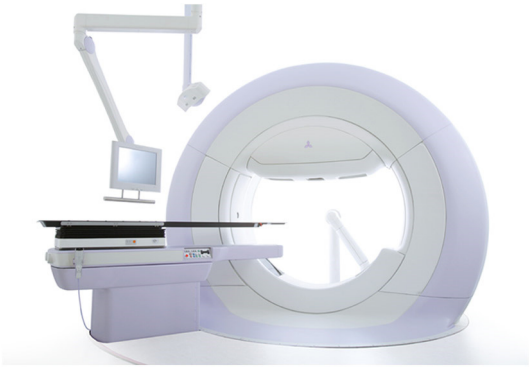
The Challenge of Innovative Cancer Treatments Enabled by Vero4DRT -Development of High-precision Dose Delivery Features for Reducing Radiation Exposure of Healthy Tissue-



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In recent years, radiation therapy outcomes have improved significantly because of the ceaseless efforts of healthcare professionals, as well as the new developments and widespread availability of high-precision radiation therapies, which were realized by the increased sophistication of control and computing technologies and the intensive and accurate delivery of radiation beams to the target tumor, while minimizing damage to the surrounding healthy tissue. On the other hand, there has been a growing need for the "more efficient" delivery of high-precision radiation therapies because of the increase in the number of cancer patients waiting for treatment. This report introduces "Vero4DRT," our radiation therapy equipment sold under the "MHI-TM2000 Linear Accelerator System" brand name. Utilizing its unique hardware structure and configuration, this system has made it possible to establish a truly innovative beam delivery method for achieving further improvements in radiation therapy outcomes.

1. Introduction

Radiation therapies have been developed along with the progress of beam delivery technologies for increasing beam concentration. "Three-dimensional (3D) conformal radiation therapy" was first developed in 1960. It was further developed into "3D conformal radiation therapy with a multi-leaf collimator (MLC)," which is moving beam radiotherapy with an MLC-shaped aperture created to fit the radiation beam shape/radiation field to the 3D shape of the tumor.

In 1994, a new beam delivery method called "intensity-modulated radiation therapy (IMRT)," in which the beam intensity in each radiation field is modulated and controlled appropriately, was developed in the U.S. IMRT plays a central role in high-precision radiation therapies, together with "stereotactic radiotherapy (SRT)" and "stereotactic radiosurgery (SRS)."

The next dramatic evolution that occurred in radiation therapy was "a movement from 3D treatment to four-dimensional (4D) treatment," by which tumor movement due to respiration and other factors could be handled by motion management technology.

"Respiratory-gated radiotherapy," the first method for treating moving targets with motion management technology, was developed in 1999. In this method, a beam is delivered to a moving target only when it enters the radiation field.

In 2011, the world's first "dynamic tracking radiotherapy," in which a beam is delivered to a moving target by tracking it continuously with real-time monitoring, was performed on a lung cancer patient using Vero4DRT at Kyoto University Hospital.

From the beginning of the 21st century, there has been rapid progress in high-precision radiation therapies through the integration of "beam control" and "image processing" technologies

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(i.e., image-guided radiotherapy; IGRT), resulting in the widespread availability of these therapies.

Mitsubishi Heavy Industries, Ltd. (MHI) has been engaged in the development, manufacturing, marketing and sales of Vero4DRT, with a desire to contribute to conquering cancer through the development of innovative beam delivery methods.

2. Unique characteristics of equipment configuration and structure

Vero4DRT is high-precision image-guided radiotherapy equipment, and the entire system was developed as an integrated system of "beam delivery techniques" and "imaging technologies" from the very beginning of its design. The entire structure, configuration and the sub-devices mounted on Vero4DRT were also designed to realize "dynamic tracking radiotherapy," which is high-precision beam delivery technology for tumors that move inside the body due to respiration and other factors (**Figure 1**).

