

Research Article

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A Dosimetric Comparison of Volumetric Modulated Arc Therapy (VMAT) with Unflattened Beams to VMAT with Flattened Beams and Tomotherapy for Head and Neck Cancer

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Abstract

Background: The purpose of this study was to compare the dose distributions and treatment delivery efficiency of volumetric modulated arc therapy (VMAT) with flattening filter free (FFF) beams (FFF-VMAT) against VMAT with flattening filter (FF) beams (FF-VMAT) and Helical Tomotherapy (HT) for head and neck cancer.

Methods: Ten patients with nasopharyngeal and oropharyngeal cancer were chosen for this planning comparison study. Three treatment plans (dual arc FFF-VMAT, dual arc FF-VMAT, and HT) were created for each patient. The three prescription dose levels of the planning target volumes were 69.96, 60, and 54 Gy in 33 fractions, using the simultaneous integrated boost technique. Comparisons of the plan quality were performed by analyzing the homogeneity, conformity, dose to the organs at risk (OARs), the number of monitor units (MUs), and beam-on time (BOT) necessary for delivering the plans.

Results: The target coverage and sparing of the OARs for FFF-VMAT were almost equivalent to those for FF-VMAT and HT. Compared to FF-VMAT, FFF-VMAT and HT significantly increased the number of MUs. The BOTs were the same for FFF-VMAT and FF-VMAT but significantly increased for HT.

Conclusion: We here present the first report of FFF-VMAT achieving a comparable plan quality with less delivery time to that of FF-VMAT and HT in head and neck cancer. FFF-VMAT is a highly efficient and feasible option for the treatment of head and neck cancer in clinical practice.

Keywords: Flattening filter free; Volumetric modulated arc therapy; Tomotherapy; Head and neck cancer

Introduction

Flattening filter-free (FFF) beams have recently become available for commercial c-arm linear accelerators. The advantages of FFF beams include a reduced peripheral dose as a result of lower head scatter and leakage, and less variation in the energy spectrum in the off-axis position compared to flattening filter (FF) beams [1]. Furthermore, another advantage of FFF beams is the shortened delivery time necessary for delivering plans, owing to the increased dose rate [2].

FFF beams are already used clinically in Helical Tomotherapy (HT), which delivers highly modulated radiation dose fluence via rotating fan beams and by moving the couch simultaneously [3]. HT has been widely used for various sites of disease, including the brain, head and neck, lungs, breasts, and pelvis. Moreover, advantages have been reported for large target volumes (e.g. craniospinal irradiation and total body irradiation) due to the absence of field gaps using this technique [4,5]. Volumetric modulated arc therapy (VMAT) is a novel innovative treatment delivery technique with simultaneously varying

dose rates, gantry rotation speeds, and multileaf collimator shapes [6]. VMAT has the potential to create plans with comparable quality to conventional static field intensity modulated radiation therapy, and offers a shorter delivery time and smaller monitor units (MUs) [7]. Recently, several planning studies have demonstrated that VMAT with FFF beams (FFF-VMAT) shows equivalent treatment plan quality to VMAT with FF (FF-VMAT) [8-10].

However, there are currently no published studies comparing FFF-VMAT with FF-VMAT and HT, which is widely applied in clinical practice for the treatment of head and neck cancer. In this study, we examined the differences in dose distribution and treatment delivery efficiency between FFF-VMAT, FF-VMAT, and HT for head and neck cancer treatment.

Materials and Methods

Patients

We recruited 10 patients with head and neck cancer (5 with nasopharyngeal cancer and 5 with oropharyngeal cancer) treated with HT (Accuray Inc., Sunnyvale, CA.) between June 2013 and December

2014. All patients were immobilized using a thermoplastic mask, and computed tomography with 2.0 mm slice thickness was performed from the skull vertex to below the clavicles for treatment planning. The prescription doses at D95 (dose covering 95% of the volume) were 69.96, 60, and, 54 Gy in 33 fractions to the high-dose, intermediate-dose, and low-dose planning target volumes (PTV), respectively. Each PTV was trimmed up to 2 mm from the skin surface. The organs at risk (OARs) included the brain stem, spinal cord, eyes, lens, optic nerves, optic chiasm, parotid glands, inner ears, oral cavity, larynx,

mandible, esophagus, and brain. A planning risk volume of 3 mm in every direction was created around the spinal cord and around the brain stem. The following dose constraints based on the RTOG 0225 protocol were set on the OARs: maximum dose for the spinal cord: <45 Gy; maximum dose of the brain stem: <54 Gy; mean dose for at least one parotid gland: <26 Gy [11]. The optimization parameter of PTV and OARs for treatment planning is shown in Table 1. This study was conducted under the regulations of the Institutional Review Board of our institution.

