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MR-guided stereotactic radiation therapy for head and neck cancers

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ABSTRACT

Purpose: MR-guided radiotherapy (MRgRT) has the advantage of utilizing high soft tissue contrast imaging to track daily changes in target and critical organs throughout the entire radiation treatment course. Head and neck (HN) stereotactic body radiation therapy (SBRT) has been increasingly used to treat localized lesions within a shorter timeframe. The purpose of this study is to examine the dosimetric difference between the step-and-shot intensity modulated radiation therapy (IMRT) plans on Elekta Unity and our clinical volumetric modulated arc therapy (VMAT) plans on Varian TrueBeam for HN SBRT.

Method: Fourteen patients treated on TrueBeam sTx with VMAT treatment plans were re-planned in the Monaco treatment planning system for Elekta Unity MR-Linac (MRL). The plan qualities, including target coverage, conformity, homogeneity, nearby critical organ doses, gradient index and low dose bath volume, were compared between VMAT and Monaco IMRT plans. Additionally, we evaluated the Unity adaptive plans of adapt-to-position (ATP) and adapt-to-shape (ATS) workflows using simulated setup errors for five patients and assessed the outcomes of our treated patients.

Results: Monaco IMRT plans achieved comparable results to VMAT plans in terms of target coverage, uniformity and homogeneity, with slightly higher target maximum and mean doses. The critical organ doses in Monaco IMRT plans all met clinical goals; however, the mean doses and low dose bath volumes were higher than in VMAT plans. The adaptive plans demonstrated that the ATP workflow may result in degraded target coverage and OAR doses for HN SBRT, while the ATS workflow can maintain the plan quality.

Conclusion: The use of Monaco treatment planning and online adaptation can achieve dosimetric results comparable to VMAT plans, with the additional benefits of real-time tracking of target volume and nearby critical structures. This offers the potential to treat aggressive and variable tumors in HN SBRT and improve local control and treatment toxicity.

Introduction

Despite the advancements in head and neck (HN) cancer treatment, approximately 15–50 % of patients will experience locoregional failure [1,2]. Reirradiation is a potential curative option for these patients. While conventional techniques such as 2D or 3D-conformal radiotherapy offer clinical benefits over systemic therapy alone, they are often linked to a high risk of toxicity [3]. With the advent of modern radiotherapy techniques, data indicates that locoregional control rates have increased from 20 % to 60 % with conventional 2D and 3D techniques to 50 %-60 % with intensity modulated radiation therapy (IMRT) [4–6].

Stereotactic body radiation therapy (SBRT) is one of the most recent and advanced image-guided radiation techniques that delivers ablative doses with exceptional conformity, typically administered in three to five fractions. In comparison to standard HN fractionation courses of 6 to 7 weeks, SBRT offers a unique opportunity for reirradiation of HN cancer within less than 2 weeks with encouraging results [7,8].

The foundations of delivering safe and top-tier treatment in HN SBRT reside in precise target and normal tissue delineation and high-gradient

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conformal dose deposition during treatment. Currently, cone beam computed tomography (CBCT) has become the standard for image guidance in HN SBRT. However, the relatively low soft tissue contrast and sometimes less distinct visualization of the treatment volume on CBCT can pose a challenge for radiation oncologist to distinguish between the tumor and nearby critical organs. The demand for diagnostic-grade imaging during treatment becomes imperative.

Recent cutting-edge technology in the integration of MRI with a linear accelerator (MRL) have empowered the MR-guided radiotherapy (MRgRT) [9–11]. The MR-Linac system facilitates concurrent MR imaging and radiation delivery, thereby enhancing the visualization of soft tissues during treatment and enabling the real-time motion monitoring [12,13]. Furthermore, the MRL system also allows for online treatment plan adaptation to accommodate the variability of patient anatomy over the treatment course [9]. Several studies have reported the utilization of online plan adaptation with a 1.5 Tesla MRL system for varied treatment sites [14–16]. However, as of now, there have been no reports on utilization of MRgRT for HN SBRT.

