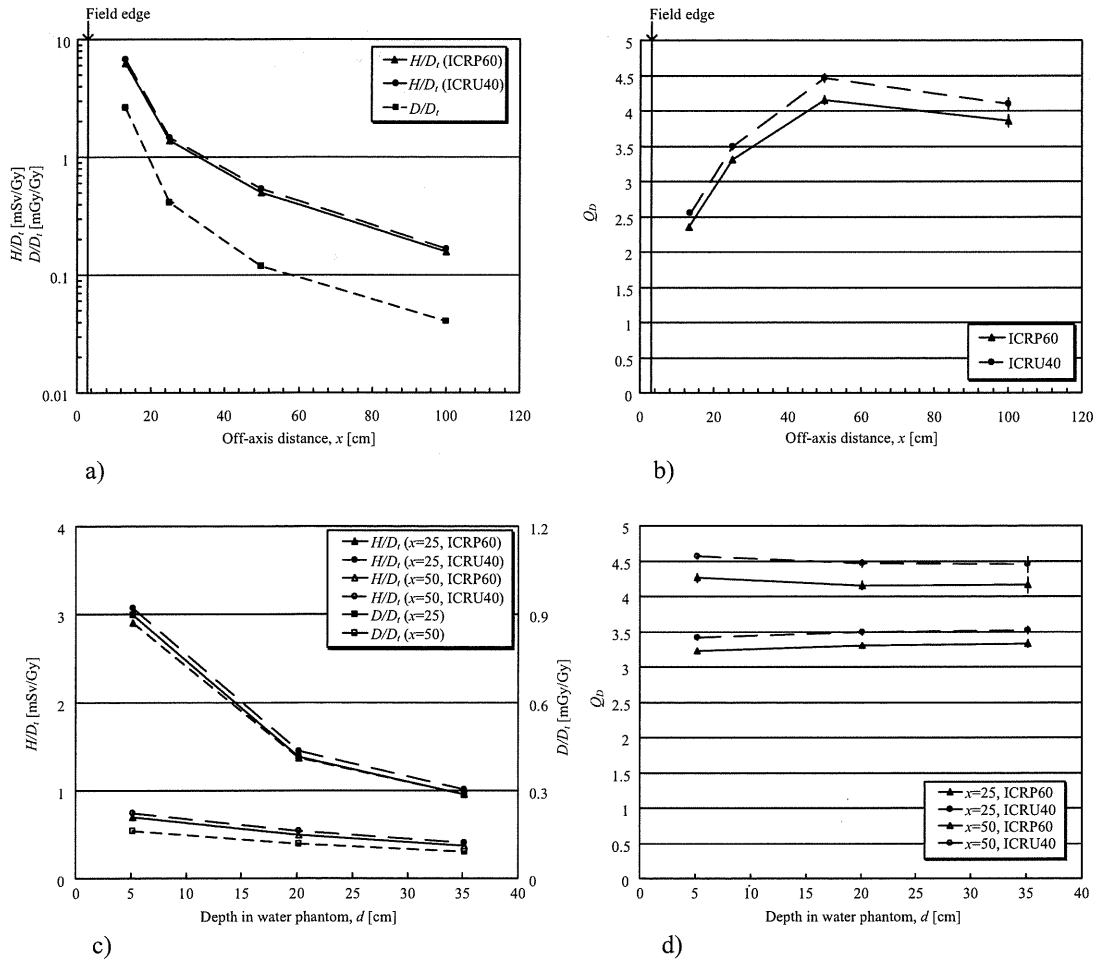


FIG. 2. Measured absorbed dose per the treatment absorbed dose at the center of the range-modulated region D/D_t, dose equivalent per the treatment absorbed dose at the center of the range-modulated region H/D_t, and dose-averaged quality factor Q_D, for the 400 MeV/u carbon beam. (a) D/D_t and H/D_t on the line of d=20 cm. (b) Q_D on the line of d=20 cm. (c) D/D_t and H/D_t on the line x=25 or 50 cm. (d) Q_D on the line x=25 or 50 cm. The error bar represents the statistical error (one standard deviation).

carbon beam. (2) Q_D for the proton beam had a dependence on d. The Q_D values at d=5 cm were higher than those at the other position by more than 1. The Q_D value for the proton beam ranged from 5.1 to 8.2, which was higher than that for the carbon beam at all positions.

Table II shows the ratio of H/D_t using $Q(y)$ of the ICRP 60 recommendation for the 235 MeV proton beam to that for the 400 MeV/u carbon beam R_H. At (50,5), H/D_t for the proton beam was about three times higher than that for the carbon beam. We attributed this to a facility dependency because the neutron ambient dose equivalent at the position has been shown by our previous study to be two times higher at NCCHE than at other proton radiotherapy facilities in Japan.[6] Another remarkable result is that R_H decreased as x decreased and d increased: R_H at (13, 20) was very low, though Q_D for the proton beam was 2.2 times higher than for the 400 MeV/u beam.

IV. DISCUSSION

In this study, we experimentally obtained absorbed doses, dose equivalents, and dose-averaged quality factors in water phantom outside of the irradiation field in passive carbon-ion and proton radiotherapies. Although the values of D/D_t and H/D_t vary according to the parameters of the beam-shaping devices and the facility as mentioned above, they can be a measure of the secondary exposure dose for patients. Table III shows the total dose equivalent per a typical prostate cancer treatment in units of mSv. It was assumed that the total prescribed dose was 66 GyE for the 400 MeV/u carbon beam and 74 GyE for the 235 MeV proton beam, respectively. Also, two opposed beams were assumed for estimating the total dose equivalent at a depth of 5 cm: The average value of those at d=5 and 35 cm. At all positions, these values are comparable to or less than those in 3D-CRT and IMRT for prostate cancer.[41–43] In particular, as the position is closer to the field edge, the total dose equivalents in carbon-ion and proton radiotherapies become obviously less that those in 3D-CRT and IMRT.

We also found different tendencies between the carbon and proton beams. (1) D/D_t and H/D_t for the carbon beam became higher than those of the proton beam as the position got closer to the field edge and farther from the phantom

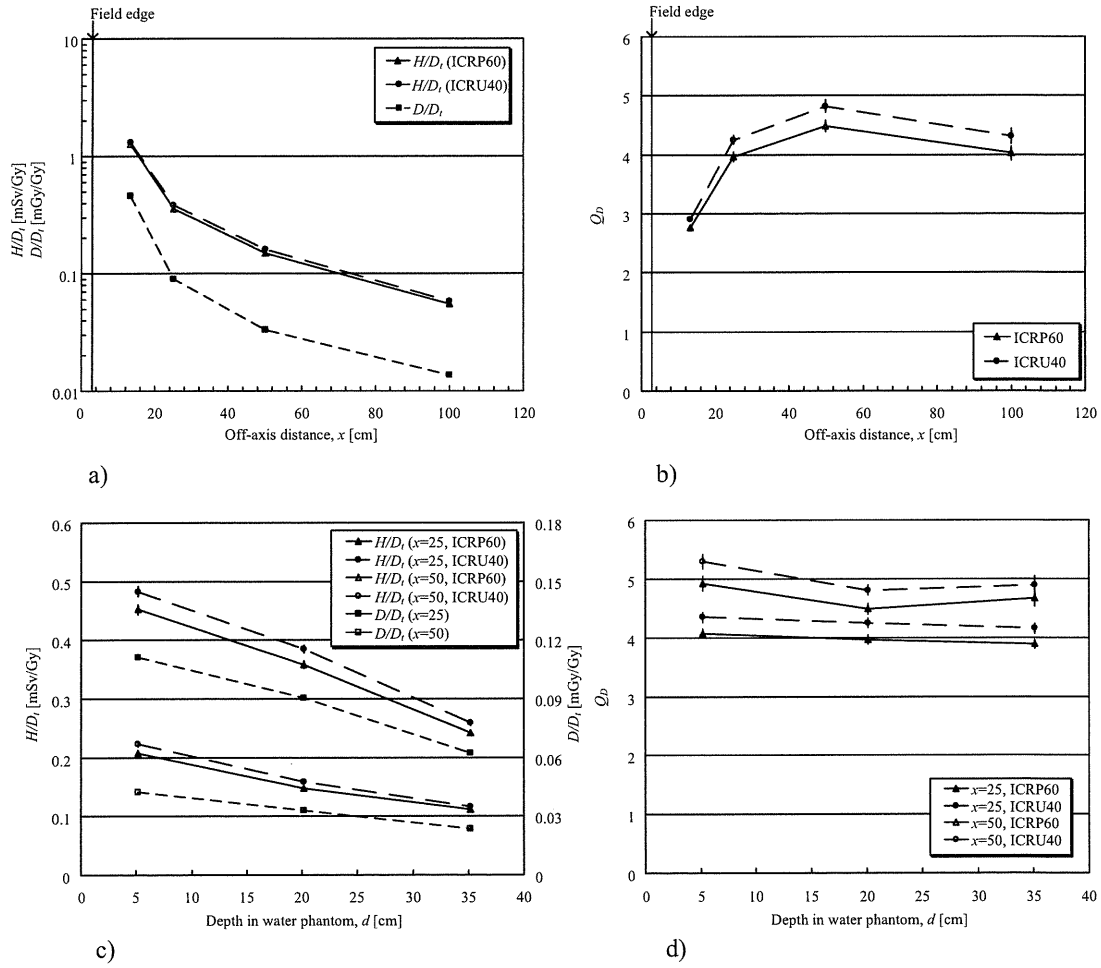


FIG. 3. Measured absorbed dose per the treatment absorbed dose at the center of the range-modulated region D/D_t, dose equivalent per the treatment absorbed dose at the center of the range-modulated region H/D_t, and dose-averaged quality factor Q_D, for the 290 MeV/u carbon beam. (a) D/D_t and H/D_t on the line of d=20 cm. (b) Q_D on the line of d=20 cm. (c) D/D_t and H/D_t on the line x=25 or 50 cm. (d) Q_D on the line x=25 or 50 cm. The error bar represents the statistical error (one standard deviation).

surface. (2) The position where Q_D starts to drop was farther from the field edge for the carbon beam than that for the proton beam. (3) Q_D for the proton beam depended on d, but Q_D for the carbon beam did not depend on d.

