Radiotherapy and Oncology 113 (2014) 72–76

Contents lists available at ScienceDirect

Radiotherapy and Oncology

journal homepage: www.thegreenjournal.com

Particle beam therapy

Dose distribution resulting from changes in aeration of nasal cavity or paranasal sinus cancer in the proton therapy

Nobuyoshi Fukumitsu *, Hitoshi Ishikawa, Kayoko Ohnishi, Toshiyuki Terunuma, Masashi Mizumoto, Haruko Numajiri, Teruhito Aihara, Toshiyuki Okumura, Koji Tsuboi, Takeji Sakae, Hideyuki Sakurai

Proton Medical Research Center, University of Tsukuba, Japan

ARTICLE INFO

Article history:
Received 13 November 2013
Received in revised form 18 August 2014
Accepted 18 August 2014
Available online 19 September 2014

Keywords:
Cancer
Nasal cavity
Paranasal sinus
Proton beam therapy
Aeration

ABSTRACT

Background and purpose: Aeration in the nasal cavity and paranasal sinus (NCPS) was investigated during the course of proton therapy (PT), and the influence of aeration on the dose distribution was determined.
Material and methods: Twenty patients with NCPS cancer (10 nasal cavity, 10 paranasal sinus) were analyzed. All the patients received a total proton beam irradiation dose of 38–78.4 Gray equivalents (GyE). Two to five CT examinations were performed during the course of treatment. The aeration ratio inside the cavity/sinus was calculated for each CT observation. Moreover, a simulation study supposing that the first treatment plan had been continued until the end of treatment was performed using the subsequent CT findings.
Results: The aeration ratio was increased in 18 patients. The largest increase was from 15% to 82%. Three patients had a simulated maximum cumulative dose in the brainstem of beyond 60 GyE, while 10 patients had a simulated maximum cumulative dose in the optic chiasm of beyond 50 GyE. The shortest simulated time period to reach the dose limitation was 21 days.
Conclusions: Aeration in the NCPS is altered during the course of PT treatment and can greatly alter the dose distribution in the brainstem and optic chiasm.

Proton therapy (PT) for cancer treatment was developed in the 1950s. A proton beam enables a rapidly increasing dose at the end of its beam range [1]. Because of its excellent dose escalation characteristics, PT is very useful for the treatment of many types of cancer, and the number of facilities for PT has been increasing worldwide in recent years. For nasal cavity or paranasal sinus (NCPS) cancers, PT enables the delivery of a high irradiation dose to the tumor without exceeding the tolerant irradiation dose to close critical organs, such as the brainstem and optic chiasm, and has been recognized as a useful treatment tool [2–5].

The NCPS region contains complicated structures such as bone, mucosa, tumor tissue, collected fluid, and air, which can alter the different proton beam ranges. Moreover, the ratios and geometrical distributions of these components are largely altered during the course of treatment in most patients. Especially, changes in the mucosal thickness, tumor volume, and collected fluid can contribute to the amount of aeration inside the NCPS. These changes can alter the proton beam range to a large degree and in an inhomogeneous manner during the course of treatment.

In particular, increases in aeration as a result of tumor shrinkage should extend the proton beam range to a greater depth. Physicians are frequently obliged to irradiate critical organs at the maximum tolerable dose during the treatment of advanced NCPS cancer patients. Therefore, slight dose distribution changes to critical organs are associated with a risk of inducing severe side effects. However, to our knowledge, no detailed reports have investigated changes in aeration and dose distribution to critical organs in NCPS cancer patients undergoing treatment with PT.

We calculated the amount of aeration inside the NCPS quantitatively and investigated the changes in aeration during the course of PT. Moreover, we conducted a simulation study under the assumption that the first treatment plan had been continued until the end of treatment using subsequent CT findings obtained during the course of treatment. Then, we investigated the changes in the dose distribution to critical organs located beneath the tumor.

Materials and methods

We analyzed 20 consecutive adult NCPS cancer patients (31–87 years old, 13 men and 7 women) examined between December 2009 and March 2013. The primary site was the nasal cavity in 10 patients, the maxillary sinus in 6, and the ethmoid sinus in 4. The

* Corresponding author. Address: Proton Medical Research Center, University of Tsukuba, 1-1-1, Tennoudai, Tsukuba 305-8575, Japan.
E-mail address: fukumitsun@yahoo.co.jp (N. Fukumitsu).

http://dx.doi.org/10.1016/j.radonc.2014.08.024

pathological findings were squamous cell carcinoma (SCC) in 8 patients, melanoma in 5, neuroblastoma in 3, adenoid cystic carcinoma in 1, cylindrical cell carcinoma in 1, poorly differentiated carcinoma in 1, and small cell carcinoma in 1. Visually, the primary tumor fully occupied the NCPS in 13 patients, occupied more than half of the NCPS in 4 patients, and occupied less than half of the NCPS in 3 patients. The number of CT examinations performed for dose planning during the course of treatment was 2–5, including first planning CT examination. The timing of the CT examinations was decided based on routine disease checks (at an interval of about 2–3 weeks), visually observed changes in the intranasal condition, cumulative irradiation doses to critical organs, or the physician's medical decision.

