Dosimetric comparison of helical tomotherapy, volume-modulated arc therapy, and fixed-field intensity-modulated radiation therapy in nasopharyngeal and cervical cancers

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Research

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Abstract

Background: To compare the dosimetric parameters of different radiotherapy plans, helical tomotherapy (HT), volume-modulated arc therapy (VMAT), and fixed-field intensity-modulated radiation therapy (FF-IMRT) for nasopharyngeal carcinoma (NPC) and cervical cancer (CC).

Methods: A total of 15 patients with NPC and 15 patients with CC were chosen for retrospective analysis and replanned for HT, VMAT, and FF-IMRT. The prescribed doses of the planning target were 2.12/69.96 Gy, 1.8/59.4 Gy for NPC and 1.8/45 Gy for CC, respectively. The dosimetric parameters of the planning target, organs at risk (OARs), and the efficiency of radiation delivery were assessed and compared using the paired-samples t-test.

Results: Compared with VMAT and FF-IMRT, HT plans significantly improved the mean conformity index (CI) and homogeneity index (HI). For the OARs, the HT plans reduced the maximum doses of most organs, such as brainstem, spinal cord, and optic nerves in NPC, and significantly reduced the volume of the high-dose region in NPC and the $V_{30}$ and $V_{40}$ of small bowel, rectum, and bladder in CC. However, VMAT evidently reduced the treatment time and improved the efficiency of radiation delivery than HT.

Conclusions: For NPC and CC, results showed that HT and VMAT possessed better homogeneity and conformity of the target and better sparing of OARs compared with the conventional FF-IMRT, and HT achieved the best effect. VMAT had the shortest radiation delivery time. The results of this study can provide guidance for the selection of appropriate radiation technologies for patients with NPC and CC who are undergoing concurrent chemoradiotherapy.

Background

Cancer, a global health issue, is expected to be the leading cause of death and the most important barrier to increasing life expectancy in the 21st century[1]. Radiation therapy (RT) plays a crucial role in the treatment of cancer, especially in nasopharyngeal (NPC) and cervical (CC) cancers. Some randomized prospective clinical trials have found that cCRT increases tumor control compared with RT alone in CC [2, 3]. cCRT has been accepted as a standard treatment for most patients with CC since 1999 [4, 5]. It is also the same in the locally advanced NPC[6]. However, cCRT can lead to considerable acute and late toxicities that affect the gastrointestinal (GI) and genitourinary (GU) tracts[4, 7, 8] in CC and aggravate the adverse effects of many normal structures that surround the nasopharynx in NPC, such as pharyngeal mucosa, parotid glands, and cranial nerves, in NPC[9, 10]. Therefore, more and more studies focus on reducing the side effects related to the treatment in patients with CC and NPC who are undergoing cCRT.

Modern radiation techniques have appeared due to the development of radiation equipment and radiation physics in recent years. Following the conventional three-dimensional conformal technique, IMRT can attain the certain specified dosimetric and clinical objectives through a computer-aided optimization process[11], and provide highly conformal dose distributions to the planning target volume (PTV), minimize the dose to organs at risk (OARs)[12, 13], and eventually reduces acute and late toxicity.
Volume-modulated arc therapy (VMAT) and helical tomotherapy (HT) are gaining more attention than conventional fixed-field intensity-modulated RT (FF-IMRT, 5/7/9-field) recently. VMAT has low monitor units (MUs) and treatment time, varying dose rates, and dynamic multileaf collimator (MLC) through a variable-speed rotational treatment mode. HT is a new computed tomography (CT)-based rotational IMRT, delivers a highly conformal dose distribution, and provides fine OARs sparing ability by using the 51 independent beam directions and 64 pneumatically driven leaves of MLC.

However, the high cost of primary equipment and maintenance of the HT treatment system leads to the rise in treatment cost, which limits its use in the clinical practice especially in the developing countries. Hence, this study aims to assess three modern IMRT techniques (HT, VMAT, and FF-IMRT) in terms of dosimetric parameters for the planning target and the OARs in CC and locally advanced NPC and determine whether the cost of HT can make a significant difference dosimetrically.

**Methods**

**Patient characteristics and CT simulation**

A total of 15 patients with AJCC Stage III/IVb NPC and 15 patients with FIGO Stage IIB CC between May 2019 and October 2019 in our hospital were chosen for this research. The selection criterion was biopsy-proven squamous cell carcinoma. The age of the eligible patients ranged from 44 years to 66 years, and the mean and median ages were 53.4 and 59 years, respectively. The thermoplastic head and neck masks were used to immobilize the patients with NPC, whereas the thermoplastic pelvic masks were used to immobilize the patients with CC. All patients were placed in a supine position and subjected to scanned CT simulations of 5 mm slice thickness by using the Philips 16-slice Brilliance big bore CT scanner (Philips Medical Systems, Amsterdam, Netherlands). Patients with CC were in a supine position with comfortably full bladder (after emptying, patients were requested for drinking 1 liter of water 30 to 45 minutes before treatment and holding urine) and a bowel preparation with oral contrast agent prior to simulation. The scanned images were from the top of the head to the carina for the patients with NPC and from the L2 vertebra to the area of 5 cm below the symphysis pubis for the patients with CC.