Figure 5 shows the measured dose distributions normalized to the total absorbed dose $yd(y)$, at (50, 20), (50, 5), (25, 20), (25, 5), (25, 35), and (13, 20) for the 400 MeV/u carbon beam and 235 MeV proton beam. These dose distributions are very helpful for understanding the differences. According to the published data,[23,25,44] the lineal energy peak of the dose distribution increases as the neutron energy increases in the neutron energy range below ~500 keV, but the peak shifts to the lower lineal energies in the neutron energy range above ~500 keV because the energy of the recoil proton increases as the neutron energy increases. The peak is below 10 keV/μm when the neutron energy is above 40 MeV. In fact, the events between ~10 and ~100 keV/μm corresponding to the proton edge are mainly due to neutrons with energy below several tens MeV. Also, the events between ~1 and ~10 keV are due to photons or high energy protons including recoil protons by high energy neutrons, and the events above the proton edge are due to heavy recoils by higher energy neutrons.

In the proton beam, the dose distributions at (25, 5) and (50, 5) were significantly different from those at other locations: The contribution between ~10 and ~100 keV/μm was higher. Dose distributions at (50, 20) and (50, 5) in the carbon beam also showed this tendency, but the tendency was not strong. This fact is the reason why the Q_D values at position closer to the phantom surface were higher, and indicates that neutrons with energy below several tens of MeV produced in the beam-shaping devices contribute strongly to the undesired dose at positions close to the phantom surface. This result also implies that the hydrogen-rich material only 20 cm thick can be very effective in decreasing the secondary exposure dose by half.

There is another unique distribution at (13, 20) in the carbon beam: The contribution between ~1 and ~10 keV/μm is the highest. As written above, these events are theoretically due to photons or high energy protons in-

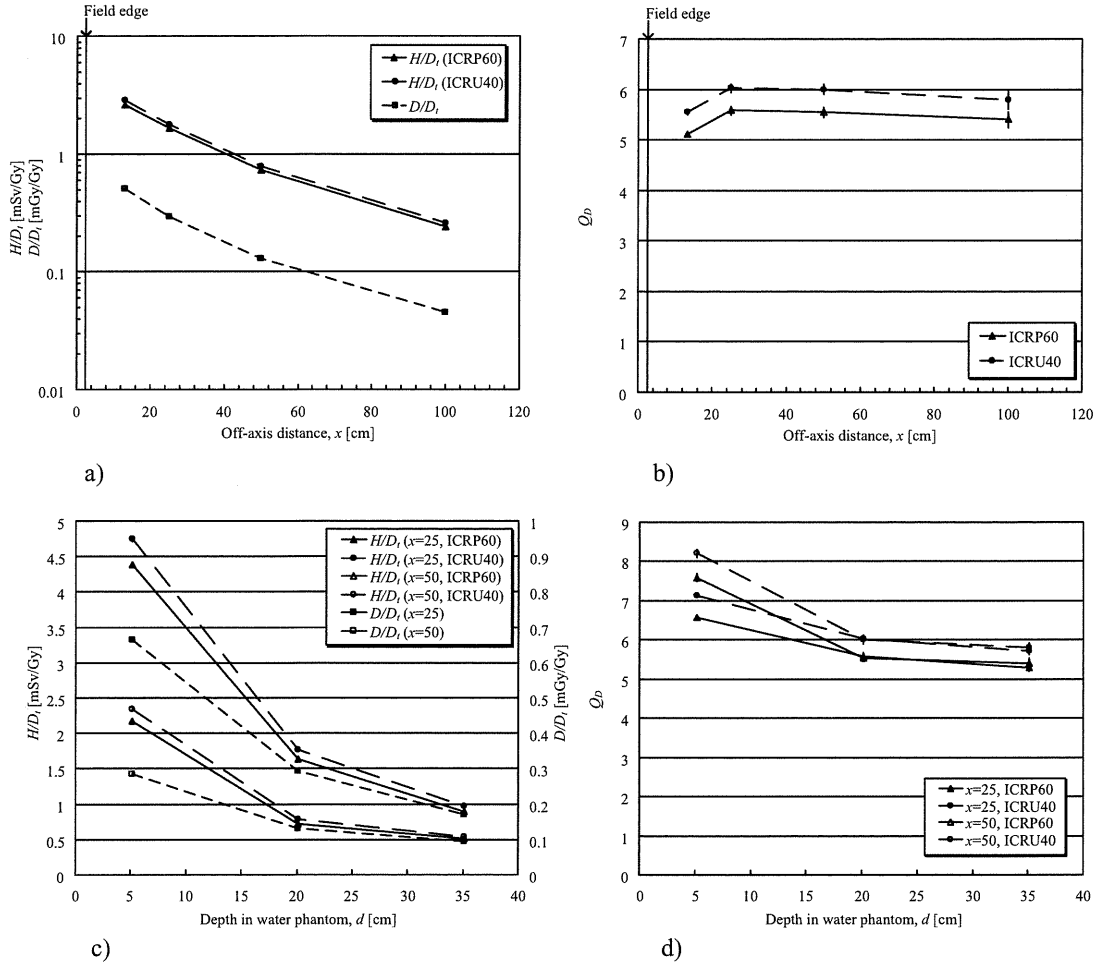


FIG. 4. Measured absorbed dose per the treatment absorbed dose at the center of the range-modulated region D/D_t, dose equivalent per the treatment absorbed dose at the center of the range-modulated region H/D_t, and dose-averaged quality factor Q_D, for the 235 MeV proton beam. (a) D/D_t and H/D_t on the line of d=20 cm. (b) Q_D on the line of d=20 cm. (c) D/D_t and H/D_t on the line x=25 or 50 cm. (d) Q_D on the line x=25 or 50 cm. The error bar represents the statistical error (one standard deviation).

cluding recoil protons by high energy neutrons. We expect that the fragmental protons of the incident carbon beam and the recoil protons produced by high energy neutrons from the breakup of the projectile and direct knock-on processes mainly contribute to these events because the peak between ~1 and ~10 keV/μm increased as the position became closer to the field edge and farther from the phantom surface. Therefore, fragmental and recoil protons with a low quality factor reduce the dose-averaged quality factors and increase the absorbed doses and dose equivalents at those positions.

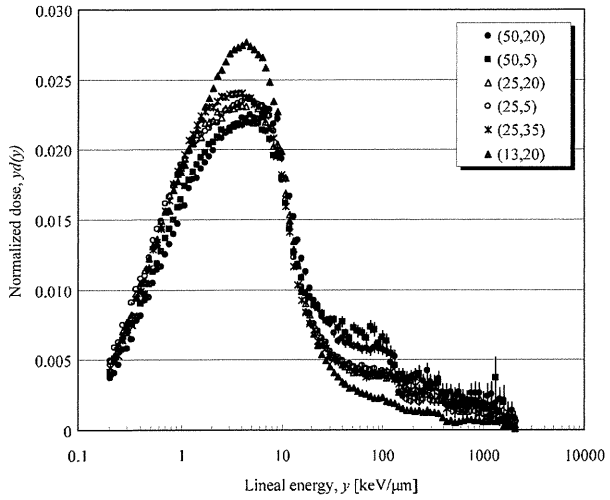
TABLE II. Ratio of dose equivalent per the treatment absorbed dose at the center of the range-modulated region H/D_t for the 235 MeV proton beam to that for the 400 MeV/u carbon beam R_H. $Q(y)$ of the ICRP 60 recommendation was used.

