of the range selection process for a non-uniform elliptical phantom using one mono-energetic arc in accordance with aspects of the present invention;

FIG. 22 is a schematic of the range selection process for a non-uniform elliptical phantom using two mono-energetic arcs according to aspects of the present invention;

FIG. 23 is a schematic of the range selection process for a non-uniform elliptical phantom using three mono-energetic arcs in accordance with aspects of the present invention;

FIGs. 24A-24D are images comparing the dosage delivered to healthy tissue under standard treatment plans to treatment plans in accordance with aspects of the present invention; and

FIGs. 25A-25B are images comparing the dosage delivered to healthy tissue under standard treatment plans to treatment plans in accordance with aspects of the present invention.

DETAILED DESCRIPTION OF THE INVENTION

Aspects of the invention are directed to methods for irradiating a planning target volume with charged particles and charged particle therapy systems. The following descriptions are meant to provide example embodiments of the present invention. The scope of the claims is not intended to be limited by any of the particular embodiments disclosed below.

- 5 -

The inventor has recognized that it would be useful to provide a charged particle therapy treatment method that combines pencil beam scanning and arc therapy techniques. The inventor has additionally recognized that utilizing a single energy for each arc or segment of an arc about the planning target volume reduces exposure time and the number of monitor units required for the treatment process. In particular, the inventor has found that with only one energy per angle, the speed of the treatment becomes limited only by the rotational speed of the gantry and the length of the arc(s) used for the treatment. The inventor has further recognized that terminating the Bragg peak in the central region of the planning target volume minimizes the dose of radiation to the surrounding healthy tissue and increases linear energy transfer (LET) of the charged particle beam in the target.

FIG. 1 shows in schematic form a method 100 for irradiating a planning target volume with charged particles. The method may be performed using a charged particle therapy system including a charged particle beam path and a gantry configured to rotate about a planning target volume. Additionally or alternatively, the charged particle therapy system may include a charged particle beam path and a patient positioning device ("PPS") configured to rotate the planning target volume, e.g., by rotating the patient. One of ordinary skill in the art will understand upon reading this disclosure that other suitable devices and/or pieces of equipment may be utilized to manipulate the charged particle beam with reference to the planned target volume.

In one embodiment, the charged particle therapy system operates in pencil beam scanning (PBS) mode. In step **110**, the charged particle therapy system delivers charged particles to a planning target volume. The planning target volume is a geometrical concept defined to deliver radiation. The planning target volume may be a uniform or non-uniform phantom for use in treatment planning, or a tumor in a patient. One of ordinary skill in the art will understand that the size and shape of the planning target volume depend on the size of the area to be treated (e.g., the tumor volume) treatment technique used, the effects of organ and patient movement, and inaccuracies in beam and patient setup.

In step **120**, a gantry is rotated during an irradiation session (e.g., during the delivery of radiation to a planning target volume of a patient) to a plurality of positions in an arc about the planning target volume. An arc includes at least a portion of 360 degrees about the planning target volume. An irradiation session may include multiple arcs, where each arc may have the same or different center of rotation and where each arc may be contained in the same plane of rotation (co-planar arcs) or not contained in the same plane of rotation (non-coplanar arcs). The gantry transports and delivers the charged particle beam into a treatment room, bends the beam until it can be incident

orthogonal to the patient and then rotates the beam around the patient. A typical gantry is comprised of large magnets, an evacuated pipe, a nozzle and a counterweight. All of the components are mounted on a large steel beam "squirrel cage" to enable the rotation of the proton beam around the patient. In a preferred embodiment, the gantry is operable to continuously rotate while simultaneously delivering charged particles to the planning target volume, which decreases treatment time and increases efficiency. The gantry may rotate continuously and deliver charged particles to a plurality of positions within the arc. The rotation may be centered on the planning target volume, or it may be centered elsewhere. In one embodiment, the gantry rotates continuously, but delivers charged particles to less than all positions within the arc, i.e., it does not deliver charged particles to the entire arc.

In an alternative embodiment, a PPS may be used to rotate the patient to a plurality of positions with respect to a fixed charged particle beam. The PPS may rotate continuously during the treatment of the patient, thereby decreasing treatment time and increasing efficiency.

In step **130**, the planning target volume is irradiated at a first energy level. Irregularly shaped planning target volumes, such as the elliptical, non-uniform phantom depicted in **FIG. 6**, may require multiple charged particle beam energy levels to deliver a dose to the entire target. In one embodiment, prior to the delivering the dose to the target volume, the planning target volume is subdivided into a plurality of sub-targets, which may form a plurality of positions towards which the charged particle beams are directed.

The charged particle beam path may terminate within the target volume such the Bragg peak is located within the planning target volume. Preferably, the particle beam path terminates within the target volume such the Bragg peak is located in a central region of the planning target volume. The Bragg peak is a pronounced peak on the Bragg curve which plots the energy loss of ionizing radiation during its travel through matter. Protons in particular tend to travel through the body tissue without significant absorption until they reach a specific point within the body. At this point, which corresponds to the Bragg peak of the proton beam, the proton energy is released. For protons, the peak occurs immediately before the particles come to rest. Thus, the region where the Bragg peak is located receives the highest dose from the charged particle beam. Tracking the central region of the planning target volume with the proton beam Bragg peak minimizes damage to surrounding healthy tissue such as, e.g., organs at risk ("OARs") and maximizes the dose and linear energy transfer (LET) received by the planning target volume from the charged particle beam.

FIG. 2 depicts a schematic diagram of the irradiation of a planning target volume according to aspects of the present invention. A circular uniform phantom represents a patient body **5** with an OAR **6** surrounding a circular uniform planning target volume **7**. The gantry (not shown) rotates continuously from position **1** to position **4** about the planning target volume **7**. In this embodiment, the gantry rotates a half arc about the planning target volume. The charged particle beam **8**, at a first energy level, enters the patient body **5** and terminates such that the Bragg peak is located in the central planar region of the planning target volume **7**. The charged particle beam **8** may be directed to one or more of the plurality of positions between position **1** and position **4**, i.e., positions **2** and **3**, or other positions not depicted. Also, the charged particle beam path may be shut off at one or more of the plurality of positions. While the charged particle beam path is shut off, the gantry does not irradiate the planning target volume, however, as described above, the gantry may continue to rotate.

As shown in **FIG. 3**, irradiation may be applied to a more complex planning target volume geometry. A uniform circular phantom represents a patient body **5** with nonsymmetrical target **7** surrounding an OAR **6**. In this embodiment, the gantry is configured to rotate isocentrically approximately 180 degrees (i.e., a half arc) about the planning target volume to a plurality of positions. The plurality of positions may be located at various points within the 180 degrees about the planning target volume, as demonstrated by example positions **10**, **11**, **12**, and **13**. The gantry delivers beams **8** at a first energy level while rotating between positions **10** and **14**. The gantry may rotate from position **10** to position **14**, or from position **14** to position **10**. Bragg peaks **9** deposit energy in the section of the plane perpendicular to beams **8** that contains the target.

Turning to **FIG. 4** an elliptical phantom represents a patient body **5** with nonsymmetrical target **7** surrounding OAR **6**. In this embodiment, the gantry is configured to complete two 180 degree (i.e., two half arc) rotations and deliver charged particles at a first and second energy level. Each rotation may correspond to a distinct energy level. As the gantry rotates about target **7** to irradiate planes **22** (corresponding to a first energy level E_1) and **23** (corresponding to a second energy level E_2), the depth ($L_1, L_2, \dots$) of each of these planes may vary for each individual gantry angle requiring the use of more than one energy ($E_1, E_2, \dots$) to deposit the dose in the PTV. While only five planes **22** and **23** are shown, irradiation may be continuous. In this embodiment, two beam energies are used due to the non-symmetrical shape of the patient body **5**. Different energies may be required to penetrate to the required depth at every angle so that the Bragg peak terminates in the target volume.

While rotating from position **15** to position **16**, the gantry delivers a charged particle beam **20** to a plane contained within the planning target volume **7**. The charged particle beam is shut off when the gantry reaches position **16**. The gantry continues to rotate and, when it reaches position **18**, the charged particle beam is turned back on at the first energy level. The charged particle beam irradiates the planning target volume at the first energy level until the gantry reaches position **19**. At this position, the charged particle beam is shut off, and the gantry stops, completing its first of two rotations.

The charged particle beam is then configured to emit charged particles at a second energy level which is distinct from the first. The gantry then rotates back from position **19** to position **15**. When the gantry reaches position **17**, the charged particle beam **21** irradiates the planning target volume **7** at a second energy level as the gantry continues to rotate. When the gantry reaches position **16**, the charged particle beam is shut off and the gantry continues to rotate until it reaches position **15**, completing its second rotation.

FIG. 5 illustrates the irradiation of a planning target volume according to principles of the present invention. In this embodiment, three distinct energy levels are used, corresponding with three gantry rotations, due to the non-symmetrical nature of the planning target volume and patient body. In this example, the gantry rotates counterclockwise with respect to the planning target volume in a continuous arc starting at position **24** and ending at position **27**. Between position **24** and position **25**, the gantry delivers a charged particle beam **28** at a first energy level E_1 to the planning target volume **7**. During this first rotation and during the two subsequent rotations, the charged particle beam path terminates such that Bragg peak is located within the planning target volume **7** in a similar fashion to **FIG. 4**. Once it reaches position **25**, the gantry shuts off the charged particle beam while continuing its rotation about the planning target volume to position **27**. The gantry then begins its second rotation, rotating clockwise with respect to the planning target volume from position **27** to position **25**. Between position **26** and position **25**, the gantry delivers a charged particle beam **29** at a second energy level E_2 . The gantry then shuts off the charged particle beam and stops. The gantry then completes a third rotation, rotating counterclockwise with respect to the planning target volume **7** from position **25** to position **27**. Between position **25** and position **26** the gantry rotates without delivering any dose and once it reaches position **26**, the charged particle beam **30** is turned back on at a third energy level E_3 . The gantry rotation and charged particle beam both stop when the gantry reaches position **27** during its third rotation.

- 9 -

One of ordinary skill in the art will understand that the gantry may rotate more than three times, and that more than three energy levels may be used in an irradiation session while still remaining within the scope of the present invention.

EXAMPLES

5 Example 1 - Proton Modulated Arc Therapy in a Circular Uniform Phantom with a symmetrical planning target volume

The delivery of a uniform dose to a planning target volume using pencil beam scanning proton modulated arc therapy was performed. **FIG. 6** shows the dose distribution in the central plane of a cylindrical phantom, and depicts the charged particle dose distribution (dose in color wash) obtained when beams are delivered as described in **FIG. 2**. A planning target volume **31** and OARs **32** and **33** were defined within a cylindrical, homogeneous phantom **34**. Planning target volume **31** is a circle 5 cm in diameter. A 166.94 MeV proton beam **35** was used in a 360 degree arc, the beam entering the planning target volume at a plurality of positions. The radiation dose was concentrated in planning target volume **31**. As shown by the dose density diagram, dose delivery to OAR's **32** and **33** was minimal.

Example 2 – Proton Modulated Arc Therapy in a Circular Uniform Phantom with a non-symmetrical planning target volume

The delivery of a uniform dose to a non-symmetrical planning target volume using pencil beam scanning proton modulated arc therapy was performed. **FIG. 7** shows the dose distribution in the central plane of a cylindrical phantom, and depicts the charged particle dose distribution obtained when beams are delivered as described in **FIG. 3**. A planning target volume **36** and OARs **37** and **39** were defined within a cylindrical, homogeneous phantom **40**. Planning target volume **36** is a 1.25 cm wide half-annulus that has the same center point as OAR **37**. OAR **37** is a cylinder 5 cm in diameter. There is a 2 mm separation between OAR **37** and planning target volume **36**. OAR **39** is a half-annulus 0.5 cm wide and is separated by 1.5 mm from the planning target volume. Once the optimal beam energy was selected, the same beam was repeated in 37 gantry positions every 5 degrees to create a 180 degree arc. Dose delivery to the OAR was minimal.

Example 3a - Proton Modulated Arc Therapy in an Elliptical Non-Uniform Phantom

Proton modulated arc therapy was applied to irregular, nonhomogeneous shapes as may be found in the human body. **FIG. 8** shows the dose distribution in the central plane of a non-uniform phantom meant to emulate a human torso, and depicts the charged particle dose distribution obtained when beams are delivered as described in **FIG. 4**. Planning target volume **41** and OARs **42** and **43**, which have the same dimensions as in the previous example, were defined in a nonhomogeneous phantom **44**.

The dose distribution was obtained after using 3 different energies, as depicted in **FIG. 5**. The results shown in **FIG. 8** indicate this treatment method could successfully be used in treatment sites with large heterogeneities such as the brain, neck, and prostate.

Example 3b – Proton Modulated Arc Therapy in an Elliptical Non-Uniform Phantom

5 The delivery of a uniform dose to a non-symmetrical planning target volume using pencil beam scanning proton modulated arc therapy was performed. The phantom modeled phantom extended 20 cm caudad/cephalad. The target was a half annulus 1 cm wide that has the same center as the central cylinder and surrounds it by 180°. There is a 3 mm separation between the central cylinder and the half annulus. 10 Therefore, the annulus has an inner radius of 2.3 cm and an outer radius of 3.3 cm with respect to the common central axis of the cylinder and the annulus. The structures extend 4 cm caudad/cephalad. The results shown in **FIG. 11** indicate that this treatment method could be successfully used in treatment sites of non-regular shaped body parts with non-homogeneous media.

15 Example 4a – Proton Modulated Arc Therapy in Real Patient Geometry

Proton modulated arc therapy was used to plan the treatment of an astrocytoma in the brain, as shown in **FIG. 9**. Planning target volume **45** was irradiated from a plurality of angles using a 180 degree gantry arc. The target is located in a non-homogenous location (i.e., the base of the skull) and the beam traverses the cranial 20 bone which has a different thickness for each of the beam angles. Dose volume histogram **46** shows better sparing of healthy tissue achieved using proton modulated arc therapy (square plot symbols) when compared with results from a standard pencil beam scanning method (triangle plot symbols). **FIGs. 24** and **25** further illustrates that the proton modulated arc therapy better spares healthy tissue when compared to 25 standard methods for irradiating a patient.

Example 4b – Efficiency Assessment for Proton Modulated Arc Therapy in Real Patient Geometry

An efficiency assessment of a brain case was planned using aspects of the invention as set forth above. The arcs were coplanar within an axial plane containing the isocenter and extended for 180° with 37 fields separated every 5°. The prescription used 30 for the target and OARs is given in table 1. The beam ranges utilized for one (1E), two (2E), and three (3E) mono-energetic arcs are plotted in **FIGs. 12, 13, and 14**, respectively.

Table 1 - dose prescription for the brain case presented

Volume Name	D _{max} (%)	Volume (%)	Prescribed dose (%)
CTV		99	98
PTV	107	98	95
Brainstem	84.6	50	68.2
Optic nerves & chiasm	78.3		
Cochlea	37.9		
Eyes	12.6		
Temp lobes	25.3*		
Pituitary	56.8		
Hippocampus	25.3		
Hypothalamus	12.6		

* Mean Dose

In the case of the 3 mono-energetic arcs for the uniform phantom case (**FIG. 14**), the beam ON sequence would start delivering the arc with 14.39 cm beam range when the gantry rotates anticlockwise from angle 90° to 65°, then turn the beam OFF from angle 65° to 290°, then turn the beam back ON from 290° to the end of the first rotation (270°). At this point, the beam energy would be reduced in order to deliver a beam with a range of 12.65 cm, which will be delivered between the arc segments going from 295° to 310° and 45° to 60°, while the gantry is rotated clockwise up to gantry angle 60° where the beam is turned OFF and the gantry stops. Finally, the gantry rotates back anticlockwise to gantry angle 45° where a beam with a range of 10.91 cm is turned back ON while the gantry keeps rotating up to 315°. At this gantry angle, the beam is turned OFF and the gantry stops; thus, concluding the treatment.

On the bases that a proton gantry rotates with an angular speed of 1 revolution per minute, the amount of time required to complete each of the beam ON/OFF sequences (and therefore the treatment time) presented in **FIGs. 12, 13, and 14** is 30 sec, 52.7 sec and 71.4 sec respectively. Thus, it is calculable that the Proton Modulated Arc Therapy ("PMAT") treatments are faster (minimum room time (MRT) = patient setup + 30 sec + patient unload) or of similar duration (MRT = patient setup + 75 sec + patient unload) than the SFO/MFO treatments, assuming that the patient load, setup, and unload time requirements are the same for each treatment plan, and considering that each beam in the SFO or MFO plans need be loaded and reset from inside the room as well as that sometimes a couch quick between beams is also needed.