**Target and normal tissue volume definition**

The CT images were transferred to the Monaco 5.11 (Elekta AB, Stockholm, Sweden) planning system for contouring. For consistency, all the contouring of the target and OARs was finished by the same radiation oncologists who had a major in head and neck and gynecological RT, respectively. The target volume delineation of NPC was based on the Radiation Therapy Oncology Group (RTOG) 2009 guidelines[16] and the Chinese NPC Clinical Staging Committee[17]. The gross tumor volume (GTV) was defined as known gross disease. Grossly positive lymph nodes were defined as any lymph node > 1 cm or nodes with a
necrotic cancer. The clinical target volume (CTV59.4) was defined as a region at high risk for microscopic disease, which included all potential routes of spread for primary and nodal diseases. The primary high-risk regions included entire nasopharynx, anterior 1/3 of clivus, skull base, pterygoid fossa, parapharyngeal space, inferior sphenoid sinus, posterior 1/4 of the nasal cavity/maxillary sinuses, inferior soft palate and retrostyloid space. High risk lymph nodes regions usually included the bilateral upper deep jugular, retropharyngeal, and level II, III, IV, and V lymph nodes. Level IB can be spared in selected patients. The OARs for the NPC included the brainstem, spinal cord, optic nerves, optic chiasm, eyes, lens, temporal lobe, parotid glands, pituitary, temporomandibular joints (TMJ), mandible, oral cavity, brachial plexus, esophagus, and larynx. The target volume delineation of CC was based on the recommendations of the RTOG 0418 protocol and the International Commission on Radiation Units and Measurements reports (ICRU) Report 62. The CTV for the CC included the gross tumor volume, cervix, parametria, uterus, uterosacral ligaments, sufficient vaginal margin from the gross disease (at least 3 cm), presacral region, and pelvic lymph drainage area. The CTV ranged from the L4–L5 vertebra to the inferior margin of the obturator foramen. The PTV was generated by expanding a uniform 7 mm margin to the CTV. The OARs for the CC included the small bowel, bladder, rectum, spinal cord and femoral heads.

### Treatment planning

All treatment planning procedures were developed by the same radiation physicist to ensure consistency. The FF-IMRT and VMAT plans were designed using the Monaco planning system version 5.11, and the HT plans were designed in the tomotherapy planning system (Accuray Inc., Madison, USA). The FF-IMRT and VMAT plans were designed to be executed using the Elekta Synergy (Elekta Ltd., Crawley, UK) equipped with 8 MV photon beams and the MLCi2 (40 pairs of MLC leaves; each one had 1 cm width at the isocenter). The prescribed doses of the PTV were 2.12/69.96 Gy, 1.8/59.4 Gy for NPC and 1.8/45 Gy for CC, respectively. The details on the dose constraints of normal tissues for the NPC and the CC plans are summarized in Table 1.
Table 1
The dose-volume constraints of normal tissues in NPC and CC

| Structures      | Dose-volume constraints |
|-----------------|-------------------------|
| **NPC**         |                         |
| Brainstem       | Dmax < 54 Gy            |
| Spinal cord     | Dmax < 45 Gy            |
| Optic nerves    | Dmax < 54 Gy or D1 < 60 Gy |
| Optic chiasm    | Dmax < 54 Gy            |
| Lens            | Dmax < 8 Gy             |
| Eyes            | Dmax < 40 Gy            |
| Pituitary       | Dmax < 60 Gy            |
| Mandible        | Dmax < 70 Gy            |
| TMJ             | Dmax < 70 Gy            |
| Brachial plexus | Dmax < 66 Gy            |
| Oral cavity     | V40 < 40%               |
| Parotid gland   | V30 < 50%               |
| Temporal lobes  | Dmax < 60 Gy or D1 < 65 Gy |
| Larynx          | V45 < 40%               |
| Esophagus       | V45 < 40%               |
| **CC**          |                         |
| Small bowel     | V30 < 50%, D\(_{\text{max}}\)<48 Gy |
| Rectum          | V30 < 50%, D\(_{\text{max}}\)<48 Gy |
| Bladder         | V40 < 35%               |
| Femoral head    | V40 < 5%                |
| Spinal cord     | D\(_{\text{max}}\) < 40 Gy |

The patients with CC received brachytherapy by using Ir\(^{192}\) source (high-dose rate) once a week and applied with 30–36 Gy/5–6f, which was dosed at the A point.

HT plans
The HT plans were done using a tomotherapy planning station with 6 MV X-ray and performed on the Tomo HD (Accuray Inc., Madison, USA). The parameters for beamlet calculation included a field width of 2.5 cm, a pitch value of 0.287, a modulation factor of 3, and a normal dose calculation grid.

VMAT plans

The VMAT plans were done in the Monaco 5.11 planning system, and an 8 MV X-ray of a Synergy linear accelerator was used. The VMAT plans were designed using a beam with double 360° arcs, which had 100 control points per arc. All VMAT plans were designed using the Monte Carlo algorithm in the Monaco 5.11 planning system.

FF-IMRT plans

The FF-IMRT plans were done in the Monaco 5.11 planning system, and an 8 MV X-ray of a Synergy linear accelerator was used. Nine evenly distributed coplanar fields with gantry angles of 200°, 240°, 280°, 320°, 0°, 40°, 80°, 120°, and 160° were used, and 20 control points were present in one beam. All FF-IMRT plans were prepared using the Monte Carlo algorithm in the Monaco 5.11 planning system. The optimization functions of the FF-IMRT plans were the same as those of the VMAT plans. The DMLC (sliding window) technique was used in the FF-IMRT plans.

Plan evaluation parameters

The data in the dose–volume histogram (DVH) obtained from all the plans were analyzed. The plan comparisons were focused on the following parameters.

PTV Coverage

The dose that received 98% volume of the PTV ($D_{98%}$), $D_{50%}$, $D_{2%}$, mean dose ($D_{mean}$), conformity index (CI), and homogeneity index (HI) were quantified to evaluate the PTV coverage. CI was used to evaluate the conformity of the prescribed dose distribution.

\[
CI = \frac{V_{t,\text{ref}}}{V_t} \times \frac{V_{t,\text{ref}}}{V_{\text{ref}}}
\]
Where $V_{tref}$, $V_t$, and $V_{ref}$ denote the target volume receiving the prescribed dose, the target volume, and the total volume covered by the prescribed dose, respectively.