Structures	Optimization objectives	Optimization priorities
PTV _{69.96 Gy}	Maximum dose <69.96 Gy	High
	Minimum dose >69.96 Gy	High
PTV _{60 Gy} - PTV _{69.96 Gy}	Maximum dose <60 Gy	Low
	Minimum dose >60 Gy	High
PTV _{54 Gy} - PTV _{69.96 Gy} - PTV _{60 Gy}	Maximum dose <54 Gy	Low
	Minimum dose >54 Gy	High
Cord	Maximum dose <45 Gy	High
Brain stem	Maximum dose <54 Gy	High
Lens	Maximum dose <5 Gy	Medium
Inner ear	Mean dose <45 Gy	Low
Oral cavity	Mean dose <40 Gy	Low
Larynx	Mean dose <45 Gy	Low
Mandible	Maximum dose <70 Gy	Medium

Table 1: The optimization parameter of PTV and OARs for treatment planning. Abbreviations: PTV: Planning Target Volume; OARs: Organs At Risk.

VMAT planning

The treatment plans were performed using Eclipse (version 11.0.31, Varian Medical Systems, Palo Alto, CA) for delivery on TrueBeam (Varian Medical Systems). The dose calculation algorithm used was the anisotropic analytical algorithm with a dose calculation grid of 2.0 mm. All RapidArc treatment plans were created with 2 full arcs for 6 MV photons. The maximal dose rates were set to 600 MU/min for FF-VMAT and 1400 MU/min for FFF-VMAT. The collimator angle was typically set to 45° to avoid tongue-and-groove effects.

Tomotherapy planning

The treatment plans were optimized in a Planning Station (version 5.0.1 or higher, Accuray Inc., Sunnyvale, CA) using a collapsed cone convolution dose calculation algorithm with a 2.0 mm calculation grid resolution. The HT plan parameters consisted of a 2.5 cm field width, 0.287 pitch (ratio of the distance travelled by the treatment couch per rotation to the fan beam thickness), and 1.8-2.5 modulation factor (maximum leaf intensity divided by average leaf intensity). The nominal dose rate at the isocenter was approximately 850 cGy/min.