Example 5 – Linear Energy Transfer (LET) Distribution with Proton Modulated Arc Therapy

LET is commonly used as an indicator of the biological power of the dose. The higher the LET, the higher the biological power of the dose. **FIG. 10** shows the LET distribution associated with proton modulated arc therapy. Planning target volume **47** received an LET in excess of 8 keV/μm while OARs **48** and **49** received very low LET values.

Example 6a – Developing a PMAT Treatment Plan for a Uniform Elliptical Phantom

The objective was to treat the central cylindrical structure using the above prescription delivered with 37 fields separated every 5° over a 180° arc going from left to right of the phantom. The OAR was an annular structure.

The range and modulation required from each field of the arc to provide full dose coverage to the target were calculated (each field has its own range and spread out Bragg peak (SOBP) width). The water equivalence distance ("WED") was also determined. This calculation, which was done in single field optimization, provides the calculated ranges (R_{TPS}) appearing in table 2. These ranges correspond to the energy of the most distal layer of each beam. As the method described in this example is premised on all beams stopping inside the target, the final range for each beam was obtained from:

$$R_{PMAT} = R_{TPS} - \frac{MOD_{TPS}}{2}$$

Where R_{PMAT} corresponds to the final range for each beam used for the PMAT calculation, and MOD_{TPS} corresponds to the modulation obtained from the TPS for each beam during the raw (free range and modulation) calculation. Table 2 is provided below.

Table 2: Relevant beam data to make PMAT plans for the uniform phantom case

Bm. No.	Bm. Angl.	Distal Range	SOBP width	R _{PMAT}	WED	1E	2E	3E
1	90	17.38	4.24	15.26	15.22	12.65	13.95	14.39
2	85	17.35	4.48	15.11	15.15			
3	80	17.16	4.56	14.88	14.88			
4	75	16.90	4.80	14.50	14.56			
5	70	16.58	4.93	14.12	14.19			
6	65	16.25	5.21	13.65	13.74			
7	60	15.78	5.26	13.15	13.24		11.34	12.65
8	55	15.38	5.34	12.71	12.75			
9	50	14.82	5.21	12.22	12.24			
10	45	14.35	5.13	11.79	11.84			
11	40	13.95	5.07	11.42	11.39			
12	35	13.56	4.96	11.08	11.15			
13	30	13.21	4.80	10.81	10.8			
14	25	12.90	4.70	10.55	10.53			
15	20	12.65	4.54	10.38	10.35			
16	15	12.43	4.41	10.23	10.23			
17	10	12.31	4.29	10.17	10.07			
18	5	12.18	4.20	10.08	10.08			
19	0	12.11	4.15	10.04	10.03			
20	355	12.17	4.17	10.09	10.06			10.91
21	350	12.25	4.32	10.09	10.06			
22	345	12.38	4.38	10.19	10.22			
23	340	12.60	4.49	10.36	10.33			
24	335	12.83	4.68	10.49	10.5			
25	330	13.10	4.74	10.73	10.76			
26	325	13.41	4.84	10.99	11.05			
27	320	13.80	4.96	11.32	11.33			
28	315	14.19	5.09	11.65	11.73			
29	310	14.59	5.10	12.04	12.09			
30	305	15.09	5.27	12.46	12.57		13.95	12.65
31	300	15.55	5.27	12.92	13.06			
32	295	15.94	5.16	13.36	13.55			
33	290	16.35	5.01	13.85	13.96			14.39
34	285	16.63	4.73	14.27	14.32			
35	280	16.90	4.63	14.59	14.63			
36	275	17.00	4.39	14.81	14.89			
37	270	17.07	4.20	14.97	14.95			

Table 2 provides the collection of ranges to use if one (1E) or two (2E) or three (3E) mono-energetic arcs were used. As set forth above, the inventor identified a potential range or combination of ranges that requires the shortest arc trajectory with

the highest possible dose conformity to the target. The ranges to use in the 1E, 2E or 3E arcs were based on a graphical method explained below.

To find the single energy solution, presented in **FIG. 15**, the middle range between the maximum and the minimum of the ranges presented in table 2 was used.

To calculate the 2 ranges required for **FIG. 16**, the range difference between maximum and minimum was equally divided in two regions, and the mid-point of the beam ranges included in each of these two regions provided the solution ranges for each mono-energetic arc: 11.34cm and 13.95cm. As illustrated in **FIGs. 15, 16, and 17**, as the number of mono-energetic arcs used increases, the distance of the points to the dashed line decreases.

The lines and arrows in the lower part of **FIGs. 15, 16, and 17** represent the beam ON and OFF sequence that could be used to deliver the mono-energetic arcs in each of the phantom cases. The sequence was based on identifying the shortest total gantry rotation to deliver all required arcs, which would represent the shortest treatment delivery time.

Example 6b – Developing a PMAT Treatment Plan for a Non-Uniform Elliptical Phantom

The objective was to treat a half annular target structure wrapped around a cylindrical OAR. PMAT treatment included an arc with 37 fields every 5 degrees over a 180 degree tilted arc, whereby beam angles 1-3 passed through less inhomogeneity than beam angles 24-27. The first angle of the arc was set at 65 degrees from the vertical.

Aspects of the process used in Example 6a were employed to determine the range required to produce PMAT plans, whereby the distal edge of the SOBP was obtained from the most distal point of the distal edge and the proximal edge of the SOBP was determined from the most proximal point of the proximal edge of the target structure.

A contouring technique, different from the technique of Example 6a, was employed to enable optimization of the uniformity of the arc by way of modifying the SOBP width. The contouring technique employed included subdividing the target structure into multiple sub-targets that served as target structures for each beam. Splitting the target into multiple sub-targets may reduce the heterogeneity of the SOBP width variation across the arc and enable the dosage to be delivered by alternative directions. The sub-targets were produced by splitting the target in wedges every 5 degrees, thereby creating 37 sub-targets, one for each beam (e.g., sub-target 1 served as the target for beam 1, sub-target 2 served as target for beam 2, etc.). **FIG. 18** illustrates the difference between the mid-SOBP range and the target WED for each beam angle. **FIG. 19** depicts the technique used to irradiate the target in the case of

- 15 -

the non-uniform elliptical phantom. **FIG. 20** illustrates the difference in the dose distribution when a single mono-energetic arc is planned using the raw data presented in **FIGs. 18** and **19**. The inventors found that the method employed in this Example may provide more conformal and homogenous dose distribution than the method in Example 6a.

The range selection for each mono-energetic arc solution was determined according to the methodologies explained above, e.g., Example 6a. **FIGs. 21-23** depict the range selection process for each beam as the number of arcs is increased from 1 to 3. The calculations employed to provide Table 3, shown below, used a lateral spot spacing of 0.5 cm.

Table 3: Relevant beam data used to plan PMAT in non-uniform phantom case

Beam Number	Beam Angle	Distal Range	SOBP Width	R _{PMAT}	WED	1E	2E		3E	
1	65	12.77	1.57	11.99	12.67	10.36	11.17		11.44	
2	60	12.12	1.63	11.31	12.98					
3	55	11.52	1.53	10.76	13.15					
4	50	10.98	1.55	10.21	12.53		9.549.05		10.36	
5	45	10.52	1.44	9.80	12.10					
6	40	10.17	1.36	9.49	11.69					
7	35	9.88	1.26	9.25	11.22					
8	30	9.69	1.29	9.05	10.92					
9	25	9.42	1.09	8.88	10.66					
10	20	9.24	0.95	8.77	10.40					
11	15	9.26	0.97	8.78	10.19					
12	10	9.18	0.90	8.73	10.09					
13	5	9.19	0.77	8.81	10.06					
14	0	9.22	0.55	8.95	9.98					
15	355	9.39	0.66	9.06	10.05					
16	350	9.53	0.65	9.21	10.07					
17	345	9.74	0.58	9.45	10.26					
18	340	10.04	0.61	9.74	10.30					
19	335	10.32	0.88	9.88	10.57					
20	330	10.66	1.17	10.08	10.85					
21	325	10.90	1.58	10.11	11.12					
22	320	10.97	1.82	10.06	11.52					
23	315	10.74	1.58	9.95	11.90					
24	310	10.75	1.70	9.90	12.39					
25	305	10.53	1.26	9.90	12.93					
26	300	10.59	1.20	9.99	12.45					
27	295	10.75	1.02	10.24	12.13					
28	290	11.03	1.08	10.49	11.90					
29	285	11.27	1.00	10.77	12.02					
30	280	11.65	1.04	11.13	12.31					
31	275	11.88	1.36	11.20	12.61					
32	270	12.08	1.45	11.36	12.91					
33	265	12.15	1.85	11.23	13.61					
34	260	11.95	1.66	11.12	13.91					
35	255	11.74	1.65	10.92	13.17					
36	250	11.34	1.21	10.74	13.00					
37	245	10.87	1.09	10.33	12.69					

Additionally or alternatively, the use of PMAT algorithms, which account for the dose in between beams not accounted for in the present step-and-shoot mode used in this Example, may desirably improve the efficacy of the treatment. For example, as can be seen in the 2E and 3E cases, the two layers the TPS imposes, even with the SOBP width at 0 cm, are very close to one another; e.g., 2E beams 4 to 27 include 9.54 cm at 113.45 MeV and 9.05 cm at 110.40 MeV and 3E beams 6 to 18 include 9.27 cm at 111.66 MeV and 8.77 cm at 108.64 MeV. Without intending to be limited to any

- 17 -

particular theory, it is believed that this effect results from current TPS providing homogenous dose coverage to the target structure at any given angle.

Although the invention is illustrated and described herein with reference to specific embodiments, the invention is not intended to be limited to the details shown.

- 5 Rather, various modifications may be made in the details within the scope and range of equivalents of the claims and without departing from the invention.

- 18 -

What is Claimed:

1. A method for irradiating a planning target volume with charged particles, comprising the steps of:

delivering the charged particles to the planning target volume with a charged
5 particle therapy system including:

a charged particle beam path; and

one or more charged particle beam path direction devices from the group
consisting of a gantry configured to rotate about the planning target volume and
a patient positioning device configured to rotate the planning target volume;

10 rotating the charged particle beam path direction devices, during an irradiation
session, to a plurality of positions within at least one arc about the planning target
volume; and

during the rotation, irradiating the planning target volume with the charged
particles at a first energy level at one or more of the plurality of positions such that, at
15 each of the one or more of the plurality of positions, the charged particle beam path
terminates within the planning target volume to produce a Bragg peak within the
planning target volume.

2. The method of claim 1, wherein the plurality of positions are located at
various points within an arc about the planning target volume.

20 3. The method of claim 1, where the plurality of positions are within the
same plane of rotation.

4. The method of claim 1, wherein the plurality of positions are within
multiple planes of rotations.

5. The method of claim 1, further comprising rotating the gantry a plurality
25 of arcs about the planning treatment volume, wherein each arc has the same center of
rotation

6. The method of claim 1, further comprising rotating the gantry a plurality
of arcs about the planning treatment volume, wherein each arc has a different center of
rotation.

30 7. The method of claim 1, wherein the rotating step comprises continuously
rotating the gantry and only irradiating the planning target volume at the plurality of
positions.

8. The method of claim 7, wherein the rotating step comprises shutting off
the charged particle beam path at positions other than the plurality of positions.

35 9. The method of claim 1, wherein the rotating step comprises rotating the
gantry at least twice about the planning target volume and wherein the irradiating step
comprises, during the first rotation, delivering charged particles at a first energy level

to the planning target volume at a first set of positions within the plurality of positions and, during the second rotation, delivering charged particles at a second energy level at a second set of positions within the plurality of positions.

10. The method of claim 9, wherein the first set of positions are different
5 from the second set of positions.

11. The method of claim 1, wherein the rotating step comprises rotating the gantry at least three times about the planning target volume and wherein the irradiating step comprises, during the first rotation, delivering charged particles at a first energy level to the planning target volume at a first set of positions within the
10 plurality of positions and, during the second rotation, delivering charged particles at a second energy level to the planning target volume at a second set of positions within the plurality of positions and, during the third rotation, delivering charged particles at a third energy level at a third set of positions within the plurality of positions.

12. The method of claim 1, wherein the charged particle therapy system
15 comprises a pencil beam scanning system.

13. The method of claim 9, further comprising, prior to the delivering step, the step of subdividing the planning target volume into a plurality of sub-targets that form the plurality of positions.

14. A charged particle system comprising
20 a charged particle beam path including charged particles; and
one or more charged particle beam path direction devices from the group consisting of a gantry configured to rotate about a planning target volume and a patient positioning device configured to rotate the planning target volume, the charged particle beam path direction devices configured to deliver charged particles while
25 rotating, such that the charged particle beam path terminates within the planning target volume to produce a Bragg peak within the planning target volume.

15. The system of claim 14, further configured to deliver the charged particle beam in pencil beam scanning mode.

16. The charged particle system of claim 14, wherein the gantry is configured
30 to rotate a plurality of times about a planning target volume and to deliver charged particles at a distinct energy level during each rotation.

17. A method for irradiating a planning target volume with charged particles, comprising the steps of:

delivering the charged particles to the planning target volume with a charged
35 particle therapy system including:

a charged particle beam path; and

- 20 -

one or more charged particle beam path direction devices from the group consisting of a gantry configured to rotate about the planning target volume and a patient positioning device configured to rotate the planning target volume; rotating the charged particle beam path with reference to the planning target
5 volume, during an irradiation session, to a plurality of positions within at least one arc about the planning target volume; and

during the rotation, irradiating the planning target volume with the charged particles at a first energy level at one or more of the plurality of positions.

18. The method of claim 17, wherein at each of the one or more of the
10 plurality of positions, the charged particle beam path terminates in a central region of the planning target volume to produce a Bragg peak in the central region.

19. The method of claim 1, wherein the charged particle beam path terminates within a central region of the planning target volume.

20. The method of claim 1, wherein the charged particle beam path
15 terminates within the planning target volume to produce a Bragg peak within the central region of the planning target volume.

21. The charged particle system of claim 14, wherein the charged particle beam path terminates within a central region of the planning target volume to produce a Bragg peak within the central region.