The CI ranges from 0 to 1, and a high CI indicates high conformal dose of the target. In accordance with the ICRU report NO.83 [18], the HI was calculated using following formula:

$$HI = \frac{D_{2\%} - D_{98\%}}{D_{50\%}}$$

HI was used to evaluate the homogeneity of dose distribution. The low HI value indicates good homogeneity of the target volume.

Organs at Risk (OARs)

For the patients with NPC, the maximum doses ($D_{max}$) of the brainstem, spinal cord, optic nerves, optic chiasm, lens, eyes, pituitary, mandible, TMJ, and brachial plexus; the mean dose ($D_{mean}$) of the larynx, oral cavity, and esophagus; the $V_{30}$ (volume that received the dose of 30 Gy) and the $D_{mean}$ of parotid glands; $D_1$ (the dose that received 1% volume of the OARs) and the $D_{max}$ of temporal lobes were determined.

For the patients with CC, the $V_5$, $V_{10}$, $V_{20}$, $V_{30}$, $V_{40}$, $D_{max}$, and $D_{mean}$ of OARs, including the small bowel, rectum, bladder, spinal cord, and femoral head (right and left), were determined.

Treatment Time

The treatment delivery time of each plan was determined and compared.

**Data analysis**

All plans were normalized to cover the 95% volume of the PTV with the prescribed dose to keep the results comparable. The data collected from the DVH of PTV and OARs were analyzed using the SPSS 19.0 (SPSS, Inc., Chicago, IL, USA). The significance of differences was tested using the paired-samples $t$-test. A $P$ value $< 0.05$ was considered statistically significant.
Results

PTV coverage

The mean volumes of PTV69.96, PTVnd, and PTV59.4 in NPC were 53.6 ± 30.3 (11.3–106.5 cc), 41.6 ± 38.9 (6.9–107.9 cc) and 674.0 ± 142.4 cc (503.3–874.0 cc), respectively. The mean volume of PTV was 1054.0 ± 126.4 cc (860.3–1281.0 cc) in CC. All HT, VMAT, and FF-IMRT plans were normalized to cover 95% of the PTV volume with ≥ 100% of the prescribed dose. The $D_{\text{max}}$ constrained in the PTV was less than 110% of the prescription dose.

The detailed results are shown in Table 2. With regard to conformal and homogeneous dose distribution to the PTV target dose distribution in NPC and CC, the HT plans, which had the lowest HI and the highest CI, was significantly better than the VMAT and FF-IMRT plans ($P<0.001$)(Fig. 1). The HT plans, which had the best $D_{\text{mean}}$ value ($P<0.001$) which is close to the prescription dose, also exhibited significant advantages over the other two plans. Compared with the conventional FF-IMRT plans, the VMAT plans provided better HI ($P=0.027$) and CI ($P<0.001$) in CC but did not show significant superiority ($P>0.05$) in NPC, only the CI of PTV59.4 was better ($P=0.016$). Typical dose distributions and dose-volume histograms of the three plans in NPC and CC are showed in Fig. 2 and Fig. 3.
Table 2
Dosimetric parameters for PTV of three plans in NPC and CC

| Parameters | IMRT | VMAT | HT | \( P^* \) | \( P^{*} \) VMAT VS IMRT | \( P^{*} \) HT VS IMRT | \( P^{*} \) HT VS VMAT |
|------------|------|------|----|--------|-----------------|-----------------|-----------------|
| NPC        |      |      |    |        |                 |                 |                 |
| PTV69.96   |      |      |    |        |                 |                 |                 |
| Dmean (Gy) | 72.10±0.49 | 72.24±0.37 | 70.63±0.23 | 0.117 | <0.001 | <0.001 |
| HI         | 0.07±0.01  | 0.07±0.01  | 0.03±0.01  | 0.217 | <0.001 | <0.001 |
| CI         | 0.75±0.04  | 0.76±0.03  | 0.82±0.04  | 0.086 | <0.001 | <0.001 |
| PTVnd      |      |      |    |        |                 |                 |                 |
| Dmean (Gy) | 72.11±0.52 | 72.30±0.25 | 70.63±0.25 | 0.409 | <0.001 | <0.001 |
| HI         | 0.07±0.02  | 0.07±0.02  | 0.03±0.01  | 0.726 | <0.001 | <0.001 |
| CI         | 0.77±0.05  | 0.78±0.04  | 0.82±0.04  | 0.184 | <0.001 | <0.001 |
| PTV59.4    |      |      |    |        |                 |                 |                 |
| Dmean (Gy) | 62.50±0.60 | 62.47±0.49 | 60.85±0.43 | 0.765 | <0.001 | <0.001 |
| HI         | 0.17±0.04  | 0.17±0.04  | 0.11±0.01  | 0.082 | <0.001 | <0.001 |
| CI         | 0.65±0.08  | 0.66±0.08  | 0.76±0.08  | 0.016 | <0.001 | <0.001 |
| CC         |      |      |    |        |                 |                 |                 |
| PTV        |      |      |    |        |                 |                 |                 |
| Dmean (Gy) | 46.45±0.33 | 46.41±0.33 | 45.81±0.15 | 0.370 | <0.001 | <0.001 |
| HI         | 0.08±0.01  | 0.07±0.01  | 0.04±0.01  | 0.027 | <0.001 | <0.001 |
| CI         | 0.78±0.04  | 0.80±0.04  | 0.86±0.03  | <0.001 | <0.001 | <0.001 |