(x,d)	R_H
(13, 20)	0.42
(25, 20)	1.20
(50, 20)	1.46
(100, 20)	1.54
(25, 5)	1.51
(50, 5)	3.13
(25, 35)	0.94
(50, 35)	1.35

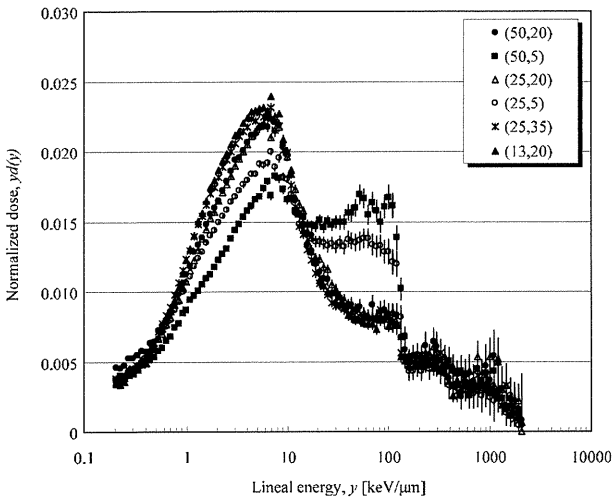
TABLE III. The total dose equivalent per a typical prostate cancer treatment in units of mSv. These values represent doses for a whole course of treatment. It was assumed that the total prescribed dose was 66 GyE for the 400 MeV/u carbon beam and 74 GyE for the 235 MeV proton beam, respectively. $Q(y)$ of the ICRU 40 recommendation was used.

(x,d)	400 MeV/u carbon	235 MeV proton
(13, 20)	187	190
(25, 20)	40.5	119
(50, 20)	14.9	52.7
(100, 20)	4.67	17.5
(25, 5)[a]	57.0	192
(50, 5)[a]	16.0	97.1

[a]Two opposed equally weighted beams were assumed.

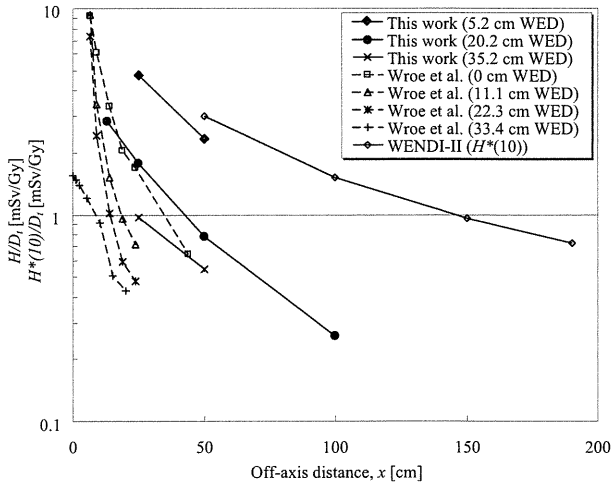


(a) 400-MeV/u carbon beam

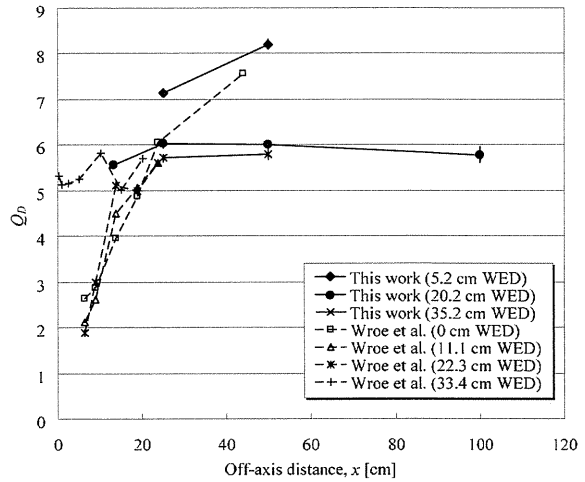


(b) 235-MeV proton beam

FIG. 5. Measured dose distributions normalized by the total absorbed dose $yd(y)$ at (50, 20), (50, 5), (25, 20), (25, 5), (25, 35), and (13, 0) for the 400 MeV/u carbon beam and 235 MeV proton beam. The error bar represents the statistical error (one standard deviation). (a) 400 MeV/u carbon beam. (b) 235 MeV proton beam.



a)



b)

FIG. 6. Comparison of measured dose equivalent per the treatment absorbed dose at the center of the range-modulated region H/D_t and dose-averaged quality factor Q_D in this study and those of Wroe *et al.* (Ref. 20) for the proton beam. Here, the $Q(y)-y$ relationship by the ICRU 40 recommendation was used in both studies. WED means the water-equivalent depth of the measured position. (a) Dose equivalent per the treatment absorbed dose at the center of the range-modulated region H/D_t. Measured neutron ambient dose equivalents, $H^*(10)/D_t$, obtained with the rem meter WENDI-II in the previous study (Ref. 6) are also shown. (b) Dose-averaged quality factor Q_D. The error bar represents the statistical error (one standard deviation).

The dose due to fragments of an incident carbon beam is one of the primary components at positions close to the field edge, which is not simulated exactly in the treatment planning system presently employed at HIMAC.[45]

As mentioned in Sec. I, two reports presenting experimental dosimetric data on the secondary exposure in a phantom for passive proton radiotherapy have been published. Since the one by Mesoloras *et al.*[18] is for proton energies less than 160 MeV, we only compared our data to the data by Wroe *et al.*[20] In their paper, they determined the dose equivalent and dose-averaged quality factor with a microdosimetric technique using a silicon-on-insulator dosimetry system for several clinical treatment configurations. We chose the configuration of theirs which was the most similar to our experimental configuration, namely, the prostate configuration (beam range in water, 28.8 cm; beam modulation, 10.4 cm; maximum field dimensions, 6.9, 7.7 cm; and precollimation field diameter, 11.2 cm).

Figure 6 shows comparisons between the results of this study and Wroe *et al.*[20] for the proton-beam values of H/D_t and Q_D. Here, the $Q(y)-y$ relationship by the ICRU 40 recommendation was used in both studies. The depth in the water phantom d was converted to the water-equivalent depth (WED) because Wroe *et al.*[20] used a Lucite phantom: d values of 5, 15, and 35 cm corresponded to WEDs of 5.2, 15.2, and 35.2 cm, respectively, considering the WED of the phantom wall. Also, our previous study's results for the neu-

tron ambient dose equivalents per the treatment absorbed dose at the center of the range-modulated region $H^*(10)/D_t$ as measured with the rem meter WENDI-II (Ref. 46) are shown.[6] [WENDI-II used in the previous study was calibrated by using an ^{241}Am–Be neutron source and then could directly output $H^*(10)$.]

The H/D_t values obtained in this study were two to three times higher than those by Wroe *et al.*[20] This difference should be attributed to the facility dependency according to our previous study. However, since the experimental data are too scarce to confirm this, more experimental data at different facilities are needed. Also, it was found that the neutron ambient dose equivalent obtained with WENDI-II in the previous paper[6] provides a conservative dose estimation compared to the dose equivalent in the phantom. This result shows that measuring the undesired dose with a rem meter such as WENDI-II is good for the first estimation because the measurement with a rem meter is convenient and easy; however, the dose measurement in a phantom is needed for accurate risk assessment of secondary cancer.

Q_D values of this study were in good agreement with those of Wroe *et al.*[20] except for our 5.2 cm WED. Since the contribution of secondary neutrons produced in the beam-shaping devices was higher at 5.2 cm WED (d=5 cm) as written above, we expect that this difference is due to the facility dependency. However, it should be true that Q_D is higher as the position is closer to the phantom surface because the contribution of secondary neutrons produced in the beam-shaping devices with a high quality factor is higher. As the position became closer to the field edge (within ~20 cm from the field edge), Q_D decreased by 2 according to Wroe *et al.*[20] This is due to the scatter of incident protons as fragmental protons in the carbon beam. Also, Wroe *et al.*[20] mentioned that Q_D is relatively constant with a value of 5–6 after the distal edge. When our data were combined with that from Wroe *et al.*,[20] the following conclusions could be made: (1) At a position close to the field edge within ~20 cm from the field edge, Q_D is 2–5. (2) At a position close to the beam-shaping devices, Q_D is 7–8. There is a possibility that this value varies depending on the facility. (3) At other positions, Q_D is 5–6, which is here defined as the equilibrium Q_D. The equilibrium Q_D should depend on the energy of the incident proton beam as shown in the carbon beam. The conclusion for Q_D can be applied to the incident carbon beam. In carbon radiotherapy, Q_D is 2–4 within ~50 cm from the field edge and the equilibrium Q_D is 4–5.

V. CONCLUSIONS

We experimentally obtained absorbed doses, dose-averaged quality factors, and dose equivalents in water phantom outside of the irradiation field in passive carbon-ion and proton radiotherapies with TEPC. These data are very useful for estimating the risk of secondary cancer in patients receiving passive radiotherapies and for verifying Monte Carlo calculations, which can provide more detailed dose distribution. The comparison between carbon-ion and proton radiotherapies was done with approximately the same parameter settings of beam-shaping devices and exactly the same experimental setup. Assuming a prostate cancer treatment in which the total prescribed dose was 66 GyE for the 400 MeV/u carbon beam and 74 GyE for the 235 MeV proton beam, the total secondary exposure doses per treatment were comparable to or less than those in 3D-CRT and IMRT at all positions. In particular, as the position became closer to the field edge, the total dose equivalents in carbon-ion and proton radiotherapies were obviously less than those in 3D-CRT and IMRT. It was also found that the distributions and values of D/D_t, H/D_t, and Q_D differed for carbon-ion and proton radiotherapies. Combining the published data for proton beam and the results obtained in this study, the distribution of Q_D in water phantom was shown for a proton beam.