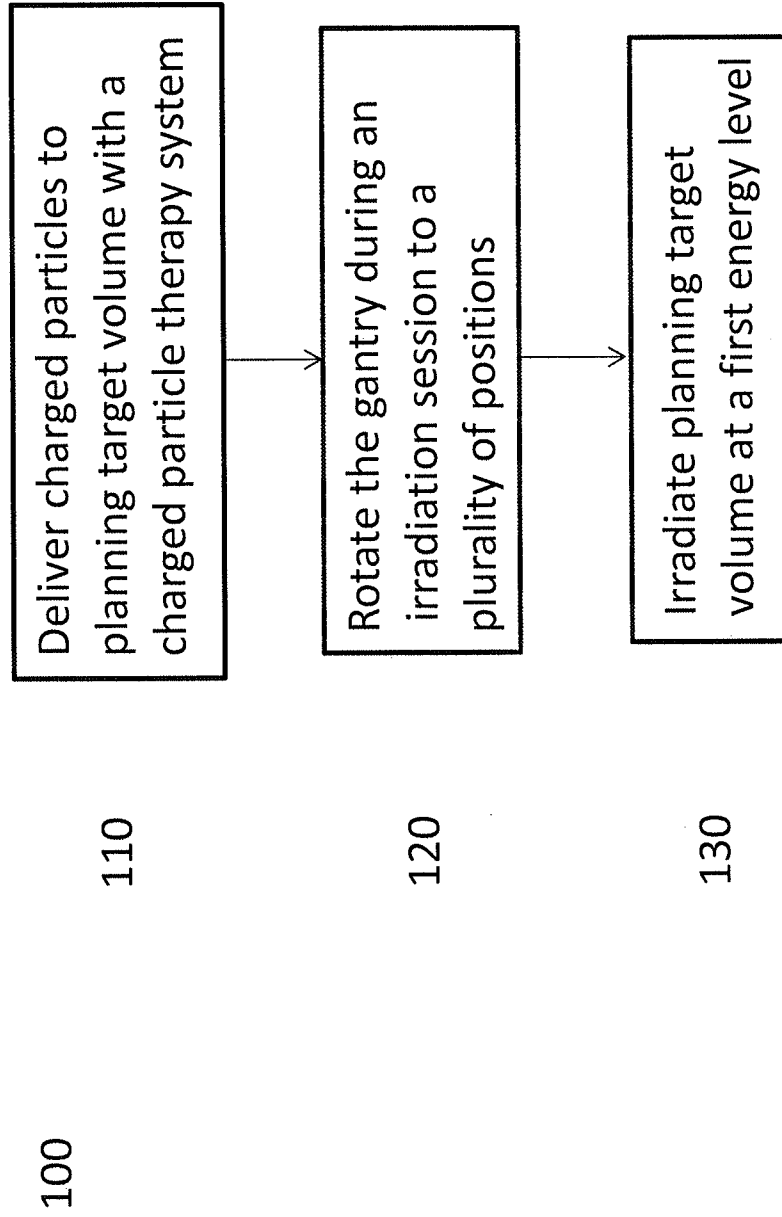


FIG. 1

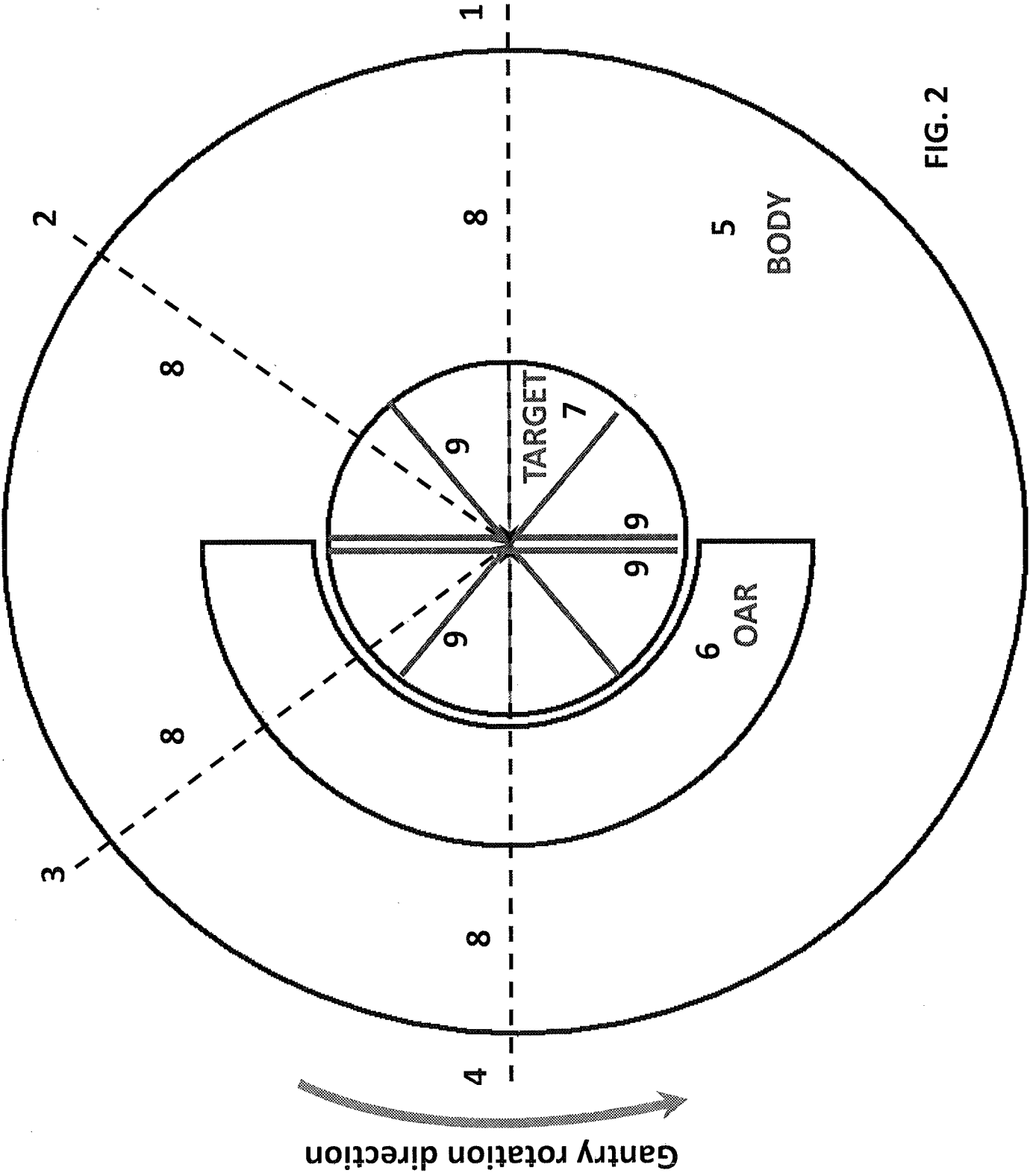
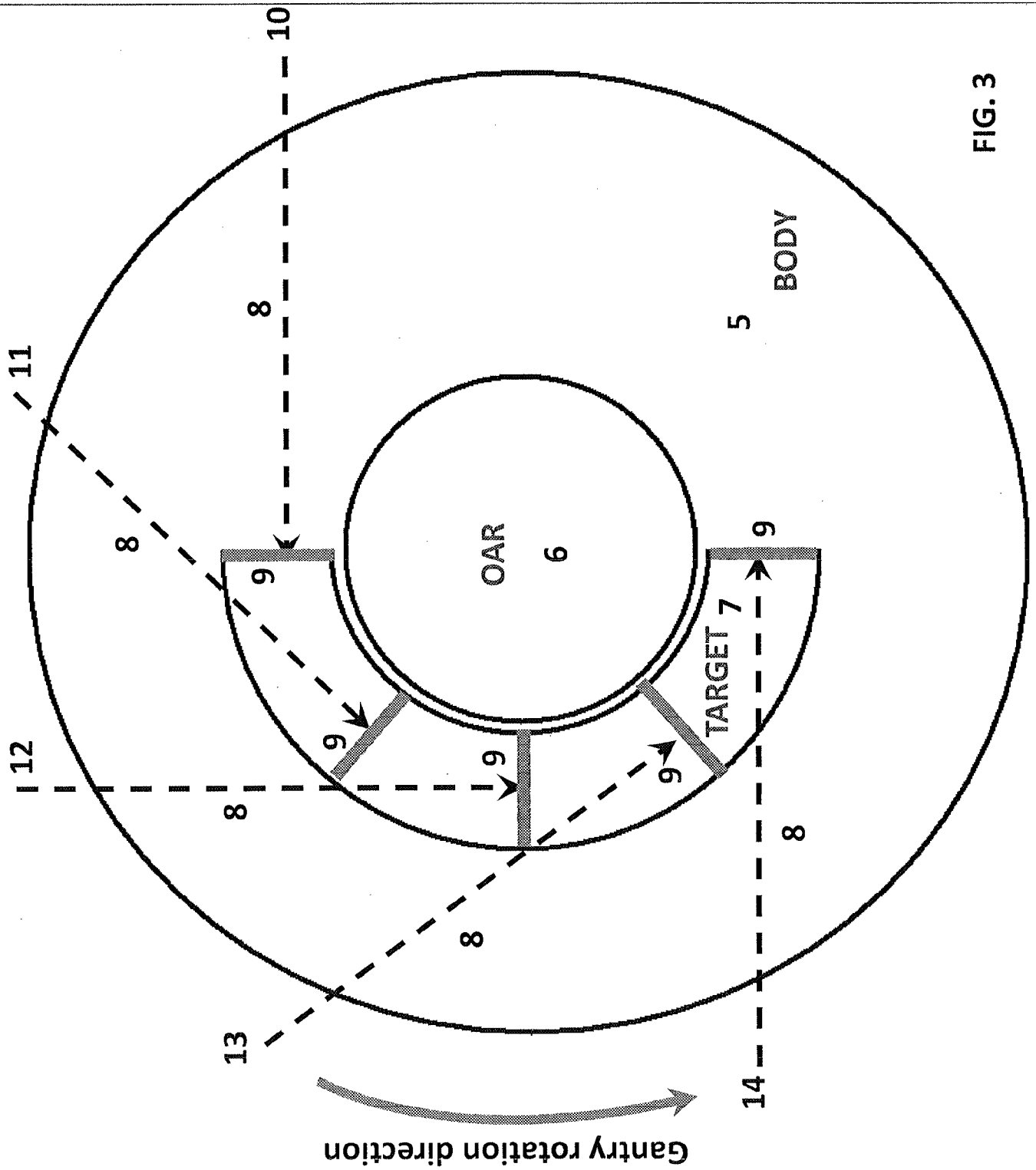


FIG. 2

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G
L

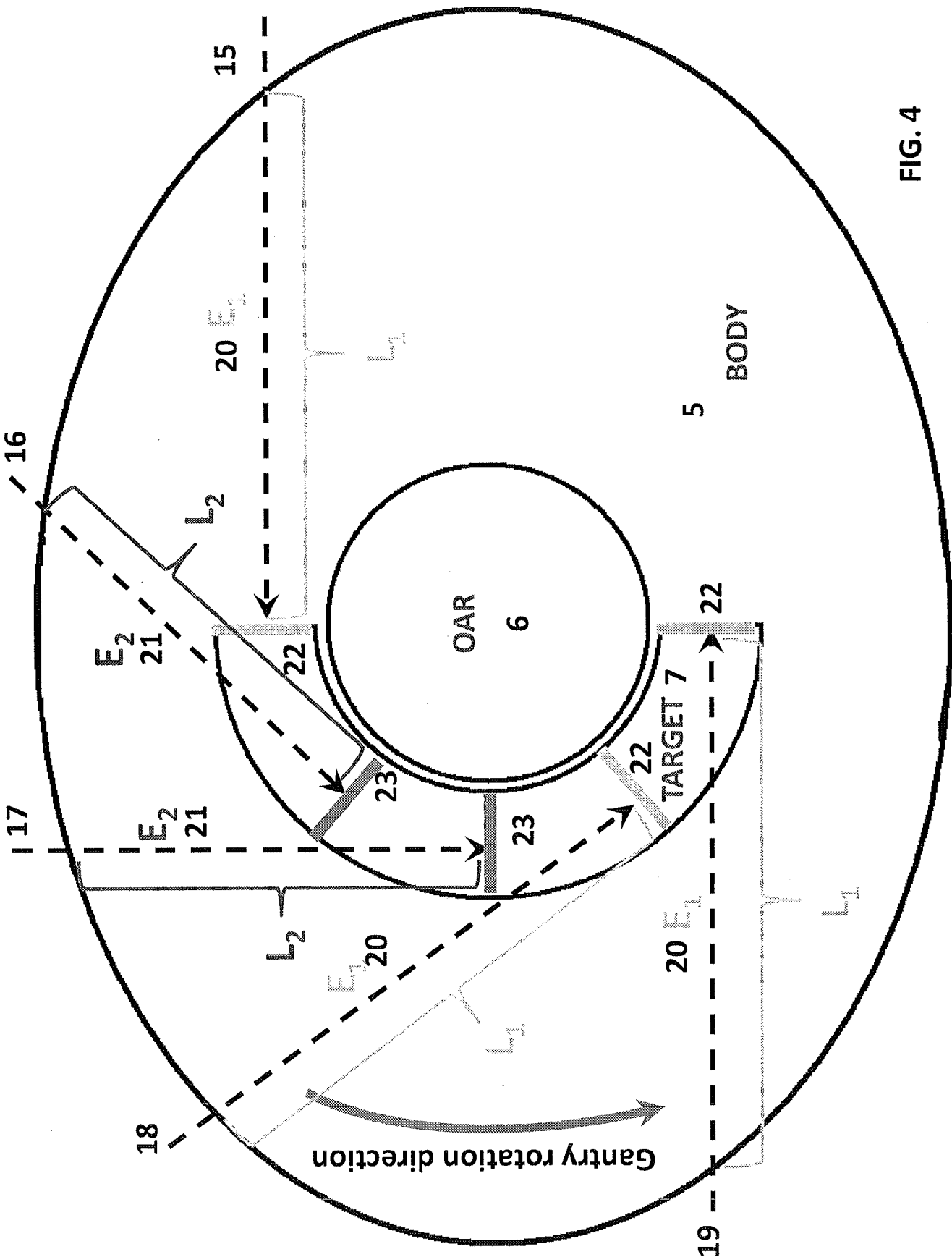
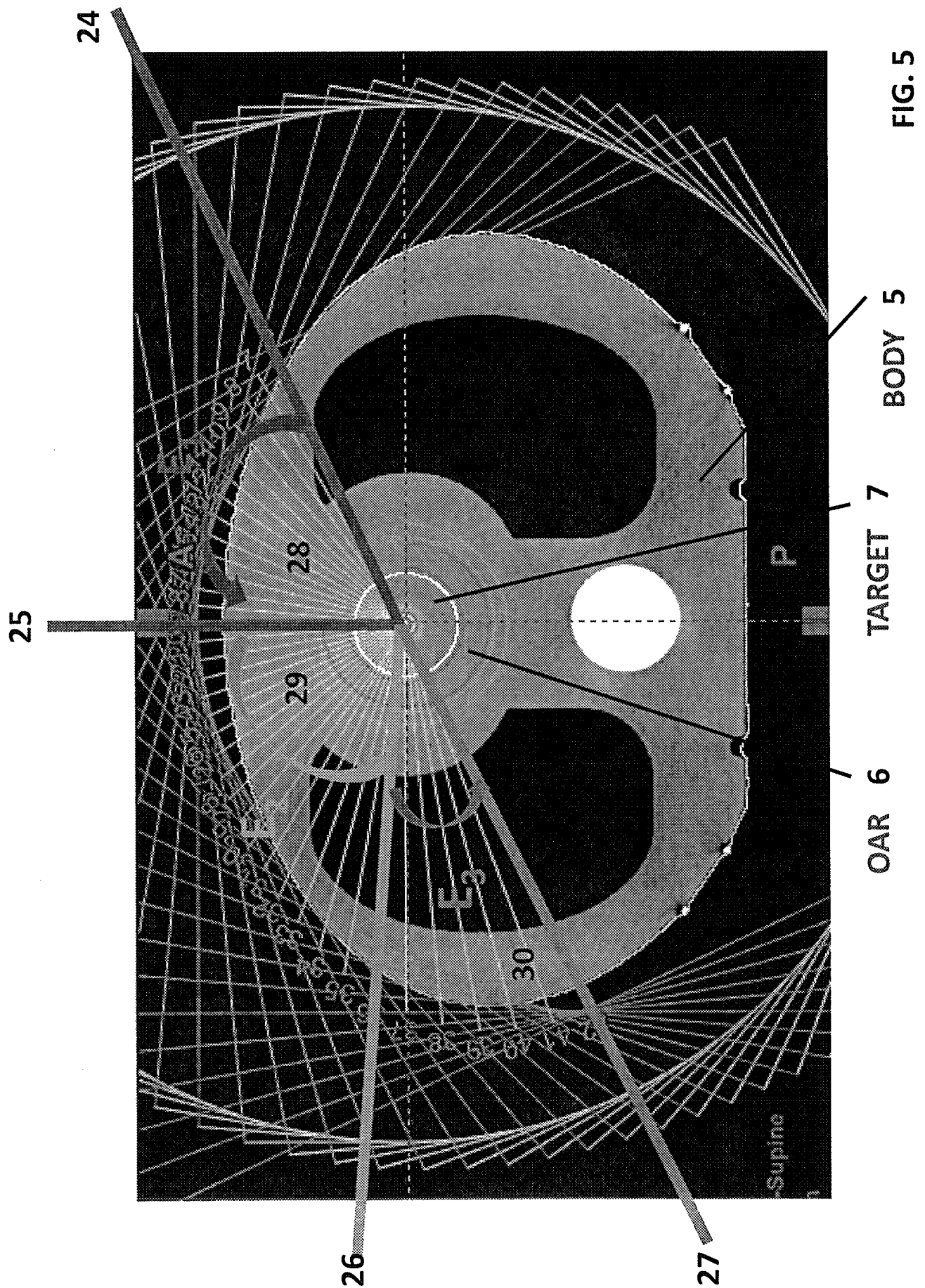
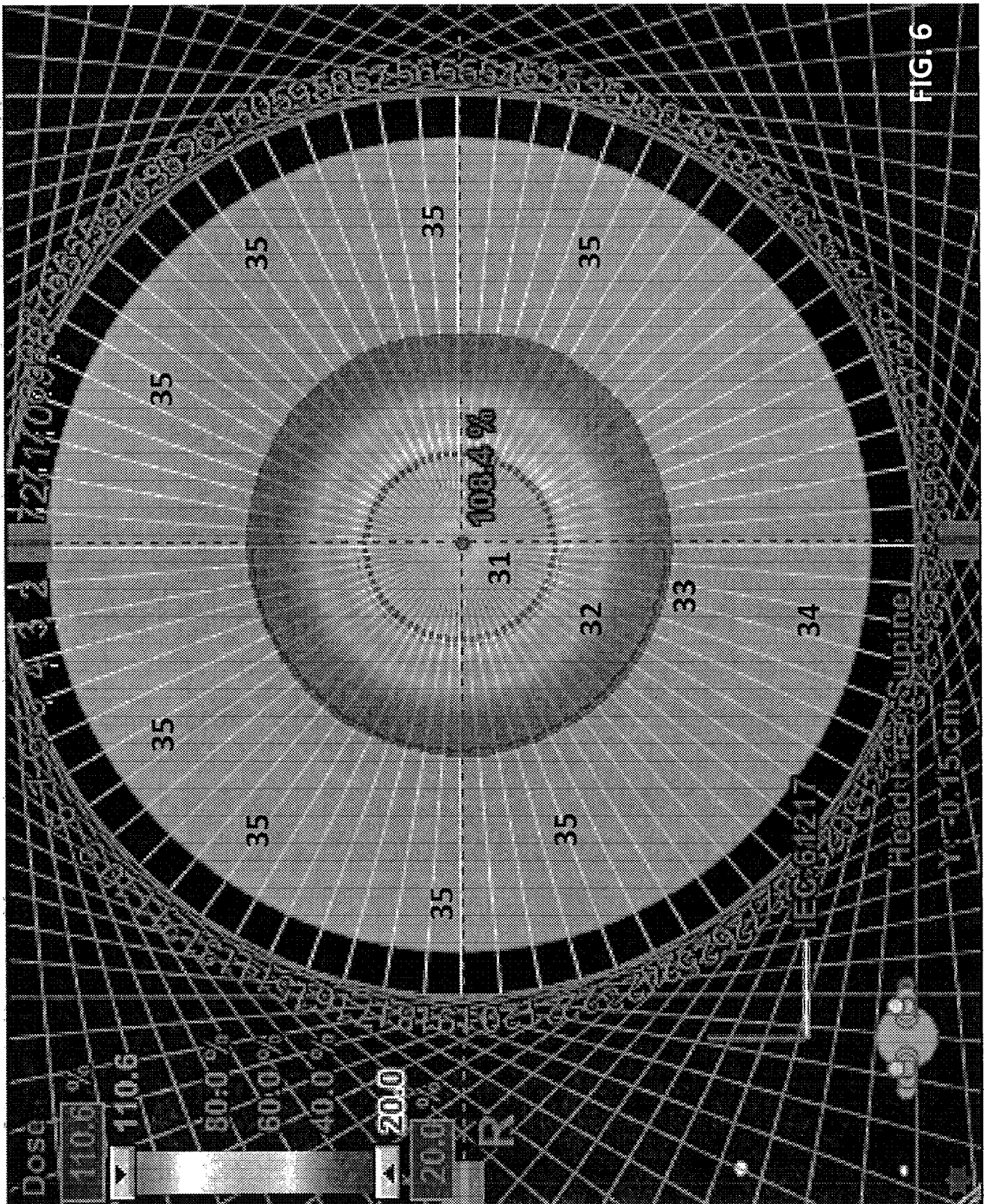


