Original Article

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Analysis of Treatment and Delay Times by Disease Site and Delivery Technique at Samsung Medical Center - Proton Therapy Center

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We have treated various disease sites using wobbling and scanning proton therapy techniques since December 2015 at the Samsung Medical Center. In this study, we analyze the treatment time for each disease site in 65 wobbling and 50 scanning treatments. Treatment times are longest for liver and lung cancer cases using the respiratory gating technique in the wobbling treatment and for cranio-spinal irradiation in pediatric patients with anesthesia in the scanning treatment. Moreover, we analyze the number of incidents causing treatment delays and the corresponding treatment delay time. The mal-functioning related to the X-ray imagers was the main reason for delays in the wobbling treatment; the delayed time decreased continually from January to June 2016, due to the attaining of proficiency in handling the mal-functioning. The main reason for delays in the scanning treatment was interlocks during scanning pattern delivery; and the interlocks has been resolved by proton therapy service engineers. Through this work, we hope to provide other institutes with useful information and insight for initial operation of proton therapy system.

Key Words: Proton therapy, Treatment time, Treatment delay time, Wobbling treatment, Line-scanning treatment

Introduction

Proton therapy can effectively enhance the survival rate of cancer patients and reduce the adverse effects of treatment because of its high dosimetric benefits compared to conventional photon and electron beam therapies[1] owing to Bragg's peak, which is a physical characteristic of proton beams. However, the high price of proton therapy is one of the critical factors preventing wide dissemination of the technique, posing a significant burden on both the patients receiving the treatment and the hospitals providing proton therapy.

The Ministry of Health and Welfare of South Korea decided to reimburse the proton therapy for most type of cancer by national health insurance in September 2015, and the application of health insurance greatly decreased the financial burden on patients. Currently, many patients who could gain dosimetric benefits from proton therapy are waiting to receive it instead of conventional therapies.

On the other hand, it is difficult for institutions to purchase proton therapy system, which are several times more expensive than conventional radiotherapy systems, and to introduce them based on the calculation of profit and loss alone in consideration of the high attendant operating costs. The costs of initial introduction of the treatment system, maintenance, and manpower are compared with profits from the treatment. In most cases, the treatment cost is estimated to be 2～3 times higher than the cost of the X-ray treatment.[2,3] The profit of proton therapy machines is inversely proportional to the time spent for each patient, which is closely related to the operation

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efficiency of a proton therapy machine. However, the average time spent for patient treatment can be determined only through actual experience because it is affected by many factors. Other institutions have conducted studies to estimate the maximum capacity of proton therapy patients as a function of the distribution of disease sites, the number of ports, tumor size, facility operating capacity, and patient treatment time.[4,5] These studies discussed the cost effectiveness of proton therapy and provide basic data for improving the efficacy of proton therapy and calculating the appropriate number of personnel involved.

The present work aims to share with other insitutions our experiences of operating a proton therapy facility as a private hospital for the first time in Korea.[6] We has conducted proton therapy with wobbling and line scanning of proton therapy system manufacture by Sumitomo Heavy Industries in Japan. Wobbling and line scanning treatments were started in December 2015 and March 2016, respectively. As of July 2016, we have completed treatments for 65 patients with wobbling and 50 patients with line scanning.

This study analyzes the average treatment time for the first, second, and later fractions of treatment and the maximum and minimum treatment times in the total treatment period for patients treated for eight months. Furthermore, the number of incidents that delayed treatment in each treatment room and the resulting treatment delay times are analyzed to construct useful information in predicting average time required for each patient for proton therapy system operation.