We are now working on verifying the Monte Carlo calculation of the dose distribution in water phantom with the experimental data from this study. We then plan to assess the organ-specific dose in an anthropomorphic phantom, which is essential to the risk assessment of the secondary cancer risk. Our final goal is to develop a system for assessing the secondary exposure dose of any patient receiving passive carbon-ion or proton radiotherapy.

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Improved dose-calculation accuracy in proton treatment planning using a simplified Monte Carlo method verified with three-dimensional measurements in an anthropomorphic phantom

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Abstract

Treatment planning for proton tumor therapy requires a fast and accurate dose-calculation method. We have implemented a simplified Monte Carlo (SMC) method in the treatment planning system of the National Cancer Center Hospital East for the double-scattering beam delivery scheme. The SMC method takes into account the scattering effect in materials more accurately than the pencil beam algorithm by tracking individual proton paths. We confirmed that the SMC method reproduced measured dose distributions in a heterogeneous slab phantom better than the pencil beam method. When applied to a complex anthropomorphic phantom, the SMC method reproduced the measured dose distribution well, satisfying an accuracy tolerance of 3 mm and 3% in the gamma index analysis. The SMC method required approximately 30 min to complete the calculation over a target volume of 500 cc, much less than the time required for the full Monte Carlo calculation. The SMC method is a candidate for a practical calculation technique with sufficient accuracy for clinical application.

(Some figures in this article are in colour only in the electronic version)

1. Introduction

In proton tumor therapy, tumor control while sparing adjacent organs requires a good treatment plan to maximize dose delivery to the target volume. The optimum plan is formulated by

evaluating the calculation results for a variety of beam configurations. The dose-calculation method must be fast and accurate.

Many facilities currently use pencil beam algorithms (PBAs) (Petti 1992, Hong 1996, Szymanowski 2001) for treatment planning. The required calculation time is relatively short and the accuracy of these algorithms is reasonable when the tumor is surrounded by structures of intermediate complexity. PBAs express the dose distribution formed by a mono-energetic proton pencil beam as a product of the depth-dose distribution in water obtained from measurements or Monte Carlo calculations and an off-axis radial function defined as a two-dimensional Gaussian function with an rms value determined by scattering in the materials along its central axis. The dose distributions of multiple pencil beams at various incident positions and energies are summed to obtain the dose distribution in the patient. Kohno *et al* developed a Range-Modulated-Pencil-Beam Algorithm (RMPBA) to shorten the calculation time while maintaining accuracy by using a measured depth-dose distribution for the combined beam rather than summing the contribution of protons at each specific energy (Kohno 2001).

Though PBAs perform well for homogeneous targets, the accuracy is decreased in targets with large lateral heterogeneity. Since the PBAs assume that the central axis is a straight line and determine the energy deposit and the lateral spread due to materials along the central axis, they do not include the effects of lateral density heterogeneity on the dose distribution. The PBAs also use a zero-thickness collimator approximation ignoring the edge scattering in the aperture collimator. These limitations decrease the dose-calculation accuracy of PBAs in heterogeneous media. In order to improve accuracy, Kanematsu *et al* developed a PBA variant that subdivides the pencil beam kernels into sub-pencil beams when it encounters a large heterogeneity (Kanematsu 2009).

The clinical application of full Monte Carlo calculations such as MCNPX (Waters 2002) or Geant4 (Agostinelli 2003) has been investigated (Paganetti 2008). Although they are capable of more accurately computing dose distribution, they require a long calculation time, up to 6 h per patient even using more powerful cluster machine than ours (Paganetti 2008). To reduce the calculation time, fast pseudo-Monte-Carlo algorithms were proposed (Li 2005, Yepes 2009).

Sakae *et al* (2000) developed a simplified Monte Carlo (SMC) method to obtain fast and accurate dose calculation in heterogeneous targets, and the accuracy of the method in simple targets was verified by Kohno *et al* (2002, 2003). Since the SMC method tracks individual particles, it includes lateral density heterogeneity effects on the dose distribution. A second advantage of the SMC method is easy implementation since it can use same input data for PBAs.

We implemented the SMC method in the clinical treatment planning system of the National Cancer Center Hospital East (NCCHE, Japan). We demonstrated the effectiveness of the SMC method by comparing the calculation results with measurement results in a heterogeneous slab phantom, and that in an anthropomorphic phantom simulating the complexity encountered in a clinical situation. The SMC results were also compared to RMPBA calculations. The data were analyzed using a number of methods, including a variant of the γ-index method (Low 1998) with an accuracy tolerance of 3 mm and 3%.

2. Materials and methods

2.1. Calculation model

A right-handed Cartesian system was used for dose-calculation coordinates in which the central beam axis coincided with the z-axis and the gantry rotated about the y-axis. Target data

in the original CT coordinate system were transformed into the dose-calculation coordinate system using the gantry and couch rotation angles.

The SMC method begins tracking individual protons at the entrance to the range compensator (RC). The initial beam parameters were provided by the effective-source model with the model parameters determined by measurements (Hong 1996, Symanovski 2001). The model provides the standard deviation of the initial angular distribution at any point on the entrance plane. The proton fluence distribution was based on the lateral-dose distribution measured without the RC and aperture collimator. In the system arrangement at the NCCHE, the RC is placed upstream of a patient-aperture collimator. For calculation of range loss and scattering of individual protons in material, polyethylene RC and 60 mm thick brass aperture collimator were divided into segments with a thickness of 1 mm along the z-axis. Patient volume was divided into cubic voxels with twice the edge length of the CT pixels. Each particle was characterized in terms of position, the direction expressed by the two projection angles, and the residual range in water. The trajectory of each particle was tracked by assuming multiple Coulomb scattering with scattered projection angles expressed as a normal random number with a standard deviation calculated using the Highland formula (Highland 1975, 1979). The energy loss of a proton in a segment of material was calculated using the water equivalent model (Chen 1979). We assumed that the relative dose deposit in a patient voxel could be obtained from the measured depth-dose distribution in water. One reason for the shorter calculation time of the SMC method compared with full Monte Carlo methods is the simplification in which the dose deposit in materials is calculated using the measured depth-dose distribution for a mono-energetic proton beam in water, and ignoring absorption and lateral scattering due to nuclear reaction. Note that use of the measured depth-dose curve in water implicitly includes some averaged effects from nuclear interactions.

The calculation method was compared to the RMPBA with the measured effective source model.

2.2. *Experiment*

We verified the calculation accuracy of the SMC method by comparing the calculation results with the measured dose distributions in the heterogeneous phantoms described in sections 2.2.1 and 2.2.2. The proton beam was extracted from the 235 MeV cyclotron at the NCCHE. For some experiments the energy was reduced using the energy-selection-system (ESS), and the beam was transferred to a passive beam spreading system using the double-scattering method (Nishio 1999, Tachikawa 1999).

A PTW 2D Array seven29™ was used for dose detection. This is a two-dimensional detector matrix containing 729 ionization chambers in a 10 mm pitch 27 × 27 array developed by ®PTW Freiburg GmbH. Spezi reported the successful application of this detector to radiation therapy and verified the performance (Spezi 2005). The sensitive volume of a unit chamber is 5 mm × 5 mm × 5 mm. The ionization chambers of the array are open to the air. The offset thickness from the entrance surface to the center of the sensitive volume is 8 mm in WEL.

To compare the calculation results and measurements under the same conditions, we corrected the calculation of depths by the offset thickness when calculating the dose distributions. We also convolved the calculation results with the detector cell size of 5 mm × 5 mm.