PT was performed in all the patients. Uniform scanning was used for the proton beam. In detail, a broad proton beam using the double-scattering method was prepared for the treatment. The beam delivery system created a homogeneous dose distribution at the prescribed dose using the spread-out Bragg peak of the proton beam. The total irradiation dose was 38 Gray equivalents (GyE) in 1 patient who had previously received X-ray radiotherapy and 56–78 GyE in the other 19 patients (Table S1). The number of beam directions was 2 or 3 (28 anterior direction (0–30 degree), 4 anterolateral (31–60 degree), 6 lateral (61–90 degree), and 6 posterolateral (more than 91 degree)) at the first planning. The dose distribution was calculated using VQA plan, Ver. 2.0 (Hitachi, Ltd). Treatment planning was modified 1–4 times during the treatment course in 19 patients, and only 1 patient received a constant irradiation field.

Aeration calculation study

The data analysis was performed using the Dr. View/LINUX image analysis software system (AJS Inc., Tokyo, Japan), as shown in Fig. S1. First, image registration of subsequent CT images was performed using the first planning CT as a reference. For image registration, we used a three-dimensional rigid registration algorithm developed by Maes et al. [6]. The rigid registration used a mutual information algorithm for which the image intensity values of the corresponding voxel pairs reached a maximum if the images were geometrically aligned. The registration error was estimated to be a maximum of 1–2 mm [6]. The registration result was visually checked, and none of the patients required manual adjustments in this study. Second, the sinus in which the tumor existed was manually contoured during the first planning CT examination. We defined the sinus in which the tumor existed as the main sinus in this study. Next, an image of the main sinus was constructed by subtracting the outside of the contoured area from the first planning CT image. For the subsequent CT image, the same contoured area was applied and the main sinus image was constructed in the same way (Fig. S1).

Images were constructed for bone, soft tissue, and air. Then, the volume of the real main sinus (A) was calculated by subtracting the bone tissue component from the original volume. The aeration ratio of the main sinus was calculated using (A) and the volume of the air (B), as shown by the equation below:

$$\text{Aeration ratio} = (B/A) \times 100\ (\%).$$

The aeration ratio of the other sinuses was also calculated in the same way.

Simulation study

We performed a simulation study of the dose distribution to the critical organs supposing that the first treatment plan had been used throughout the course of treatment. We applied the same irradiation conditions (beam energy, isocenter, irradiation field, bolus, and spread-out Bragg peak length) used during the first treatment plan to the subsequent CT. The dose distribution was calculated using a pencil beam algorithm. The brainstem, optic chiasm, contralateral retina, and brain were manually contoured on each CT, and a comparative study was performed.

Analysis

We calculated the aeration ratio, simulated irradiation dose of the brainstem, optic chiasm, retina, brain, and clinical target volume (CTV). Data are expressed as the mean value ± standard deviation. The cumulative dose was calculated as the biological effective dose of 2 GyE ($\alpha/\beta = 3$). The dose limit was set at 60 GyE for the brainstem and 50 GyE for the optic chiasm [7,8]. The dose limit for the retina was set at 45 GyE for the whole organ, and for the brain was set at 60 GyE for 1/3 of the volume [8]. In the analysis of the irradiation dose of the CTV, we calculated the dose received by 95% of the target volume (D95%) in each CT, then examined the alteration of the dose coverage during the treatment course. A paired t-test of the aeration ratio was performed between the first planning CT and last CT during the treatment course.

Results

The aeration change in the main sinus ranged from −8% to 67% (18% ± 19%). The aeration ratio increased in 18 patients, and the values for the last CT examination were higher than those for the first planning CT examination ($P = 0.0002$). The values in 11 of the 18 patients increased more than twofold, with a doubling time of 38 days. The largest increase was from 15% to 82%. In contrast, the aeration change in the other sinuses ranged from −27% to 20% (0% ± 12%). The aeration ratio increased in 12 patients, decreased in 7 patients, and did not change in 1 patient. Overall, the aeration in the other sinuses did not change remarkably (Fig. 1).

Three patients had a simulated maximum cumulative dose to the brainstem of beyond 60 GyE. The shortest period during which the cumulative dose would have reached 60 GyE was 38 days. Ten patients had a simulated maximum cumulative dose to the optic chiasm of beyond 50 GyE. The shortest period during which the cumulative dose would have reached 50 GyE was 21 days. The maximum cumulative dose to the retina was 3.9 GyE and much less than 45 GyE (Fig. 2). Regarding the brain, all patients showed the cumulative dose as 0 GyE. In contrast, the D95% of the CTV was changed 102 ± 4% during a total of 45 times of the subsequent CT, and the lowest value was 91% compared to the first planning CT.

Fig. 3 shows an example of a simulation in which the dose distribution in the brainstem and optic chiasm would have changed as the aeration progressed.

Discussion

The appearance of NCPS changes rapidly and considerably during the course of radiation treatment. The presence of a tumor sometimes creates an obstacle to mucus outflow; thus, massive fluid collection is indistinguishably intermixed with the tumor in the NCPS. In general, the volume of a radio-sensitive tumor decreases rapidly. As the tumor volume is reduced, the blockade is loosened and the outflow of the collected fluid occurs, allowing aeration to progress rapidly. On the other hand, the size of a radio-resistant tumor decreases slowly or occasionally increases. Mucosal thickening as an early side effect of irradiation may progress. Accordingly, the alteration of the aeration in the NCPS is difficult to predict. In our study, 18 of the 20 patients exhibited