Dosimetric difference amongst 3 techniques: TomoTherapy, sliding-window intensity-modulated radiotherapy (IMRT), and RapidArc radiotherapy in the treatment of late-stage nasopharyngeal carcinoma (NPC)

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ABSTRACT

To investigate the dosimetric difference amongst TomoTherapy, sliding-window intensity-modulated radiotherapy (IMRT), and RapidArc radiotherapy in the treatment of late-stage nasopharyngeal carcinoma (NPC). Ten patients with late-stage (Stage III or IV) NPC treated with TomoTherapy or IMRT were selected for the study. Treatment plans with these 3 techniques were devised according to departmental protocol. Dosimetric parameters for organ at risk and treatment targets were compared between TomoTherapy and IMRT, TomoTherapy and RapidArc, and IMRT and RapidArc. Comparison amongst the techniques was done by statistical tests on the dosimetric parameters, total monitor unit (MU), and expected delivery time. All 3 techniques achieved similar target dose coverage. TomoTherapy achieved significantly lower doses in lens and mandible amongst the techniques. It also achieved significantly better dose conformity to the treatment targets. RapidArc achieved significantly lower dose to the eye and normal tissue, lower total MU, and less delivery time. The dosimetric advantages of the 3 techniques were identified in the treatment of late-stage NPC. This may serve as a guideline for selection of the proper technique for different clinical cases.

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Introduction

Nasopharyngeal carcinoma (NPC) is a common type of head and neck cancer in Southeast Asia. The deep-seated location of the lesions renders radical surgery infeasible. Moreover, NPCs, especially of the undifferentiated type, are highly responsive to radiation. This made radiotherapy the mainstream treatment for nonmetastatic NPC. Treatment of NPC has been challenging owing to the close proximity of the lesions to nearby organs at risk (OARs). To reduce treatment complications without compromising tumor control, delivery of highly conformal radiation dose is necessary. This is usually achieved by modern radiotherapy technologies that can produce highly conformal radiation dose distribution. This requirement is particularly important in the treatment of late-stage NPC, where primary tumors are often extensive, and cases of tumor encroaching or extending to nearby normal tissues such as the optical pathways, brainstem, spinal cord, and temporal lobes are not uncommon. In addition, cervical lymph nodes are often part of the treatment target, and bulky metastatic lymph nodes are often present. This makes sparing of parotid glands, glottic larynx, and constrictor muscles extremely difficult.

The use of intensity-modulated radiotherapy (IMRT) in the treatment of NPC has been shown to reduce dose to OARs, with satisfactory results in the local control of T3-T4 diseases. In recent years, volumetric-modulated arc therapy (VMAT), such as RapidArc, implemented by modulated gantry rotation speed, dose rate, and multileaf collimator (MLC) pattern in linear accelerator, is gaining thrust because of its dosimetric performance being rival to conventional IMRT, yet with a significantly reduced treatment time. On the contrary, Helical TomoTherapy delivers highly modulated radiation dose fluence by a linear accelerator mounted on a rotating gantry, coupled with fast-switching binary MLC and movable couch. TomoTherapy has also shown promising dosimetric advantage in the treatment of NPC. IMRT, VMAT, and TomoTherapy are the focus of radiotherapy treatment of NPC nowadays. Yet, few publications focused on the treatment of this challenging cancer type have been reported to compare amongst the 3 techniques.
In treatment centers with a heavy load of patients with NPC, and which is equipped with these treatment technologies, it is crucial to identify the relative merits and demerits of individual techniques. Cases with different clinical requirements can be triaged to be treated with the best option. It is the aim of this article to illustrate and discuss the strengths of individual methods based on the dosimetric study that was performed on selected patients.

Methods and Materials

Ten patients with late-stage NPC (5 Stage III and 5 Stage IV, according to American Joint Committee on Cancer seventh edition staging system)10; 9 males and 1 female) treated with TomoTherapy or IMRT were selected for the study.