2.2.1. Slab phantom. The heterogeneous slab phantom depicted in figure 1 was used for evaluation of the SMC method. We investigated lateral density heterogeneity effects on dose

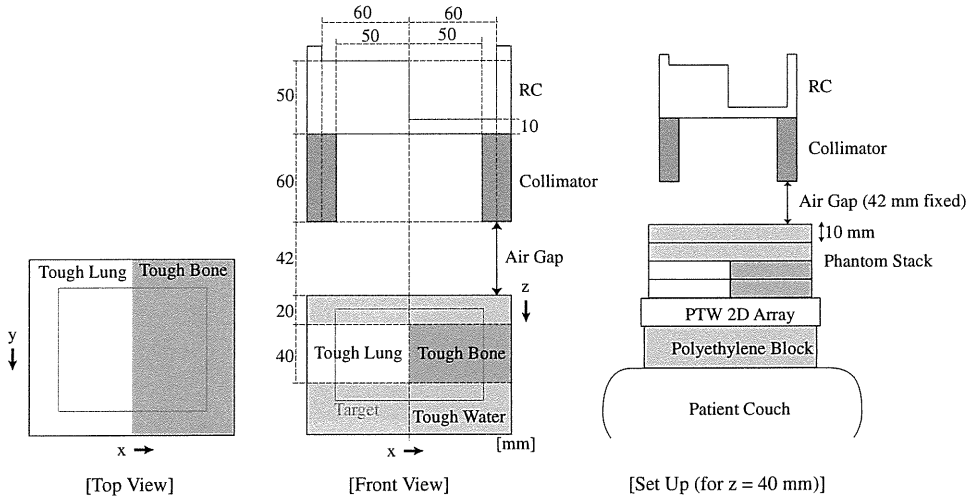

Figure 1. Experimental arrangement of heterogeneous slab phantom, RC and aperture collimator. The red line indicates the target region.

distribution using a 150 MeV proton beam passing through a ridge filter with a spread-out Bragg peak (SOBP) width of 80 mm. The phantom was constructed by combining 10 mm thick component slabs made from Tough Water (TW), Tough Lung (TL), and Tough Bone (TB) (®Kyoto Kagaku Co., Ltd). The water-equivalent–thickness ratios (Takada 2008) of TW, TL and TB are 1.01, 0.34 and 1.40, respectively. We designed the RC and the aperture collimator for the cube-shaped target with a volume of 800 cc (indicated by the red line in figure 1).

Lateral dose distributions were measured at depths of $z = 0$ mm, 20 mm, 40 mm, 60 mm, 80 mm and 90 mm. A stack of the phantom slabs was mounted on the detector to measure the dose distribution in each depth as shown in figure 1. When a different phantom stack was mounted, we fixed the distance between the aperture collimator and the phantom entrance surface by adjusting the vertical position of the patient couch. Since the chamber pitch was 10 mm, we shifted the detector by 5 mm in the x and y directions to obtain measurements with a lateral sampling pitch of 5 mm. Each measurement was repeated three times at each depth and averaged to obtain the lateral-dose distribution.

The simulation required approximately 40 min with a target voxel size of 1 mm per side using 1.14×10^8 generated protons on four cores (two dual-core 2.4 GHz AMD Opteron CPUs, four jobs running in parallel). All the dose data sets were normalized at a point ($x =$ 30 mm, $y = 60$ mm) in a flat dose region for comparison of measurements and calculations. The estimated mean statistical error of the calculated dose in the target region was 1% rms, and that of the convolved calculated dose was 0.2% rms. Reduction of the error in the convolved calculated dose came from the larger voxel size.

2.2.2. RANDO phantom. We used the head portion from a RANDO® phantom produced by the Phantom Laboratory® to simulate the complex arrangement of materials experienced in clinical applications. The RANDO phantom mimics the density distribution in the human head using resins with various compositions. Figure 2 contains the median sagittal and median horizontal CT images and the PTV. The phantom is composed of horizontal layers of 25 mm thick. We measured the dose distributions in the layers with the z-index numbered from 1

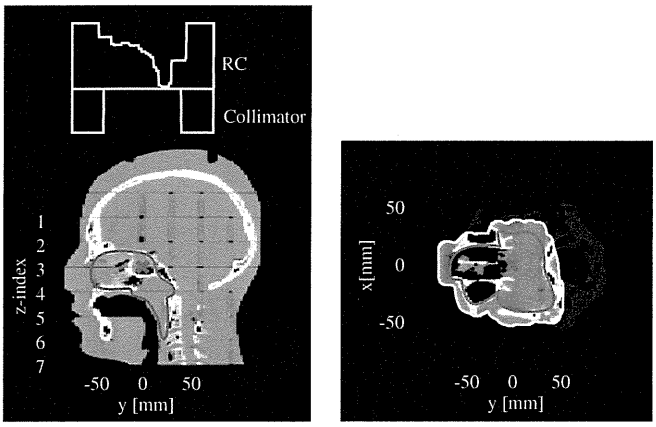

Figure 2. Median sagittal and median horizontal CT images of the head portion from the RANDO phantom. The iso-center (red cross), PTV (red line) and RC and collimator shape (white line) are also depicted.

to 7 as shown in the figure. To simulate clinical situations, we followed the actual patient treatment procedure: obtaining a CT, delineating the PTV, determining the beam direction, manufacturing the corresponding RC and aperture collimator, aligning the reference surface markers on the phantom with laser cross-hairs and irradiating the phantom on the patient couch. We designed a treatment plan assuming a head and neck cancer with a volume of approximately 500 cc. The smearing distance of the RC (Kooy 2008) was taken at 4.5 mm. Since the measurement plane was limited to the horizontal plane due to the layered structure of the phantom, the irradiation direction was also limited to downward from the top of the head. Although the results have no clinical significance due to the unrealistic selection of the irradiation direction, it simulates the dose distribution in the complex heterogeneous region typically found in the head and neck cases.

We used a 235 MeV proton beam with a SOBP width of 80 mm. We mounted a stack of phantom layers on the detector to measure the dose distribution in each measurement plane. The distance between the aperture collimator and the phantom entrance surface was fixed by adjusting the couch height, again. The reported results are the average of three measurements. To estimate the effect of set-up errors on the dose distribution, we repeated the set-up and measurement procedure three times on the $z = 4$ layer where a complicated lateral-dose distribution was expected.

The simulation required approximately 30 min when the target voxel size was 1.17 mm on a side and the number of generated particles was 4.68×10^7 on four cores (two dual-core 2.4 GHz AMD Opteron CPUs, four jobs running in parallel). All the dose data sets were normalized with reference to the dose at the iso-center for comparison. The estimated mean statistical error of the calculated dose in the target region was 1.2% rms, and that of the convolved calculated dose was 0.25% rms.

3. Results

3.1. Slab phantom

Figure 2 compares the iso-dose distributions obtained from (a) measurements, (b) the SMC calculation and (c) the RMPBA calculation. In the figure, we note that the high-dose region

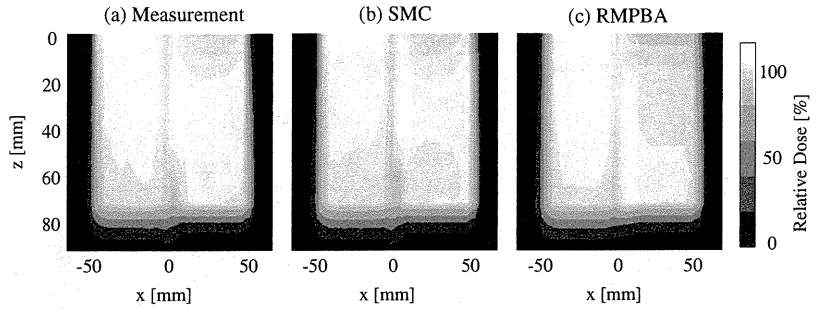

Figure 3. Iso-dose distributions in the heterogeneous slab phantom from (a) measurements, (b) the SMC and (c) the RMPBA. The measurements were obtained at $z = 0$ mm, 20 mm, 40 mm, 60 mm, 80 mm and 90 mm.

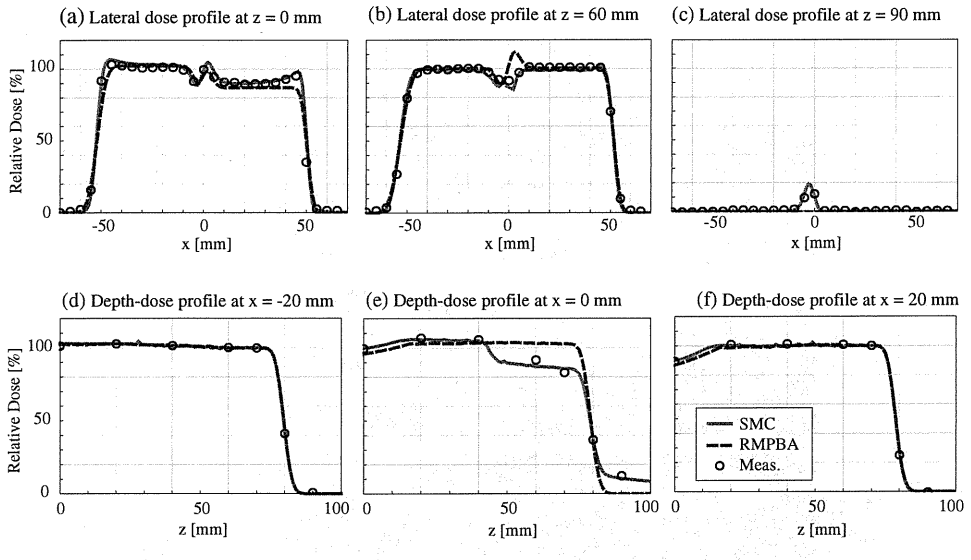

Figure 4. Dose profiles in the heterogeneous slab phantom: solid lines indicate the SMC prediction, dashed lines indicate the RMPBA prediction, and open circles represent measurements. Figures (a)–(c) are lateral-dose profiles at $z = 0$ mm, 60 mm and 90 mm. Figures (d)–(f) are depth-dose profiles at $y = -20$ mm, 0 mm and 20 mm. Since the estimated measurement error from three measurements in each set-up is less than 1.0%p-p of the normalization dose, error bars are not displayed (smaller than circles).