* \( P \) value was computed by paired \( t \) test
OARS

The DVH data for the OARs in NPC and CC are listed in Table 3 and Table 4.
| OARs         | IMRT  | VMAT  | HT    | \( P^* \) | VMAT VS IMRT | HT VS IMRT | HT VS VMAT |
|-------------|-------|-------|-------|-----------|---------------|-------------|-------------|
| Brainstem   |       |       |       |           |               |             |             |
| Dmax (Gy)   | 53.77±1.33 | 53.16±1.26 | 51.84±1.95 | 0.006 | <0.001 | 0.002 |
| Spinal cord |       |       |       |           |               |             |             |
| Dmax (Gy)   | 43.99±1.03 | 42.99±1.15 | 41.34±1.57 | 0.022 | <0.001 | <0.001 |
| Optic nerve left | | | | | | | |
| Dmax (Gy)   | 55.46±2.98 | 54.46±4.13 | 52.07±3.14 | 0.040 | <0.001 | 0.002 |
| Optic nerve right | | | | | | | |
| Dmax (Gy)   | 55.05±2.39 | 55.11±3.13 | 50.90±3.24 | 0.881 | <0.001 | <0.001 |
| Optic chiasm | | | | | | | |
| Dmax (Gy)   | 42.52±11.57 | 41.88±11.82 | 42.67±7.26 | 0.378 | 0.912 | 0.600 |
| Lens left   |       |       |       |           |               |             |             |
| Dmax (Gy)   | 7.43±1.64  | 7.16±1.94  | 5.47±0.82  | 0.346 | <0.001 | 0.001 |
| Lens right  |       |       |       |           |               |             |             |
| Dmax (Gy)   | 7.69±1.28  | 7.46±1.36  | 5.82±0.62  | 0.502 | <0.001 | <0.001 |
| Eye left    |       |       |       |           |               |             |             |
| Dmax (Gy)   | 35.72±4.70 | 33.06±6.68 | 28.13±5.25 | 0.011 | <0.001 | 0.001 |
| Eye right   |       |       |       |           |               |             |             |
| Dmax (Gy)   | 35.92±3.29 | 33.62±5.62 | 26.62±4.59 | 0.018 | <0.001 | <0.001 |
| Pituitary   | | | | | | | |

* \( P^* \) value was computed by paired \( t \) test
| OARs            | IMRT       | VMAT       | HT         | \( P^* \)   |
|-----------------|------------|------------|------------|-------------|
|                 |            |            |            | VMAT VS IMRT | HT VS IMRT | HT VS VMAT |
| Dmax (Gy)       | 58.22 ± 4.97 | 58.54 ± 5.35 | 52.32 ± 6.78 | 0.375       | < 0.001     | < 0.001     |
| Mandible       |            |            |            |             |             |             |
| Dmax (Gy)       | 67.39 ± 3.87 | 67.76 ± 3.83 | 66.61 ± 4.20 | 0.249       | 0.234       | 0.095       |
| TMJ left        |            |            |            |             |             |             |
| Dmax (Gy)       | 61.07 ± 2.53 | 59.16 ± 3.54 | 57.85 ± 3.42 | 0.001       | < 0.001     | 0.004       |
| TMJ right       |            |            |            |             |             |             |
| Dmax (Gy)       | 60.23 ± 4.88 | 58.58 ± 5.17 | 57.10 ± 5.36 | 0.016       | < 0.001     | 0.027       |
| Brachial plexus |            |            |            |             |             |             |
| left            |            |            |            |             |             |             |
| Dmax (Gy)       | 63.93 ± 2.19 | 64.32 ± 2.18 | 63.25 ± 3.79 | 0.132       | 0.363       | 0.177       |
| Brachial plexus |            |            |            |             |             |             |
| right           |            |            |            |             |             |             |
| Dmax (Gy)       | 64.20 ± 2.63 | 64.79 ± 3.00 | 63.27 ± 4.10 | 0.074       | 0.171       | 0.022       |
| Oral cavity     |            |            |            |             |             |             |
| Dmean (Gy)      | 38.06 ± 1.48 | 38.44 ± 1.79 | 37.68 ± 1.57 | 0.404       | 0.356       | 0.229       |
| Parotid gland   |            |            |            |             |             |             |
| left            |            |            |            |             |             |             |
| Dmean (Gy)      | 33.81 ± 1.34 | 33.38 ± 1.87 | 33.64 ± 1.04 | 0.471       | 0.683       | 0.664       |
| V30 (%)         | 50.58 ± 2.52 | 49.96 ± 2.70 | 45.23 ± 1.73 | 0.537       | < 0.001     | < 0.001     |
| Parotid gland   |            |            |            |             |             |             |
| right           |            |            |            |             |             |             |
| Dmean (Gy)      | 34.71 ± 1.08 | 33.86 ± 1.72 | 33.87 ± 1.13 | 0.036       | 0.048       | 0.975       |

* \( P \) value was computed by paired \( t \) test
| OARs            | IMRT     | VMAT     | HT       | \( P^* \) | VMAT VS IMRT | HT VS IMRT | HT VS VMAT |
|-----------------|----------|----------|----------|-----------|--------------|------------|------------|
| V30 (%)         | 51.15 ± 1.68 | 50.44 ± 2.06 | 45.56 ± 2.14 | 0.359     | < 0.001      | < 0.001    |            |
| Temporal lobe left |         |          |          |           |              |            |            |
| Dmax (Gy)       | 65.16 ± 3.94 | 64.79 ± 3.80 | 62.09 ± 3.73 | 0.071     | < 0.001      | < 0.001    |            |
| D1 (Gy)         | 59.38 ± 1.26 | 59.13 ± 1.84 | 58.23 ± 1.28 | 0.429     | 0.006        | 0.028      |            |
| Temporal lobe right |       |            |          |           |              |            |            |
| Dmax (Gy)       | 63.90 ± 1.39 | 64.08 ± 1.69 | 60.46 ± 0.77 | 0.659     | < 0.001      | < 0.001    |            |
| D1 (Gy)         | 58.87 ± 0.85 | 59.35 ± 1.05 | 58.00 ± 1.00 | 0.080     | 0.001        | < 0.001    |            |
| Larynx          |          |          |          |           |              |            |            |
| Dmean (Gy)      | 43.22 ± 1.08 | 41.99 ± 2.07 | 39.56 ± 0.98 | 0.024     | < 0.001      | 0.001      |            |
| Esophagus        |          |          |          |           |              |            |            |
| Dmean (Gy)      | 30.41 ± 6.63 | 28.80 ± 6.58 | 28.18 ± 5.91 | 0.007     | < 0.001      | 0.371      |            |