Patient setup and simulation

Each patient was immobilized in a supine position with a thermoplastic shell. Intravenous contrast-enhanced computed tomography (CT) simulation was performed at 3-mm intervals from the vertex to 5 cm below the sternoclavicular notch with a 16-slice Brilliance Big Bore CT (Philips Medical Systems, Cleveland, OH). Magnetic resonance images were coregistered with the CT images for tumor delineation.

Contour delineation

The target volumes were delineated by clinical oncologists, and details of the delineation guidelines are described in a previous article.10 The OARs including the brainstem, spinal cord, optic nerves, optic chiasm, eyes, lens, temporal lobes, parotid glands, auditory structures, constrictor muscles, larynx, and mandible were contoured on axial CT slices. Planning OAR volumes were generated with 3-mm setup margin for OARs (brainstem, optic nerves, optic chiasm, and eyes) and 5-mm margin for spinal cord.

Treatment planning

Both RapidArc and IMRT plans were generated with 6-MV photon beam in a linear accelerator equipped with 120 Millennium MLC using Eclipse treatment planning system (Eclipse version 8.6, Varian Medical Systems, Palo Alto, CA). Dose calculation was performed with anisotropic analytic algorithm. RapidArc plans were devised by the use of 2 coplanar full arcs. Collimators were rotated by 10° to 20° to minimize the effect of tongue and groove. IMRT plans were devised by using 9 coplanar beams. One or 2 noncoplanar beams were added if necessary, as this might improve tumor coverage with acceptable treatment delivery time. TomoTherapy plans were generated with 6-MV photon beam using TomoTherapy Planning Workstation (TomoHD version 1.0.0, Accuray Inc., Sunnyvale, CA). Dose calculation was performed with superposition or convolution algorithm. The planning parameters were as follows: field width = 2.5 cm, pitch = 0.43, and modulation factor = 3 to 3.5. The planning parameters described previously reflected the common planning practice in our institution, which were derived with the aim of generating treatment plans of sufficient quality with reasonable treatment time.

The priority (or penalty) settings in the optimization process for all 3 techniques differ owing to the different optimization algorithms employed. To ensure consistency of planning techniques, all treatment plans were devised by physicists with over 1-year clinical experience in IMRT, RapidArc, and TomoTherapy planning. Planning requirements and techniques for planners were also aligned by training, standard protocol, and procedures of the department. All planning target volumes (PTVs) were aimed to achieve a volume of 98% covered by the prescription dose. The maximum target dose was limited to less than 115% of the prescribed dose. For OARs, dose constraints were designed to limit the maximum dose to be less than 54 Gy for the brainstem, optic nerves, optic chiasm, and eyes; 45 Gy for the spinal cord; and 6 Gy for the lens. If PTV coverage was not severely compromised, the following constraints were also employed: mean dose was not to exceed 50 Gy for auditory structures; 50 Gy for constrictor muscle; and 45 Gy for the glottic larynx. Median dose was not to exceed 30 Gy for the individual parotid glands. Maximum dose was not to exceed 70 Gy for the temporal lobe.

Statistical analysis

For serial organs (brainstem, optic nerves, optic chiasm, eyes, spinal cord, and mandible), the dosimetric parameter of D98 was taken for the individual parotid glands) for evaluation. OAR sharing properties of serial and parallel organs (larynx, constrictor muscle, lens, auditory instrument, temporal lobe) were assigned to record D92 and Dmedian. Besides, normal tissue mean dose (NTMD), denoted by the mean dose of the whole patient body contour minus all clinical target volumes, was calculated as a metric to represent radiation dose to healthy tissues.