around $x = 0$ mm extends to a region deeper than 50 mm only in the RMPBA. Such differences of dose distribution are shown more clearly in lateral- and depth-dose profiles of figure 4. The SMC method reproduced the measurement results better than the RMPBA in three regions. The first is the peripheral high-dose region around $x = \pm 50$ mm in figure 4(a) that is influenced by the scattered and energy-degraded protons interacting with the edge of the aperture collimator. The SMC method accurately reproduced the measured dose distribution, while the RMPBA does not take into account edge-scattered proton paths and cannot reproduce the dose distribution well in this region. The second region is a dose reduction at depths between $z = 40$ mm and $z = 70$ mm in the vicinity of $x = 0$ mm (figures 4(b) and (e)). This area is influenced by protons passing through both the thicker section of the RC and the

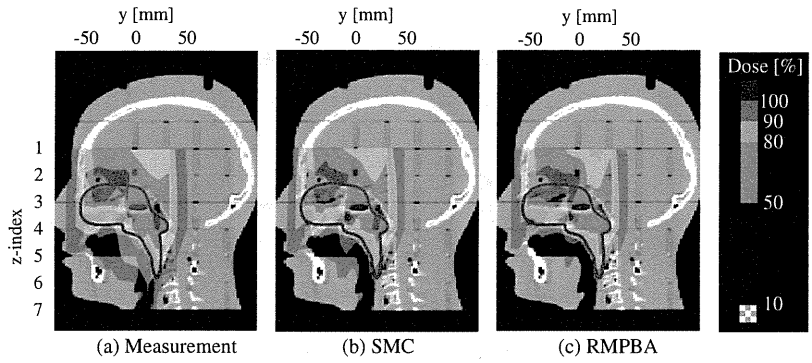

Figure 5. Median sagittal iso-dose distributions in the anthropomorphic phantom from (a) measurements, (b) the SMC and (c) the RMPBA.

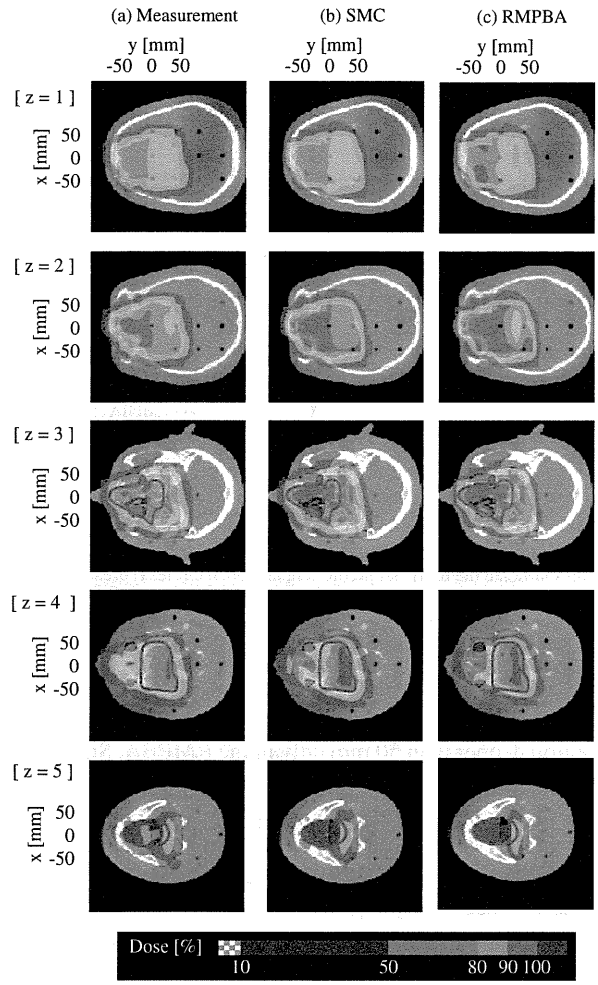

Figure 6. Horizontal iso-dose distributions in the anthropomorphic phantom. The red lines show the target region.

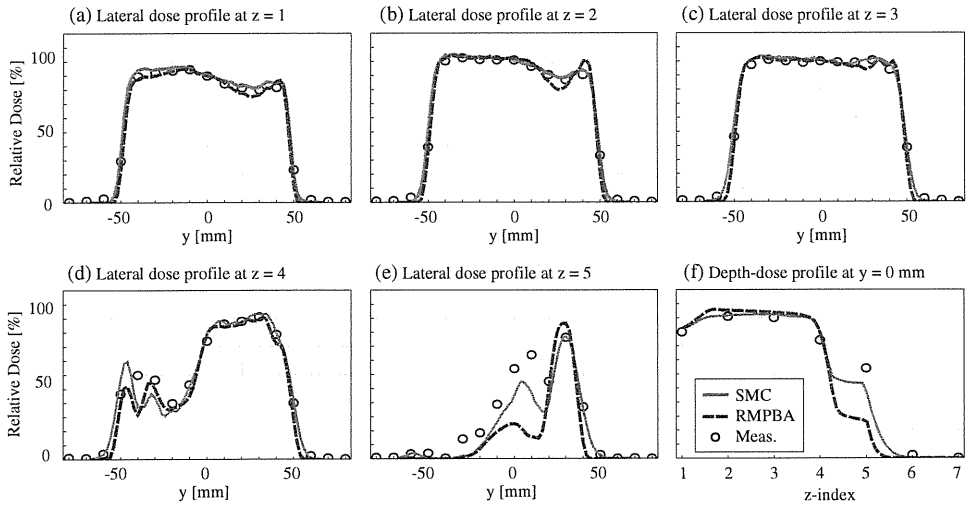

Figure 7. Lateral- and depth-dose profiles in the anthropomorphic phantom. The solid lines depict calculation results using the SMC, the dashed lines depict calculation results from the RMPBA, and the hollow circles represent measurements. Figures (a)–(e) are lateral-dose profiles on the $z = 1$, 2, 3, 4 and 5 levels, and figure (f) is a depth-dose profile at $y = 0$ mm. Since the estimated measurement error from three measurements in each set-up is less than 1.3%p-p of the normalization dose, error bars are not displayed (smaller than circles).

higher-density region in the phantom. The third region is a low-dose region near $x = 0$ mm at a depth of $z = 90$ mm (figures 4(c) and (e)) formed by protons passing through both the thinner section of the RC and the lower-density region in the phantom. Note that this region is located deeper than the target distal boundary. The RMPBA could not reproduce the dose in this region due to the disregard of irregular proton paths mentioned above while the SMC could.

Both the SMC and the RMPBA perfectly reproduced the depth-dose distribution in the region lacking lateral heterogeneity (figures 4(d) and (f)). The difference in calculation accuracy between the SMC and the RMPBA in figure 4(e) was caused by the difference in operation between the two algorithms; the SMC method tracks almost all proton paths while some paths in the RMPBA are missing.

3.2. RANDO phantom

Figures 5 and 6 describe the iso-dose distributions in the median sagittal plane and horizontal planes obtained using (a) measurements, (b) the SMC calculation and (c) the RMPBA calculation. We ignored the $z = 6$ and $z = 7$ planes because almost no protons reached these levels. The number of measurement points irradiated with more than 10% of the normalization dose was 80, 82, 88, 88 and 41 for $z = 1$ through 5. Apparent discrepancy between the target distal boundary and the dose distal boundary can be attributed to difference between the displayed depth and the measured depth by the detector with a cover thickness of 8 mm WEL. Since our interest is focused on difference between measurements and calculations, this is not a major issue here. In the figures, you will note that both the SMC and the RMPBA reproduced the overall measured distribution in some accuracy. Yet there are some local differences shown in dose profiles of figure 7: (a)–(e) are lateral profiles at $z = 1$–5, and (f) is a distal profile at

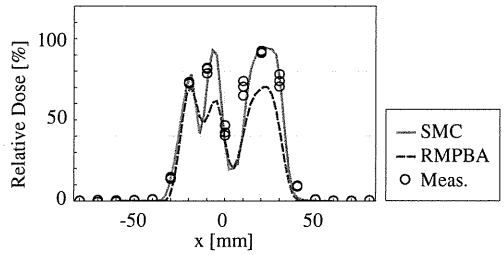

Figure 8. Effect of alignment error on dose distribution in the anthropomorphic phantom along the x-axis at $y = -20$ mm on the $z = 4$ layer. The dose errors caused by set-up misalignment are large at $x = 10$ mm and $x = 30$ mm where the dose gradient is large. Since the estimated measurement error from times measurements in each set-up is less than 0.7%p-p of the normalization dose, error bars are not displayed (smaller than circles).