Materials and Methods

1. Proton therapy

The proton therapy machine in our institution is a product of Sumitomo Heavy Industries, Japan, and consists of a cyclotron that accelerates protons at an energy of 230 MeV, a beam transport line, and two rotating gantries. The first rotating gantry has a multi-purpose nozzle that can perform both wobbling and line-scanning treatments. The second rotating gantry has a dedicated nozzle for line-scanning treatments. The wobbling treatment method irradiates a uniform dose at the maximum block radius by rotating a pencil beam with x- and y-axis scanning magnets in an elliptical trajectory and passing the beam through a scatterer. The proton range is modulated by using a range compensator. Spread-out Bragg's peaks (SOBP) are generated by using ridge filters. Thus, the wobbling treatment technique produces the desired three-dimensional dose distribution by using a ridge filter, a block, and a compensator. The line-scanning method obtains the desired dose distribution by changing the position of the pencil beam with scanning magnets to a predefined position. It then accumulates the dose in a direction parallel to the irradiation axis by changing the energy of each pencil beam. Unlike the wobbling treatment, this method can perform intensity-modulated proton therapy because it obtains a 3D dose distribution by changing the energy and position of each pencil beam. Unique features of this system include a multi-leaf collimator installed in the multipurpose nozzle which effectively shapes the beam for wobbling treatment and a helium chamber installed in the scanning dedicated nozzle which can minimize the air scattering effect.

Raystation (Raysearch Laboratory AB, Stockholm, Sweden) is installed as a treatment planning system and Mosaiq (Eleckta AB, Stockholm, Sweden) is installed as an oncology information system (OIS) at Samsung Medical Center. For patient position verification, VeriSuite (MedCom, Darmstadt, Germany) is installed which provide cone beam computed tomography (CBCT) for three-dimensional image verification and two orthogonal kV-X-ray images for two-dimensional image verification.

The entire proton therapy machine, including the beam transport line, the mechanical structure of the nozzle, and the software network must be in good condition. If any of the above component has a problem, the proton beam cannot be irradiated and patient treatment may be delayed. Thus, Sumitomo Corporation service engineers are stationed in our institution to respond to emergencies, and many spare parts for various components are on hand. Treatment may be delayed, however, if any component fails for which we have no spare parts.

Among cancers treated with wobbling method, lesions in liver and lung experience movement owing to respiration, and respiratory gating therapy is performed to minimize the uncertainty of the irradiation position and dose in consideration of these movements. For respiratory gating technique, 4D CT (four-dimensional computed tomography) which is established by reorganizing the CT images by respiration cycle is taken for simulation and a treatment plan. To deliver the dose according to the treatment plan, respiratory gating or breath-holding techniques should be performed with gating system of Anzai Medical (Japan) and a proprietary breathing training program is required.

2. Treatment time by disease site

In gantry room 1, the wobbling treatment has been conducted from December 2015 until the present. In this study, patient data between December 2015 and March 2016 were excluded from the analysis because it was believed that the characteristics of treatment time were not reflected due to frequent treatment delays in this period.

Patients receiving the wobbling treatment were analyzed in the first rotating gantry and patients receiving the line-scanning treatment in the second rotating gantry. The 65 wobbling treatment patients were divided into nine cancer sites: brain, head and neck, chest (for which the gating technique was not used), lung (for which the gating technique was used), spine, liver, abdomen, pelvis, and other sites. The line-scanning treatment was performed in the second rotating gantry for a total of 50 patients divided into eight cancer sites: brain, head and neck, chest (for which the gating technique was not used), lung (for which the gating technique was used, abdomen), pelvis, prostate, and cranio-spinal irradiation (CSI). Patient treatment time was analyzed from April to July 2016 for both wobbling and line-scanning treatment methods. The treatment time for the first fraction, the average treatment time for the second and later fractions, the maximum treatment time, and the minimum treatment time were analyzed for each patient and for each disease site. The treatment time was defined as the time between entry into and exit from the treatment room, and the data used in this study were recorded by radiotherapist.

3. Treatment delay

The smooth operation of the proton therapy machine presupposes the integrity of the machine parts and software and no errors in the network. However, various problems and interlocks are bound to occur during operation for various reasons. In this study, various delay incidents during treatment were collected and analyzed for each treatment room from January 2016, when proton therapy was started, until June 2016. For the wobbling treatment, which was performed in the first rotating gantry, data for 25 weeks were collected from the third week of January to the second week of June. For the line-scanning treatment, data for 13 weeks were collected from the first week of April to the second week of June. The daily average number of incidents that caused treatment delays and the average daily treatment delay times in minutes were analyzed for each treatment room.