* \( P \) value was computed by paired \( t \) test
Table 4  
Dose-volume histogram comparisons for the main OARs of three plans in CC

| OARs   | IMRT          | VMAT          | HT            | P*        | VMAT VS IMRT | HT VS IMRT | HT VS VMAT |
|--------|---------------|---------------|---------------|-----------|--------------|------------|------------|
|        |               |               |               |           |              |            |            |
| Small bowel |               |               |               |           |              |            |            |
| V5 (%) | 92.40 ± 8.78  | 92.63 ± 8.76  | 95.11 ± 8.33  | 0.440     | 0.001        | 0.001      |            |
| V10 (%)| 84.27 ± 8.57  | 84.15 ± 8.57  | 88.10 ± 9.33  | 0.636     | 0.011        | 0.011      |            |
| V20 (%)| 64.12 ± 7.26  | 63.82 ± 5.94  | 61.02 ± 4.54  | 0.664     | 0.006        | 0.004      |            |
| V30 (%)| 42.71 ± 5.14  | 41.95 ± 5.49  | 36.73 ± 5.74  | 0.081     | 0.001        | 0.001      |            |
| V40 (%)| 24.42 ± 5.38  | 22.82 ± 4.85  | 20.06 ± 5.22  | 0.001     | 0.001        | 0.001      |            |
| Dmax (Gy)| 47.95 ± 0.52 | 48.05 ± 0.75  | 46.69 ± 0.54  | 0.391     | 0.001        | 0.001      |            |
| Dmean (Gy)| 26.42 ± 2.41 | 26.11 ± 2.26  | 25.58 ± 1.95  | 0.009     | 0.001        | 0.005      |            |
| Rectum |               |               |               |           |              |            |            |
| V5 (%) | 99.45 ± 1.27  | 99.23 ± 1.51  | 99.67 ± 0.89  | 0.139     | 0.083        | 0.071      |            |
| V10 (%)| 98.15 ± 2.79  | 97.11 ± 3.15  | 97.76 ± 3.15  | 0.006     | 0.547        | 0.318      |            |
| V20 (%)| 87.99 ± 5.09  | 81.14 ± 5.52  | 69.99 ± 2.77  | 0.001     | 0.001        | 0.001      |            |
| V30 (%)| 51.51 ± 1.92  | 49.27 ± 2.23  | 42.66 ± 4.11  | 0.001     | 0.001        | 0.001      |            |
| V40 (%)| 18.79 ± 3.61  | 19.23 ± 3.61  | 19.42 ± 2.58  | 0.357     | 0.514        | 0.863      |            |
| Dmax (Gy)| 47.69 ± 0.65 | 47.71 ± 0.44  | 46.61 ± 0.38  | 0.924     | 0.001        | 0.001      |            |
| Dmean (Gy)| 30.52 ± 0.87 | 29.61 ± 0.86  | 28.17 ± 0.66  | 0.001     | 0.001        | 0.001      |            |

* P value was computed by paired t test
| OARs       | IMRT       | VMAT       | HT         |          |          |          |
|------------|------------|------------|------------|----------|----------|----------|
|            |            |            |            | VMAT VS  | HT VS    | HT VS    |
|            | IMRT       |            |            |          | IMRT     | VMAT     |
| V5 (%)     | 100.00 ± 0.00 | 100.00 ± 0.00 | 100.00 ± 0.00 | -        | -        | -        |
| V10 (%)    | 100.00 ± 0.00 | 100.00 ± 0.00 | 99.98 ± 0.07 | -        | 0.334    | 0.334    |
| V20 (%)    | 99.53 ± 0.73 | 98.72 ± 2.01 | 79.61 ± 3.71 | 0.138    | 0.001    | 0.001    |
| V30 (%)    | 79.81 ± 6.99 | 77.26 ± 9.45 | 52.07 ± 2.54 | 0.164    | 0.001    | 0.001    |
| V40 (%)    | 37.55 ± 1.57 | 36.53 ± 2.12 | 35.07 ± 3.69 | 0.015    | 0.003    | 0.030    |
| Dmean (Gy) | 36.75 ± 0.72 | 36.28 ± 1.03 | 31.88 ± 0.81 | 0.021    | 0.001    | 0.001    |

**Spinal Cord**

|               | IMRT       | VMAT       | HT         |          |          |          |
|---------------|------------|------------|------------|----------|----------|----------|
| Dmax (Gy)     | 38.62 ± 1.61 | 35.94 ± 2.32 | 29.99 ± 3.54 | 0.001    | 0.001    | 0.001    |