In this study, we conducted a dosimetric comparison between Monaco (Elekta, Stockholm, Sweden) IMRT treatment plans for Elekta Unity MRL and RayStation (RaySearch Laboratories, Stockholm, Sweden) volumetric modulated arc therapy (VMAT) plans for Varian TrueBeam sTx (Varian Oncology System, Palo Alto, CA), which represents our current practice. Additionally, we evaluated the adaptive planning process using simulated setup errors, and presented the outcomes of our treated HN SBRT patients.

Method

Reference plan comparison

We randomly selected 14 patients who were reirradiated (between years 2014 to 2020) with HN SBRT on one of several head and neck prospective trials at our institution (institutional review board approved). These included patients with small unresectable disease (<60 cc tumor volume) treated on our phase II randomized stereotactic onco-ablative reirradiation trial (SOAR; 2016–1065), those who received postoperative SBRT reirradiation after surgical salvage for recurrent disease on our prospective head and neck reirradiation registry (PA14-1098) in which larger target volumes are allowed, and those receiving non-reirradiation SBRT for benign tumors (PA14-0194) or enrolled on our phase 2 trial utilizing SBRT for laryngeal cancer (2016–1023). Because the planning metrics and critical avoidance structures differ significantly among skull base, mucosal and neck subsites, we selected patients from these 3 major reirradiation subsites (6 skull base patients, 3 mucosal patients, and 5 neck patients) [8].

These patients were treated on TrueBeam sTx with VMAT treatment plans generated in RayStation. The prescription doses ranged from 27 to 45 Gy in 3–5 fractions (8–9 Gy per fraction), treated every other day. The primary planning target volumes (PTVs) varied from 1.4 cm^3 to 180.8 cm^3, while the total PTVs, including primary PTV and lower dose level target volumes for each patient, ranged from 12.0 cm^3 to 362.8 cm^3. One neck patient had a larger primary PTV of 180.8 cm^3, while the primary PTVs for other patients were all within 50 cm^3. All patients also had subclinical risk target volumes contoured around the primary PTVs to receive lower doses to cover sites of high subclinical risks.

TrueBeam sTx is equipped with a 2.5 mm multileaf collimator (MLC) and beams are configured with a 100 cm source-axis distance (SAD). Clinical VMAT plans consist of 2 to 4 arcs using 6 MV photon energy. The number of arcs depends on the complexity of the plan. For skull base plans, which are typically more challenging to spare critical organs, 3 to 4 arcs are commonly utilized, incorporating non-coplanar arcs with couch kick as well as various MLC angles.

The SBRT plans were re-planned using the Monaco treatment planning system (TPS) for Elekta Unity MRL to achieve comparable PTV coverages and adhere to organ-at-risk (OAR) constraints in VMAT plans. The general clinical goals for 3 and 5 fraction reirradiation and non-reirradiation treatment plans are outlined in Table 1. The reirradiation tolerance for spinal cord was based on time-dependent recovery [17]. Elekta Unity comprises a 1.5 T MR imaging system and a 7 MV beam Linac, featuring a 7.2 mm MLC and a 143.5 cm SAD. It's important to note that only sagittal traveling MLCs are available for IMRT planning. The Monaco IMRT (rIMRT) plans utilize 12–15 beams evenly distributed around the patients.

VMAT and rIMRT plans are compared using the following dosimetric metrics: primary PTV coverage, PTV mean and maximum dose, Paddick conformity index (PCI)[18], target homogeneity index (HI), gradient index (GI), and the patient body volume receiving 20 % of prescribed dose (V20%). HI is defined as a ratio of D2% to D98%, and GI is defined as the ratio of V50% to V100%, where D2% and D98% represent the dose levels received by 2 % and 98 % of the target volume, and V50% and V100% represent the volumes enclosed by the 50 % and 100 % isodose lines, respectively.