Results

1. Treatment time by disease site

For the wobbling treatment, treatment sites were classified into brain, head and neck, chest (for which the gating technique was not used, hereinafter termed ‘chest’), lung (for which

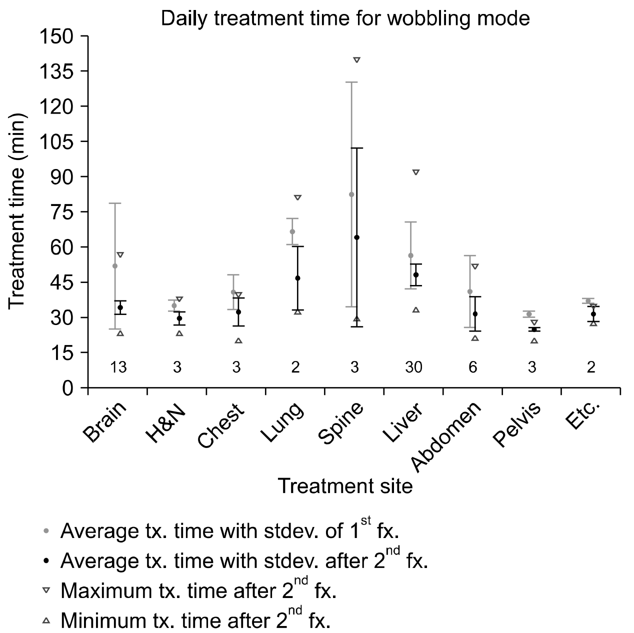

Fig. 1. Site-specific daily average of proton treatment time for the wobbling mode. Pink: averaged treatment time with standard deviation only for the first fraction of treatment. Blue: averaged treatment time with standard deviation after the second fraction of treatment. The standard deviation of each graph is indicated by upper and lower bars and average values are denoted by solid dots in the middle of the range. Red upward (downward) triangles are minimum (maximum) values of treatment time after the second fraction of treatment. At the bottom of the graph, the number of patients for each treatment site are presented. tx.: Treatment, fx.: fraction.

the gating technique was used, hereinafter 'lungs'), spine, liver, abdomen, pelvis, and other sites. The treatment time for the first fraction, the average treatment time for the other fractions, the maximum treatment time, and the minimum treatment time are shown in Fig. 1. In Table 1, the average treatment time for liver lesions was 48.1 minutes and the average treatment time for lung lesions was 46.6 minutes. The average treatment times for liver and lung sites were longer by 35.6% and 31.6%, respectively, than the average treatment time of 35.4 minutes for other lesions.

Brain lesions showed the greatest difference in treatment time between the first fraction and the other fractions. The average treatment time for the first fraction was 51.8 minutes, whereas the average treatment time for the other fractions was 34 minutes, and the standard deviation was 26.8 minutes. This suggests that the first fraction took more time to set up. The average treatment time excluding the first fraction was 29.6 minutes for the head and neck, 32.3 minutes for the chest, 64.1 minutes for the spine, 31.5 minutes for the abdomen, and 24.8 minutes for the pelvis. Thus, wobbling treatments took approximately 30 minutes, on average. The average time required to treat the first fraction was 51.8 minutes for the brain,

Table 1. Treatment time of each site for the wobbling mode.

(min)	Brain	Head and neck	Chest excluding lung	Lung	Spine	Liver	Abdomen	Pelvis	Other
Avg_1st	51.8	35.0	40.7	66.5	82.3	56.4	41.0	31.3	37.0
Avg_tx	34.0	29.6	32.3	46.6	64.1	48.1	31.5	24.8	31.4
Std_1st	26.8	2.5	7.4	5.5	47.9	14.3	15.3	1.3	1.0
Std_tx	2.8	2.8	5.9	13.6	38.2	4.7	7.4	0.8	3.2
Min	23.0	23.0	20.0	32.0	29.0	33	21.0	20.0	27.0
Max	57.0	38.0	40.0	81.0	140.0	92.0	52.0	28.0	35.0
N	13	3	3	2	3	30	6	3	2

Site-specific daily average proton treatment times for the wobbling mode.
Avg_1st: Average value of treatment time for the first fraction, Avg_tx: average value of treatment time after the second fraction, Std_1st: standard deviation of treatment time for the first fraction, Std_tx: standard deviation of treatment time after the second fraction, Min: minimum value of treatment time after the second fraction, Max: maximum value of treatment time after the second fraction, N: number of samples.

Table 2. Treatment time of each site for the scanning mode.