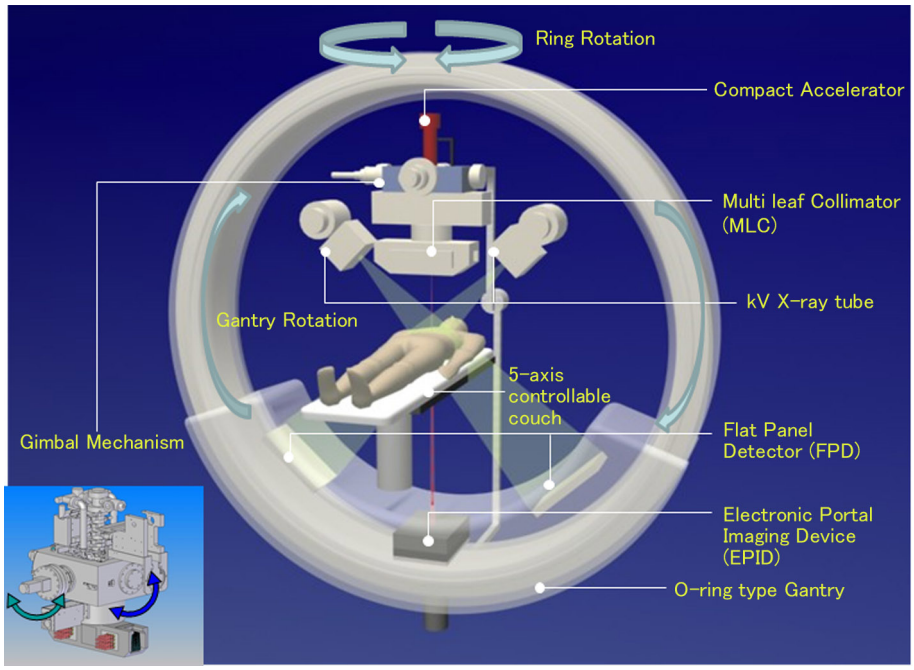

Figure 1 System Structure and Configuration of Vero4DRT

As Vero4DRT is highly flexible in its structure, configuration and mechanisms, both individual and synchronized controls are available. Therefore, new innovative beam delivery techniques can be added by upgrading the software.[1,2,3,4]

(1) A highly-rigid O-ring type gantry makes it possible for the tumor to be targeted by a therapeutic X-ray beam from any angle or direction along the gantry with high precision.

(2) Beam delivery from any angle or direction is available not only in the "coplanar" plane (an imaginary plane perpendicular to the patient lying on the couch) with gantry rotation, but also at the "non-coplanar" points (outside of the coplanar plane) with ring rotation. The "coplanar" and "non-coplanar" beam deliveries (gantry and ring motions) are separately controllable. This function therefore enables multiport radiation therapy, including both coplanar and non-coplanar beam deliveries, without changing the patient's posture (couch position or robotics angle).

(3) Neither of the two unique devices, which are shown below, can be found on any radiation therapy system other than Vero4DRT. With these devices, Vero4DRT can not only correct a minute displacement of the therapeutic beam axis, but also allow a therapeutic beam to track a moving tumor in real time.

One of these devices is a "compact C-band standing wave accelerator" that delivers therapeutic X-ray beams. It is one-third the size of traditional accelerators and has been equipped with radiation therapy equipment for the first time anywhere in the world.

The other is a "gimbal mechanism," on which the X-ray head (accelerator system) and MLC (multi-leaf collimator) are mounted. It enables therapeutic X-ray beams to move and swing.

(4) Two types of imaging systems are built into the O-ring gantry ("all-in-one" system). One system consists of two pairs of "a kV X-ray tube and a flat panel detector (FPD)." In the other system, "an electronic portal imaging device (EPID)" is used to produce images to monitor the treatment results by therapeutic X-ray beams. This "all-in-one" system contributes significantly to the increase in throughput of high-precision radiation therapies.

3. Expanded applicable body region for dynamic tracking radiotherapy

Moving tumors have conventionally been treated by "delivering a beam covering the entire area where the tumor moves" or "delivering a beam that only irradiates when the tumor is in the radiation field." The former method, however, needs to deliver a high dose to the surrounding healthy tissue, while the latter requires a longer time to treat a patient.

"Dynamic tracking radiotherapy" was developed to solve these problems using a method to "deliver an X-ray beam continuously by concentrating it only on a moving tumor," which had long been a fervent wish of healthcare professionals.

"Dynamic tracking radiotherapy" was approved by MHLW based on the Japanese Pharmaceutical Affairs Law in May 2010. In September 2011, the treatment was started for lung cancer patients at Kyoto University Hospital, by inserting multiple gold-spherical markers inside the patient's bronchi.

With Vero4DRT, dynamic tracking radiotherapy as mentioned above can be performed utilizing two pairs of kV imaging systems and a gimbal mechanism.[4]

In dynamic tracking radiotherapy, the beam is delivered according to the following steps (**Figure 2**).

(1) Continuously and simultaneously detect the "positions of IR markers attached/set on the outer surface of patient's abdominal wall (respiratory signals)" and the "3D position of the tumor that moves inside the body from respiration and other factors."

(2) Build a correlation model (4D Model) between the detected respiratory signals (IR markers) and the position of the moving tumor.

(3) Estimate a real-time tumor position based on the real-time respiratory signals obtained during treatment via the 4D Model.

(4) Make a therapeutic X-ray beam direction to track and follow the real-time position of the tumor, using a gimbal mechanism.

(5) Deliver therapeutic X-rays continuously while the beam is tracking the moving tumor until the prescribed dose is completely delivered.

