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ORIGINAL ARTICLE

Comparison of three-dimensional vs. conventional radiotherapy in saving optic tract in paranasal sinus tumors

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Summary

Purpose: *To assess the possibility of delivering a homogeneous irradiation with respect to maximal tolerated dose to the optic pathway for paranasal sinus (PNS) tumors.*

Methods: *Treatment planning with conformal three-dimensional (3D) and conventional two-dimensional (2D) was done on CT scans of 20 patients who had early or advanced PNS tumors. Four cases had been previously irradiated. Dose-volume histograms (DVH) for the planning target volume (PTV) and the visual pathway including globes, chiasma and optic nerves were compared between the 2 treatment plannings.*

Results: *The area under curve (AUC) in the DVH of the globes on the same side and contralateral side of tumor involvement was significantly higher in 2D planning ($p<0.05$), which caused higher integral dose to both globes. Also, the AUC in the DVH of chiasma was higher in 2D treatment planning ($p=0.002$). The integral dose to the contralateral optic nerve was significantly lower with 3D planning ($p=0.007$), but there was no significant difference for the optic nerve which was on the same side of tumor involvement ($p>0.05$). The AUC in the DVH of PTV was not significant (201.1±16.23 mm^3 in 2D planning vs. 201.15±15.09 mm^3 in 3D planning). The volume of PTV which received 90% of the prescribed dose was 96.9±4.41 cm^3 in 2D planning and 97.2±2.61 cm^3 in 3D planning ($p>0.05$).*

Conclusion: *3D conformal radiotherapy (RT) for PNS tumors enables the delivery of radiation to the tumor with respect to critical organs with a lower toxicity to the optic pathway.*

Key words: conventional treatment planning, paranasal sinus tumors, radiotherapy, three dimensional conformal treatment planning, treatment planning

Introduction

PNS and nasal cavity carcinomas represent 3-4% of head and neck cancers. A 3-year overall survival rate of 50% has been reported for patients with all stages of disease, and the main cause of treatment failure is local recurrence [1,2]. Complete resection represents the major prognostic factor for survival [3-5]. When RT is used alone or postoperatively to treat macroscopic residual disease, dose escalation > 65 Gy has been reported to correlate with improvement in local control [5,6].

Eye complications are the most frequent and significant complications of RT. When only a portion of the ipsilateral eye is irradiated (medial one third), it is possible to preserve vision in the majority of the patients. When there is extensive disease in the orbit, however, the entire eye is irradiated to a high dose with almost certain loss of vision; however, these same patients would require orbital exenteration if treated by surgery. The risk for bilateral blindness can be reduced by use of CT and MRI scans for improved treatment planning and knowledge of the tolerance of the optic nerve [7]. Also, advances in radiation technology and imaging techniques have led to major improvements in the quality of dose delivery to the PNS tumors. These improvements have caused a decrease in complications in organs at risk (OARs), especially the ocular pathway.

The aim of this study was to assess the possibility of delivering a homogeneous irradiation with respect to maximal tolerated dose to the optic pathway for PNS tumors.

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Methods

This study was designed as a retrospective analysis and involved patients with PNS tumors who were referred to the Radiation Oncology department for definitive or postoperative RT. Cases that received re-irradiation due to tumor recurrence were also enrolled. Tumor stage was classified according to AJCC 2002 staging system [8].

Twenty patients were enrolled onto this study. They were treated with 3D conformal RT. CT scans of these patients were reviewed and the PTV and OARs including optic globes, optic nerves, and chiasma were contoured again. 2D treatment planning was performed on the CT scans of these patients. Both treatment plannings were arranged for megavoltage cobalt-60 machine.

Clinical target volume (CTV) was defined as the pretreatment gross tumor volume and macroscopic extension in the imaging (CT) findings, the surgery reports, biopsy and physical examination findings, and was contoured. PTV included the CTV plus an additional uniform 5 mm expansion. The treatment volume was not reduced because of the dosimetric constraints to the optic pathway.

The maximal doses tolerated by the OARs were the doses prescribed by Emami et al. in 1991 [9]. The maximal dose was limited to 50 Gy to the chiasma and the optic nerves and to 45 Gy to the globes with respect to the eye retina. The choice of portal incidence was determined by the maximal dose tolerated by the OARs except in the case of definitive RT for tumors that involved them, in which a minimum dose of 60 Gy was delivered. In all of the cases the aim of treatment planning was to spare the contralateral globe and optic tract.

