Original Article

Dosimetry Comparison between Volumetric Modulated Arc Therapy with RapidArc and Fixed Field Dynamic IMRT for Local-Regionally Advanced Nasopharyngeal Carcinoma

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ABSTRACT

Objective: A dosimetric study was performed to evaluate the performance of volumetric modulated arc radiotherapy with RapidArc on locally advanced nasopharyngeal carcinoma (NPC).

Methods: The CT scan data sets of 20 patients of locally advanced NPC were selected randomly. The plans were managed using volumetric modulated arc with RapidArc and fixed nine-field coplanar dynamic intensity-modulated radiotherapy (IMRT) for these patients. The dosimetry of the planning target volumes (PTV), the organs at risk (OARs) and the healthy tissue were evaluated. The dose prescription was set to 70 Gy to the primary tumor and 60 Gy to the clinical target volumes (CTV) in 33 fractions. Each fraction applied daily, five fractions per week. The monitor unit (MU) values and the delivery time were scored to evaluate the expected treatment efficiency.

Results: Both techniques had reached clinical treatment's requirement. The mean dose (D_{mean}), maximum dose (D_{max}) and minimum dose (D_{min}) in RapidArc and fixed field IMRT for PTV were 68.4±0.6 Gy, 74.8±0.9 Gy and 56.8±1.1 Gy; and 67.6±0.6 Gy, 73.8±0.4 Gy and 57.5±0.6 Gy ($P<0.05$), respectively. Homogeneity index was 78.85±1.29 in RapidArc and 80.34±0.54 ($P<0.05$) in IMRT. The conformity index (CI: 95%) was 0.78±0.01 for both techniques ($P>0.05$). Compared to IMRT, RapidArc allowed a reduction of D_{mean} to the brain stem, mandible and optic nerves of 14.1% ($P<0.05$), 5.6% ($P<0.05$) and 12.2% ($P<0.05$), respectively. For the healthy tissue and the whole absorbed dose, D_{mean} of RapidArc was reduced by 3.6% ($P<0.05$), and 3.7% ($P<0.05$), respectively. The D_{mean} to the parotids, the spinal cord and the lens had no statistical difference among them. The mean MU values of RapidArc and IMRT were 550 and 1,379. The mean treatment time of RapidArc and IMRT was 165 s and 447 s. Compared to IMRT, the delivery time and the MU values of RapidArc were reduced by 63% and 60%, respectively.

Conclusion: For locally advanced NPC, both RapidArc and IMRT reached the clinic requirement. The target volume coverage was similar for the different techniques. The RapidArc technique showed some improvements in OARs and other tissue sparing while using reduced MUs and delivery time.

Key words: Volumetric modulated arc therapy; Intensity-modulated radiotherapy; Dosimetry; Target volume; Nasopharyngeal carcinoma

INTRODUCTION

Recently, nasopharyngeal carcinoma (NPC) patients more likely have received intensity-modulated radiotherapy (IMRT) than three dimensionals' conformal radiotherapy (3D-CRT). The IMRT has got better dose distribution in target volume and lower dose for organs at risk (OARs), especially for the parotids[1-3]. But IMRT needs complex plan management, more fixed fields and monitor units (MUs) especially for NPC which has large target volume, more OARs and more overlapping of target volume. All of the above may bring the prolonging of the treatment time (for example, 7–9 fixed-field dynamic IMRT needs about 7–10 minutes of treatment delivery) which may cause the increasing of the movement of the swallowing and the position shift during the treatment, so that the clinical efficacy may be reduced consequently.

Generally, the number of the fixed fields can increase the freedom of the plan management, and the development of the volumetric modulated arc therapy

technique brings the design of the treatment plan to a new stage which can produce various optimization methods based on the differences of the peak value optimization[4]. Nowadays, RapidArc was developed mainly by the optimization of the multi-leaf collimators shape, the change of the dose rate delivery and the rotation of the gantry[5-8]. It was based on the volumetric modulated arc therapy technique and can obtain the similar distribution of the fixed IMRT. The analytical anisotropic algorithm (AAA) system was used for dose calculation[9], and GLAaS[10] and PTW-729[11] methods were applied for quality control to ensure the accuracy and security in the clinical application[12].