Evaluation tools

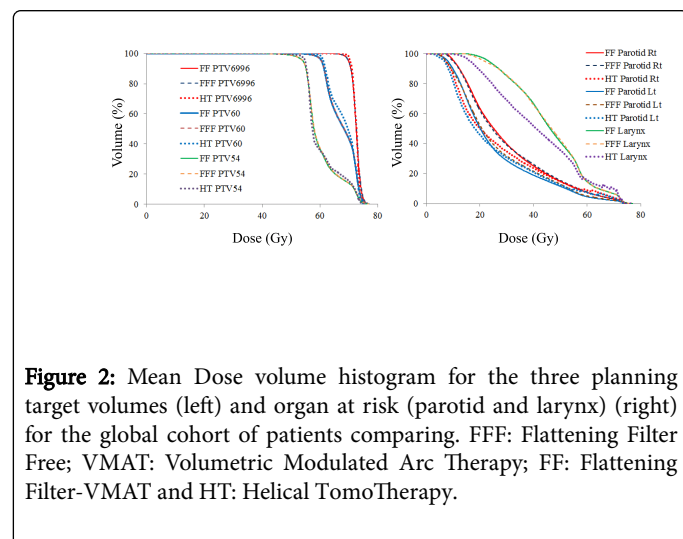
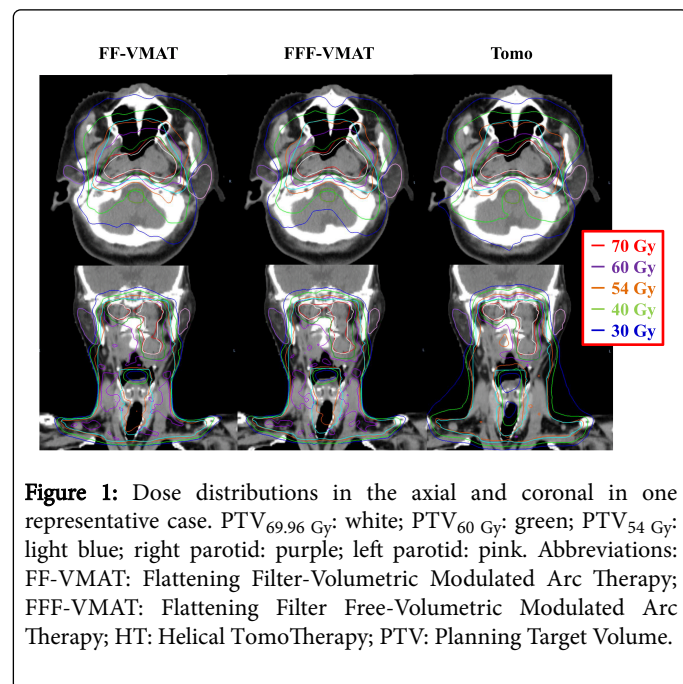
Quantitative evaluation and comparison of the plans were performed based on cumulative dose-volume histograms (DVHs). For the PTV, the homogeneity index (HI) and conformity index (CI) were used as comparison metrics between FFF-VMAT, FF-VMAT, and HT plans. HI was defined as $(D_{2\%} - D_{98\%}) / D_{50\%}$, where $D_{2\%}$, $D_{98\%}$ and $D_{50\%}$ indicate the doses received by 2%, 98%, and 50% of the volume, respectively [12]. CI was calculated as V_{pi} / PTV , where V_{pi} and PTV represent the volume receiving a dose equal to or greater than the prescribed dose and PTV volume, respectively [13]. In the evaluation of the OAR dose, the maximum point doses to the spinal cord and brain stem were determined, and the mean doses to the parotid gland, larynx, and body were recorded. Moreover, we calculated the integral body dose [14]. Finally, the number of MUs and the beam-on time (BOT) were evaluated for comparisons of the delivery efficiency.

Statistical analysis

Comparison between pairs of groups was performed using the non-parametric Mann-Whitney U test due to the small sample number [15]. A p-value of <0.05 was considered to indicate statistical significance.

Results

The typical dose distributions obtained using FFF-VMAT, FF-VMAT, and HT are presented in Figure 1. Figure 2 shows the average cumulative DVHs (10-patient average) for the PTV and OARs. Table 2 summarizes the results of the statistical analyses for the difference in the PTV, OARs, and delivery efficiency between the three techniques.



	FF-VMAT Average (SD)	FFF-VMAT Average (SD)	HT Average (SD)
Global max (Gy)	76.9 (1.4)	76.7 (1.1)	74.4 (0.8)*
PTV6996 D _{2%} (Gy)	75.0 (0.9)	75.1 (0.9)	73.6 (0.9)*
PTV6996 D _{98%} (Gy)	68.8 (0.2)	68.8 (0.3)	69.9 (0.1)*
Conformity index	1.036	1.046	1.167*
Homogeneity index	0.084	0.086	0.051*

Brain stem max (Gy)	42.4 (9.2)	42.3 (9.1)	38.7 (9.6)
Cord max (Gy)	41.9 (1.2)	42.2 (1.2)	38.4 (2.3)*
Rt parotid mean (Gy)	26.7 (6.9)	26.6 (7.1)	24.4 (6.4)
Lt parotid mean (Gy)	27.6 (13.3)	27.8 (13.5)	27.3 (15.5)
Larynx mean (Gy)	44.6 (11.3)	44.6 (11.4)	42.2 (11.6)
Body mean (Gy)	13.8	13.6	15.2
Integral body dose (Joules)	160.6 (35.7)	158.1 (34.7)	172.4 (38.0)
Treatment time (sec)	120	120	290.5*
MU	621	726.3	4053.7*

Table 2: Results of the analysis of the difference in the dosimetric parameters in the planning target volume and organs at risk and delivery efficiency among the three techniques. Asterisks indicate statistical significance (FFF-VMAT vs. HT ($p < 0.05$)). Numbers in parentheses represent one standard deviation. Abbreviations: FF-VMAT: Flattening Filter-Volumetric Modulated Arc Therapy; FFF-VMAT: Flattening Filter Free-Volumetric Modulated Arc Therapy; HT: Helical Tomotherapy.