To evaluate the dosimetric outcome in treatment targets, the target coverage, the dose homogeneity, and the dose conformity were addressed by the D98, homogeneity index (HI), and conformity number (CN), respectively. D98 was taken for all PTVs. HI was recorded for PTV1p and PTV1n, and CN was taken for 70 Gy targets (PTV1p1 + PTV1n1), 66-Gy targets (PTV1p2 + PTV1n2), and 60-Gy targets (PTV1n3 + PTV1n3). HI and CN of the treatment targets were taken with the following definition:

\[
HI = \frac{V_{D92}/C2}{V_{D98}}
\]

\[
CN = \frac{TV_{D92}}{TV_{D98}} \times \frac{TV_{D98}}{TV_{D92}}
\]

where TVD98 is the volume of PTV target covered by 98% of prescribed dose, TV is the volume of PTV target, and VD92 is the volume of the body covered by 98% of prescribed dose. An HI value of 0 suggested perfect homogeneity, and a CN value of 1 suggested perfect conformity.

For all of the aforementioned dosimetric parameters, Wilcoxon signed rank test was used to investigate significance of differences in TomoTherapy vs IMRT, RapidArc vs IMRT, and TomoTherapy vs RapidArc. A 2-tailed p < 0.05 was considered statistically significant. Analysis was performed using statistical software (SPSS, Chicago, IL).

Besides the dosimetric parameters, monitor unit (MU) of individual plans was recorded. Expected delivery time for these plans were calculated based on a nominal dose rate of 400 MU/min for IMRT; maximum dose rate of 600 MU/min and gantry rotation speed of 75 seconds per rotation for RapidArc; and 882 MU/min dose rate for TomoTherapy. For IMRT and RapidArc, 20 seconds was added to each coplanar field to simulate the time needed for field loading and parameter checking, and 45 seconds was added to each noncoplanar field to cater for the extra time in couch rotation. Wilcoxon signed rank test was used to test the significance of difference in MU and expected delivery time.

Results

Figures 1 and 2 show the plots of the dosimetric parameters in treatment targets. Table 1 shows the dosimetric parameters of treatment targets that show significant difference amongst the treatment techniques. TomoTherapy performed significantly better conformity in 70 and 66 Gy isodose levels. Conformity for the 60 Gy isodose level was similar in TomoTherapy and RapidArc, and both were better than IMRT. It was noted that HI did not achieve statistical significance amongst the techniques nor were the target coverage D98 for all PTVs, except PTV1n1, which was about 1% higher in IMRT than the other 2 treatment options. The dose distributions in the nasopharynx of a typical case, for each of the 3 techniques, are shown in Fig. 3.

Results of statistical analysis for OARs are shown in Table 2. All other dosimetric parameters not shown in the table did not achieve significant difference amongst the techniques.

Table 3 shows the total MU and the expected delivery time for each treatment plan. The delivery time was significantly different between RapidArc vs IMRT (p = 0.005) and TomoTherapy vs RapidArc (p = 0.005), but not between TomoTherapy vs IMRT (p = 0.646).

Discussions

To the best of our knowledge, this is the first article on the dosimetric comparison amongst sliding-window IMRT, RapidArc, and Helical TomoTherapy for radiotherapy treatment of late-stage NPC. These treatment techniques differed in radiation delivery method. They also differed in the implementation software (e.g., optimization and dose calculation algorithm) and hardware (e.g., MLC and flattening filter design). It was expected that these intrinsic differences would result in advantages of one method over the others in different dosimetric aspects. This article focused on the identification of these aspects via a treatment planning study. Although planning studies were often subjected to
uncertainties from case selection and differences in practice amongst planner, among others, effort was made to minimize these effects by selection of typical NPC cases as well as the standardization of treatment planning practice in a team of planners by training and guidelines. It was, however, conceivable that results could differ if different treatment planning parameters were used, for example, number of beams or arcs in IMRT or RapidArc and choice of modulation factor and field width in TomoTherapy. The parameters used in this study were those commonly used in our daily planning practices and were decided based on literature review and planning experience. In finalizing the parameters, balance had to be struck between plan quality and treatment time. Results of the comparisons are discussed later.