Currently, multiple centers compared the dose distribution of the both techniques and generally suggested that volumetric modulated arc therapy with RapidArc was a rapid, safe and accurate radiotherapy technique for many tumors like gliomas, brain metastases and some lung tumors according to the preliminary results[13-17].

NPC needs large and complex target volume and has many OARs around, so that complicated fields' management was necessary. Therefore, in this study, RapidArc was compared at the reference of the fixed 9-field IMRT in dosimetry for locally advanced NPC.

MATERIALS AND METHODS

Patients' Characteristics

Twenty cases of location CT scan data (layer 3 mm) was randomly selected from the locally advanced NPC patients who had received radiotherapy (RT) continuously in Radiotherapy Department, Beijing Cancer Hospital. The patients' characteristics are shown in Table 1, and the clinical stage was according to the Stage of NPC (AJCC 2002) followed as below. Among these 20 patients, three patients had been diagnosed as T4 and six patients as N3. The gross tumor volume (GTV) was ranged from 51.4 cm^3 to 421.8 cm^3 and the median volume was 130.9±83.2 cm^3.

Table 1. Patients' General and Clinical Characteristics

Parameters (20 cases)	Values
Age (y)	48 (23−70)
Sex (male:female)	7:3
Stage III	13
Stage IV	7

Treatment Plan Management

Two treatment plans were performed for each patient. RapidArc was compared to the fixed 9-field coplanar dynamic IMRT in dosimetry. The Eclipse system from the Varian Company (Denver, USA) was used for the two RT plans, with 6MV-X ray and 120 multi-leaf collimator in it. Considering the large target volume of the locally advanced NPC and complex OARs around, the double-arc plan was adopted for RapidArc and the coplanar fixed 9-field plan was selected for IMRT. Meantime, the AAA 8.6 edition system was applied for calculation.

The simultaneous boost plan was used and the dose prescribed as: GTV 70 Gy/33f, 95% planning target volume (PTV) 60 Gy/33f was generated by 5-mm outer margin of clinical target volume (CTV) and 5 mm apart from the skin at least.

The quality control of the plan was in accordance with the standard dose-volume histogram (DVH) of $D_{98\%}$ and $D_{2\%}$ which represent the doses of 98% and 2% PTV and they indicated the minimum and maximum doses of the plan respectively. The conformity index (CI) of the target volume is expressed as $CI_{95\%}=(PTV_{60Gy}/V_{PTV})\times(PTV_{60Gy}/V_{60Gy})$[18]. PTV_{60Gy} represents the volume receiving the prescription dose 60 Gy in the target volume, V_{PTV} stands for the volume of the PTV, V_{60Gy} is in the name of the volume which has received the prescribed dose. The homogeneity index (HI) of the target volume is defined as $HI=100\times[1-(D_{5\%}-D_{95\%})/D_{mean}]$[15]. OARs, $D_{33\%}$, D_{mean}, $D_{50\%}$, and $D_{66\%}$ were adopted to evaluate the dose distribution of both sides of the parotids. D_{mean} and D_{max} (the maximum dose which was defined as the dose received by less than 2 ml volume of the following OARs) were applied to evaluate the dose of the lens, spinal cord, mandible and optic nerves. For the healthy tissue, integrity absorption dose (DoseInt) was used as the evaluation standard accompanied by D_{mean} and V_{10Gy} at the same time. The time interval of the treatment delivery and the MU values of the techniques were also compared.

Statistical Analyses

The SPSS 13.0 (SPSS Inc., IL, USA) was applied for statistical data management and analysis, and double-side *t*-test was employed to compare the difference between two treatment plans at statistically significant level of $P<0.05$. The null hypothesis of no difference in dosimetry between study groups was tested with the use of the log-rank test at a two-sided level of significance of 0.05. Confidence intervals were calculated and study groups were compared by means of the log-rank test. All other hypothesis tests were two-sided at a significance level of 0.05.