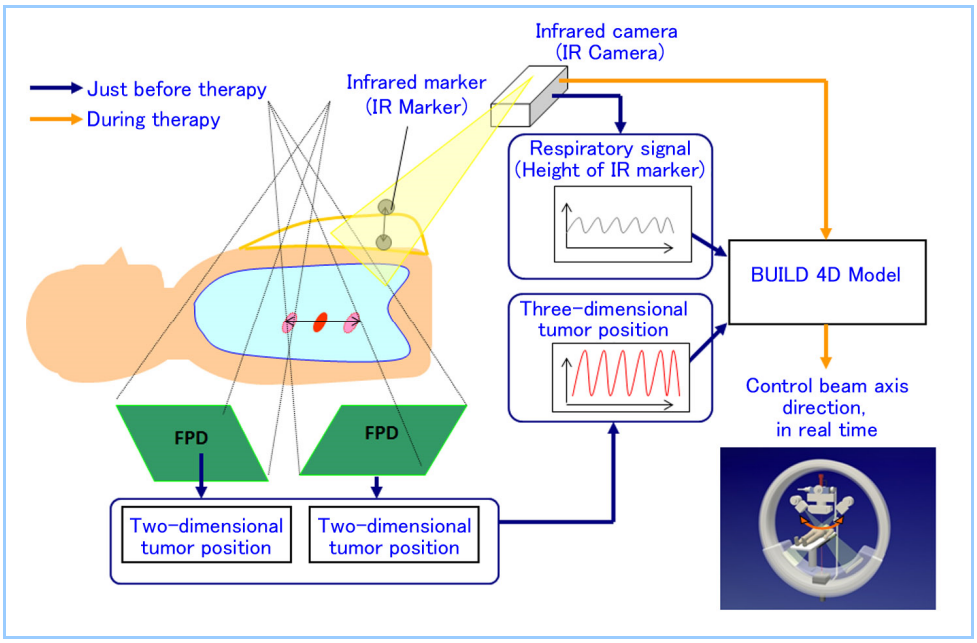

Figure 2 Mechanism drawing of Dynamic Tracking Radiotherapy

This dynamic tracking radiotherapy is performed by estimating the real-time tumor position inside the body, based on the fact that the movement of the tumor is highly correlated with the vertical movement of the abdominal wall. Steps (1) and (2) are carried out just before the treatment, and steps (3) through (5) are performed during treatment.

The 3D position of a tumor that moves in a lung can be detected using several gold spherical markers (1.5 mm in diameter) that have been inserted beforehand in the bronchi near the tumor with an endoscope and detected automatically by the system.

The tumors, which move inside the body with respiration but are located in other organs such as the liver and pancreas, can be automatically detected using thin, coiled gold markers called "long markers," which are percutaneously inserted near the tumor (**Figure 3**).[5, 6]

Both sphere-type and coiled-type markers have already been approved as medical devices based on the Japanese Pharmaceutical Affairs Law.

The advanced image processing technology that enables the automatic detection of these markers is a true essential technology for applying a cutting-edge "dynamic tracking radiotherapy" to more body regions and for increasing its treatment cases.

In March 2013, Kyoto University Hospital started dynamic tracking radiotherapy for liver cancer patients using long markers.

Figure 3 Gold markers inserted into patient's body for Dynamic Tracking Radiotherapy

4. Truly innovative beam delivery method: Development of Dynamic Wave Arc (DWA)

Conventional radiotherapy equipment has a mechanical structure to rotate the entire machine, which is equipped with an accelerator to deliver therapeutic X-ray beams, enabling the delivery of beams from any angle or direction along the gantry, but only within the "coplanar" plane (an imaginary plane perpendicular to the patient). Unlike conventional equipment, Vero4DRT can individually and separately control the gantry rotation and the ring rotation, as described in section 2. These rotations can also be controlled synchronously. By utilizing this unique characteristic, we have developed a new beam delivery technique called "Dynamic Wave Arc (DWA)," with which therapeutic X-ray beams can be delivered to the tumor, thereby minimizing the exposure to at-risk organs, by selecting an effective beam path compared with conventional ones (**Figure 4**).

(DWA has not been approved by Japan's MHLW based on the Pharmaceutical Affairs Law, as of January 2014.)