**Planning target volumes**

TomoTherapy allows radiation from multiple angles and thus eliminated high-dose spread at discrete beam directions (as in IMRT) that may undermine dose conformity. Other articles on dosimetric comparison of delivery techniques for NPC treatment also revealed favorable dose conformity in TomoTherapy. Regarding dose homogeneity, it was generally reported that TomoTherapy was better than linac-based techniques. This was echoed in our study with homogeneity slightly better in TomoTherapy, though statistical significance was not reached. Results of comparison in dose homogeneity between IMRT and dual-arc RapidArc or VMAT were less consistent in other
Homogeneity was observed between the 2 techniques. Candidate benefits of TomoTherapy encroaching on the optical structures may be a weakness of TomoTherapy in NPC treatment. Tumors with extended angles away from optic nerves and eyeball, thus further widening the difference with TomoTherapy. Conceivably, this was a major weakness of TomoTherapy in NPC treatment. As compared with IMRT and RapidArc, mean doses to glottic larynx were reduced by 7.5 and 5.1 Gy, respectively, and to constrictor muscles by 8.4 and 3.8 Gy, respectively.

OAR—Lens

TomoTherapy achieved significantly lower dose in lens, with an averaged reduction of 0.63 Gy compared with IMRT and 1.92 Gy compared with RapidArc. The difference in MLC transmission between 120 Millennium MLC in linear accelerators (1.5%) and the binary MLC in Helical TomoTherapy (0.5%) contributed to this saving. Moreover, as the collimator is rotated in RapidArc fields to minimize tongue-and-groove effect, the lens that is located superior to treatment target is then exposed to collimator opening, which further increased the doses.

OAR—Eyes and optic nerves

Sparing of optical structures was best achieved by RapidArc. For eye, RapidArc achieved 6.7 Gy less radiation dose when compared with IMRT, and 10.3 Gy less compared with TomoTherapy. For optic nerves and optic chiasm, the difference was only significant between TomoTherapy and RapidArc, which was approximately 10 Gy. With the field width of 2.5 cm and the helical fashion of dose delivery in TomoTherapy, a significant dose spillage to regions superior to the treatment target was evident. This effect was accentuated in cases where the optical structure was located immediately above the treatment target, and this was in concordance with the comparison performed between Pinnacle VMAT and TomoTherapy and between step-and-shoot IMRT and TomoTherapy. RapidArc was able to provide direct radiation into targets at angles away from optic nerves and eyeball, thus further widening the difference with TomoTherapy. Conceivably, this was a major weakness of TomoTherapy in NPC treatment. Tumors with extensive involvement encroaching on the optical structures may be candidate benefiting more from RapidArc rather than TomoTherapy.

Table 1

<table>
<thead>
<tr>
<th>Parameter</th>
<th>TomoTherapy vs IMRT</th>
<th>RapidArc vs IMRT</th>
<th>IMRT vs RapidArc</th>
</tr>
</thead>
<tbody>
<tr>
<td>CN—70 Gy</td>
<td>0.017</td>
<td>0.007</td>
<td>NS</td>
</tr>
<tr>
<td>CN—66 Gy</td>
<td>0.005</td>
<td>0.005</td>
<td>NS</td>
</tr>
<tr>
<td>CN—60 Gy</td>
<td>0.007</td>
<td>NS</td>
<td>0.009</td>
</tr>
<tr>
<td>PTVn1—D&lt;sub&gt;max&lt;/sub&gt;</td>
<td>0.005</td>
<td>NS</td>
<td>0.021</td>
</tr>
</tbody>
</table>

NS denotes statistical nonsignificance (p > 0.05).

Articles 12-14,16-18 and in our study, no significant difference in homogeneity was observed between the 2 techniques.