	Brain	Head and neck	Chest (without gating)	Lung (with gating)	Abdomen	Pelvis	Prostate	CSI
Avg_1st	48.6	40.1	37.6	76.2	66.0	38.6	50.0	91.4
Avg_tx	30.2	29.7	29.8	66.9	39.7	24.9	31.6	60.0
Std_1st	5.8	4.9	4.9	18.5	4.9	8.1	10.8	32.9
Std_tx	3.0	3.8	1.1	23.9	10.8	3.0	2.8	17.8
Min	22.00	20	22	33.00	22	20	24	22
Max	60.00	99	51	170.00	69	42	70	114
N	10	15	3	4	2	3	3	10

Site-specific daily average proton treatment times for the scanning mode.
CSI: Cranio-Spinal Irradiation, Avg_1st: average value of treatment time for the first fraction, Avg_tx: average value of treatment time after the second fraction, Std_1st: standard deviation of treatment time for the first fraction, Std_tx: standard deviation of treatment time after the second fraction, Min: minimum value of treatment time after the second fraction, Max: maximum value of treatment time after the second fraction, N: number of samples.

35 minutes for the head and neck, 40.7 minutes for the chest, 82.3 minutes for the spine, 41 minutes for the abdomen, 31.3 minutes for the pelvis, and 37 minutes for other sites. The minimum treatment time was 20 minutes for lesions excluding lung and liver lesions and the maximum treatment time was 140 minutes for the spine, followed by the liver at 92 minutes, and the lungs at 81 minutes.

The analysis results of the line-scanning treatment are shown in Fig. 2 for the brain, head and neck, chest, lung, abdomen, pelvis, prostate, and CSI. In table 2, the average treatment time was 30.2 minutes for the brain, 29.7 minutes for the head and neck, 29.9 minutes for the chest, 39.7 minutes for the abdomen, 24.9 minutes for the pelvis, 31.7 minutes for the prostate, and 60 minutes for CSI. The lung treatments took 67 minutes because of using the respiratory gating technique.

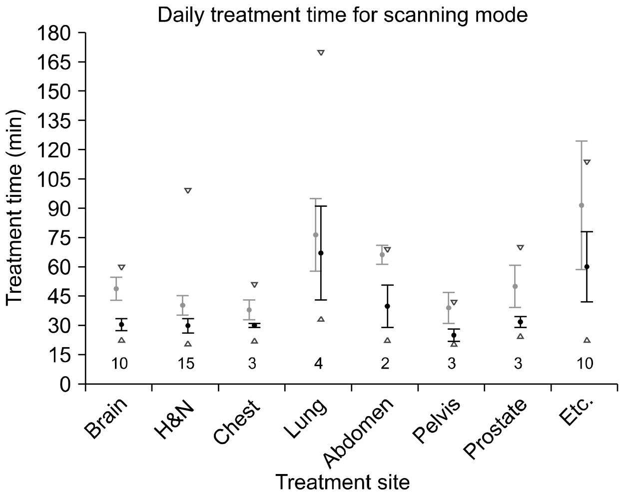

Fig. 2. Site-specific daily average of proton treatment time for the scanning mode. Pink: averaged treatment time with standard deviation only for the first fraction of treatment for each patient. Blue: averaged treatment time with standard deviation after the second fraction of treatment. The standard deviation of each graph is indicated by upper and lower bars and average values are denoted by solid dots in the middle of the range. Red upward (downward) triangles are minimum (maximum) values of treatment time after the second fraction of treatment. At the bottom of the graph, the boxed numbers are the numbers of patients for each treatment site. tx.: Treatment, fx.: fraction.

The average treatment time for the first fraction was 48.6 minutes for the brain, 40 minutes for the head and neck, 37.7 minutes for the chest, 66 minutes for the abdomen, 38.7 minutes for the pelvis, 50 minutes for the prostate, and 91.4 minutes for CSI. The minimum treatment time was approximately 20 minutes, and the maximum treatment time was 170 minutes for the lungs (there was a problem with image matching), followed by 114 minutes for CSI.

2. Treatment delay

Treatment delays for the wobbling treatment were analyzed between the third week of January and the second week of June. The daily average treatment delays and the daily average number of incidents that caused delays during this period are shown in Fig. 3. The daily average treatment delay was 38.3 minutes in January, 38.3 minutes in February, 46.8 minutes in March, 22.1 minutes in April, 12.3 minutes in May, and 17.3 minutes in June. The daily average number of incidents that delayed treatment was 5.1 in January, 4.3 in February, 4 in March, 2.9 in April, 1.2 in May, and 2.2 in June.