**Femoral head-L**

|               | IMRT       | VMAT       | HT         |          |          |          |
|---------------|------------|------------|------------|----------|----------|----------|
| V5 (%)        | 94.79 ± 11.69 | 96.29 ± 9.20  | 98.69 ± 3.79  | 0.165    | 0.096    | 0.115    |
| V10 (%)       | 82.73 ± 16.97 | 93.98 ± 12.53 | 93.10 ± 10.07 | 0.001    | 0.001    | 0.338    |
| V20 (%)       | 48.11 ± 14.09 | 58.93 ± 14.98 | 30.31 ± 3.48  | 0.001    | 0.001    | 0.001    |
| V30 (%)       | 22.72 ± 10.05 | 22.45 ± 9.71   | 9.79 ± 3.93   | 0.906    | 0.001    | 0.001    |
| V40 (%)       | 2.62 ± 2.35  | 2.49 ± 2.05   | 0.05 ± 0.10   | 0.659    | 0.001    | 0.001    |
| Dmean (Gy)    | 20.57 ± 3.96  | 22.72 ± 3.84   | 17.58 ± 1.19  | 0.001    | 0.003    | 0.001    |

**Femoral head-R**

|               | IMRT       | VMAT       | HT         |          |          |          |
|---------------|------------|------------|------------|----------|----------|----------|
| V5 (%)        | 96.65 ± 6.43  | 97.01 ± 6.75  | 99.52 ± 1.74  | 0.591    | 0.063    | 0.094    |
| V10 (%)       | 82.98 ± 16.52 | 91.50 ± 10.55 | 92.31 ± 8.26  | 0.010    | 0.007    | 0.548    |

* P value was computed by paired t test
| OARs     | IMRT        | VMAT        | HT         | \(P^*\)        | VMAT VS IMRT | HT VS IMRT | HT VS VMAT |
|----------|-------------|-------------|------------|----------------|--------------|-------------|-------------|
| V20 (%)  | 46.34 ± 16.35 | 58.87 ± 15.19 | 31.24 ± 3.05 | 0.008          | 0.004        | 0.001       |
| V30 (%)  | 22.04 ± 9.36  | 19.69 ± 7.32  | 9.64 ± 4.03  | 0.308          | 0.001        | 0.001       |
| V40 (%)  | 1.92 ± 2.63   | 0.99 ± 1.29   | 0.01 ± 0.02  | 0.081          | 0.013        | 0.011       |
| Dmean (Gy) | 20.27 ± 3.91 | 22.03 ± 3.13 | 17.62 ± 0.76 | 0.039          | 0.013        | 0.001       |

* \(P^*\) value was computed by paired \(t\) test

In the RT of NPC, results showed that the \(D_{\text{max}}\) values to the brainstem, spinal cord, optic nerves, lens, eyes, pituitary, TMJ left, and temporal lobes in HT plans were significantly lower than those in FF-IMRT and VMAT plans (\(P \leq 0.01\)). HT also performed significantly better dose sparing for the \(V_{30}\) of parotid glands, \(D_1\) of temporal lobes, and \(D_{\text{mean}}\) of larynx, compared with FF-IMRT and VMAT (\(P < 0.05\)). Compared with FF-IMRT, VMAT significantly decreased the \(D_{\text{max}}\) of the brainstem, spinal cord, optic nerve, eyes, TMJs, and temporal lobe and the \(D_{\text{mean}}\) of the larynx and esophagus (\(P < 0.05\)) (Table 3).

As for CC cases, GU and GI are the major concerns in clinical practice. Therefore, our aim was to keep the dose of small bowel, rectum, and bladder as low as possible. The HT plans resulted in a significantly lower dose to the small bowel than the FF-IMRT and VMAT plans, and these results were best seen at the \(V_{20}\), \(V_{30}\), \(V_{40}\), \(D_{\text{max}}\) and \(D_{\text{mean}}\) (\(P < 0.01\)). However, HT did not work well in the protection of low-dose area, as evidenced by the higher \(V_5\) and \(V_{10}\) than those of the FF-IMRT and VMAT. Furthermore, HT significantly improved the rectal sparing for the \(V_{20}\) and \(V_{30}\) as evidenced by 13–20% reduction compared with those of FF-IMRT and VMAT (\(P < 0.001\)), and also resulted in decreased \(D_{\text{max}}\) and \(D_{\text{mean}}\). In the bladder, the \(V_{20}\), \(V_{30}\), \(V_{40}\), and \(D_{\text{mean}}\) in HT were significantly lower (4–34% reduction) compared with those in IMRT and VMAT (\(P < 0.05\)). In the femoral head, HT decreased the \(V_{20}\), \(V_{30}\), \(V_{40}\), and \(D_{\text{mean}}\) compared with VMAT and IMRT (\(P < 0.05\)) and increased the \(V_{10}\) compared with FF-IMRT (\(P < 0.01\)). In addition, HT resulted in decreased \(D_{\text{max}}\) in the spinal cord by 12–22% compared with FF-IMRT and VMAT. Compared with FF-IMRT, VMAT showed significant advantage in dose sparing for the \(V_{40}\) of the small bowel; \(V_{10}\), \(V_{20}\), and \(V_{30}\) of the rectum; \(V_{40}\) of the bladder; and \(D_{\text{max}}\) of the spinal cord (\(P < 0.05\)) (Table 4).

**Treatment time**
The treatment delivery time of the three treatment techniques in NPC and CC were determined to study the execution efficiency of the three RT technologies. The mean treatment delivery times of FF-IMRT, VMAT, and HT in NPC were 7.49 ± 0.32, 4.40 ± 0.29, and 7.59 ± 0.40 min, respectively. Similarly, the mean treatment delivery times of FF-IMRT, VMAT, and HT in CC were 7.79 ± 0.33, 4.87 ± 0.27, and 8.85 ± 0.86 min, respectively. Compared with FF-IMRT and HT, VMAT had the highest execution efficiency in NPC and CC.