FIG. 4





Fields	Dose Prescription	Field Alignments	Plan Objectives	Optimization Objectives	Dose Statistics	Calculation Models : Plan Sum:				
Fractionation Id	Dose / Fraction [cGy]	Number of Fractions	Total Dose [cGy]	Target Volume	Primary Reference Point [Volume]	Total Dose at Primary [cGy]	Relative Dose at Primary [%]	Prescribed Percentage [%]	Plan Normalization Mode	Plan Normalization Value [%]
F1	500.0	12	6000.0	TARGET FA	TARGET FA [TARGET_FA]	6000.0	100.0	100.0	No plan normalization	100.0

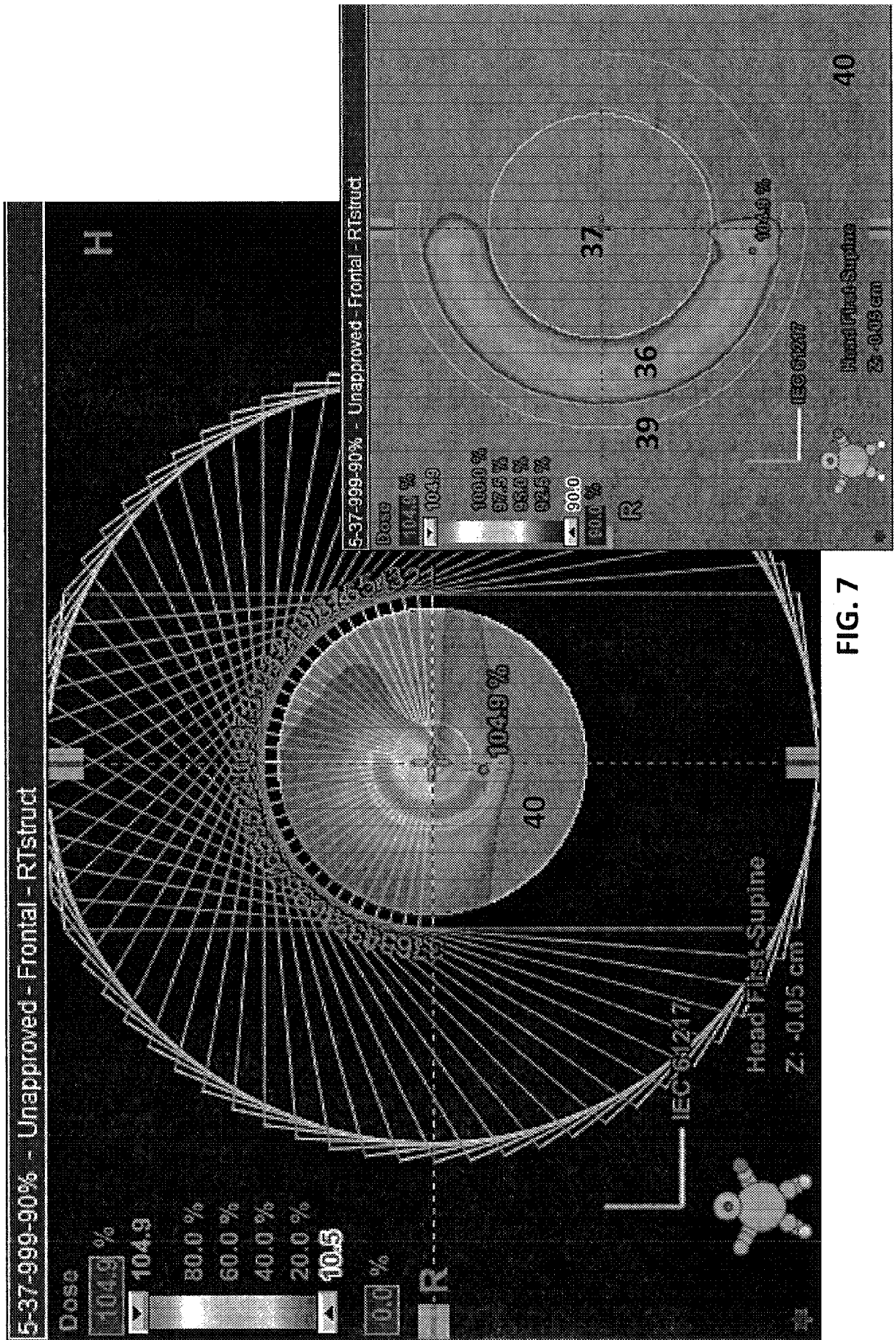


FIG. 7

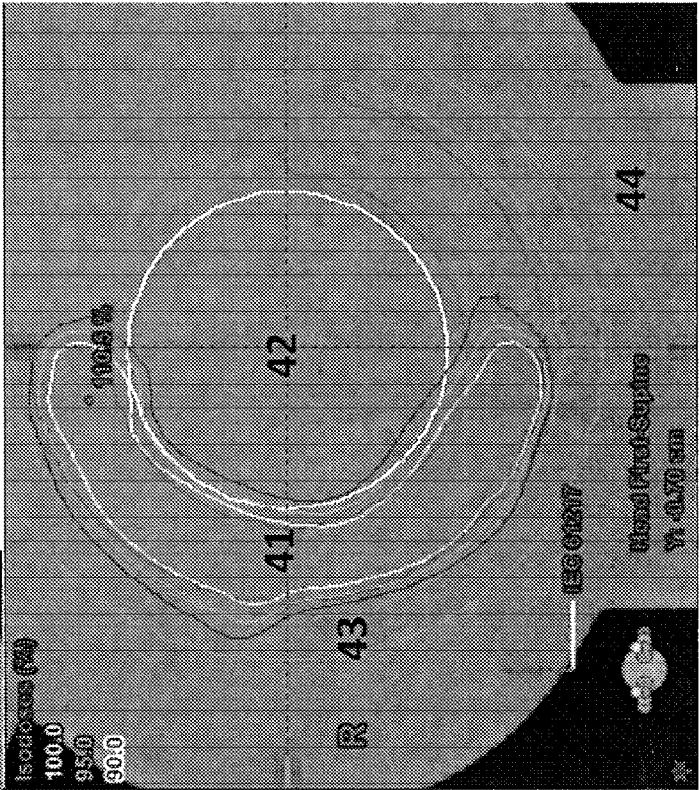
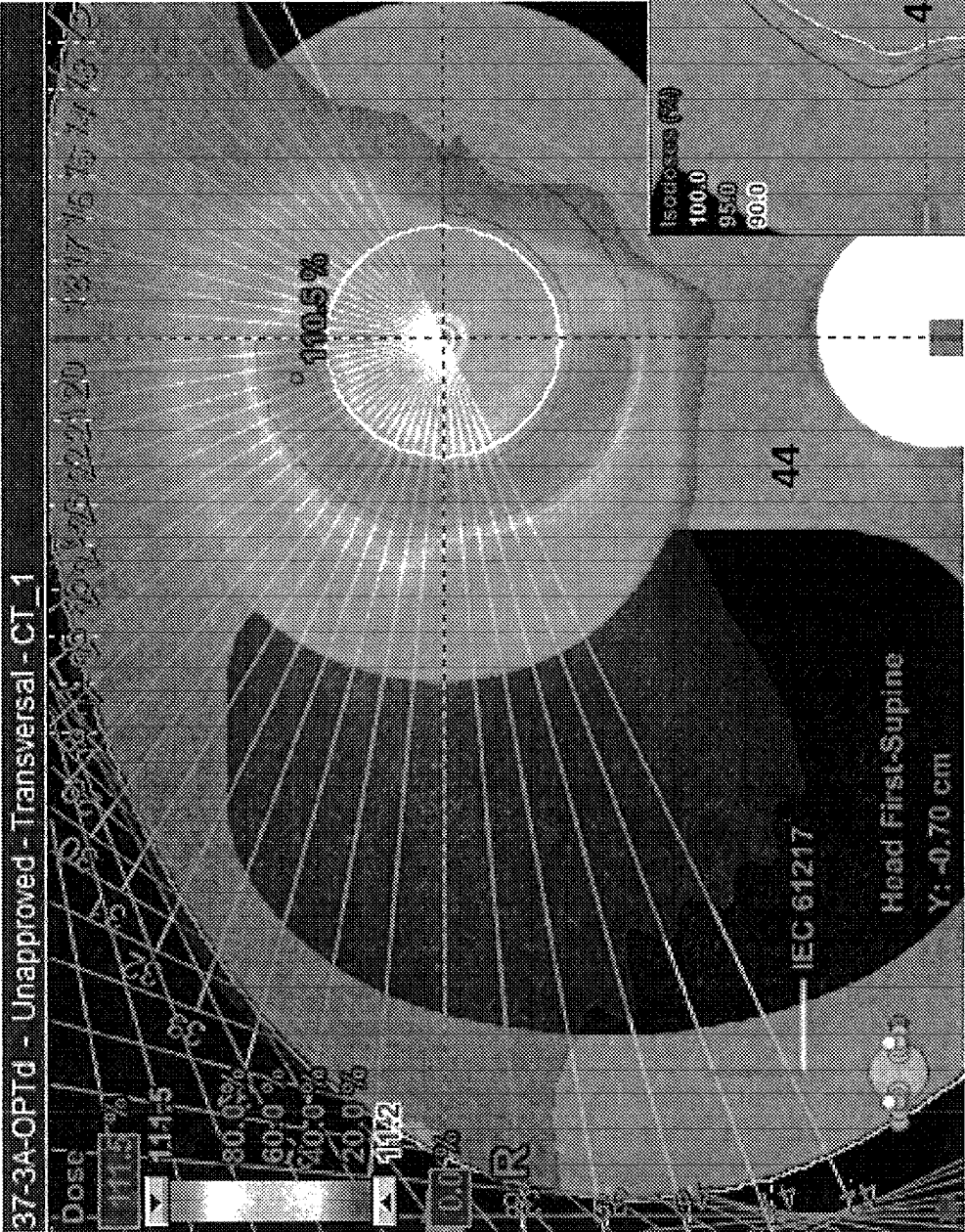