The treatment delay for line-scanning therapy was analyzed between the first week of April and the second week of June.

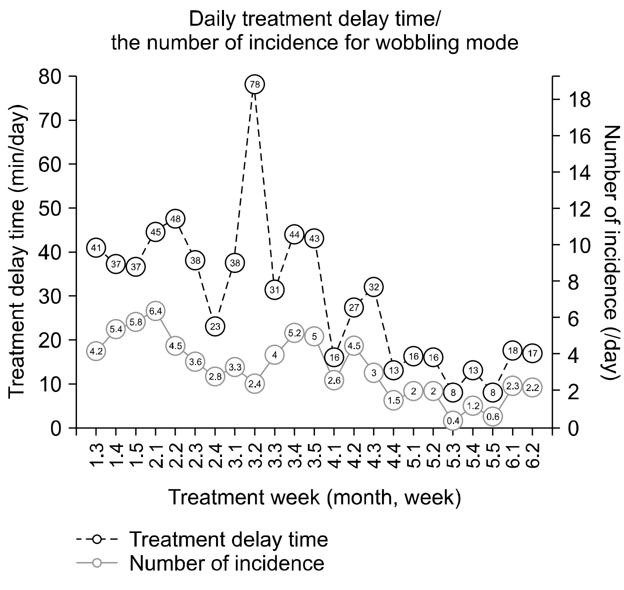

Fig. 3. The number of incidents causing treatment delays and average delay time for the wobbling mode. Left axis/blue dots: daily averaged treatment delay time at that week. Right axis/red line: daily average number of incidents during the given week.

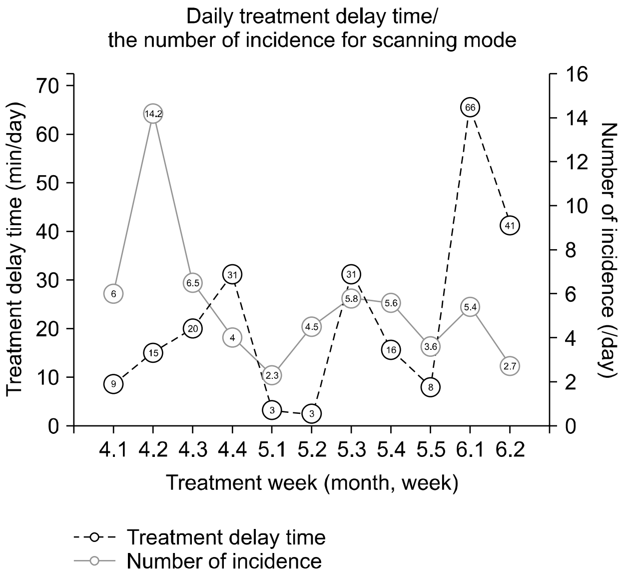

Fig. 4. The number of incidents causing treatment delays and average delay time for the line-scanning mode. Left axis/blue dots: daily averaged treatment delay time during the given week. Right axis/red line: daily average number of incidents during the given week.

The daily average treatment delay and daily average number of incidents that caused treatment delays during this period are shown in Fig. 4. The daily average delay was 18.6 minutes in April, 12.1 minutes in May, and 53.4 minutes in June. The daily average number of incidents that delayed treatment was 7.7 in April, 4.4 in May and 4 in June.

Discussion

1. Treatment time by disease site

1) Wobbling treatment: The reason for the high standard deviation of treatment time of brain for the first fraction was that two out of thirteen patients took 103 and 120 minutes, respectively. Excluding these two patients, the average treatment time was 40.9 minutes and the standard deviation was 8.1 minutes for the first fraction, which are not much different from those of other lesions.

In the case of spine lesions, one of the three patients in this category took 150 minutes for the first fraction and 118 minutes on average for the other fractions. The treatment times of the remaining two patients were 48 minutes for the first fraction and 37 minutes for the other fractions. These data distributions are biased owing to the small number of samples available. If the number of patients per lesion is large, then the data distribution would follow the normal distribution and the deviation decreases.