The PCI value is typically to or less than 1, and a value close to 1 indicates higher conformality. The HI value is generally higher than 1, and a value close to 1 signifies greater uniformity. Similarly, a GI value is typically greater than 1, with a smaller value indicates a quicker dose fall-off.

The paired sample *t*-test will be employed to compare the metrics of rIMRT and VMAT plans, with a significance level set at 0.05 for the p-value.

Adaptive plan evaluation

Elekta Unity limits couch motion only in the superior-inferior direction. Any detected shift through registration will need an adaptive plan to be generated for a new isocenter on patient anatomy. There are two types of adaptation techniques exist on Unity: 'adapt-to-position' (ATP) and 'adapt-to-shape' (ATS). The ATP workflow enables plan adaptation based on the online patient position. In this workflow, the online MRI image is rigidly registered to the reference plan image. Subsequently, the isocenter position on the reference image is updated. The pre-treatment plan is then recalculated or reoptimized to replicate or improve the target coverage from the reference. Since the recalculation or re-optimization occurs on the reference image and contours, no contour adjustments can be made, and no optimization objectives can be modified.

The second workflow, ATS, enables plan adaptation based on the daily patient anatomy, with optimization performed on the daily MRI. Following the registration, the contours from the reference image are automatically propagated onto the daily online MRI using deformable image registration. If needed, these contours can be edited by a radiation oncologist. Unlike the ATP re-plan, which uses an optimizer based on a warm-start optimization, the ATS re-plan is a full treatment re-plan with new IMRT segments and is based on the daily MR images and corresponding contours. During the planning process, the optimization objectives can also be fine-tuned to improve the plan.

In this study, we assess the dosimetry of both ATP and ATS plans using simulated positioning errors for 5 patients (3 mucosal patients and 2 skull base patients). The original reference plans were generated on simulation CT images. Same-day simulation MR images were available for these patients and were utilized to simulate the daily online MRIs. The planning contours and the IMRT plan from the simulation CT were replicated onto the simulation MR. This MR and the corresponding optimized plan will serve as the reference image and reference plan (rIMRT) to evaluate the adaptive planning process.

To simulate the daily setup uncertainties, the simulation MRIs were then mathematically shifted by +2 mm and +4 mm in the lateral and vertical directions to simulate and test the online ATP and ATS planning workflow. While ATP plans were optimized using the reference image with isocenter updated based on detected shifts through registration, we also evaluated the recalculated ATP (ATPcalc) plans which were

Table 1
Clinical goals and dose constraints for head and neck SBRT plans.

Structures	Clinical goals/Dose constraints			
PTVs	V100% > 95 % Dmax < 120 % (skull base) Dmax < 110 % (mucosal, neck)			
OARs	No hot spot if in target, as low as reasonably achievable if outside of or away from target			
	Reirradiation 27 Gy/3 fractions	Reirradiation 45 Gy/5 fractions	Non-Reirradiation 27 Gy/3 fractions	Non-reirradiation 45 Gy/5 fractions
Brainstem	Dmax < 10 Gy	Dmax < 13 Gy	Dmax < 21 Gy V15 Gy < 0.5 cm^3	Dmax < 23 Gy V21Gy < 0.5 cm^3
Spinal cord	Dmax < 9 Gy	Dmax < 12 Gy	Dmax < 18 Gy V17 Gy < 0.3 cm^3	Dmax < 21 Gy V20Gy < 0.3 cm^3
Optic apparatus	Dmax < 9 Gy	Dmax < 12 Gy	Dmax < 17 Gy	Dmax < 18 Gy
Carotids	Dmax < 20 Gy	Dmax < 30 Gy	Avoid hot spot if in target V20 Gy < 0.1 cm^3 for target > 0.5 cm away	V30Gy < 0.1 cm^3
Cochlea	Dmax < 21 Gy	Dmax < 21 Gy	Dmax < 18 Gy	Dmax < 23 Gy,
Mandible	V12Gy < 3 cm^3	V20Gy < 3 cm^3		V20Gy < 3 cm^3
Temporal Lobe	Dmax < 18 Gy V12Gy < 3 cm^3	Dmax < 27 Gy V18Gy < 3 cm^3	Dmax < 23 Gy V15 < 3 cm^3	Dmax < 27 Gy V18Gy < 3 cm^3