Discussion

Cancer is a major public health problem worldwide and is the second leading cause of death in the United States. The cancer mortality rate has been declining since 1991 due to the increased precision in surgery and RT, the maturity of diagnostic imaging technology, and the development of molecular targeted therapy or immunotherapy[19]. Therefore, attention should be paid to the side effects related to the treatment and the quality of life of patients with cancer and the local control rate of tumor. RT is one of the main treatments for cancers. Being one of the few hospitals equipped with several advanced linear accelerators (nine linear accelerators, including Versa HD and HT) in China, our hospital has unique advantages in the dosimetric study of IMRT, VMAT, and HT. Reports about comparing dosimetric parameters of FF-IMRT, VMAT, and HT with regards to the PTV and OARs in two cancers in different sites (NPC and CC) are rare. Therefore, this study aims to estimate the dosimetric superiority of the three RT techniques and provide guidance for the technique selection in patients with NPC and CC.

NPC and CC were chosen as research subjects because most of these two cancers are squamous cell carcinoma, which has good radiosensitivity and prognosis. Moreover, these two cancers have relatively complex-shaped tumorous regions and important adjacent OARs for sparing. Therefore, exploring the feasible and optimal radiotherapeutic techniques is critical to accomplish high conformal treatment plans and acquire good OAR sparing. Given that the RT principle of CC is the external beam RT and brachytherapy, GU and GI are the major concerns. Hence, our aim was to keep the dose to the small bowel, rectum, and bladder as low as possible in CC. For NPC, many dose constraint organs surround the PTV, and RT may cause acute or late adverse effects of these structures. Our study aimed to decrease the dose and the volume of these structures that were irradiated.

Previous studies have confirmed that the modern IMRT have demonstrated significantly steeper dose gradient around the target compared with the conventional 3D-CRT[20, 21]. Growing Evidences have shown that HT can sculpt radiation doses to complex-shaped tumorous regions and avoid high-dose regions to OARs through the rapid opening and closing of leaves in a collimator rotating around the patient[22]. Therefore, HT is frequently used in various diseases[23−26], including NPC and CC[27, 28], nowadays. In this study, results showed that the three IMRT techniques met the clinical demand, but HT showed an evidently sharp dose gradient with the optimal HI and CI in NPC and CC. Moreover, VMAT offered better results in PTV coverage and dose conformity than FF-IMRT. Therefore, on the basis of these results, HT was the recommended RT technique to ensure the local control of tumors and improve the prognosis of patients with NPC and CC during RT treatment.
In addition to the conformity and homogeneity of the target, HT also showed a significantly better sparing of the surrounding OARs. In CC, the high-dose volume of the small bowel, rectum, and bladder is associated with the GI and GU toxicities after RT\cite{29–31}. Limiting the high-dose radiation delivered to the small bowel, rectum, and bladder can reduce the occurrences of acute and late GI and GU toxicities\cite{32, 33}. Therefore, the $V_{30}/V_{40}$ of the small bowel, rectum, and bladder are the major concerns in clinical practice and usually the parameters in the dose constraints of OARs. In our study, results showed that compared with the FF-IMRT plans, the HT plans decreased the $V_{30}$ and $V_{40}$ of the small bowel by 14.0% ($P<0.001$) and 17.9% ($P<0.001$), respectively; the $V_{30}$ of the rectum by 17.2% ($P<0.001$); and the $V_{30}$ and $V_{40}$ of the bladder by 34.8% ($P<0.001$) and 6.6% ($P=0.003$), respectively. The HT plans also had evident advantages in the above parameters compared with VMAT ($P<0.05$). Therefore, the HT plans notably reduced the high-dose volume, the $D_{mean}$, and the $D_{max}$ of the small bowel, rectum, and bladder, which may contribute to a marked decrease in the acute/late GI and GU toxicities. At the same time, the sparing of the HT in the $V_{40}$ of bladder and rectum was not as good as that in the $V_{30}$ which may be because the bladder and rectum were closely adjacent to PTV or partially overlapping and the primary principle of plan designing is to ensure the coverage of PTV. In NPC, the nasopharynx is adjacent to some critical organs, such as brainstem, lens, and optic nerves. Parts of the tumor are often underdosed, which may cause low local control rate, to protect these critical organs\cite{34}. The high dose and volume of irradiated normal tissues usually cause severe adverse effects, such as dysphagia and radiation mucositis, which may interrupt radiation. Therefore, decreasing the dose and volume of normal tissues, which surround the radiation regions, is crucial. In our study, results showed that compared with the FF-IMRT and VMAT plans, the HT plans significantly decreased the $D_{max}$ of the brainstem, spinal cord, optic structures, pituitary, TMJ, temporal lobes, and larynx (Table 3). Moreover, the HT plans decreased the $V_{30}$ of the parotid glands compared with the FF-IMRT ($P<0.001$) and VMAT ($P<0.001$) plans. Therefore, the HT plans may decrease the radiotherapeutic adverse effects by reducing the doses and volume of irradiated normal organs in CC and NPC.

The reasons for the significant advantages of the HT plans over the FF-IMRT and VMAT plans in PTV coverage and OAR sparing were as follows. First, the linac of HT can rotate 360° continuously with 51 beam angles optimized with the couch moving continuously at the same time. Second, HT delivers radiation in the form of helical tomoscan by using constant beam widths of 1, 2.5, and 5 cm. Finally, HT is equipped with a pneumatic binary MLC system with rapid leaf transition times. In addition, the on-board megavoltage CT (MVCT) of HT allows daily setup validation. The margin expanding from the CTV to the PTV can be decreased because the setup errors are reduced by daily setup verification, resulting in the reduced dose of OARs. The MVCT can be used to perform adaptive RT planning, which can eliminate the volume variation of the target and OARs between intrafractions.