In the case of the pelvis, the treatment time for the first fraction was 31.3 minutes and the average treatment time was 24.8 minutes. Thus, the treatment times were shorter than those of other sites. The shorter treatment time for pelvic lesions was mostly due to the use of a small number of fields and alignment of patient positions using only 2D X-ray images. Compared to brain lesions, for which CBCT was performed every week or every day, the shorter image guide time had the effect of reducing the total treatment time.

The respiratory gating technique used in the treatment of lung and liver lesions requires pre-work to determine the in-phase positions of the internal organs by acquiring respiratory signals and image guiding (e.g., fluoroscopy). Furthermore, such methods as gating or breath-holding, which irradiate the proton beam only at the appropriate time, require additional timing of the proton beam. Therefore, lung and liver lesions for which respiratory gating therapy is performed have longer treatment times than other lesions. The average treatment times for the lung and liver were 46.6 minutes and 48.1 minutes, respectively. The average treatment times of these two organs were 53.2% and 57.2% longer than the average for the other lesions excluding lung, liver and spine, respectively. The difference in treatment time was greater in the first fraction. The lung treatments were delayed by 68.5% to 66.5 minutes and liver treatments by 42.9% to 56.4 minutes compared with the average treatment time of 39.5 minutes for lesions excluding the lung, liver, and spine.

2) Line-scanning treatment: The line-scanning treatment requires less time to replace treatment accessories because it does not use blocks and compensators, unlike the wobbling treatment. The treatment time for the first fraction was 48.6 minutes for the brain, 40.1 minutes for the head and neck, 37.7 minutes for the chest excluding the lung, 76.3 minutes for the lung, 66 minutes for the abdomen, 38.7 minutes for the pelvis, 50 minutes for the prostate, and 91.4 minutes for CSI. The average treatment time was 31 minutes, and the first fraction took 46.8 minutes for lesions excluding the lungs and CSI, which take an especially long time. For CSI, multi-isocenters (brain, upper spine, lower spine, etc.) in a given fraction are treated, necessitating multiple treatment times. Furthermore, we performed CSI treatments of pediatric patients in cooperation with anesthesiologists in our institution, and brain boost field after pediatric CSI takes longer compared to adult because the patient is anesthetized.

In the case of lung lesions, for which the respiratory gating technique is performed for line-scanning treatment, the average treatment time was 67 minutes and the treatment time for the first fraction was 76.3 minutes because the beam delivery required a significant amount of time. For pediatric patients, who were anesthetized for CSI treatment, the average treatment time was 60 minutes and the treatment time for the first fraction was 91.4 minutes. The reason for such long treatment times is that the scan pattern download and beam delivery takes around three or four minutes for each beam port because the size of each field is almost 40 cm along the y-axis. Furthermore, four to five fields are used in total, including two fields on either side of the brain and two to three fields on the spine. Thus, the amount of work for each CSI patient is twice as much as for other general patients. In addition, the isocenters vary for each field, and additional time is required to perform image guidance.

The average treatment time used to calculate the cost of proton therapy was estimated in other institutes as 10 minutes for prostate cancer,[7-9] 30 minutes for lung cancer if respiratory gating therapy is performed,[10,11] 30 minutes for head and neck cancer,[12-14] and 20 minutes for skull-base chordoma.[15-17] Note that in the above examples, the estimated treatment time for prostate cancer was for treating only one field per day, and the estimated treatment time for lung cancer was for performing the gating technique after fluoroscopy using two or more treatment fields every day. It should be noted that these were not actual treatment times. Furthermore, since the proton treatment system does not have a separate simulator as with the X-ray treatment system, it inevitably takes more time compared to conventional therapies because treatment simulations such as reproduction of patient position are conducted in the first fraction.

Since the 3D dose distribution of proton therapy changes very rapidly, image guidance is essential. The time required for proton therapy must be compared with the image-guided treatment rather than to conventional treatments without image guidance. According to the data concerning differences in treatment times depending on the presence or absence of image guidance,[18] the average treatment time of the conventional IMRT treatment increased by 3.5 minutes from 10.5 minutes to 14.0 minutes, and the treatment time for the first fraction increased by 9 minutes from 10 minutes to 19 minutes.[19] In our institution, CBCT was done for all patients in the first fraction, and the additional setup time owing to CBCT imaging took more than 5 minutes on average considering the rotation speed of 1 rpm (rotations per minute) and CBCT reconstruction time. If the image is guided with a 2D kV image instead of CBCT, this time is reduced to less than one minute.