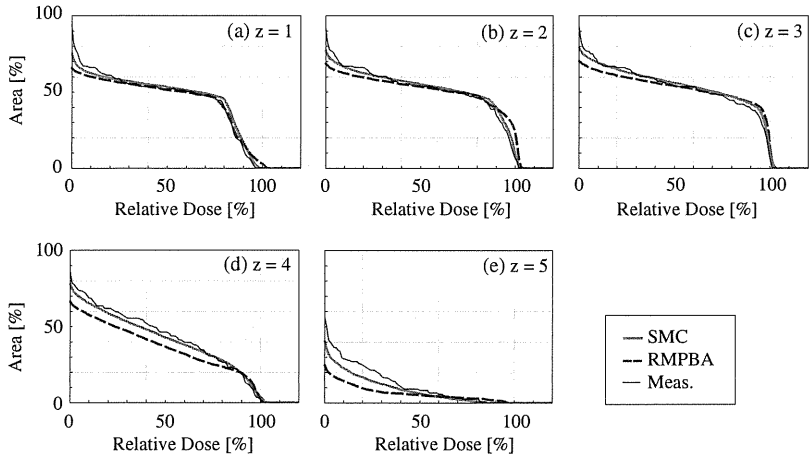

Figure 9. Comparison of dose-surface histograms in each plane from measurements, SMC calculation and PBA calculation. The black solid lines depict the measurement data, the red solid lines depict the SMC results and the blue dashed lines depict the RMPBA results.

$y = 0$ mm. Figures 4(a)–(c) show that both calculations reproduce measurements well with minor local differences. In contrast, we note large discrepancy between measurements and calculations and difference between the SMC and the RMPBA in a part of figures 4(d)–(f). The discrepancy between measurements and calculations is caused by the range uncertainty of the phantom and the large dose gradient in the distal fall-off part of the Bragg curve. The difference between the SMC and the RMPBA notably found in figures 4(e) and (f) is caused by the fact that the RMPBA disregards dose contribution of protons passing through the irregular paths along the phantom and reaching the deep region and underestimates the dose in the deep region.

We also examined the dose error caused by misalignment of the RC, aperture collimator, phantom and detector. Figure 8 depicts three lateral-dose profiles on the $z = 4$ layer of the head phantom following three separate set-up procedures. The figure also contains the SMC and the RMPBA calculation results for the case of no set-up error. The $z = 4$ layer was selected since it includes a region with a large dose gradient in the lateral direction that is

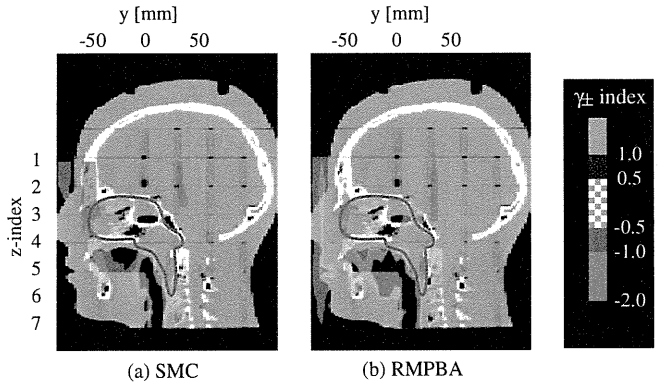

Figure 10. The $\gamma_{\pm}$-index distributions in the median sagittal plane of the anthropomorphic phantom from (a) the SMC and (b) the RMPBA. The RMPBA exhibits a larger underestimated region than the SMC.

sensitive to set-up error. The measured dose error due to misalignment was a maximum of 9.2%p-p of the normalization dose. Such a large dose error can be attributed to an estimated set-up error of ± 0.5 mm and the large dose gradient. The misalignment error is consistent with error of the alignment system using laser cross-hairs.

Figure 8 compares the dose-surface histograms (DSH) obtained from measurements, the SMC calculation and the RMPBA calculation in each measurement plane. The SMC method is superior to the RMPBA, which underestimates the dose in deeper regions. The difference in calculation accuracy between the two algorithms arises from consideration or disregard of irregular proton paths in heterogeneous media. The dose underestimation observed in the $z = 5$ layer even by SMC is caused by uncertainty in the CT-value-to-range conversion and by the large low-density region representing the oral cavity present in this layer. Since most protons in this region have a small residual range, the dose in this region is very sensitive to small uncertainties in the proton range.

4. Discussion

We evaluated the calculation accuracy using the γ-index method (Low 1998). This method simultaneously evaluates the dose difference and the distance to agreement quantitatively. We newly defined a signed-gamma-index ($\gamma_{\pm}$-index) at each measurement position to differentiate between overestimation and underestimation of the dose:

$$\gamma_{\pm}(\boldsymbol{r}_m) = \frac{D_c(\boldsymbol{r}_m) - D_m(\boldsymbol{r}_m)}{|D_c(\boldsymbol{r}_m) - D_m(\boldsymbol{r}_m)|} \times \min_{r_c} \left[\sqrt{\frac{(D_c(\boldsymbol{r}_c) - D_m(\boldsymbol{r}_m))^2}{D^2_{\text{tolerance}}} + \frac{(\boldsymbol{r}_c - \boldsymbol{r}_m)^2}{r^2_{\text{tolerance}}}} \right], \tag{1}$$

where D_m and D_c represent the measured and calculated doses, r_c and r_m are the calculated and measured positions, and the parameters $D_{\text{tolerance}}$ and $r_{\text{tolerance}}$ are the tolerance error values of the dose and the distance. The acceptable error in proton therapy dose calculation for heterogeneous targets is not clearly defined at present. We followed the recommendations of Low (1998) for photon therapy, and used 3% for $D_{\text{tolerance}}$ and 3 mm for $r_{\text{tolerance}}$ in this paper. We also defined the pass rate as the fraction of calculation points satisfying the condition of $-1 < \gamma_{\pm} < 1$.

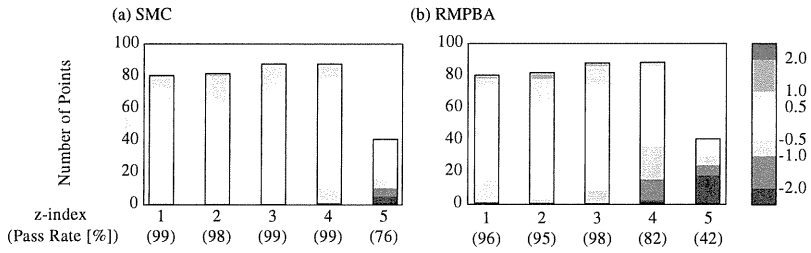

Figure 11. $\gamma_{\pm}$-index histogram for (a) the SMC and (b) the RMPBA. The $\gamma_{\pm}$-index in the stacked bar chart is shown in decreasing order from top to bottom. The number of points contained in a range of signed gamma index is indicated by the height of each bar. The pass rate is printed under the z-index.

Figure 10 illustrates the $\gamma_{\pm}$-index distributions on the median sagittal plane for (a) the SMC and (b) the RMPBA. Figure 5 contains stacked bar charts representing the $\gamma_{\pm}$-index for (a) the SMC and (b) the RMPBA. We expressed the $\gamma_{\pm}$-index scale using various intensities of red to highlight positive regions and blue for negative regions. The color intensity is proportional to the absolute value of the $\gamma_{\pm}$-index. The pass rates in individual horizontal planes are also indicated under the z-index of the measurement planes. While calculation results obtained using the SMC method agreed well with the measurement results for layers $z = 1$–4, the pass rates for the RMPBA method fell below 90% in the $z = 4$ and 5 layers due to underestimation of the dose. Therefore, the SMC method is superior in the calculation accuracy to the RMPBA. Since the SMC method can accurately reproduce the measured dose distribution in complex media within a reasonable calculation time, it is capable of improving the accuracy of dose calculations in clinical situations.

5. Conclusion

We implemented the SMC method in the treatment planning system of the NCCHE in order to improve dose-calculation accuracy in heterogeneous targets. The SMC method is easy to implement because it can use the same input data for PBAs. We verified the effectiveness of the SMC method by comparing the calculation results to the dose distributions measured at different depths in a heterogeneous slab phantom using a two-dimensional detector. We also measured the dose distributions at seven horizontal planes in an anthropomorphic phantom. For both these cases, we found that the SMC method reproduced the measured dose distributions better than the RMPBA. In the slab phantom, we found that the RMPBA overestimated the dose in shallow regions and underestimated the dose in deep regions due to disregard of some proton paths in the heterogeneous region. The same tendency was also found for the RMPBA dose calculations for the anthropomorphic phantom. Since PBAs fundamentally have a risk of disregarding some proton paths, they may underestimate the dose in deep region for the case with large heterogeneity around the target.

We evaluated the treatment plan using the $\gamma_{\pm}$-index analysis and found that the SMC method reproduced the measured dose distributions well within the accuracy tolerance of 3 mm and 3% in almost all regions. In addition, the calculation time required for the SMC method was about 30 min for a typical clinical case (target volume of 500 cc). The SMC method provides the higher calculation accuracy than RMPBA within a reasonable time, even for such a complex case. Since verification of the effectiveness of the SMC method is required

for many clinical cases, we have begun a retrospective comparison between the SMC and PBA methods using previous proton therapy cases.