FIG. 8

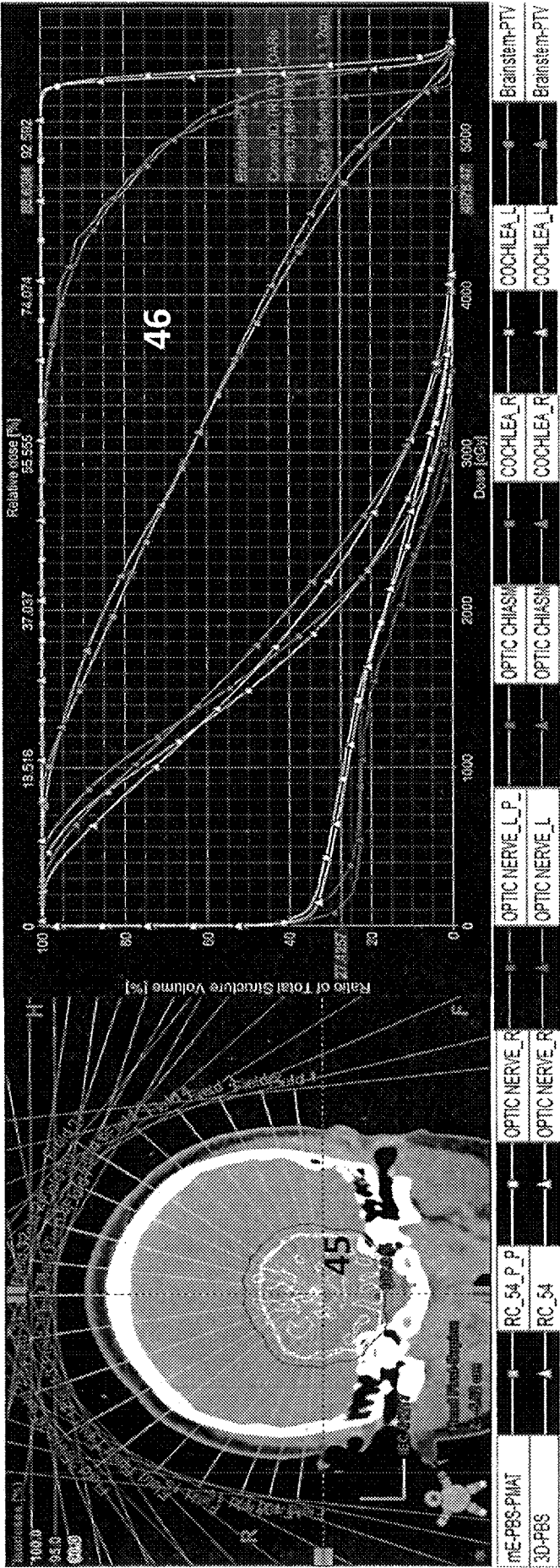


FIG. 9

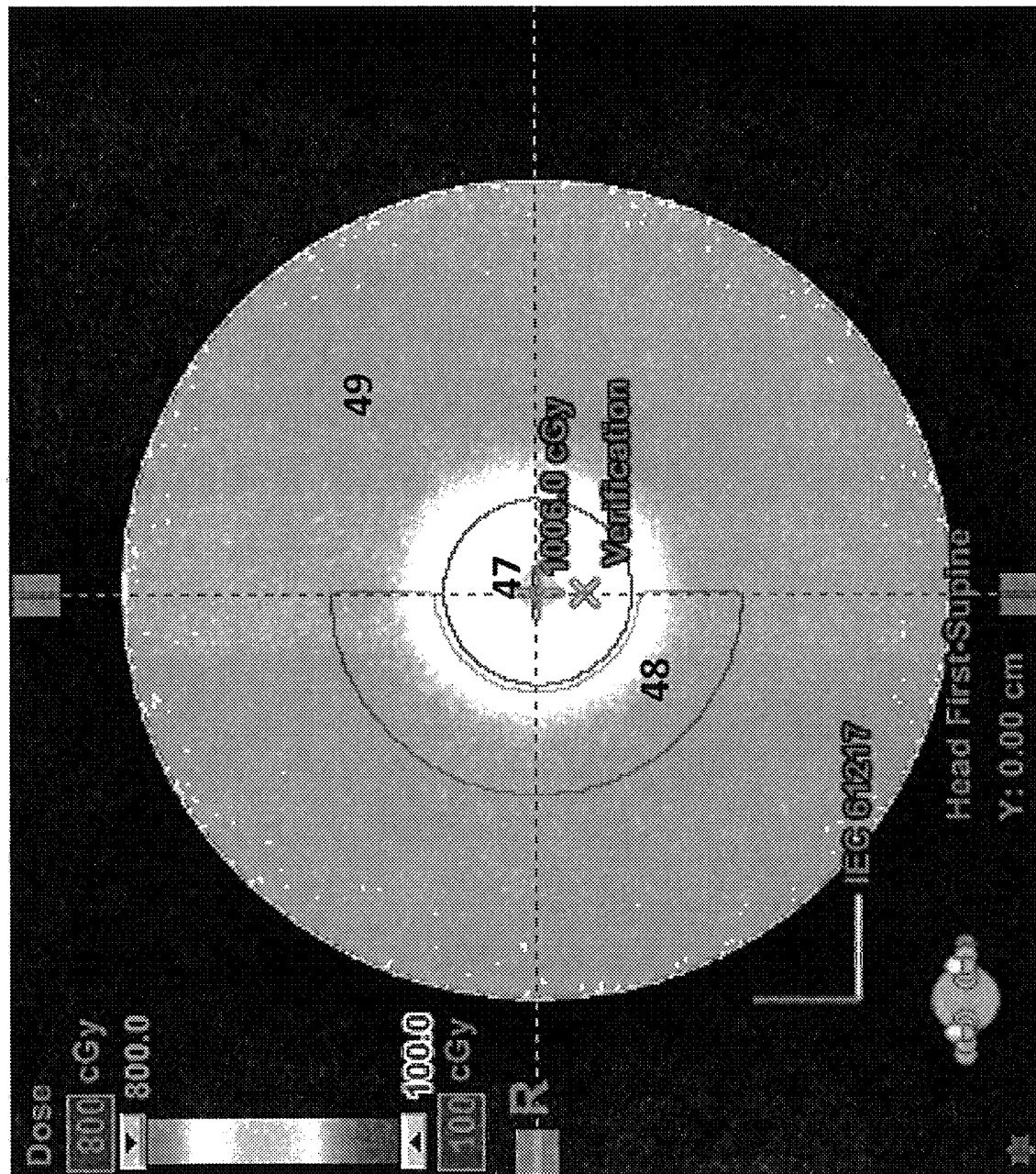


FIG. 10

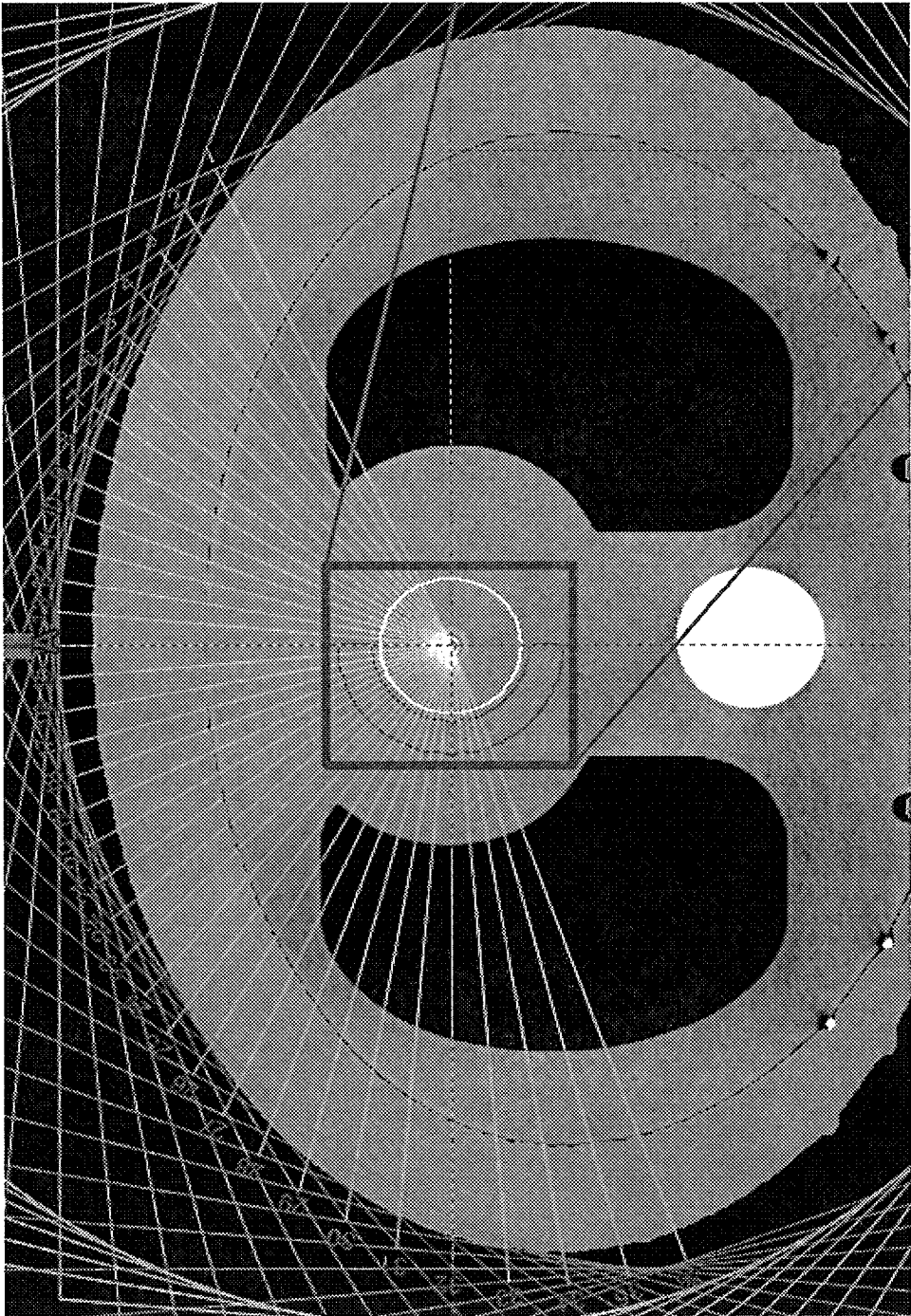


FIG. 11

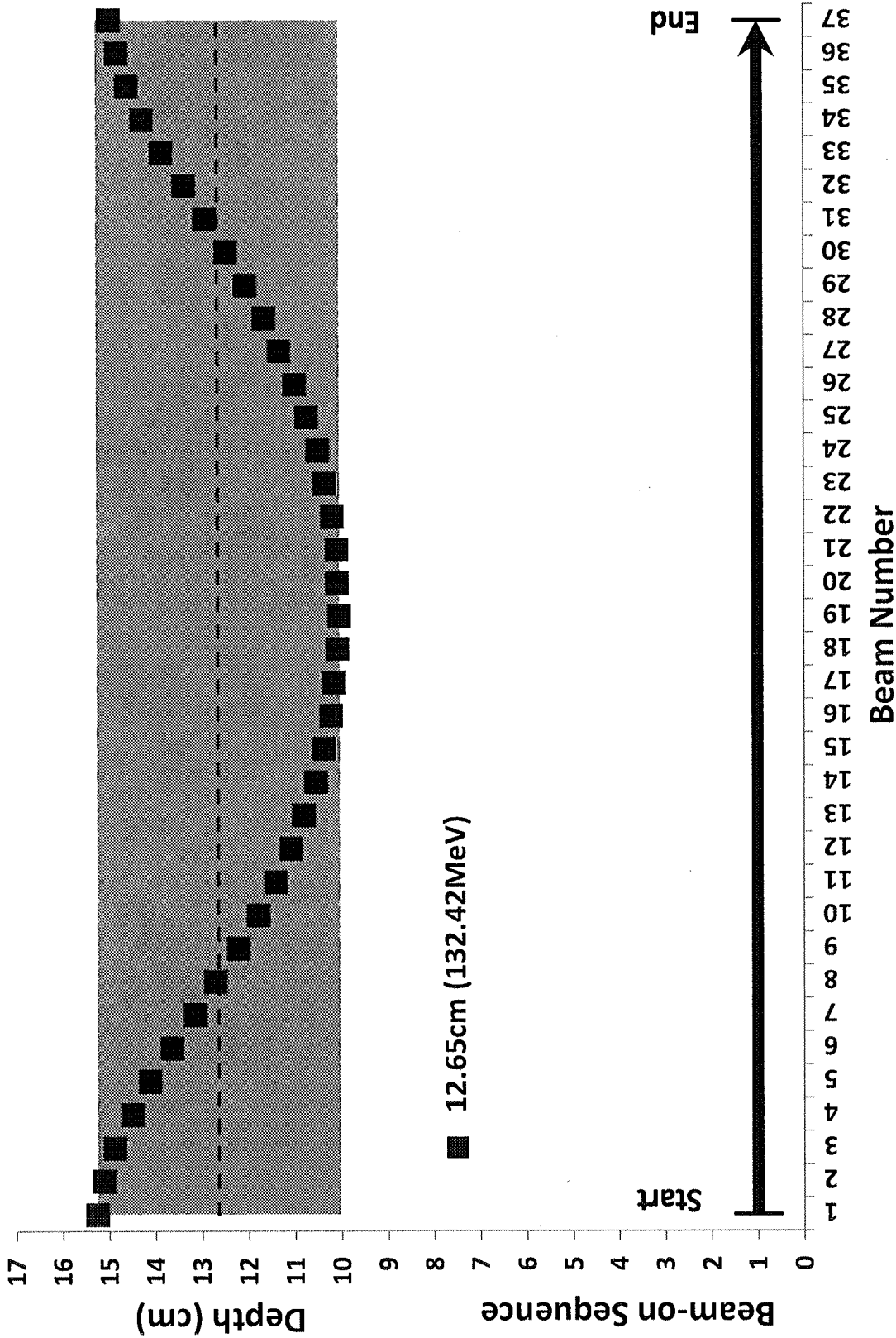


FIG. 12

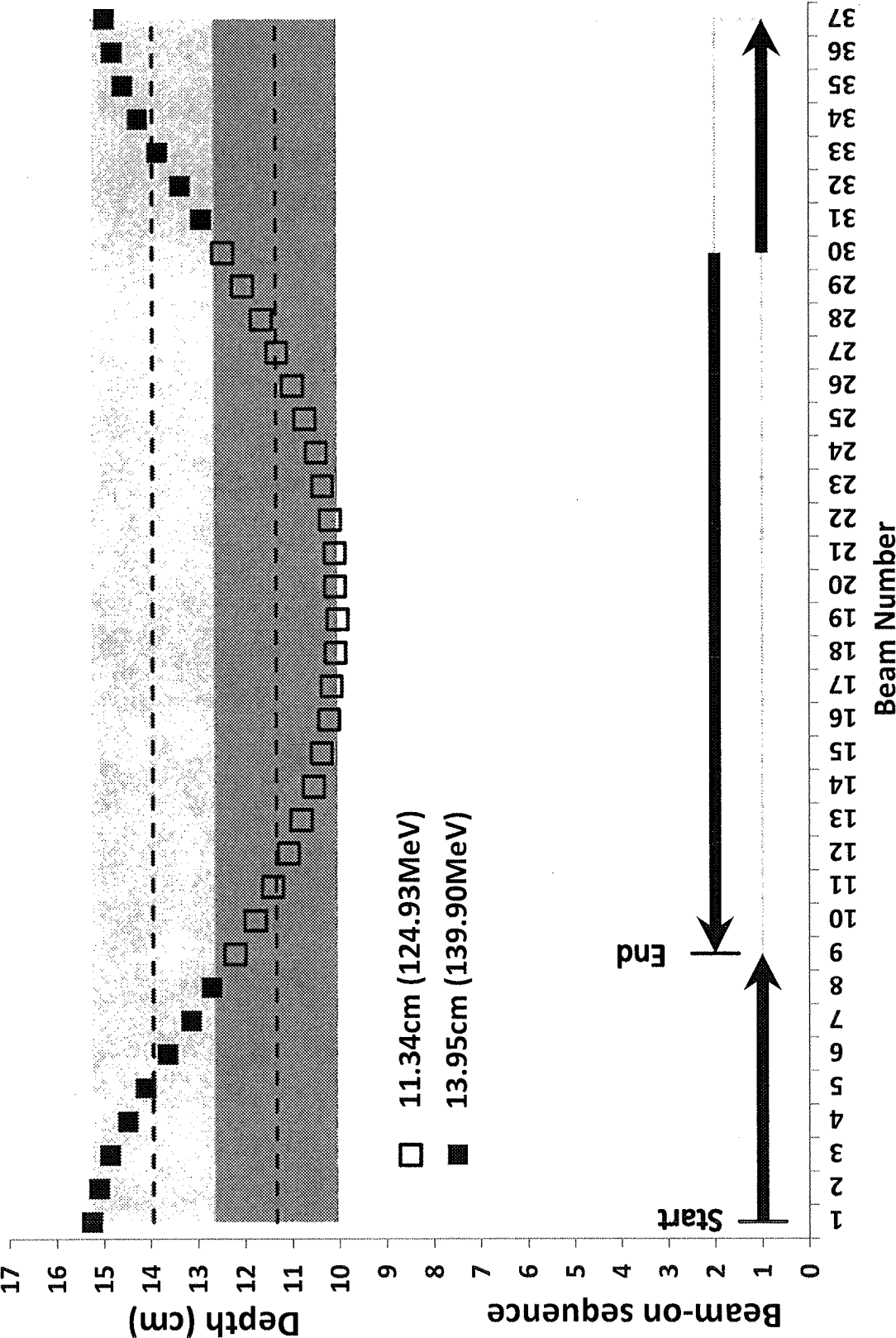


FIG. 13

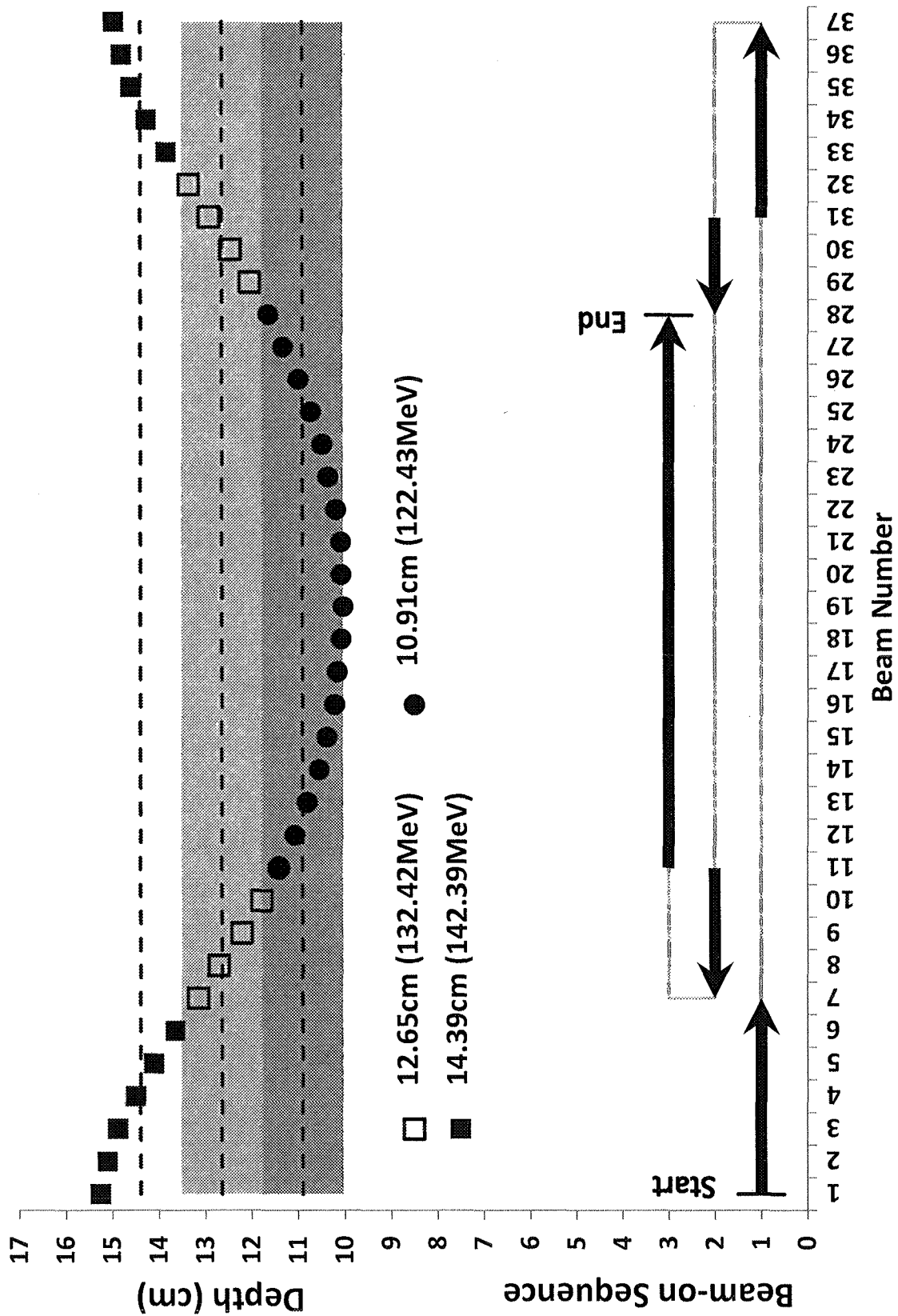


FIG. 14

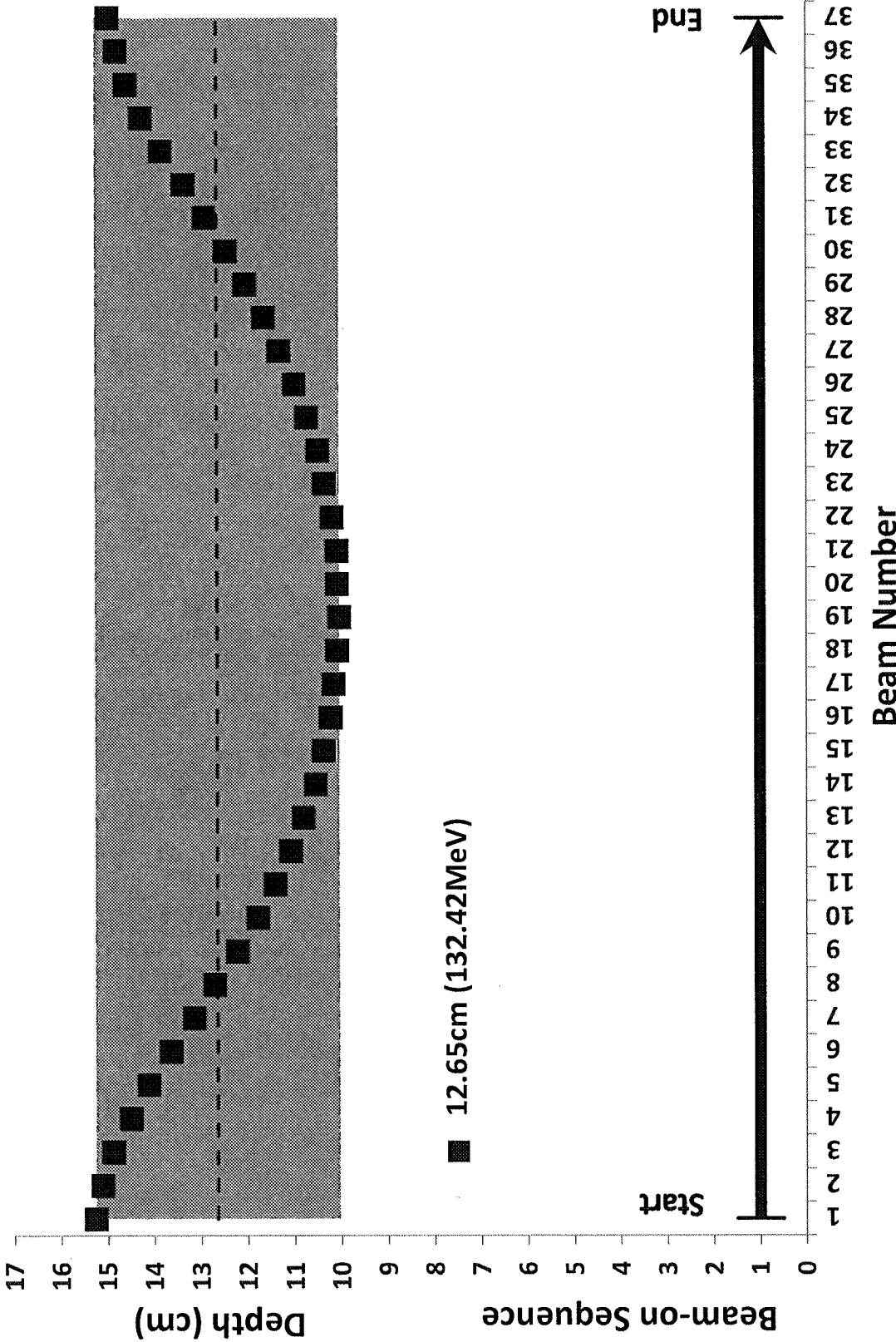


FIG. 15

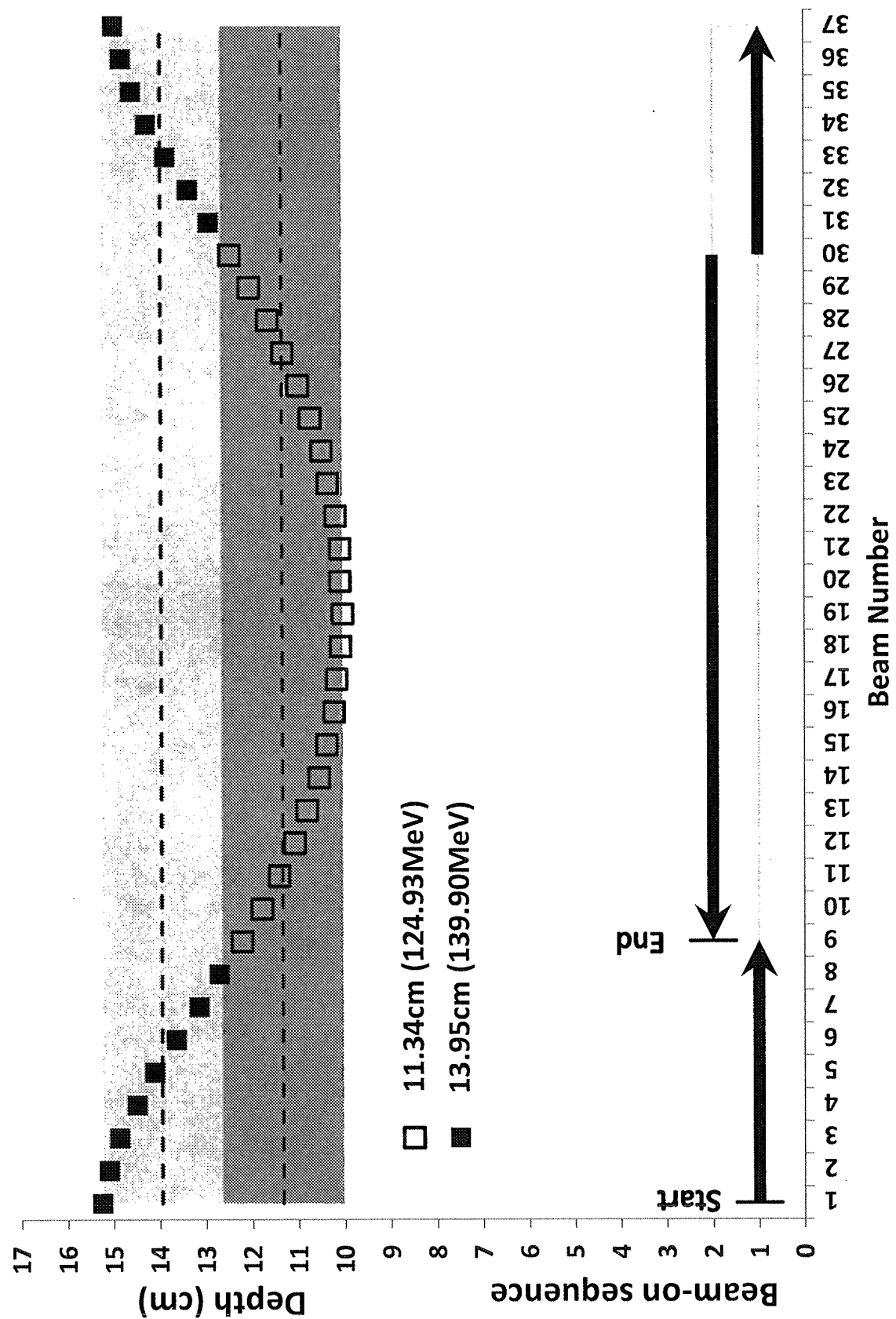


FIG. 16

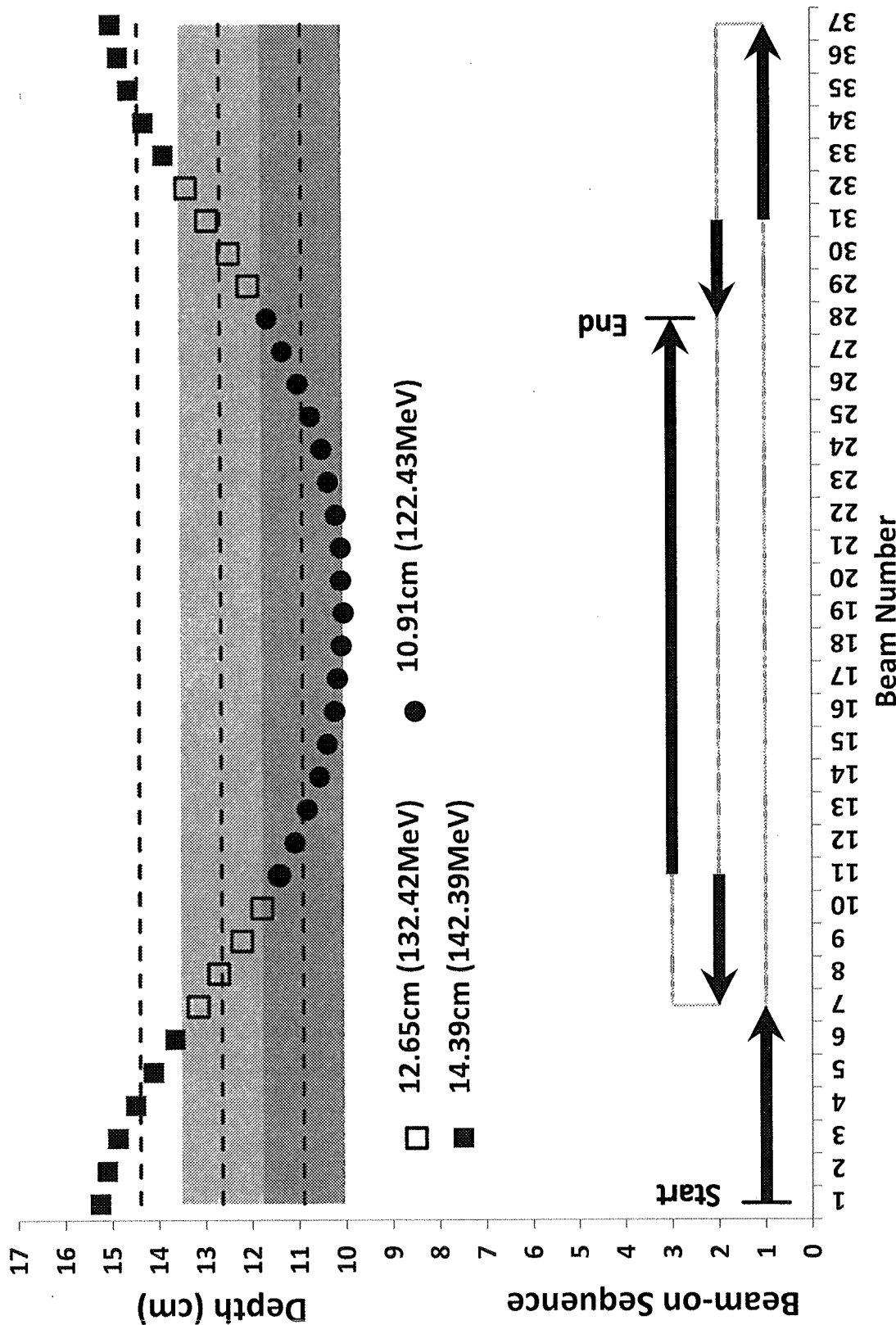


FIG. 17

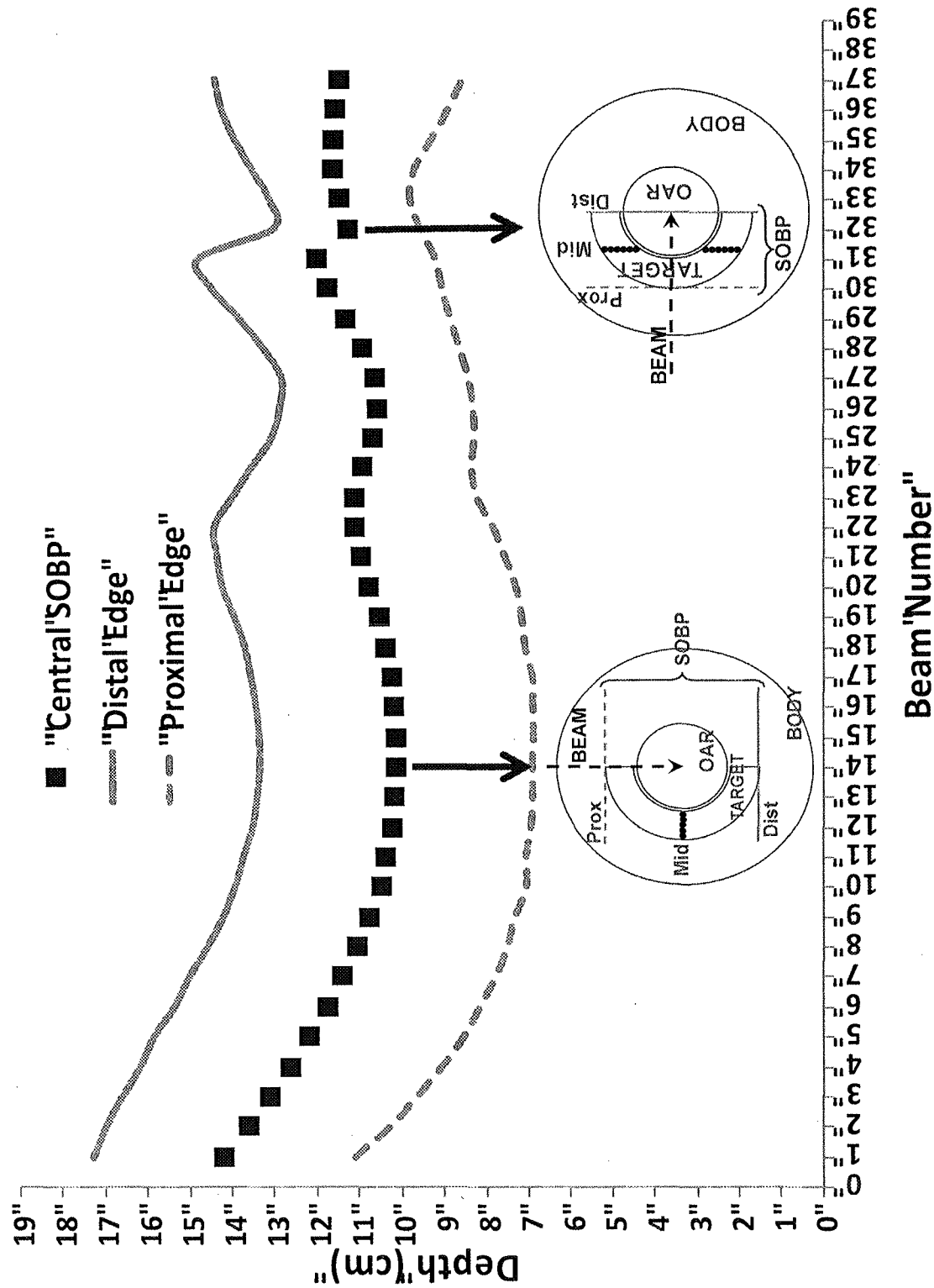


FIG. 18

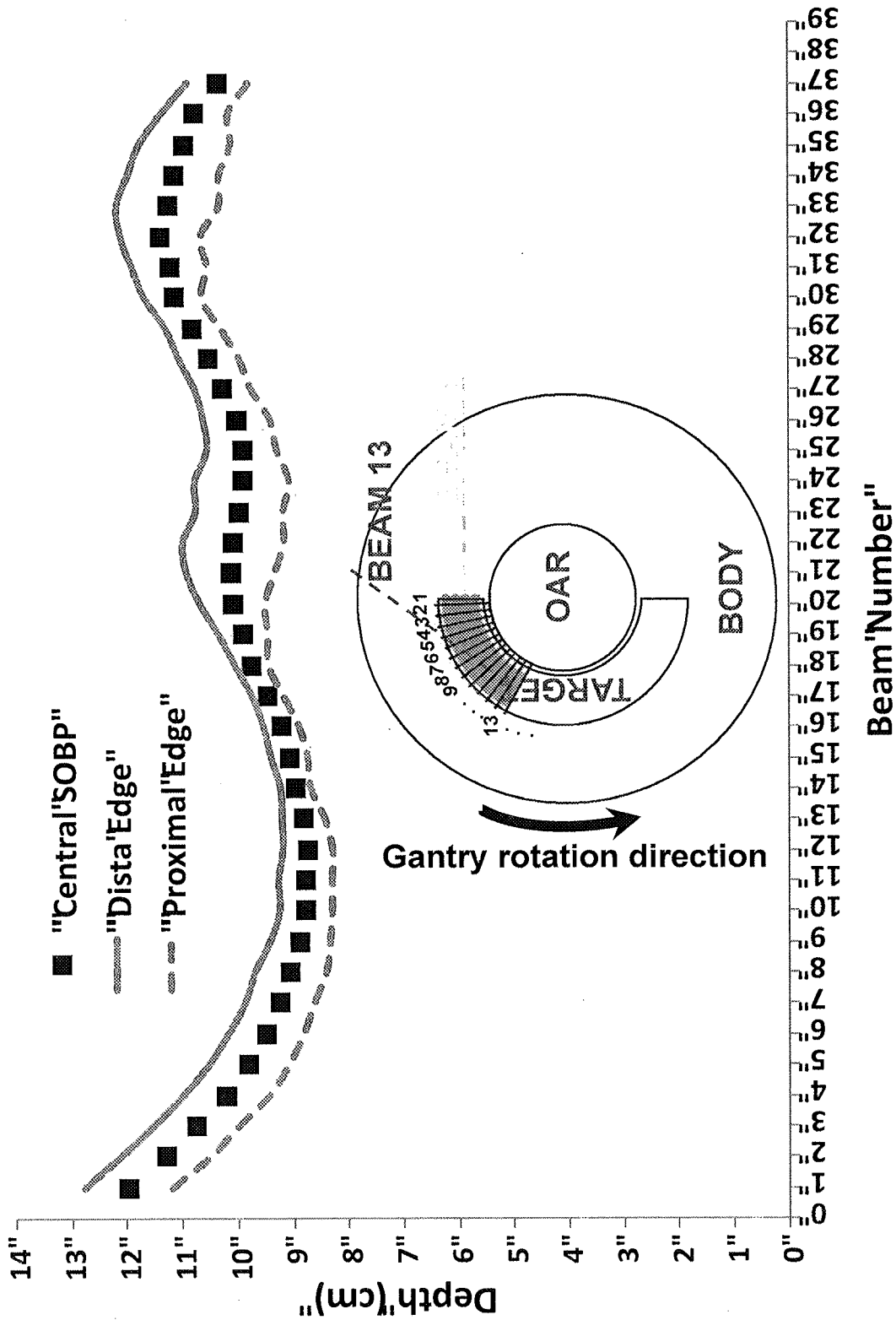


FIG. 19

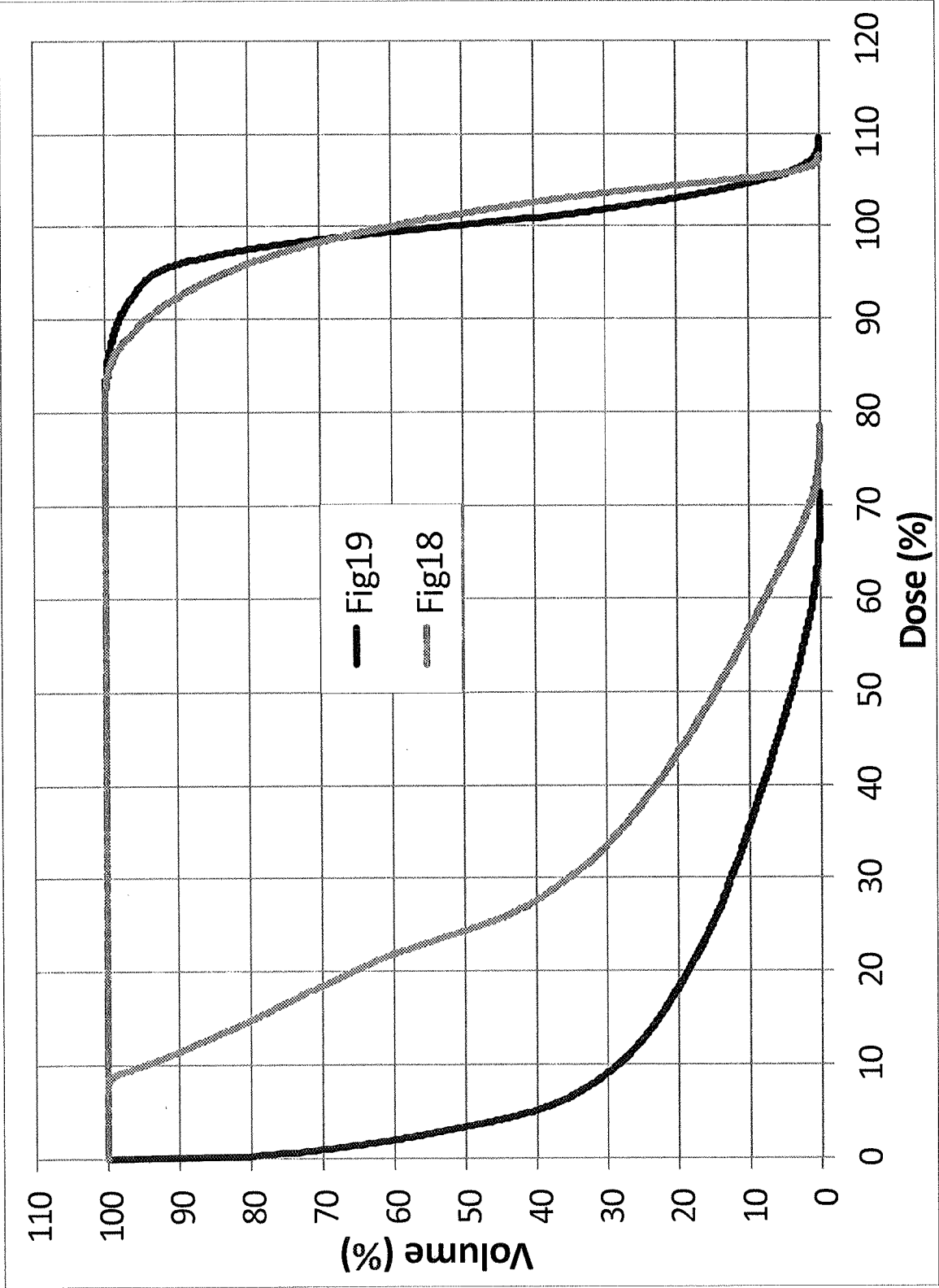


FIG. 20

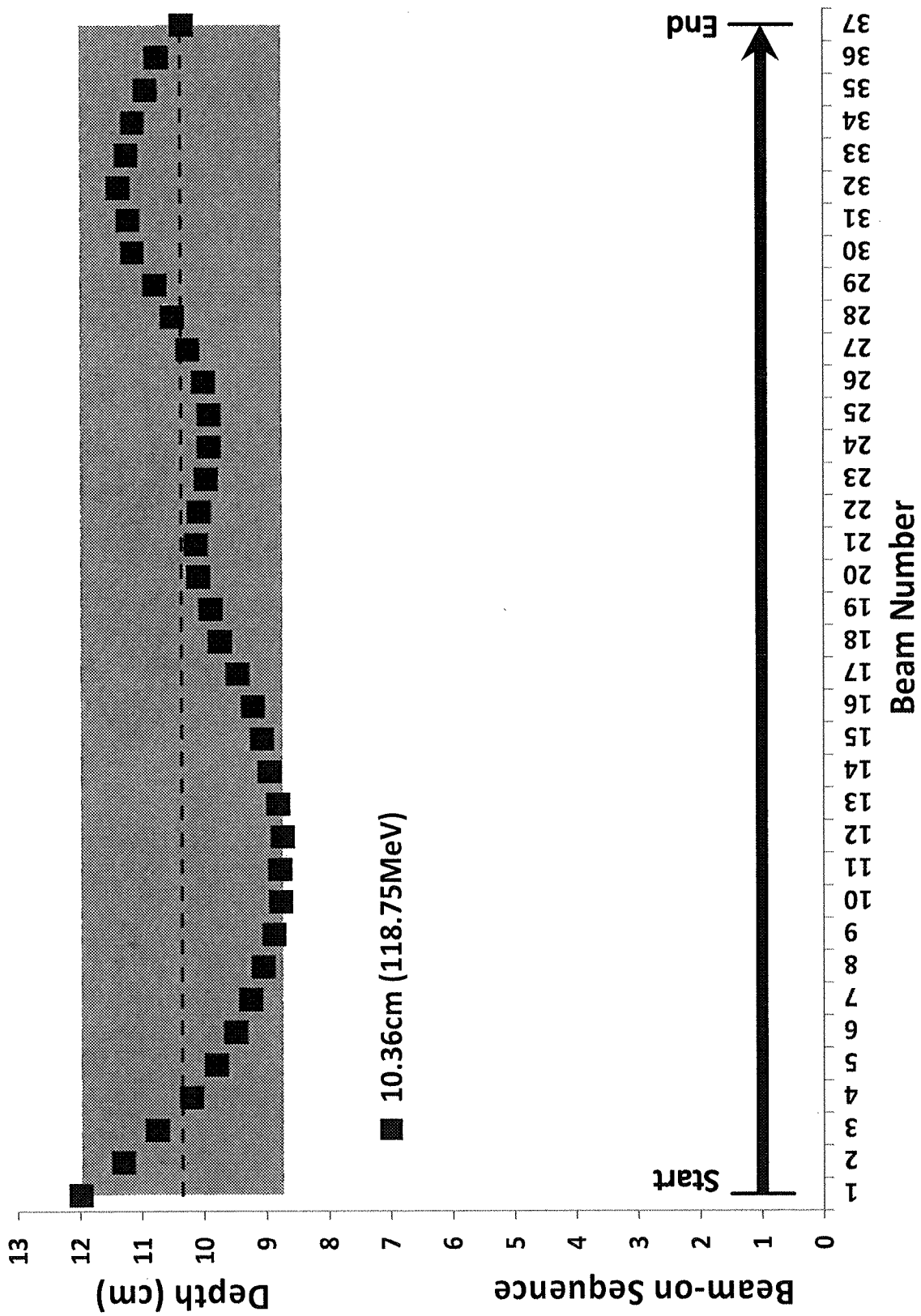