If the treatment time is classified by item, it can be divided into patient guide and entry, patient position reproduction and image guidance, beam irradiation, and patient discharge. Time management efficiency can be improved if the elapsed time for each item is recorded and managed. The present study did not analyze this, but a follow-up study will analyze the elapsed time for each item. Among the aforementioned items, the time required for patient position reproduction and image guidance has the greatest variation by patient and has more room for reduction compared to other items. To this end, we are considering a method to proceed with treatment without CBCT acquisition if the set-up uncertainty in image guidance with 2D kV images is within the set-up uncertainty considered in the plan. It is expected that the time required for image guidance can be reduced with increased confidence in the results at our institution after starting proton therapy. Furthermore, with use of the respiratory gating technique, the position reproduction and beam irradiation time can be reduced if tumors are treated within the internal tumor volume (ITV) during free breathing rather than gating.

2. Treatment delay time

In the case of wobbling treatment, both the treatment delay and the number of incidents are continuously decreasing. This is closely related to the increase in the proficiency of the engineers at our institution and of the SHI engineers who have been in charge of operational support. In the case of wobbling treatment, the main cause of treatment delays was delays or errors in the response of the X-ray panel, which is an image guidance device. It seems that the treatment delay and the number of incidents decreased because of experience gained, allowing incidents to be addressed in advance or to be responded rapidly. Since May, the daily number of incidents causing delays has been less than two cases, and the delay time has been less than 15 minutes, which represent levels that do not interfere with treatment.

The daily average treatment delay of 78 minutes in the second week of March was caused by a different incident from the general case owing to the replacement of an RF tube in the cyclotron. These delays and errors can be gradually reduced by ongoing equipment use and error resolution, and require establishment of various clinical confirmation procedures to solve them.

The delay cases for line-scanning treatment have been managed by experienced radiotherapists and engineers trained through wobbling treatment to less than five cases on average and less than 30 minutes of treatment delay since April. The cause of delays for the line-scanning treatment was the interlocks of machines during the delivery of scanning patterns. Examples of this include cases where the position inaccuracy of a pencil beam exceeded the permissible criterion or the intensity modulation of the pencil beam over time exceeded the acceptable limit. The line- scanning treatment generates interlocks owing to diverse causes and many institutions are managing them at a level that does not affect treatment. In the future, interlocks can be reduced by readjusting the acceptable limits of equipment and using more realistic parameters. The daily average number of delays in the second week of April, which was 14.2 cases, was caused by interlocks that repeatedly occurred for one patient; however, the resulting delay time was 15 minutes on a daily average, which was not large. The daily average treatment delay in the first week of June was 65.6 minutes, which resulted from incidents that prevented beam irradiation owing to hardware defects encountered during the process of checking the initial position of the proton pencil beam. This problem was solved on the same day, and the treatment was conducted.

Conclusion

The proton therapy machine at Samsung Medical Center started its first treatment on December 28, 2015, and has performed wobbling and line-scanning treatments for various lesions. In this study, the treatment time for each lesion was analyzed for 65 patients for the wobbling treatment and 50 patients for the line-scanning treatment. The maximum treatment time was associated with liver and lung lesions for which the respiratory gating technique was performed and with CSI and brain lesions in pediatric patients treated under anesthesia.

Furthermore, the daily average number of incidents that caused treatment delays in each room was analyzed. The main cause of delays in the wobbling treatment was problems with X-ray panels, which showed a declining trend from the third week of January to the second week of June. The declining trend could be explained by the increasing proficiency of the operators. The main reason for delays in the line-scanning treatment was the interlock that occurred during the delivery of the scanning pattern, and this problem was solved by technical support provided by the proton engineers.

The treatment time analyzed in this study is a part of the overall treatment process including treatment simulation, establishment of a treatment plan, and the quality assurance of the patient treatment plan. More work is needed to analyze the effects of proton therapy in comparison with treatment costs through such methods as activity-based cost analysis.[20]

We hope that this study will contribute to the early operation of proton therapy facilities in other institutions.

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