Abbreviations: SBRT, stereotactic body radiation therapy; PTV, planning target volume; OAR, organ at risk; V100, volume receiving 100 % of prescription dose; VxGy, volume receiving x Gy; Dmax, maximum dose;

obtained by calculating ATP plans on the corresponding +2 mm or +4 mm shifted MR images with deformed contours. These ATPcalc plans were believed to be more representative of the delivered plan. The quality of the daily adaptive plans was evaluated in terms of target coverage and dose to OARs.

Clinical treatment workflow

We used the ATS workflow for treating our HN SBRT patients. The outline of the workflow is summarized as follows:

Reference Plan rIMRT generation:

1. Contouring and plan optimization on simulation CT in Monaco
2. Plan and contours are copied to simulation MR; objectives adjusted to finalize the rIMRT

Treatment:

3. Daily MRI scan on treatment day
4. Registration of reference image and daily MRI
5. Contours transferred from reference plan to daily MRI using deformable image registration
6. Online evaluation of contours by radiation oncology and physicist
7. ATS planning including objective adjustment and optimization based on daily contours
8. Daily adaptive Plan approval by radiation oncologist
9. Secondary dosimetry calculation
10. Approved plan sent to treatment console

To date, we have treated four patients on Unity. The selection of these patients was based on anatomical deviations observed in the target area between the simulation CT and simulation MRI. Attending radiation oncologists were present at the treatment console to verify and edit contours, and review the final adaptive plans. Physicists were also present to deform contours, generate ATS plans, perform secondary calculations, and ensure the smooth delivery of all planned fields.

Outcomes data for these patients were collected. Treatment-related toxicities were coded based on the Common Terminology Criteria for Adverse Events (CTCAE, version 5.0).

Results

Reference plan comparison

Fig. 1 presents the comparison of VMAT plans and rIMRT plans for all 14 patients. The rIMRT plans were normalized to achieve equivalent PTV coverage, while all clinical goals for OARs were met. In Fig. 1(a), the PTV metrics, GI and V20% are depicted as ratios between rIMRT and VMAT plans for uniform presentation. PTV coverage, PCI and HI demonstrate comparability between the two planning techniques, although PTV mean and maximum doses were typically higher in rIMRT plans with a p-value < 0.05. While the GI is approximately 10 % higher in rIMRT plans, this difference lacks significance. The higher GI suggests more dose spreading to nearby normal tissue. The low dose bath index, V20%, indicates that the 20 % Rx dose isodose line encompasses approximately 42 % more volume in rIMRT plans (Fig. 1a). The p-values for the paired comparison are displayed beneath the plot.

Because skull base plans are more challenging due to critical OARs with strict tolerance, we divided patients into two groups: skull base ($n = 6$) and mucosal/neck ($n = 8$). Dosimetric metrics were compared between VMAT and rIMRT plans for these two groups separately. While the PTV maximum doses were higher in rIMRT plans for both groups, it was statistically significant only for the musosal/neck group (p-value = 0.001). GI was approximately 16 % increase in rIMRT plans for the mucosal/neck group, compared to only 3 % increase for the skull base group, both not significant. Additionally, no impact of target volume on dosimetric metrics was observed.

In Fig. 1(b), the difference in OAR doses between rIMRT plans and VMAT plans is depicted. The results for carotid and temporal lobe pertain to ipsilateral structures. It's evident that in rIMRT plans, the maximum doses to critical organs were adjusted to align with clinical goals, rendering them comparable to VMAT plans. However, the mean doses of these OARs typically exhibited higher values in rIMRT plans.