RESULTS

Dosimetry Analysis of Target Volume

Table 2 shows the comparison of the dose distribution of the PTVs and the CI and HI of the target volumes. According to the clinical requirement, D_{mean} and D_{max} of the PTV were lower while D_{min} was slightly higher and statistically significant for IMRT. The $CI_{95\%}$ of RapidArc and IMRT were both 0.78±0.07 ($P>0.05$). However, the HI for RapidArc and IMRT were 78.9±1.3 and 80.4±0.5, respectively ($P<0.05$).

Dosimetry Comparison of OARs and Healthy Tissues

Table 3 manifests the dose comparison of the OARs for the two plans. As we can see, the plans were similar in the mean dose of the spinal cord and had no differences at statistically significant levels ($P<0.05$). With

the standard of the clinical treatment, the mean dose of RapidArc for the brain stem was really lower than that of IMRT; however, for the maximum dose, IMRT was indeed very low. The mean and maximum doses of the lens were similar in two plans and have no differences at statistically significant levels ($P>0.05$). For both sides of the optic nerves, the doses (except for the maximum dose of the right optic nerve) in RapidArc were less than that in IMRT, the differences were statistically significant at $P<0.05$ levels. The maximum doses for the mandible of the RapidArc and IMRT plans were similar in statistically significant level ($P<0.05$) with the mean doses less than 50 Gy for the both, while the former was lower at statistically significant levels ($P<0.05$) in the mean dose.

Table 2. PTV dose distribution comparison of two RT techniques

Indices	RapidArc	IMRT	P
PTV D_{mean} (Gy)	68.4±0.6	67.6±0.6	<0.05
PTV D_{max} (Gy)	74.8±0.9	73.8±0.5	<0.05
PTV D_{min} (Gy)	56.8±1.1	57.5±0.6	<0.05
$CI_{95\%}$	0.78±0.07	0.78±0.07	>0.05
HI	78.9±1.3	80.4±0.5	<0.05

CI: conformity index; HI: homogeneity index. In table 2, both of PTV D_{mean} and PTV D_{max} in RapidArc were slightly higher and statistically significant than those in IMRT. The $CI_{95\%}$ of RapidArc and IMRT were the same and the HI for RapidArc was lower than that of IMRT at statistically significant level ($P<0.05$).

Table 3. Dose comparison of OARs for two plans

Indices	RapidArc	IMRT	P
Spinal cord D_{mean} (Gy)	27.7±1.4	27.8±1.7	>0.05
Spinal cord D_{max} (Gy)	33.7±1.7	33.5±1.2	>0.05
Brain stem D_{mean} (Gy)	23.9±2.8	27.9±2.2	<0.05
Brain stem D_{max} (Gy)	45.2±2.4	43.6±1.7	<0.05
Mandible D_{mean} (Gy)	46.6±2.5	50.5±2.1	<0.05
Mandible D_{max} (Gy)	73.8±1.8	74.0±2.1	>0.05
Left lens D_{mean} (Gy)	5.3±0.5	5.4±0.7	>0.05
Left lens D_{max} (Gy)	6.2±0.5	6.2±0.7	>0.05
Right lens D_{mean} (Gy)	5.3±0.4	5.2±0.6	>0.05
Right lens D_{max} (Gy)	6.2±0.4	6.4±0.7	>0.05
Left optic nerve D_{mean} (Gy)	32.8±5.2	37.6±4.9	<0.05
Left optic nerve D_{max} (Gy)	53.5±4.2	55.6±3.0	<0.05
Right optic nerve D_{mean} (Gy)	32.9±5.6	37.6±4.6	<0.05
Right optic nerve D_{max} (Gy)	51.6±8.9	55.1±2.6	>0.05

The D_{mean} of RapidArc for the brain stem was really lower than that of IMRT. As was shown above, the D_{mean} and the D_{max} for the left optic nerve of RapidArc were really lower than that of IMRT. For the D_{mean} of the mandible, RapidArc was also lower than IMRT ($P<0.05$).