PTV coverage

For dose homogeneity, FFF-VMAT showed statistically inferior results compared with HT ($p < 0.05$). However, significant improvement in the target conformity was observed for FFF-VMAT compared with HT ($p < 0.05$). The dose homogeneity and target conformity were similar for FFF-VMAT and FF-VMAT.

Sparing constrained OARs

For the spinal cord maximum dose, HT resulted in a significantly lower dose than FFF-VMAT and FF-VMAT ($p < 0.05$), with the dose constraint met in all cases. The HT plans tended to be slightly better in terms of the mean parotid and larynx dose sparing. However, the difference in these parameters between HT and FFF-VMAT were not significant. In terms of the mean body dose and the integral body dose, there was no significant difference between FFF-VMAT and FF-VMAT, and although the mean body dose and the integral body dose of the HT plan tended to be higher than those of FFF-VMAT and FF-VMAT, it was not statistically significant.

Delivery parameters

As compared with FF-VMAT, the number of MUs for FFF-VMAT significantly increased by 17.1% ($p < 0.05$). The number of MUs for HT was 5.46 times higher compared to that for FFF-VMAT ($p < 0.05$). The delivery time for FFF-VMAT was equal to that for FF-VMAT, and FFF-VMAT resulted in a 57.6% reduction in the BOT compared to HT ($p < 0.05$).

Discussion

In recent years, there has been an increasing interest in conventional c-arm linear accelerators using FFF beams. The benefits of FFF beams include reduced head scatter, head leakage, and residual electron contamination [1].

Furthermore, many researchers have shown that FFF-VMAT might allow OAR dose reduction without sacrificing target dose coverage in comparison with FF-VMAT [8-10]. However, all of these previous reports focused only on the comparison between FFF and FF beams obtained from conventional c-arm linear accelerators, and the present study is the first report regarding the dosimetric comparison of FFF-VMAT relative to FF-VMAT and HT, which is already widely used in clinical practice for head and neck cancer. When new radiation therapy delivery techniques are applied, they should be assessed by comparing them to clinically widespread technologies. Herein, we demonstrated that FFF-VMAT for head and neck cancer resulted in equivalent plan quality compared with FF-VMAT and HT. Zhuang et al. reported that FFF-VMAT for nasopharynx cancer showed inferior conformity and heterogeneity for PTVs in comparison with FF-VMAT [16]. Moreover, the dose sparing of OARs (parotid, brain stem, etc.) with FFF-VMAT were poorer than those of FF-VMAT. The authors speculated that the reason for this phenomenon might be due to the use of rather large field sizes and complex target volumes. However, our data showed that FFF-VMAT achieved comparable plan quality to that of FF-VMAT. The homogeneity and conformity for PTVs were similar between the FF-VMAT and FFF-VMAT plans. In terms of the OARs (cord brain stem, parotid, and larynx) sparing, no significant differences were observed between FF-VMAT and FFF-VMAT in this study. This phenomenon may be related to the different settings of the objective parameters of the target and OARs. We found that the maximum dose of the spinal cord in HT was significantly lower than that in FFF-VMAT, which is consistent with the previously published reports [17,18]. Meanwhile, in contrary to our results, other researchers have shown that the maximum cord dose for HT is either equal to or higher than the FF-VMAT data [19,20]. Moreover, Lu et al. reported that FF-VMAT provided better parotid sparing in comparison with HT while our study showed HT plans tended to be slightly better [20]. The reason for this discrepancy is likely because it is not possible to determine precisely the same planning objectives as a result of using different optimization algorithms of the different planning systems.