The minimal dose delivered to the PTV was 50 Gy in the adjuvant setting. In cases of incomplete or no surgery, the goal was to deliver 66-70 Gy to PTV. Two to three individually shaped coplanar isocentric field arrangements were designed. The dose per fraction was the same in 2D and 3D treatment planning for each patient. The patients were treated with 5 fractions per week. In patients who had clinically or histologically demonstrated cervical lymph node involvement, neck was included in separate fields.

DVH for the PTV and the visual pathway were calculated and compared in the two treatment plannings. AUC in the DVHs were calculated for each OAR and the PTV in both treatment plannings. Since the axes of the diagram of DVH showed the dose and volume of the irradiated tissues, the AUC determined the integral dose of those tissues.

In addition, the volume of each OAR that received 100% (V 100%) of the prescribed dose was estimated from the DVHs and compared in both treatment plannings. The volume of the PTV that received 90% of the dose (V 90%) was also determined by the DVH.

Statistical analysis

Paired t-test was used for data analysis. This test shows the average and the standard deviation in both groups and compares the difference of the averages. P-value describes the comparison of the two treatment plannings for each person. For example, in the first patient 2D and 3D treatment planning is compared and when p-value is significant, this means that in this patient there is a significant difference between the two treatment plannings. A p-value<0.05 was considered as statistically significant.

Results

Between November 2004 and May 2007, 20 patients (6 women, 14 men) with PNS tumors received RT. This was given as definitive treatment in 10 patients while the remaining received it as postoperative RT. The patient median age was 50.5 years (range 14-70). Tumor histological types were: 7 adenoid cystic carcinomas (ACC), 3 small round cell tumors, 2 squamous cell carcinomas (SCC), 2 aesthesioneuroblastomas, 1 chondrosarcoma, 1 giant cell granuloma, 1 osteogenic sarcoma, 1 poorly differentiated carcinoma and 2 undifferentiated carcinomas.

Three cases had received re-irradiation to paranasal sinuses with an interval of 24-50 months due to recurrent disease. There were 7 cases with early-stage lesions and 13 cases with advanced disease. Tumor localization was the maxillary sinus in 15 and the ethmoid sinus in 5 cases. Surgery was performed in 10 patients with one case achieving macroscopic complete tumor removal. The remaining had unresectable tumors due to their large size or medically inoperable situations. One of the patients had received neoadjuvant chemotherapy.

The median dose was 60 Gy (range 46-70) for patients who had received definitive RT and 60 Gy (range 50-60) for cases who had undergone surgery. The median number of fields was 3 (range 2-3). The median dose per fraction was 2 Gy (range 1.8-2.5).

AUC in the DVH of the globes, optic nerves and chiasma in conventional and conformal treatment planning and p-values are summarized in Table 1.

The percentage of the volume of each OAR which

Table 1. Area under the curve (AUC) in the dose-volume histograms of the globes, optic nerves and chiasma

Organ	*AUC (2D§) ±SD*	*AUC (3D*) ±SD*	*p-value*
Globe 1†	173.6±57.7	137.9±59.9	0.004
Globe 2#	101.3±79.4	58±33.01	0.006
Optic nerve 1†	188±53.07	182±55.3	>0.05
Optic nerve 2#	151.8±69.8	125.2±54.1	0.007
Chiasma	180.5±39.9	159.5±52.2	0.002

§2D treatment planning, *3D treatment planning, †same side of tumor involvement, #contralateral side of tumor involvement
SD: standard deviation

Table 2. The percentage of the volume of OARs receiving 100% of total dose of radiotherapy

Organ	*2D§ % ±SD*	*3D* % ±SD*	*p-value*
Globe 1†	53±35.9	30.05±25.29	0.006
Globe 2#	24.8±35.9	8.1±5.6	0.04
Optic nerve 1†	84.6±28.1	69.05 ±32.4	0.04
Optic nerve 2#	54.05±35.6	32.7 ±20.6	0.005
Chiasma	82.5±23.7	70.4 ±27.1	0.000

§2D treatment planning, *3D treatment planning, †same side of tumor involvement, #contralateral side of tumor involvement, OAR: organs at risk, SD: standard deviation

received 100% of the total RT dose in each treatment planning is illustrated in Table 2.