For both sides of the parotids, we performed detailed analysis in different volumes. The D_{mean}, $D_{33\%}$, $D_{50\%}$ and $D_{66\%}$ were all lower for IMRT. However, all of them above had no statistical differences between both sides of the parotids (Table 4). Figure 1 shows a demographic of the two different plans.

Table 4. Comparison of dose distribution for parotids

Indices	RapidArc	IMRT	P
Left parotids D_{mean} (Gy)	32.9±7.5	32.0±3.6	>0.05
Left parotids $D_{33\%}$ (Gy)	34.2±7.5	32.2±5.3	>0.05
Left parotids $D_{50\%}$ (Gy)	30.8±12.7	27.0±3.2	>0.05
Left parotids $D_{66\%}$ (Gy)	25.3±8.5	24.2±2.3	>0.05
Right parotids D_{mean} (Gy)	33.4±9.8	33.4±7.9	>0.05
Right parotids $D_{33\%}$ (Gy)	35.1±10.2	33.7±9.1	>0.05
Right parotids $D_{50\%}$ (Gy)	29.1±11.3	28.8±9.8	>0.05
Right parotids $D_{66\%}$ (Gy)	26.0±11.7	26.0±9.5	>0.05

The D_{mean}, $D_{33\%}$, $D_{50\%}$ and $D_{66\%}$ for both sides of the parotids of RapidArc were likely higher than that of IMRT but not statistically significant.
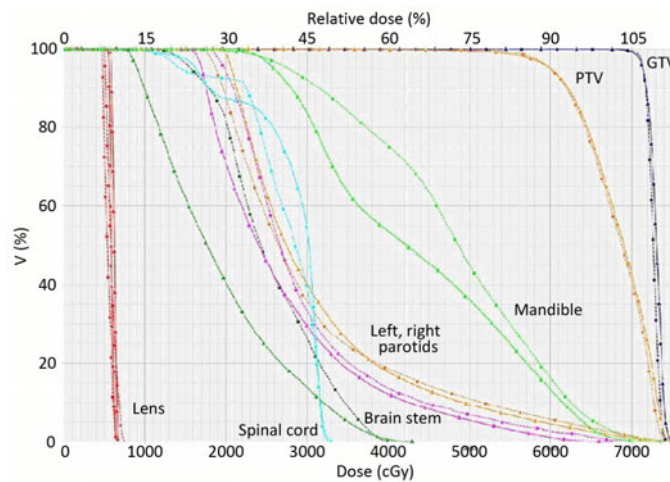
Figure 1. DVH for two treatment plans. The solid lines represent the doses of the different OARs and target volume in different volumes for RapidArc, and the dotted lines stand for those of IMRT. RapidArc appeared some priority in the mandible and the brain stem visually.

There was no clear definition of the radiation dose to the healthy tissue. But in principle, lower integrity absorption dose (DoseInt) and smaller radiation volume are better. The D_{mean} and DoseInt were significantly lowered ($P<0.05$) for RapidArc. The radiation volume of 10 Gy was smaller for IMRT, but has no statistical significance (Table 5).

Comparison of MU Value and Treatment Time Interval

Figure 2 shows the MU values and time interval for the treatment plans. The mean MU value of RapidArc was 550, reduced by 60% compared to that of IMRT with the mean MU value of 1379. The mean treatment time of RapidArc was 165 s, reduced by 63% compared to that of IMRT with the mean time of 447 s.

Table 5. Dose comparison of the healthy tissue

Indices	RapidArc	IMRT	*P*
Healthy tissue D_{mean} (Gy)	29.0±2.2	30.1±2.2	<0.05
Volume of ≤10Gy (cm^3)	5,745±1,150	5,708±1,142	>0.05
DoseInt (Gy×cm^3)	216,190±41,308	224,491±43,318	<0.05

DoseInt: integrity absorption dose. The D_{mean} and DoseInt of the healthy tissue were lowered significantly ($P<0.05$) for RapidArc than IMRT.