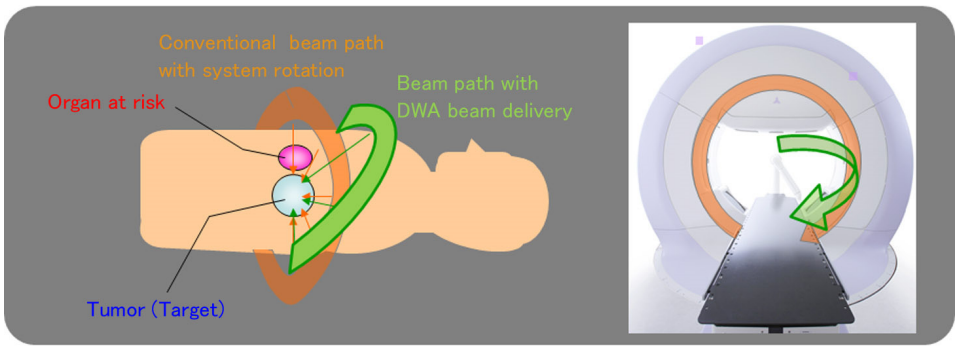

Figure 4 Beam path in Dynamic Wave Arc (DWA) Radiotherapy

In conventional beam deliveries, a controlling method such as point-to-point (PTP) control is used, because there are no other parameters to be controlled other than the gantry position. However, in DWA radiotherapy, each beam has to pass along the pre-designated path and therefore, the "continuous-path" control method for controlling the gantry axis and the ring axis synchronously has been adopted in Vero4DRT.

In this control method, "⊿R (ring rotational distance per unit time) /⊿G (gantry rotational distance per unit time)" has to be maintained "constant" within each segment, as shown in **Figure 5**.

Since the "rotational distance per unit time" is determined by "the rotational speed x unit time," the speed ratio between the synchronous gantry- and ring-axis rotations has to always be the same to maintain a constant "⊿R/⊿G."

In other words, in DWA radiotherapy, the ratio between gantry and ring rotational speeds has to be maintained as designated within each segment.

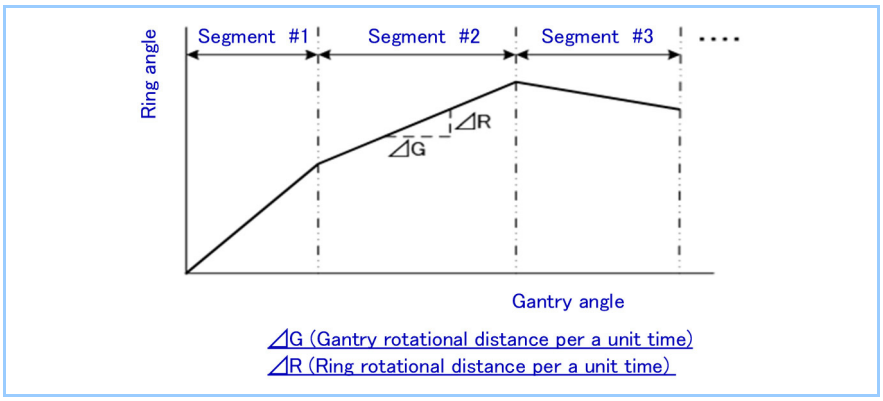

Figure 5 Beam Path Control, during DWA (Dynamic Wave Arc) beam delivery

To satisfy these requirements, we have adopted a control method in which when the trajectory goes into the next segment with a different speed ratio, the gantry or ring accelerates at the beginning of the segment, moves at a constant speed once it reaches a designated level, and decelerates at the end of the segment to stop, so that the beam axis follows the pre-designated path stably and reliably (**Figure 6**).

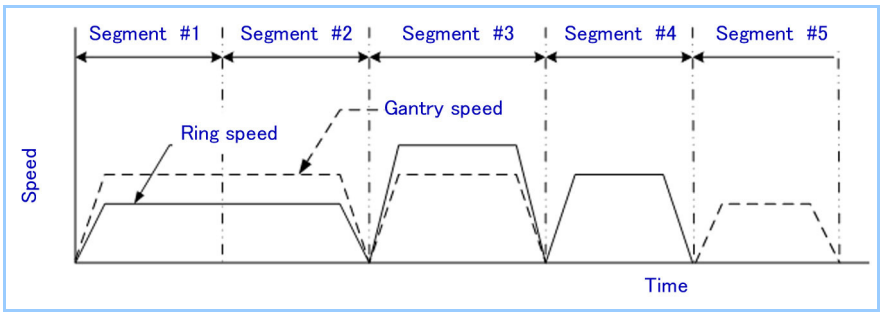

Figure 6 Beam Path Control, during DWA (Dynamic Wave Arc) beam delivery: "Continuous path" control method in case of different speed values in each segment.

5. Conclusion

As advancement for further concentrated dose application to the required tissue while decreasing the exposure of the surrounding healthy tissue, we have developed innovative and completely-new beam delivery techniques, such as the method to expand the applicable body region for dynamic tracking irradiation and the DWA beam delivery method.

We strongly hope to contribute to the betterment of society by continuing to strive to conquer cancer through the application of the functionalities we develop for clinical practice. We also would like to provide the future technology of radiotherapy by listening to the opinions and comments of patients and medical staff working in actual clinical practice.

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