FFF beams contribute to time-efficient treatment delivery because of a higher dose rate. However, our data demonstrated that FFF-VMAT shows no advantage in terms of the treatment delivery efficiency compared to FF-VMAT. Although using a larger dose per fraction increases the benefit of reduction in the delivery time, the benefit of a standard fractionation dose with 2 Gy is not significant [2]. The reason for this observation is that the VMAT BOT is governed mostly by the gantry rotation speed and not the dose rate.

FF-VMAT and FFF-VMAT resulted in significantly faster treatment delivery compared HT. Faster treatment delivery using VMAT may lead to reductions in the risk of intrafractional motion. There are several reports for a wide variety of disease sites regarding the treatment delivery time of VMAT in comparison with HT, demonstrating that the BOT for VMAT is significantly shorter than that for HT [18].

Of note, the MUs for FFF-VMAT were always higher than those for the FF-VMAT, owing to following reasons: 1) the lateral dose profiles of FFF beams show a significant difference from those of FF beams; 2) the intensity of FFF beams decreases with increasing off-axis distance; and 3) larger field sizes for FFF beams correspond to higher peaks. Although our data showed that FFF-VMAT required a higher number of MUs in comparison with FF-VMAT, the mean body dose for FFF-VMAT was equivalent to that for FF-VMAT, which is consistent with

previously published results [10]. A possible explanation for these findings is that FFF beams provide a lower head scatter and electron contamination compared to FF beams.

Moreover, HT exhibited a higher mean body dose compared to FFF-VMAT and FF-VMAT, although this was not statistically significant. Several studies have reported that the normal tissue integral dose for HT is significantly higher than that for VMAT [21,22]. In recent years, HT has offered a dynamic jaw delivery mode that reduces longitudinal dose spreading in addition to a conventional static jaw delivery mode, and Sterzing et al. reported that the dynamic jaw mode resulted in reduction of the mean integral dose compared to the conventional static jaw mode [23].

There are several potential limitations of our study. One issue is that our study was performed in a relatively small number of patients, and thus, further rigorous large-scale studies are warranted. Moreover, as mentioned above, it is difficult to determine precisely the equivalent constraint parameter settings due to the usage of different treatment planning systems and optimization algorithms for a planning comparison study [14]. However, this dosimetric comparison might bring several insights of the differences of each method, despite these limitations.

Conclusions

This is the first report of FFF-VMAT achieving equivalent plan quality to that of FF-VMAT and HT while saving treatment time in head and neck cancer. Although some significant differences in the dosimetric parameters were observed, they remained small and probably have no, or very limited, clinical impact. Our results indicate that FFF-VMAT for head and neck cancer is an efficient and feasible strategy for clinical practice.

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References

1. Georg D, Knoos T, McClean B (2011) Current status and future perspective of flattening filter free photon beams. *Med Phys* 38: 1280-1293.
2. Lang S, Shrestha B, Graydon S, Cavelaars F, Linsenmeier C, et al. (2013) Clinical application of flattening filter free beams for extracranial stereotactic radiotherapy. *Radiother Oncol* 106: 255-259.
3. Fenwick JD, Tomé WA, Soisson ET, Mehta MP, Rock Mackie T (2006) Tomotherapy and other innovative IMRT delivery systems. *Semin Radiat Oncol* 16: 199-208.
4. Corvo R, Zeverino M, Vagge S, Agostinelli S, Barra S, et al. (2011) Helical tomotherapy targeting total bone marrow after total body irradiation for patients with relapsed acute leukemia undergoing an allogeneic stem cell transplant. *Radiother Oncol* 98: 382-386.
5. Peñagaricano JA, Papanikolaou N, Yan Y, Youssef E, Ratanatharathorn V (2005) Feasibility of cranio-spinal axis radiation with the Hi-Art tomotherapy system. *Radiother Oncol* 76: 72-78.
6. Otto K (2008) Volumetric modulated arc therapy: IMRT in a single gantry arc. *Med Phys* 35: 310-317.
7. Matuszak MM, Yan D, Grills I, Martinez A (2010) Clinical applications of volumetric modulated arc therapy. *Int J Radiat Oncol Biol Phys* 77: 608-616.
8. Reggiori G, Mancosu P, Castiglioni S, Alongi F, Pellegrini C, et al. (2012) Can volumetric modulated arc therapy with flattening filter free beams