FIG. 21

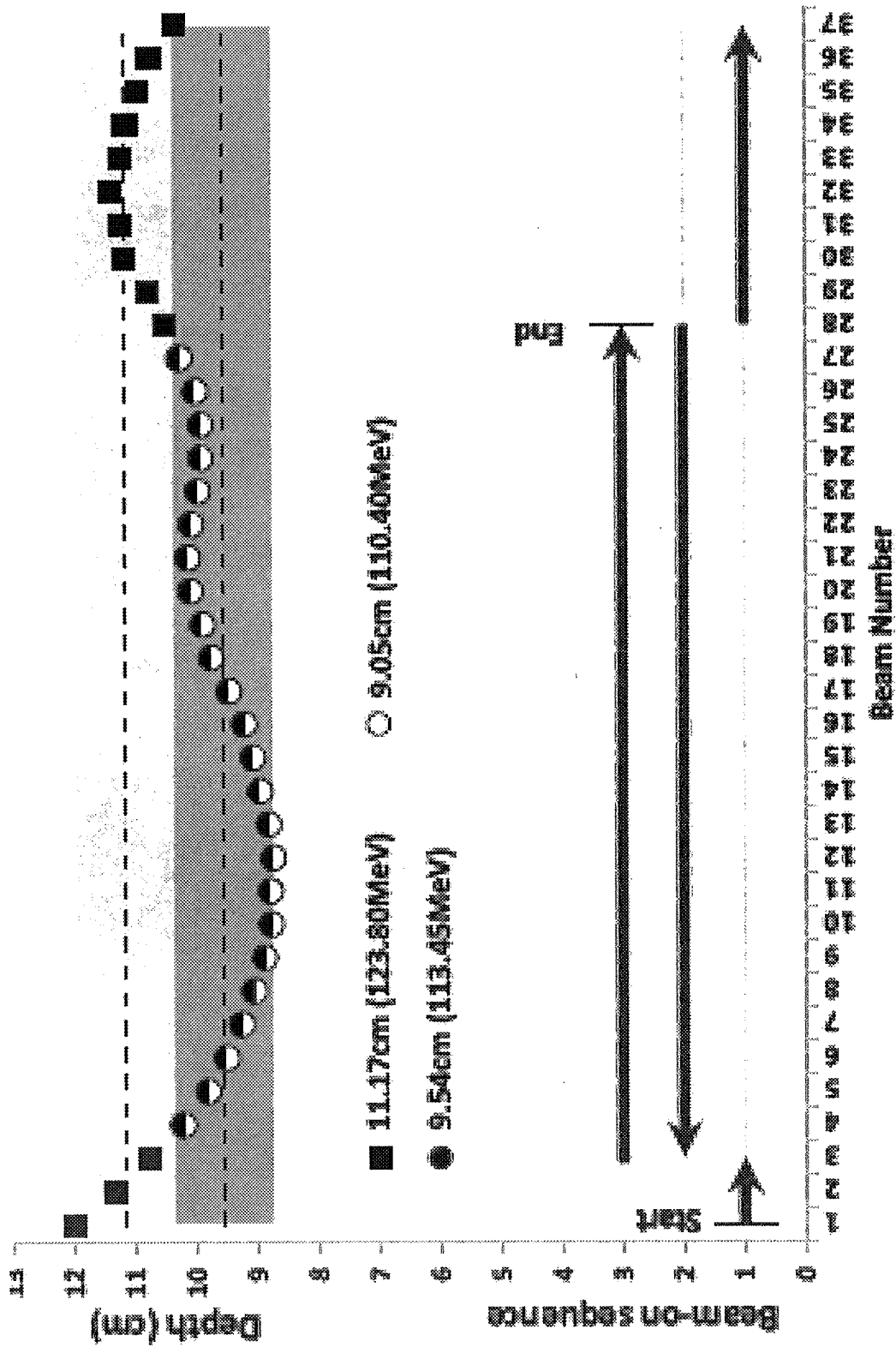


FIG. 22

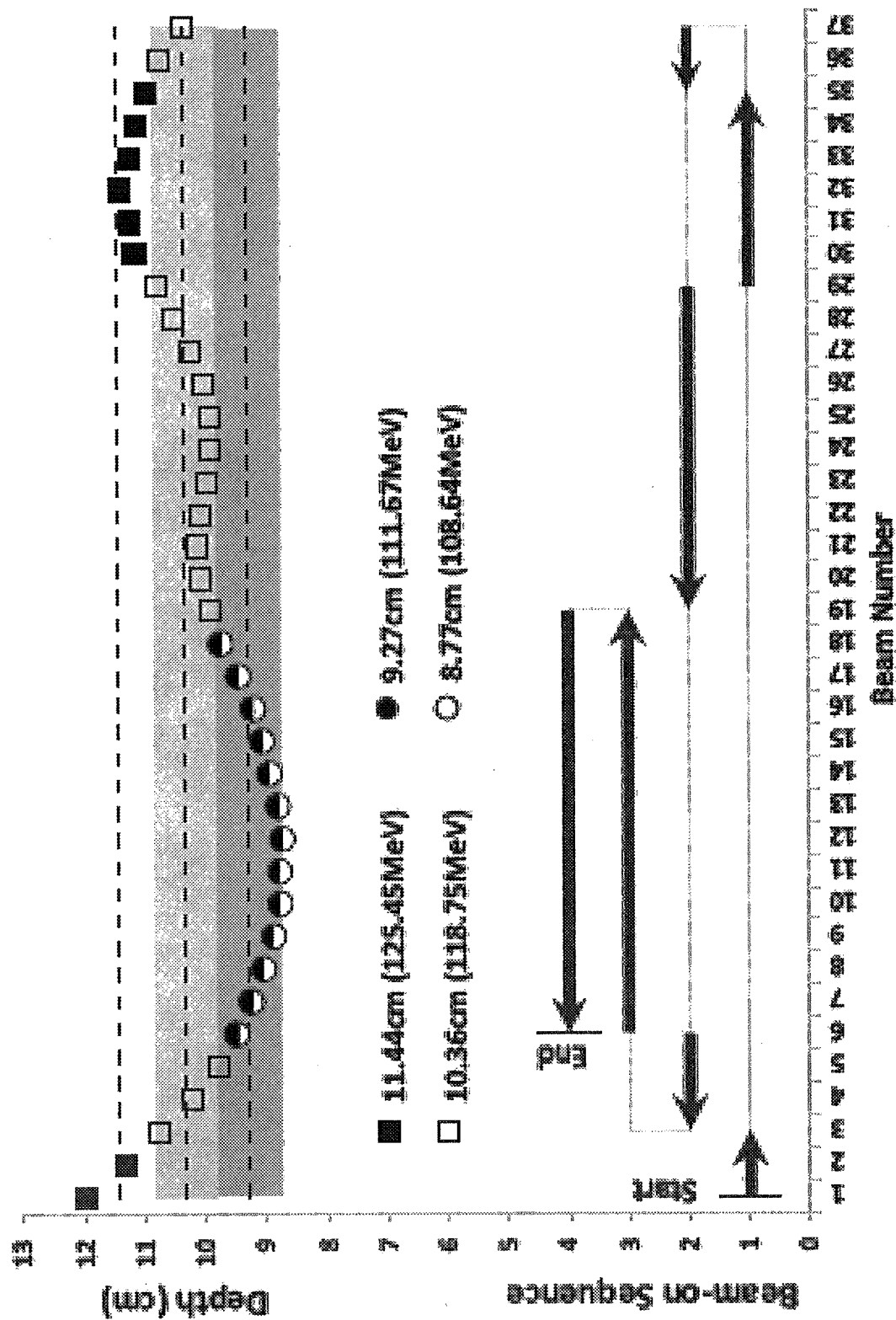


FIG. 23

FIG. 24A

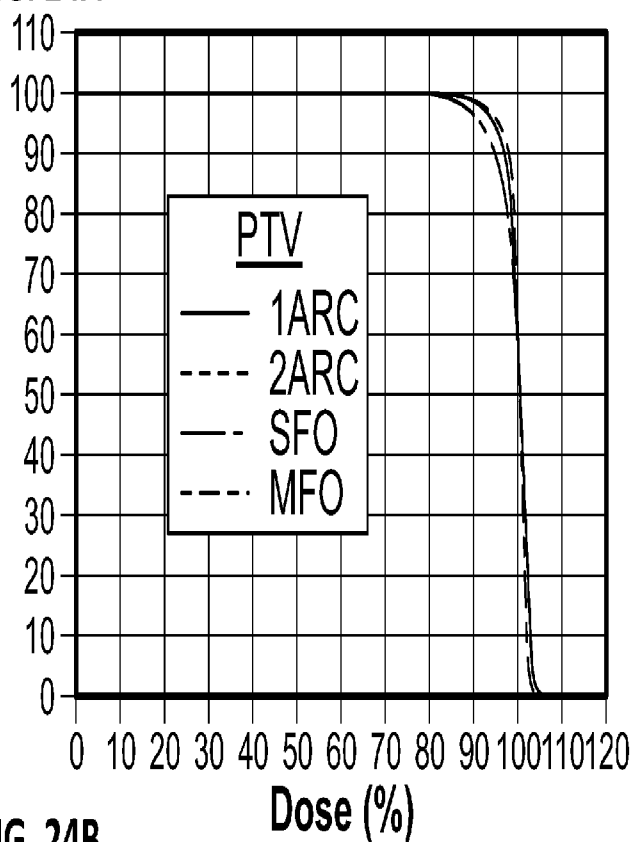


FIG. 24C

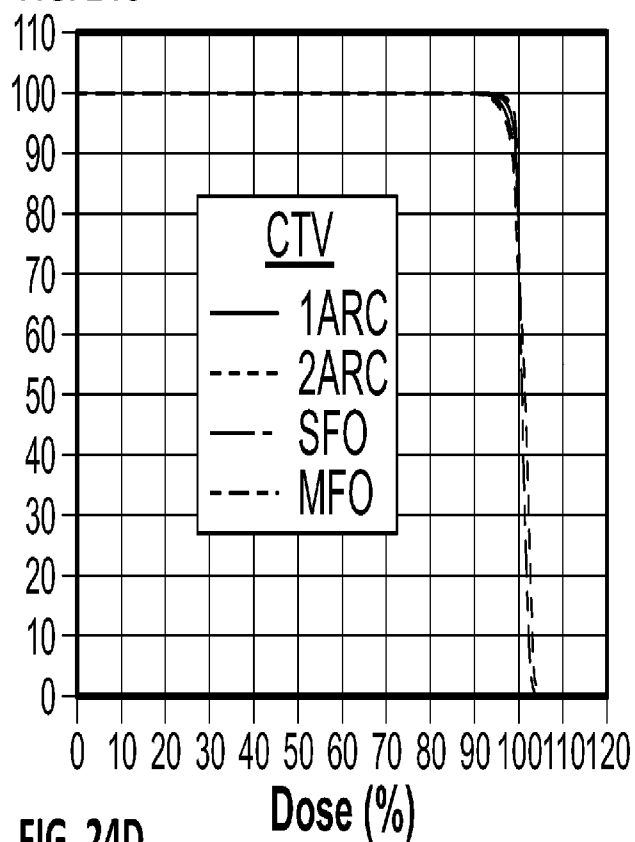


FIG. 24B

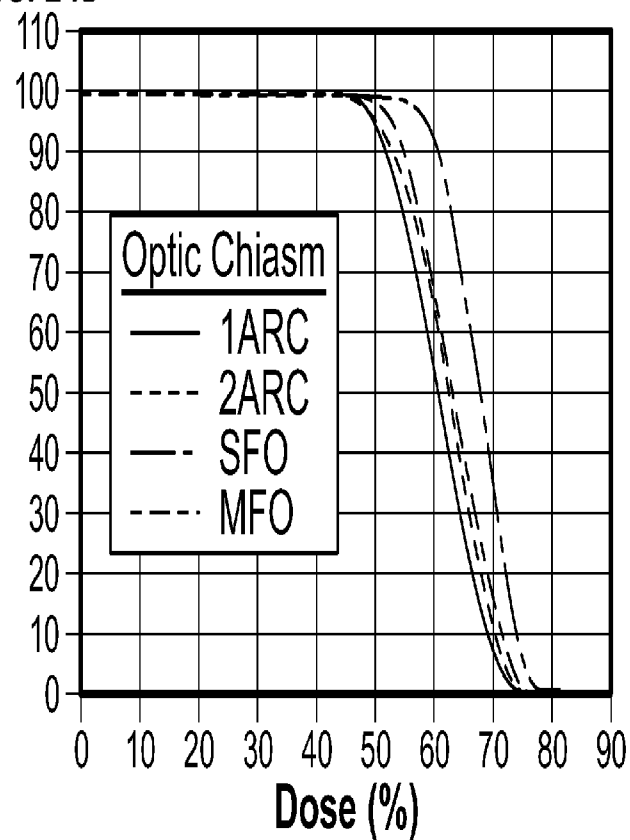


FIG. 24D

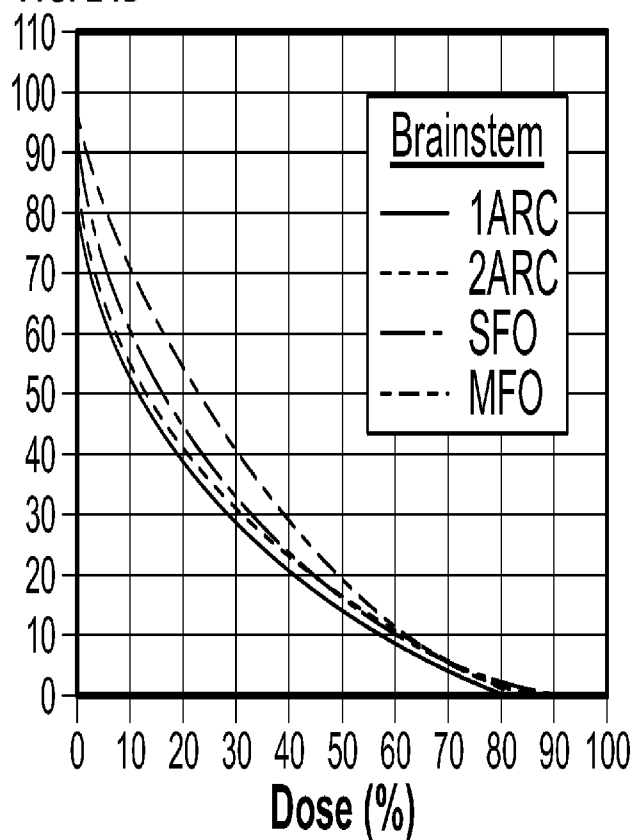


FIG. 25A

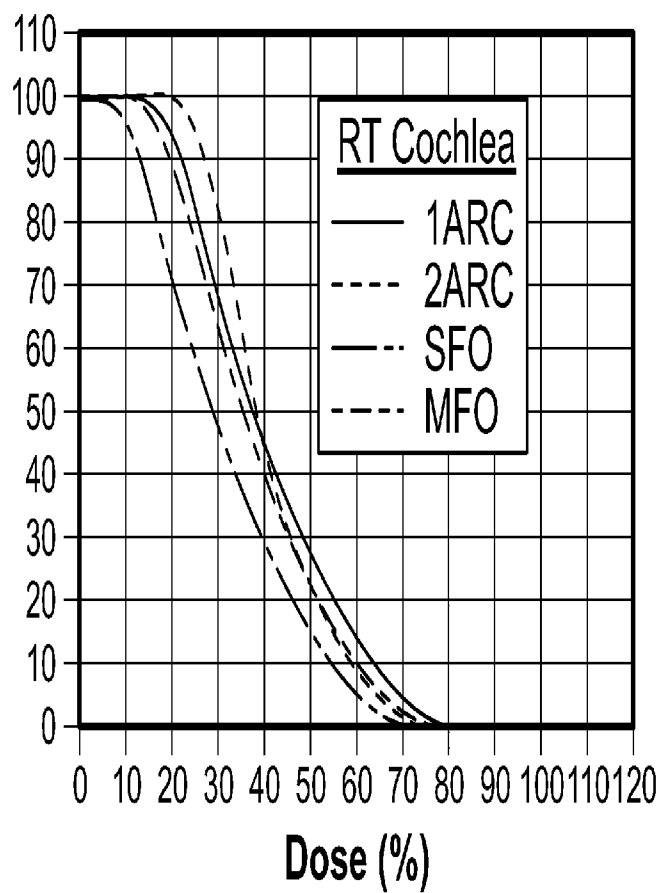
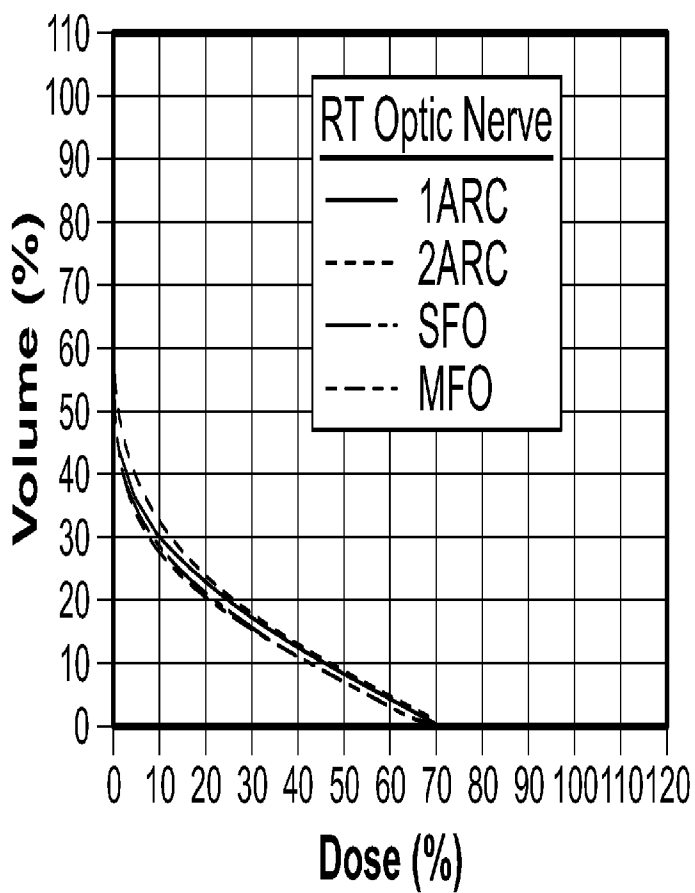


FIG. 25B



INTERNATIONAL SEARCH REPORT

International application No.

PCT/US15/41160

A. CLASSIFICATION OF SUBJECT MATTER

IPC(8) - A61N 5/10; G21K 1/02; H05H 7/12 (2015.01)

CPC - A61N 5/1042, 5/1048, 5/1067