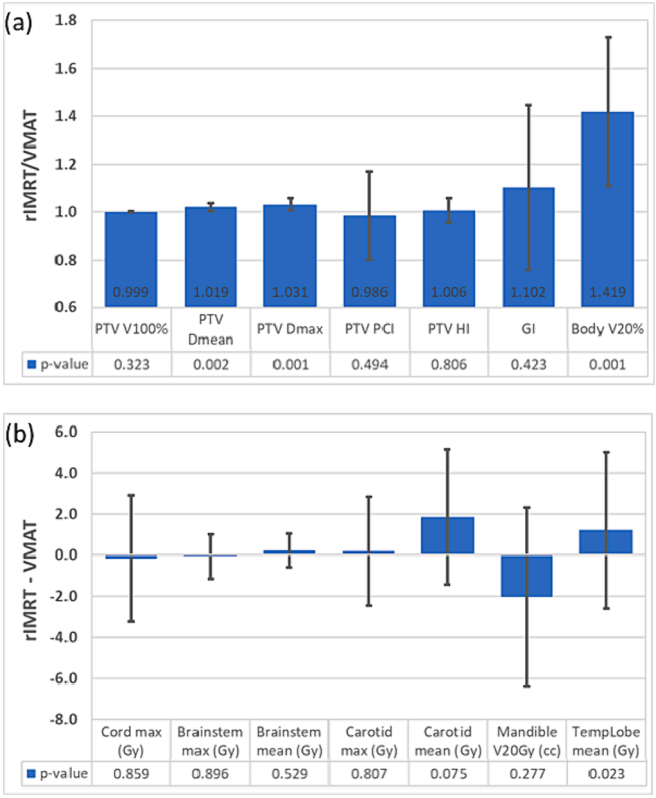

Fig. 1. Comparison between Monaco reference rIMRT plans and RayStation VMAT plans for 14 head and neck SBRT patients. (a) ratio of rIMRT plans to VMAT plans for PTV metrics, GI and body V20%; (b) difference of rIMRT plans from VMAT plans for OARs. Abbreviations: SBRT, stereotactic body radiation therapy; PTV, planning target volume; VMAT, volumetric modulated arc therapy; PCI, paddick conformity index; HI, homogeneity index; GI, gradient index.

Notably, the higher mean dose to the ipsilateral temporal lobe displayed statistical significance.

Adaptive plan evaluation

For the simulated +2 mm and +4 mm image shifts, we observed a mean registration error of 0.3 mm in Monaco (range: 0.0–0.7 mm). As illustrated in Fig. 2, we conducted a comparison among ATP plans, ATS plans and re-calculated ATP plans (ATPcalc) against the reference plan rIMRT.

The PTV coverage in ATP plans were generally comparable to those in reference plans, except for one skull base patient who experienced a 6 % PTV coverage decrease (from 98 % PTV coverage to 92 %) in the ver2mm plan in order to meet OAR dose constraints. However, 50 % of the ATPcalc plans showed that the PTV coverage were >2 % lower compared to the reference plans, with a maximum difference of 6.4 % occurred for a skull base patient. In contrast, the PTV coverage in ATS plans consistently matched the reference plans. The PTV maximum dose and body V50% in ATP plans were generally higher than those in the reference plans, and these might become worsened in ATPcalc plans. ATS plans, on the other hand, successfully addressed and improved these metrics.

The maximum doses to cord, brainstem and carotid also exhibited higher values compared to those in the reference plans, although they remained within tolerance limits. As anticipated, the ATS workflow offered the opportunity to reoptimize the plan, resulting in achieving lower or comparable dose for these structures.

The ATP plans generally required 3–5 min for optimization, whereas ATS plans, including contour deformation and editing and plan optimization, took an average of 15–20 min. In cases involving larger target volumes requiring editing, and/or adjustment to planning, an additional 10–20 min could be expected.

