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# Volumetric modulated arc therapy with robust optimization for larynx cancer

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ABSTRACT

*Purpose:* The aim of this study was to perform a comparison between robust optimization and planning target volume (PTV)-based optimization plans using volumetric modulated arc-therapy (VMAT) by evaluating perturbed doses induced by localization offsets for setup uncertainties in larynx cancer radiation therapy.
*Methods:* Ten patients with early-stage (T1-2N0) glottis carcinoma were selected. The clinical target volume (CTV), carotid arteries, and spinal cord were contoured by a radiation oncologist. PTV-based and robust optimization plans were normalized at $D_{50\%}$ to the PTV and $D_{98\%}$ to the CTV, respectively. Both optimization plans were evaluated using perturbed doses by specifying user defined shifted values from the isocenter. CTV dose ($D_{98\%}$, $D_{50\%}$, and $D_{2\%}$), homogeneity index (HI) and conformity index ($CI_{95\%}$, $CI_{80\%}$, and $CI_{50\%}$), as well as doses to the carotid arteries and spinal cord were compared between PTV-based and robust optimization plans.
*Results:* The robust optimization plans exhibited superior CTV coverage and a reduced dose to the carotid arteries compared to the PTV-based optimization plans ($p < 0.05$). HI, $CI_{95\%}$ and the dose to the spinal cord did not significantly differ between the PTV-based and robust optimization plans ($p > 0.05$). The robust optimization plans showed better $CI_{80\%}$ and $CI_{50\%}$ compared to the PTV-based optimization plans ($p < 0.05$). Plan perturbed evaluations showed that the robust optimization plan has small variations in the doses to the CTV, carotid arteries, and spinal cord compared to the PTV-based optimization plan.
*Conclusions:* The robust optimization plan may be a suitable treatment method in radiotherapy for larynx cancer patient.

## 1. Introduction

Conventional radiotherapy (CRT) delivered with opposed-lateral beams is a highly effective treatment for early-stage (T1-2N0) glottis carcinoma and achieves excellent rates of larynx preservation and cancer eradication. Long-term local control for patients with T1 and T2 tumors is achieved in approximately 90% and 75% of the population, respectively, and cancer-specific survival rates of more than 95% have been reported [1–3]. In the case of the treatment of larynx cancer using CRT, common carotid arteries receive radiation doses that are essentially equivalent to the prescription due to their close proximity to the target. Intensity-modulated radiotherapy (IMRT) and volumetric modulated arc therapy (VMAT) have been used by several research groups to reduce the dose to the carotid arteries [4–8]. VMAT can significantly decrease treatment times using a variable gantry speed, dose rate, and rapid dynamic multi-leaf collimator motion during treatment delivery of head and neck cancers. This approach has been shown to be advantageous in the treatment of larynx cancer patient.

Planning target volume (PTV)-based optimization plans have been widely used in radiation therapy to account for position uncertainties relative to the target volume during treatment delivery. To compensate for these variations, a larger PTV margin can be used to increase the probability of sufficient target coverage. However, there is a risk of irradiation of a larger volume of nearby organ-at-risk (OAR). Robust optimization plan is an alternative method that could replace the PTV margin-based plan. This plan directly uses the clinical target volume (CTV) as the primary target during the plan optimization. The robust optimization plan for intensity-modulated proton therapy (IMPT) is widely used for several treatment sites [9–11]. The photon robust optimization plan also facilitates significantly more robust dose distribution to targets and OARs than the PTV-based optimization plan [12–18]. This approach has been investigated to achieve coverage of

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the breast CTV with setup variations [12,13], or to cover the dose to moving targets through breathing cycles in lung tissue [14,15]. The robust optimization plan using partial-arc VMAT has been shown to be effective for targets at the periphery of the body because when the setup error occurs in the lateral direction, the depth of the tumor either increases or decreases [16]. The larynx is located within the anterior aspect of the neck. That is, it is located at the periphery of the body. We speculated that a larynx cancer patient may benefit from a partial-arc VMAT robust optimization plan due to the location. In addition, VMAT robust optimization might allow for the creation of radiation treatment plans with sharp dose gradients between the CTV and the carotid arteries.