Figure 2. The MU value and treatment time for the two plans.

DISCUSSION

As mentioned above, the treatment time interval is much shorter for RapidArc which may bring the promotion of the biologic effect. Although accuracy and repeatability of the RapidArc had been evaluated in some studies, there is no dose comparison for the two treatment plans in NPC patients currently.

In this research, the enrolled patients were satisfied with clinical treatment. The data of RapidArc implied that the dose distribution may be improved for some OARs and we can get more accurate plans, but this is not the point of the study. Moreover, in the program of the optimum, the weight for the target volume and the OARs were not clearly defined. Therefore, the dosimetry comparison for the two plans has its limitation.
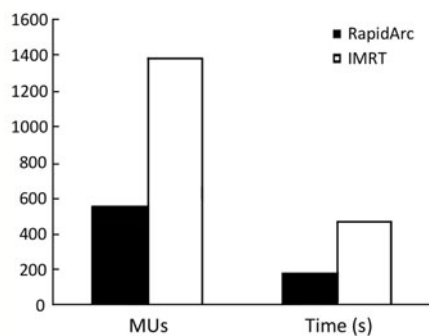
The double-arc RapidArc was selected to guarantee the dose distribution due to a large targeting volume and lots of OARs for NPC patients. The reduction of the healthy tissue dose may decrease the risk of the secondary primary carcinoma, which needs follow up to clarify. The MU value was reduced by 60% meanly for RapidArc.

The result showed the 63% reduction of the mean treatment time can decrease the effect of the organ movement, and affect treatment effectiveness. In American Society for Therapeutic Radiology and Oncology (ASTRO) meeting in 2009, it was reported by Wang that the swallowing frequency was 3–19 times in one treatment fraction (11 minutes meanly in IMRT), the time interval was 4.8 secends for swallowing, and the shift of the target volume was 3.13–12.32 mm during the course. The data demonstrated that the position shift and the swallowing movement would inevitably lower the accuracy of the target volume because of the fairly long time interval for the treatment delivery of the head and neck cancer, thereby decreasing the clinical treatment effectiveness. Therefore, RapidArc can increase the accuracy of the radiotherapy and improve the effectiveness of the treatment by reducing the time interval of the delivery.

Furthermore, the reduction of the fraction treatment time may increase the biologic effect of radiotherapy. Shibamoto, et al.[19] showed that between two fractions of radiotherapy, sublethal repair occurred in 2–3 minutes or longer time, while using breast cancer cell strain EMT 6 and head and neck squamous cell strain SCCVn of mice *in vitro*.

The previous data about RapidArc and fixed field IMRT showed that the treatment time interval was less than 2.5 minutes for RapidArc and about 7–9 minutes for the fixed field IMRT (7–9 fields generally). The superiority of RapidArc in this work was the obvious reduction of the MU value and the treatment time[20,21]. Therefore, we believe that RapidArc may promote the clinical result since it can reduce the shift of the patient location[20] and the influence of the swallowing movement on the OARs during the delivery.

To achieve satisfactory dose distribution, it will take more than 17 hours for the plan optimization to RapidArc for one locally advanced NPC while only 0.5–1 hour is needed for IMRT. Consequently, the calculation system for the RapidArc plan needs to be improved in future studies.

In conclusion, for the local advanced NPC, RapidArc can reach similar target conformity comparing to IMRT for target dose distribution and homogeneity, and IMRT is a little better than RapidArc. Compare to IMRT, though the parotids received higher dose for RapidArc, it would not damage parotids statistical significantly; brain stem, mandible and both sides of the optic nerves had better dose distribution in RapidArc plans; for the lens and spinal cord, the dose distribution was similar in both plans. Considering the mean dose of the healthy tissue and the integrity absorbed dose, RapidArc was superior to IMRT. The reduction of the treatment time and the MU value were notable for RapidArc.

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