- play a role in stereotactic body radiotherapy for liver lesions? A volume-based analysis. *Med Phys* 39: 1112-1118.
9. Nicolini G, Ghosh-Laskar S, Shrivastava SK, Banerjee S, Chaudhary S, et al. (2012) Volumetric modulation arc radiotherapy with flattening filter-free beams compared with static gantry IMRT and 3D conformal radiotherapy for advanced esophageal cancer: a feasibility study. *Int J Radiat Oncol Biol Phys* 84: 553-560.
10. Zwahlen DR, Lang S, Hrbacek J, Glanzmann C, Kloeck S, et al. (2012) The use of photon beams of a flattening filter-free linear accelerator for hypofractionated volumetric modulated arc therapy in localized prostate cancer. *Int J Radiat Oncol Biol Phys* 83: 1655-1660.
11. Lee N, Harris J, Garden AS, Straube W, Glisson B, et al. (2009) Intensity-modulated radiation therapy with or without chemotherapy for nasopharyngeal carcinoma: radiation therapy oncology group phase II trial 0225. *J Clin Oncol* 27: 3684-3690.
12. [No authors listed] (2010) Prescribing, Recording, and Reporting Photon-Beam Intensity-Modulated Radiation Therapy (IMRT): Contents. *J ICRU* 10: NP.
13. Feuvret L, Noel G, Mazon JJ, Bey P (2006) Conformity index: a review. *Int J Radiat Oncol Biol Phys* 64: 333-342.
14. Cozzi L, Dinshaw KA, Shrivastava SK, Mahantshetty U, Engineer R, et al. (2008) A treatment planning study comparing volumetric arc modulation with RapidArc and fixed field IMRT for cervix uteri radiotherapy. *Radiother Oncol* 89: 180-191.
15. Mann HB, Whitney DR (1947) On a test of whether one of two random variables is stochastically larger than the other. *Ann Math Statist* 18: 50-60.
16. Zhuang M, Zhang T, Chen Z, Lin Z, Li D, et al. (2013) Advanced nasopharyngeal carcinoma radiotherapy with volumetric modulated arcs and the potential role of flattening filter-free beams. *Radiat Oncol* 8: 120.
17. Jacob V, Bayer W, Astner ST, Busch R, Kneschaurek P (2010) A planning comparison of dynamic IMRT for different collimator leaf thicknesses with helical tomotherapy and RapidArc for prostate and head and neck tumors. *Strahlenther Onkol* 186: 502-510.
18. Rong Y, Tang G, Welsh JS, Mohiuddin MM, Paliwal B, et al. (2011) Helical tomotherapy versus single-arc intensity-modulated arc therapy: a collaborative dosimetric comparison between two institutions. *Int J Radiat Oncol Biol Phys* 81: 284-296.
19. Clemente S, Wu B, Sanguineti G, Fusco V, Ricchetti F, et al. (2011) SmartArc-based volumetric modulated arc therapy for oropharyngeal cancer: a dosimetric comparison with both intensity-modulated radiation therapy and helical tomotherapy. *Int J Radiat Oncol Biol Phys* 80: 1248-1255.
20. Lu SH, Cheng JC, Kuo SH, Lee JJ, Chen LH, et al. (2012) Volumetric modulated arc therapy for nasopharyngeal carcinoma: a dosimetric comparison with TomoTherapy and step-and-shoot IMRT. *Radiother Oncol* 104: 324-330.
21. Khalifa J, Vieilleuvigne L, Boyrie S, Ouali M, Filleron T, et al. (2014) Dosimetric comparison between helical tomotherapy and volumetric modulated arc-therapy for non-anaplastic thyroid cancer treatment. *Radiat Oncol* 9: 247.
22. Pasquier D, Cavillon F, Lacornerie T, Touzeau C, Tresch E, et al. (2013) A dosimetric comparison of tomotherapy and volumetric modulated arc therapy in the treatment of high-risk prostate cancer with pelvic nodal radiation therapy. *Int J Radiat Oncol Biol Phys* 85: 549-554.
23. Sterzing F, Uhl M, Hauswald H, Schubert K, Sroka-Perez G, et al. (2010) Dynamic jaws and dynamic couch in helical tomotherapy. *Int J Radiat Oncol Biol Phys* 76: 1266-1273.