Outcome of clinical patients

The information of the four patients treated on Unity and their treatment outcomes were shown in Table 2. While all OAR doses were within tolerance, the PTV coverages in daily adaptive plans were 97.1 % ± 2.3 % comparing to 97.6 % ± 2.2 % in reference plans. The treatment time was between 40 and 60 min.

With the exception of Patient 3 who experienced recurrent disease and passed away due to widespread progression, the other three patients are still alive at the time of our study presentation. Patients 1 and 2, treated in 2020, have not exhibited any chronic toxicities thus far. Patient 4, treated in 2022, developed grade 1 osteoradionecrosis at 9 months post SBRT. Notably, the SBRT treatment area for this patient had been partially treated by prior radiation up to 30 Gy.

Discussion

The MR Linac provides the benefit of real-time imaging and adaptive planning with superior soft tissue visualization. This exceptional image quality assists oncologists in precisely delineating the tumor target and OARs, ultimately resulting in accurate radiation delivery. Combined with the adaptive planning, this technique holds the potential to treat patients with reduced PTV margins, and to offer the opportunity for optimal planning adjustments on a daily basis.

In comparison to modern Linac, the limitations of Elekta Unity MRL planning include coplanar IMRT with a restricted 90-degree collimator angle and 7.2 mm leaf width at 143.5 cm SAD. Conversely, our clinical HN SBRT cases are planned on TrueBeam STx, which allows non-coplanar volumetric arc therapy and 2.5 mm minimum leaf width. When comparing VMAT plans and Monaco IMRT plans, both achieved the clinical goals for target and OARs doses. However, Monaco IMRT plans exhibit a higher spread of doses to normal tissue, resulting in a higher gradient index, a higher low dose bath volume, and a higher integral dose. Additionally, achieving comparable results for the PTV mean and maximum doses in Monaco IMRT plans proved challenging compared to VMAT plans due to the same machine limitations. An evident example is the strict control of PTV maximum dose in VMAT plans for mucosal cases in our practice, aimed at reducing toxicity, which is challenging to attain in Monaco IMRT plans. Clinicians must carefully balance these drawbacks, on a case-by-case basis, against the advantages of improved treatment accuracy provided by MRI soft tissue contrast and adaptive planning.

SBRT procedures often require patients to remain on the treatment table for a longer period due to the use of volumetric imaging to verify target alignment. While both simulation CT and MR images can serve as reference images for generating reference plan, we propose utilizing MR images for SBRT cases on MRL, and the simulation MR and treatment MR following same protocol or sequences. Opting for a MR image as a reference on the MRL offers multiple advantages. Not only does it reduce registration errors, it also augments the accuracy of contour deformation. This, in turn, minimizes contour editing time and consequently shortens the overall treatment duration.

The ATP workflow is generally more efficient than the ATS workflow as it necessitates less effort in contouring and plan optimization. However, due to the sharp dose gradient in HN SBRT, ATP may not be adequate to achieve the required plan quality in adaptive planning. Our study revealed that even test images without anatomical deformation can lead to up to a 6 % PTV coverage loss and an increase in OAR doses when ATP plans on reference image are re-calculated on simulated daily images with only shifts. The disparity is particularly noticeable in skull base cases. In SBRT procedures, where high ablative doses are administered daily, the ATS workflow is strongly recommended to ensure the