Acknowledgments

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PHYSICS CONTRIBUTION

THE DEVELOPMENT AND CLINICAL USE OF A BEAM ON-LINE PET SYSTEM MOUNTED ON A ROTATING GANTRY PORT IN PROTON THERAPY

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Purpose: To verify the usefulness of our developed beam ON-LINE positron emission tomography (PET) system mounted on a rotating gantry port (BOLPs-RGp) for dose–volume delivery-guided proton therapy (DGPT).
Methods and Materials: In the proton treatment room at our facility, a BOLPs-RGp was constructed so that a planar PET apparatus could be mounted with its field of view covering the iso-center of the beam irradiation system. Activity measurements were performed in 48 patients with tumors of the head and neck, liver, lungs, prostate, and brain. The position and intensity of the activity were measured using the BOLPs-RGp during the 200 s immediately after the proton irradiation.
Results: The daily measured activity images acquired by the BOLPs-RGp showed the proton irradiation volume in each patient. Changes in the proton-irradiated volume were indicated by differences between a reference activity image (taken at the first treatment) and the daily activity-images. In the case of head-and-neck treatment, the activity distribution changed in the areas where partial tumor reduction was observed. In the case of liver treatment, it was observed that the washout effect in necrotic tumor cells was slower than in non-necrotic tumor cells.
Conclusions: The BOLPs-RGp was developed for the DGPT. The accuracy of proton treatment was evaluated by measuring changes of daily measured activity. Information about the positron-emitting nuclei generated during proton irradiation can be used as a basis for ensuring the high accuracy of irradiation in proton treatment. © **2010 Elsevier Inc.**

Dose–volume delivery guided proton therapy (DGPT), Beam ON-LINE PET system on rotating gantry port (BOLPs-RGp), Target nuclear fragment reaction.

INTRODUCTION

Proton therapy is a form of radiotherapy that enables the concentration of a dose onto a tumor by the use of a scanned or modulated Bragg peak. Therefore, it is very important to evaluate the proton-irradiated volume accurately.

Recently, to ensure the high accuracy of proton therapy, imaging studies of positron-emitting nuclei that are generated by target nuclear fragment reactions involving incident protons and nuclei from a patient's body have been performed (1–14). The annihilation gamma rays from the positron-emitting nuclei were measured by a positron emission tomography (PET) system (specifically a beam OFF-LINE PET system using commercial PET apparatus or PET-computed tomography [CT] apparatus postirradiation or a beam ON-LINE PET system in a proton treatment room). The beam OFF-LINE PET system using the commercial PET-CT apparatus has the advantage of being able to easily acquire fusion images and the ability to reconstruct three-dimensional images. However, the time required for the movement of the patient to the PET room (10–30 min) and the resulting deterioration of the statistical accuracy of the acquired data are large disadvantages. With the beam ON-LINE PET system, capturing a large view and the acquisition of three-dimensional images are difficult because of geometrical problems caused by the beam direction and the PET apparatus (7, 15, 16).

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The ability to take daily PET images with a high statistical accuracy while the patient remains in the proton irradiation room is a large advantage. Besides, availability of a cone beam (CB) CT system or CT apparatus in the irradiation room can offer the possibility of daily and in situ monitoring of the patient's anatomy. A prototype beam ON-LINE PET system (BOLPs) was previously constructed for basic research (10), and verification of the proton-irradiated volume in a patient's body was confirmed using a PET apparatus and a PET-CT apparatus (beam OFF-LINE PET system) (13).

A BOLPs mounted on a rotating gantry port (BOLPs-RGp) was constructed in our proton treatment room. Activity measurement and PET imaging were performed in 48 patients with tumors of the head and neck, liver, lungs, prostate, and brain during proton treatment at our facility. The position and intensity of the activity were measured daily using the BOLPs-RGp immediately after proton irradiation. Using the activity measurement, we were able to confirm whether the proton beam irradiation of the tumor was reproducibly performed during the treatment period. Moreover, changes in the activity distribution were observed as the volume of the tumor changed, and these changes were related to the delivery dose, changes in the body shape and position of the patient, and the physiologic changes. The PET images from the BOLPs-RGp were sufficient to provide high-quality proton treatment.

METHODS AND MATERIALS

Design of a beam ON-LINE PET system mounted on an RGp

Via the detection of pairs of annihilation gamma rays emitted from the generated radioactive nuclei of a patient's body, the BOLPs-RGp is designed to determine the position and activity of the positron-emitting nuclei generated in patients by proton irradiation. Figure 1 is a picture of the BOLPs-RGp. The BOLPs-RGp was developed as a standardized system for use with proton therapy devices. During proton therapy, the detector heads have many degrees of freedom and the system allows remote control adaptation to each new proton beam condition and a patient's position. As a result, the measurement of the activity distribution is simple.

A planar positron imaging system (Hamamatsu Photonics K. K., Hamamatsu, Japan) (17) was newly arranged for the BOLPs-RGp. In comparison to the system used previously (10), the 24 detector units mounted on each detector head were increased to 36 detector units, and each unit was composed of 11 × 10 arrays of BGO ($Bi_4Ge_3O_{12}$) crystals with a crystal size of 2 × 2 × 20 mm^3. Furthermore, the 2,400 crystals were increased to 3,600 crystals. The gap of each unit became 3.3 mm from 11.0 mm for minimizing dead space in the detector. The field of view (FOV) became 164.8 × 167.0 mm^2 from 120.8 × 186.8 mm^2. The maximum field size is 185.0 × 185.0 mm^2 in the rotating gantry port with the BOLPs-RGp. Therefore, the FOV can almost cover each treatment site of the head and neck, liver, lungs, prostate, and brain for a proton treatment in our facility. However, in case of prostate, the depth activity distribution is not measured in the entrance of the incident proton beam. The BOLPs-RGp was mounted on and the center of its detection area was aligned with the iso-center of the rotating gantry in the treatment room of the proton therapy facility at our center. A PET image reconstructed by a back-projection method

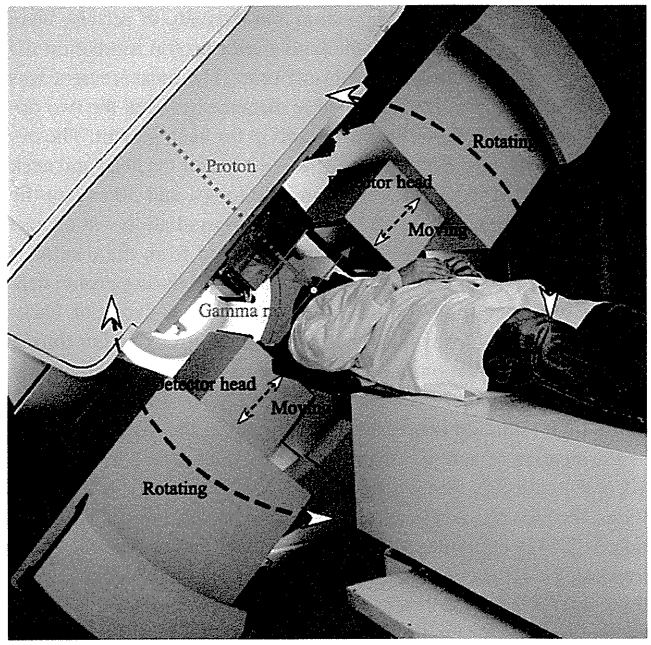

Fig. 1. Setup of the BOLPs-RGp, which is mounted on the rotating gantry port of our proton treatment room.

along the axis of the proton beam direction is always included in the FOV of the opposing detectors together with the axis of the rotating angle of the gantry system. The distance between the two opposing detector heads of the BOLPs-RGp can be adjusted from 30 to 100 cm. When the activity is not being measured, the detector head is stored inside the wall of the gantry device. The position resolution of this system is about 2 mm for the full width at half maximum in the case of use of ^{22}Na point source. The maximum data collection rate for the coincident detection of pair annihilation gamma rays is about 4,000 counts/s/cm^2 (kcps/cm^2). The accuracy of the measurements of activity distribution by this system was verified by a prototype beam ON-LINE PET system (10). The measured data are stored using in the software's list mode format. The activity image is renewed every second. The information of the on-off time points of beam irradiation is recorded in the data, and the image can be restructured according to this information. The PET data from the irradiation field of each patient are managed throughout each treatment day.

The detection efficiency of the distance between the detector heads was calibrated by using the thin-flat acrylic container filled with ^{18}F-solution. The calibration is used for a correction of the imaging uniformity and the detection sensitivity. The attenuation coefficient of 511-keV gamma rays in the patient's body was calculated by the patient's CT image data. They are used for a construction of the activity imaging. The correction of the photon scattering in the patient's body is not considered for the activity imaging. Furthermore, the photons scattered in the patient's body outside the FOV are detected by the effect of the geometry of the detector head. Therefore, the activity image is contaminated by about 10% background in this system. As the result, the position resolution of the activity distribution will become large more than 2 mm in the clinical case of a proton therapy.

Activity measurement in a patient during proton treatment

The measurement of activity was performed daily in 48 cases involving tumors of the head and neck, liver, lungs, prostate, and brain