DVH for the PTV was calculated. AUC for PTV was 201.1±16.23 mm^3 in 2D planning and 201.15±15.09 mm^3 in 3D planning (p >0.05). The volume of PTV that received 90% of the prescribed dose (V90%) was 96.6 ±4.41 cm^3 in 2D planning and 97.2 ±2.61 cm^3 in 3D planning (p >0.05).

Discussion

Because of the heterogeneity of PNS tumors and the different treatment approaches, most reports include small numbers of patients. There is a wide variety of radiotherapeutic techniques for the treatment of these tumors. In addition, due to the presence of sensitive OARs near the tumors and the unpredictable tumor growth, the arrangement of the fields is worthwhile.

In 2003 Padovani et al. assessed local disease control, survival, and clinical and dosimetric prognostic factors in 25 patients with locally advanced maxillary or ethmoid sinus carcinomas treated by 3D conformal RT. Surgery was performed in 22 patients and was macroscopically complete in 16 cases. Seven patients received chemotherapy (concomitant with RT in 4). Tumor conformity index, normal tissue conformity index, and global conformity index were defined for the 95% and 90% isodoses. The median radiation dose to the planned treatment volume was 63 Gy. The maximal doses tolerated by the structures involved in vision were respected, except tumors that involved the optic nerve. After a median follow-up of 25 months, 14 local tumor recurrences developed. The major prognostic factors were central nervous system involvement by disease and the presence of nonresectable tumors [10].

In a retrospective analysis, 85 patients with PNS and nasal cavity cancers underwent postoperative RT at the Memorial Sloan-Kettering Cancer Center. Seventy-six patients underwent CT simulation and 53 were treated with either 3D conformal RT (n = 23; 27%) or intensity-modulated (IMRT ; n = 30 or 35%). With a median follow up for surviving cases of 60 months, none of the patients who had undergone CT simulation and were treated with modern techniques developed grade 3-4 late complications of the eye. The authors concluded that emerging tools, such as 3D conformal treatment and, in particular, IMRT for PNS tumors, may minimize the occurrence of late complications associated with conventional RT techniques [11].

As seen in Table 1, the difference in AUC in the DVH of the globes and chiasma in conventional treatment planning was significantly greater than in conformal treatment planning which caused higher integral dose to both globes. In addition, it reflected more side effects in these areas. Also, this significant difference can be obviously seen in the optic nerve in the contralateral side of tumor involvement. Although the optic nerve of the same side of tumor involvement had less AUC in 3D treatment planning, it was not significantly different.

It was noticed that the percentage of the volume of OARs receiving 100% of the total dose of RT was reduced in conformal treatment planning. This can result in minimizing the occurrence of late complications associated with RT techniques. The minimal tolerance dose (TD) is defined as TD 5/5 (the RT dose that could cause no more than a 5% severe complication rate within 5 years after treatment and is based on RT at 2 Gy per fraction, 5 fractions per week). Similarly, TD 50/5 shows the probability of 50% complication rate within 5 years [12]. In a study conducted by Emami et al. in 1991, normal tissue tolerance to therapeutic irradiation based on available data showed that TD 5/5 for optic nerves and chiasma were 50 Gy and TD 50/5 were 65 Gy, resulting in blindness [9]. We observed good results by reducing dose delivery to OARs with the exception of the optic nerve on the same side of tumor involvement. In a study by Brizel et al. in 1999, dose distributions of traditional vs. conformal beam orientations in PNS malignancies were compared. The percentage of optic nerves and chiasma receiving >80% of the average target dose (V80) was reduced by conformal planning [13].

It is well known that the aim of RT is to deliver maximum homogeneous dose to the tumor, sparing the OARs. The results of our study show that 3D conformal treatment planning delivered less total dose to OARs; therefore, the rate of late complications might be decreased. We did not follow the patients for these late side effects of treatment. It may be a good practice to compare late complications of the optic pathway in both groups.

Paired t-test done to compare the difference of AUC for PTV between these two plannings showed no significant difference. Also, the volume of PTV which received 90% of the prescribed dose (V90%) did not show significant difference in the two treatment planning methods. Moreover, recurrence rate in the two groups might be different due to better homogenicity of radiation in conformal planning that can be studied in the follow up of the cases.

Conclusion

Although conformal RT planning is considered optimal in paranasal sinus carcinomas, there might be still some risks for late complications in normal tissues. Better delineation of PTV with the assistance of imaging methods could result in reducing OARs complications postradiotherapy. New irradiation techniques such as IMRT could facilitate the delivery of more radiation dose to PTV while respecting the maximal dose tolerated by normal tissues.

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