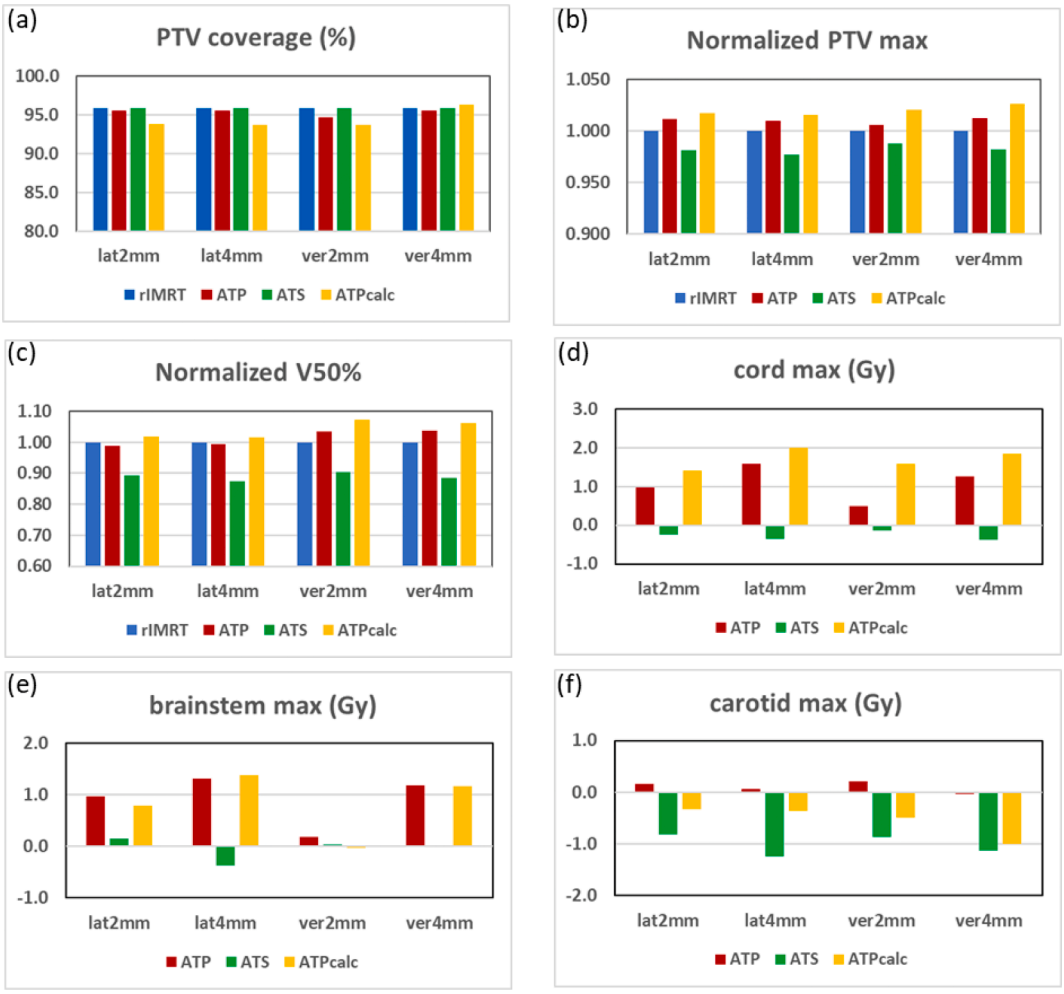

Fig. 2. Comparison of ATP, ATS and ATPcalc plans to rIMRT plan for simulated lateral 2 mm (lat2mm), 4 mm (lat4mm), and vertical 2 mm (ver2mm), 4 mm (ver4mm) shifts on PTV coverage (a), normalized PTV max (b) and normalized V50% (c). ATP, ATS and ATPcalc plans were normalized to corresponding rIMRT plans. The difference of Cord maximum (d), brainstem maximum (e), and carotid maximum (f) on ATP, ATS and ATPcalc plans from rIMRT plans were also shown for simulated shifts. Abbreviations: PTV, planning target volume; rIMRT, reference IMRT plan; ATP, adapt-to-position; ATS, adapt-to-shape; ATPcalc, recalculated ATP plan on shifted image.

delivery of high-quality plans whenever feasible.