The purpose of this study is to investigate the efficacy of VMAT robust optimization plans for larynx cancer patients. A dosimetric study was performed to compare robust optimization plans with the corresponding PTV-based optimization plan. The perturbed dose was calculated for both optimization plans with respect to the localization offset of the patient.

## 2. Methods

### 2.1. Treatment planning

In this study, the use of clinical materials was approved by the Institutional Review Board of Hiroshima University (E-1223). Ten glottis carcinoma cancer patients who were previously treated in our clinic were selected. Radiation treatment planning images were acquired with an Optima computed tomography (CT) 580W (GE Healthcare, Milwaukee, WI, USA) with a tube potential of 120 kV, gantry rotation time of 0.5 s, slice thickness of 1.25 mm and tube current of 350 mA. A thermoplastic mask (CIVCO Medical Solutions) was used to minimize day-to-day setup errors. Patients were instructed not to swallow during acquisition of the planning CT. Radiation treatment plans were created using the RayStation treatment planning system (TPS) Version 6.2.0 (RaySearch Medical Laboratories AB, Stockholm, Sweden), which was commissioned with the TrueBeam STx (Varian Medical Systems, Palo Alto, CA) linear accelerator. CTV, carotid arteries, and spinal cord were contoured by a radiation oncologist. CTV was defined as the borders of the bottom of the hyoid bone superiorly, the bottom of the cricoid cartilage inferiorly, and included the anterior commissure. The PTV was created by the expansion of the CTV with 5 mm around and 3 mm posteriorly, in order to reduce the dose to the carotid arteries [8]. The CTV volume was 20.8 ± 5.9 cc (15.0–36.6 cc) and the PTV volume was 46.9 ± 9.9 cc (36.3–72.4 cc). A PTV + 3 mm ring was created to conform the dose to the PTV, and a PTV + 8 mm ring was used to reduce the dose to healthy tissues. The organ-at-risk (OAR) of the carotid arteries and spinal cord extended 1 cm superiorly and inferiorly beyond the PTV.

Two types of VMAT plans were prepared for each patient (PTV-based and robust optimization plans). The partial arc range for the PTV-based optimization plan was started from 140° to 220° counter-clockwise and was chosen in a rotating manner near the target to avoid normal tissue, reporting that partial-arc VMAT significantly reduced mean dose to the normal brain [19]. The robust optimization plan was created using the same arc range as the PTV-based optimization plan, and the plan function in the RayStation treatment plan is based on the minimax optimization, as described by Fredriksson et al. [9]. The minimax optimization method minimizes the objective function value such that the prescription dose is valid even in the worst-case scenario that addresses setup uncertainty. The shifted values from the isocenter were 5 mm in the anterior, left-right and superior-inferior directions, except for 3 mm posteriorly. A total of seven scenarios were generated based on the selected uncertainty. The isocenter was automatically placed at the center of the PTV and a beam energy of 6 MV was selected. The collimator angle was fixed at 5°. To simplify the display of the results, all plans were prescribed 2 Gy in 1 fraction. The PTV-based optimization plan was normalized so that 50% (relative volume) of the PTV received 100% of the prescription dose ($D_{50\%}$), while the robust optimization plan was normalized so that 98% (relative volume) of the CTV received 100% of the prescription dose ($D_{98\%}$). The doses to the carotid artery and spinal cord using the larynx VMAT were planned according to an in-house protocol based on the as low as reasonably achievable (ALARA) principle. The spinal cord dose was constrained as $D_{2\%}$ (near to the maximum dose) of < 25%. In the process, the carotid artery doses were minimized while maintaining the dose to the CTV. An example of cost functions for PTV-based and robust optimization plans are listed in Tables 1 and 2. The VMAT treatment plan was calculated using the collapsed cone convolution superposition (CCCS)-based algorithm and the TPS dose grid size was 2.0 × 2.0 × 2.0 mm$^3$. The final gantry spacing was fixed at 4°, and a total of 71 control points were expected within one partial arc.