OAR—Auditory instrument

RapidArc achieved the best dose sparing of auditory instrument, but significance was reached only in the comparison between IMRT and RapidArc. The reduction in mean dose with RapidArc as compared with IMRT was 3.4 Gy. Similar result in comparing the dose to the middle ear for skull base head and neck cancer between IMRT and VMAT was reported by Chen et al.19

OAR—Parotid glands

Rotational therapy generally favored parotid gland sparing, owing to the wider range of angles for beam entry, allowing avoidance of the organ. A number of articles12,14,15,20 advocated the advantage of TomoTherapy in parotid gland sparing as compared with static field IMRT. This was in line with the result of this study. Significant reduction in the mean dose to parotid glands by TomoTherapy compared with IMRT was observed, with a magnitude of 5.8 Gy. The mean dose to parotid glands in RapidArc was higher than that of TomoTherapy and lower than that of IMRT, but no significant difference was found between RapidArc and the other 2 techniques. Previous articles12,20 employing 7-field IMRT showed significantly inferior parotid sparing as compared with VMAT. Clemente et al.14 in his article compared 9-field IMRT against VMAT and no statistical significance was found in parotid sparing. Another article by Stieler et al.21 showed 9-field IMRT conferred better sparing of parotid glands than 7-field IMRT but was still inferior to VMAT. Together with results obtained in this study, it seemed possible that the number of fields in IMRT was decisive in the outcome of comparison against VMAT.

OAR—Mandible

TomoTherapy achieved significantly lower dose when compared with the other 2 techniques, the reduction in Mandible D<sub>02</sub> being 1.6 Gy compared with IMRT and 2.4 Gy compared with RapidArc. As Mandible is often located in close proximity to PTVs.
of the nasopharyngeal tumor, the better conformity achievable in TomoTherapy was expected to be the major factor that contributed to the lower dose to Mandible.

**MU and NTMD**

Of the 3 treatment techniques, RapidArc resulted in the lowest NTMD, and the reduction was significant when compared with IMRT or TomoTherapy (1.9 and 1.6 Gy reduction compared to IMRT and TomoTherapy, respectively). Lower total MU in RapidArc treatment, leading to less radiation dose transmitted through the MLC, was apparently the major contributing factor. In our study, the ratio of total MU for RapidArc, IMRT, and TomoTherapy was 1:2.4:13.3. It should be noted the NTMD calculated by treatment planning computers did not account for head leakage, and thus the true mean dose to normal tissues should be greater than the NTMD reported here, with magnitude depending on the total MU and the head leakage ratio. Concern of radiation-induced secondary malignancy was reported previously. However, in our opinion, the real effect of the issue remained uncertain.

**Expected delivery time**

RapidArc showed significant shorter expected delivery time than IMRT or TomoTherapy, with an average saving of approximately 7 minutes as compared with the other 2 techniques. Shorter delivery time increases machine throughput and is also favorable for patients who cannot remain stable on the couch for a long time.

Finally, the treatment planning time was not addressed in this study owing to the difficulty to record the exact amount of time spent on individual plans when the planners might be involved in different tasks at the same time. However, it was our general experience that a shorter planning time was needed to construct a TomoTherapy plan, slightly more for IMRT, and substantially more was needed to create a RapidArc plan. The average required planning time differ by a factor of 2, especially for difficult plans, between TomoTherapy and RapidArc techniques. It has to be admitted that the comment was not based on objective evidence, and the result could be affected by planners’ experience, speed of computer, and version of treatment planning software. However, this remained to be one of our concerns in the selection of techniques for the case.

This study was aimed at assessing the comparative advantages of the 2 Eclipse-based modulation therapy (RapidArc and IMRT) and Helical TomoTherapy. A previous article on NPC was focused on Pinnacle-based VMAT and step-and-shoot IMRT techniques; the results of which may be vastly different from the comparative study of these in the current article. In addition, unlike most early reports,
we used noncoplanar beams in IMRT if necessary, which provided an extra dimension in optimizing dosimetry during treatment planning. Because of this study, a comparison chart (Table 4) was drawn that may serve as a quick reference for oncologists to aid in selection of patients for the appropriate treatment technique.

References