This study primarily focuses on the dosimetry of the Monaco IMRT plans for Elekta Unity MRL, comparing them to RayStation VMAT plans, and assessing the quality of the Monaco adaptive plans. One main limitation of this study is the exclusion of the assessment of different dose calculation algorithms. Monaco employs a Monte Carlo (MC)-based dose calculation engine, known for its widely accepted accuracy, albeit with a longer calculation time. In contrast, the VMAT plans generated in RayStation for this study use a collapsed cone (CC)-based algorithm, which has been tested to achieve an accuracy within 3 % [19–21]. It is important to note that the accuracy of dose calculation in these TPSs depends on the precision of beam modeling during TPS commissioning. For SBRT planning, careful TPS commissioning is essential, especially when dealing with small fields [22].

Conclusion

We demonstrate that MRgRT, with high resolution soft tissue contrast imaging and real-time tracking, has the potential to improve the precision in treatment delivery upon existing linac-based HN SBRT platforms without a compromise in planning metrics or clinical goals. The use of Monaco treatment planning and online adaptation can achieve dosimetric results comparable to VMAT plans, with the additional benefits of real-time tracking of target volume and nearby critical structures. This offers the potential to treat aggressive and variable tumors in the HN region and improve local control and treatment toxicity. Further research involving a larger cohort of treated patients will provide a clearer understanding of the MRgRT technique for HN SBRT.

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Table 2
Head and neck patients receiving SBRT on Elekta Unity MR-Linac.

Patient	1	2	3	4
Age	50	48	67	63
Stage	Metastatic	Metastatic	Metastatic	Metastatic/ residual
Target	Left Neck	Left Neck	Left Neck	Right BOT
Histology	Salivary duct carcinoma	HPV- SCC	HPV- SCC	HPV + SCC
SBRT start	Sep 2020	Nov 2020	Feb 2021	Aug 2022
SBRT Rx Dose (Gy)	36/6fx	35/5fx	27/3fx	27/3fx
Primary.PTV volume (cm^3)	17.1	16.1	29.2	149.4
Prior RT	None	None	None	Partial
OS FU (months)	32	32	12, Death	12
LC FU (months)	20	32	5, Recurrent	11
Acute Toxicities	Grade 2 (pain)	None	None	Grade 1 (pain)
Chronic Toxicities	None	None	None	Grade 1 (ORN) at 9 months post SBRT

Abbreviations: OS, overall survival; FU, follow-up; LC, local control; RT, radiation treatment; HPV, human papillomavirus; SCC, squamous cell carcinoma; ORN, osteoradionecrosis; BOT, base of tongue; SBRT, stereotactic body radiation therapy; PTV, planning target volume; fx, fraction.

Therapy.

CRediT authorship contribution statement

He Wang: Conceptualization, Writing – original draft, Formal analysis, Methodology. **Jinzhong Yang:** Conceptualization, Writing – original draft, Formal analysis, Methodology. **Anna Lee:** Data curation, Writing – review & editing. **Jack Phan:** Writing – review & editing, Supervision. **Tze Yee Lim:** Data curation, Writing – review & editing. **Clifton D. Fuller:** Writing – review & editing, Supervision. **Eun Young Han:** Data curation, Writing – review & editing. **Dong Joo Rhee:** Data curation, Writing – review & editing. **Travis Salzillo:** Data curation, Writing – review & editing. **Yao Zhao:** Writing – review & editing, Supervision. **Nitish Chopra:** Data curation, Writing – review & editing. **Mary Pham:** Data curation, Writing – review & editing. **Pam Castillo:** Data curation, Writing – review & editing. **Angela Sobremonte:** Data curation, Writing – review & editing. **Amy C. Moreno:** Writing – review & editing, Supervision. **Jay P. Reddy:** Writing – review & editing, Supervision. **David Rosenthal:** Writing – review & editing, Supervision. **Adam S. Garden:** Writing – review & editing, Supervision. **Xin Wang:** Conceptualization, Writing – original draft, Formal analysis, Methodology.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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