**Table 1**
The cost function used in the PTV-based optimization.

| Region of interest | Dose objective | weight |
|---|---|---|
| PTV | $D_{min}$ > 195 cGy | 10 |
| | $D_{max}$ < 205 cGy | 10 |
| carotid artery_left | $D_{50}$ < 80 cGy | 5 |
| | $D_{max}$ < 125 cGy | 5 |
| carotid artery_right | $D_{50}$ < 80 cGy | 5 |
| | $D_{max}$ < 125 cGy | 5 |
| spinal cord | $D_{max}$ < 50 cGy | 5 |
| 3 mm Ring | $D_{max}$ < 180 cGy | 3 |
| 8 mm Ring | $D_{max}$ < 100 cGy | 3 |

*Abbreviation:* x mm ring; ring-shaped expansion with a distance of x mm from PTV; Dx, dose to the x percentage volume of the region of interest.

For each patient, the final calculated dose, dose volume histogram (DVH) curves, and dose statistics were recorded. Dosimetric comparisons between the PTV-based and robust optimization plan were performed. The delivered dose to the CTV, homogeneity index (HI), conformity index (CI), OAR and Monitor Unit (MU) were investigated. Dosimetric parameters were computed to evaluate the $D_{98\%}$ (near to minimum dose), $D_{95\%}$, and $D_{50\%}$ CTV dose. For the OARs, the average and the $D_{2\%}$ doses were investigated. HI was calculated using the following formula [20]:

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

where $D_{2\%}$, $D_{98\%}$ and $D_{50\%}$ are doses that cover 2%, 98% and 50% of the CTV, respectively. CI was calculated using the following formula [21]:

$$CI = \frac{VRI}{TV}$$

where VRI is the volume of the reference isodose and TV is the CTV volume. The $CI_{95\%}$, $CI_{80\%}$, and $CI_{50\%}$ were calculated, and the

**Table 2**
The cost function used in the robust optimization.

| Region of interest | Dose objective | weight | Robust |
|---|---|---|---|
| CTV | $D_{min}$ > 195 cGy | 10 | on |
| | $D_{max}$ < 205 cGy | 10 | on |
| carotid artery_left | $D_{50}$ < 80 cGy | 5 | on |
| | $D_{max}$ < 125 cGy | 5 | on |
| carotid artery_right | $D_{50}$ < 80 cGy | 5 | on |
| | $D_{max}$ < 125 cGy | 5 | on |
| spinal cord | $D_{max}$ < 50 cGy | 5 | on |
| 3 mm Ring | $D_{max}$ < 180 cGy | 3 | |
| 8 mm Ring | $D_{max}$ < 100 cGy | 3 | |

*Abbreviation:* x mm ring; ring-shaped expansion with a distance of x mm from PTV; Dx, dose to the x percentage volume of the region of interest. Robust; “on” means the robust function is used for the region of interest.

corresponding reference isodose percentages were 95%, 80%, and 50%, respectively.

### 2.2. Perturbed dose evaluation

The following method was used to investigate the variation of the dose indices caused by setup errors. For perturbed dose evaluation, the isocenter of the patient were rigidly shifted 5 mm in the anterior, left-right and superior-inferior directions, except for 3 mm posteriorly. In the case of the CTV, the evaluation metrics included the perturbed doses of $D_{98\%}$, $D_{50\%}$, and $D_{2\%}$. In the case of the OARs, the average dose and $D_{2\%}$ were evaluated.

### 2.3. Statistical analysis

All the data represented the averages and standard deviations, with ranges in parentheses. Data were analyzed using the Wilcoxon signed-rank test with a statistically significance set at $p < 0.05$, using the free Software R Version 3.5.1 (www.r-project.org).