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)

IPC(8): A61N 5/01, 5/10; G21K 1/02; H05H 7/12 (2015.01); CPC: A61N 5/1042, 5/1043, 5/1044, 5/1045, 5/1047, 5/1048, 5/1067, 5/107; G21K 1/043, 1/046; H05H 7/12

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)

PatSeer (US, EP, WO, JP, DE, GB, CN, FR, KR, ES, AU, IN, CA, INPADOC Data); Google; Google Scholar; ProQuest; KEYWORDS: irradiating planning target volume charged particles therapy system beam path patient positioning device rotate arc energy level Bragg peak

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 2009/0296885 A1 (BOEH, L. et al.) December 3, 2009; figure 1; paragraphs [0023-0028, 0041-0045]	1-21
A	US 7,692,168 B2 (MORIYAMA, K. et al.) April 6, 2010; entire document	1-21
E, Y	US 2015/0041665 A1 (THE TRUSTEES OF THE UNIVERSITY OF PENNSYLVANIA) February 12, 2015; entire document	1-21

☐ Further documents are listed in the continuation of Box C.☐ See patent family annex.

* Special categories of cited documents:

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

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"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

29 September 2015 (29.09.2015)

Date of mailing of the international search report

23 OCT 2015

Name and mailing address of the ISA/

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