Nevertheless, HT plans have also some drawbacks. Vernat \cite{35} and Pasquier \cite{36} have reported that HT increases the normal tissue volume of the low-dose region compared with IMRT and VMAT in oropharyngeal and prostate cancers. Xie\cite{37} has reported that the HT plan increases the $V_5$ and the $V_{10}$ of the lung and heart compared with the IMRT and the VMAT plans for left-sided breast cancer. Therefore,
the application of HT in lung and breast cancers is still controversial. Our results were consistent with those of the abovementioned studies. The volumes of OARs in the low-dose radiation region, such as the $V_5$ and the $V_{10}$ of small bowel and $V_{10}$ of femoral heads, increased in the HT plans of CC. However, the acute/late GI and GU toxicities were associated with the volume of the high-dose region in pelvic radiation. In addition, for NPC cases, most OARs were serially organized structures, which were closely related to $D_{max}$. Thus, our study focused on the $D_{max}$ of most OARs except parotid glands instead of the low-dose volumes. For parotid glands, the $V_{30}$ and the $D_{mean}$ were evaluated on the basis of the RTOG guidelines. Therefore, HT showed significant advantages in CC and NPC.

Compared with FF-IMRT, VMAT exhibited better dose distribution of target and better sparing of OARs. In addition, compared with FF-IMRT and HT, VMAT reduced the treatment time and improved the treatment efficiency while ensuring the treatment effect. Compared with FF-IMRT and HT, VMAT reduced the treatment delivery time by 37.5% and 55.0%, respectively, in CC and by 41.3% and 42%, respectively, in NPC. Several studies have reported that VMAT has achieved higher dose conformity of PTV and better sparing of OARs with a shorter treatment delivery time than FF-IMRT in terms of plans of different cancers[38–40]. Shortened treatment time may reduce the influence of uncertain factors, the probability of patients’ movement, and patients’ discomfort. Therefore, VMAT is the appropriate treatment technique for patients who cannot stay in position for a long time due to physical or mental discomfort.

There were some limitations in our study. Firstly, we compared the dosimetric parameters drawn from three IMRT techniques (i.e., FF-IMRT, VMAT, and HT). We only used a 9-field coplanar arrangement for FF-IMRT and a two-arc coplanar beam configuration for VMAT to reduce the complexity of comparisons, because the evidence suggested that these two techniques were the best choice to obtain better target coverage and better OARs sparing in FF-IMRT and VMAT for NPC and CC radiotherapy [41–43]. Secondly, we did not optimize plans considering the dose of bone marrow dose in CC. GU and GI are the major concerns during the RT. Hence, our aim was to keep the dose of small bowel, rectum, and bladder as low as possible. And so far, there is no consensus on bone marrow sparing strategy. Additionally, the limited sample size in our study may result in insufficient statistical power to show significance in some of the dosimetric parameters. Therefore, further clinical trials with large sample sizes focusing on the clinical significance of HT in NPC and CC are essential in the future.

**Conclusion**

For patients with NPC and CC, the HT and VMAT plans showed improvements in target coverage and OAR sparing compared with the FF-IMRT plans. The HT plans achieved the optimal conformity and homogeneity of the PTV coverage and the optimal sparing of OARs. VMAT evidently reduced the treatment time and improved the efficiency of radiation delivery, which can reduce the patients’ discomfort and probability of movement during the treatment. Also, the treatment cost of VMAT was lower than that of HT. Therefore, our results may provide guidance for the technique selection in patients with NPC and CC who are undergoing RT.
Declarations

Ethics approval and consent to participate

This study complied with the Helsinki Declaration and approval from the Ethics Committee of Harbin Medical University Cancer Hospital (Harbin, China) was obtained. All patients provided their informed consents for the publication of their images/data.

Consent for publication

Not applicable.

Availability of supporting data

Not applicable.

Conflict of interest statement

All the authors declare that there are no conflicts of interest.

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Author contributions

SS. Y and YY. Z designed the study. S.L and SS. Y contoured the target and OARs. DY. Y, XY. H, and X. L performed the design of the treatment planning. DY. Y and L. W collected the data. DY. Y, S. L, and SS. Y wrote and revised the manuscript. S. L and YL. B polished the language. All authors reviewed and approved the final version.

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Abbreviations

NPC - nasopharyngeal carcinoma; CC - cervical cancers; HT - helical tomotherapy; VMAT - volume-modulated arc therapy; FF-IMRT - fixed-field intensity-modulated radiation therapy; OARs - organs at risk; CI - conformity index; HI - homogeneity index; cCRT - Concurrent chemoradiotherapy; GI - gastrointestinal; GU - genitourinary; IMRT - intensity-modulated radiation therapy; PTV - the planning target volume; MUs - monitor units; MLC - multileaf collimator; CT - computed tomography; AJCC - American Joint Committee on Cancer; FIGO - International Federation of Obstetrics and Gynaecology; RTOG - Radiation Therapy
Oncology Group; GTV - gross tumor volume; TMJ - temporomandibular joints; RT - radiation therapy; 3D-CRT - 3-dimensional conformal radiotherapy.

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**Figures**
Figure 1

Conformity index (CI) and homogeneity index (HI) for planning target volume (PTV) with IMRT (Circle), VMAT (square), and HT (triangle). A: cervical cancer; B: nasopharyngeal carcinoma.
Figure 2
Typical dose distributions and dose-volume histograms of the three plans in NPC. A: Typical dose distributions. (A) FF-IMRT, (B) VMAT, (C) HT plans. B: dose-volume histograms for PTV69.96(red), PTVnd(brown), PTV59.4(purple), Brainstem(blue), Optic nerve(orange), Parotid gland(pink), and Temporal lobe(green).
Figure 3

Typical dose distributions and dose-volume histograms of the three plans in CC. A: Typical dose distributions. (A) FF-IMRT, (B) VMAT, (C) HT plans. B: dose-volume histograms for the PTV (purple), Small bowel (cyan), Rectum (blue), Bladder (orange), and Femoral heads (dark yellow).