## 3. Results

### 3.1. Treatment planning dose evaluation

Fig. 1 shows one example of the dose distributions and DVHs of the PTV-based and robust optimization plans for the same patient. In the original plan, the CTV doses, HI, CI, OAR doses and MU using the PTV-based and robust optimization plans are shown in Table 3, with data shown as group averages with ranges for all directions. Statistically significant differences were observed in the CTV and carotid arteries dosimetric indices for the PTV-based and robust optimization plans. The $D_{98\%}$, $D_{50\%}$ and $D_{2\%}$ doses to the CTV using the robust optimization plan was on average 2.7%, 2.0% and 1.3% higher than those using the PTV-based optimization plan, respectively ($p < 0.05$). $D_{2\%}$ doses to the left and right carotid arteries in the robust optimization plans were on average 11.5% and 9.5% lower than those of the PTV-based optimization plans, respectively ($p < 0.05$). In contrast, the HI, $CI_{95\%}$ and dose to the spinal cord did not significantly differ between the PTV-based and robust optimization plans ($p > 0.05$). The latter exhibited a better $CI_{80\%}$ and $CI_{50\%}$ compared to the PTV based on the optimization plan ($p < 0.05$). The robust optimization plans were on average 15.7% less than the total MU compared to the PTV-based optimization plans ($p < 0.05$).

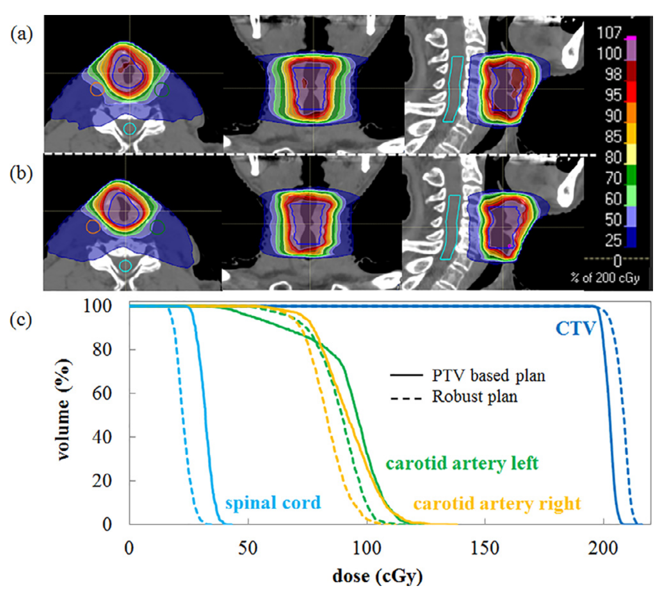


**Fig. 1.** Dose distributions calculated by (a) PTV-based and (b) robust optimization plans for a patient with larynx cancer; (c) comparison of the dose volume histograms (DVHs) between PTV-based (solid line) and robust optimization (dashed line) plans for the same patient. The CTV is shown as a blue line. Compared with the PTV-based optimization plan, the robust optimization plan resulted in lower doses to the carotid arteries, and spinal cord, and higher dose to the CTV. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

### 3.2. Perturbed dose evaluation

Table 4 compares the doses to the CTV, carotid arteries, and spinal cord obtained from the rigidly shifted plan between the PTV-based and robust optimization plans overall perturbation, with data shown as group averages with ranges for all directions. The $D_{98\%}$ dose to the CTV using the robust optimization plan was 1.0% higher on average than that of the PTV-based optimization plan ($p < 0.05$). The CTV perturbed doses of $D_{98\%}$ for the PTV-based and robust optimization plans were covered by more than a minimum of 92.5% and 94.0% of the prescribed dose for all patient. The $D_{2\%}$ doses to the left and right carotid arteries in the robust optimization plans were on average 7.6% and 8.5% lower than those of the PTV-based optimization plans, respectively ($p < 0.05$). The variation of $D_{2\%}$ of the left and right carotid arteries were 23.4 cGy versus 16.5 cGy and 25.2 cGy versus 22.8 cGy for the PTV-based and the robust optimization plans, respectively. In addition, the variation of $D_{2\%}$ of the spinal cord for the PTV-based and the robust optimization plans were 8.3 cGy and 5.3 cGy, respectively.

### 3.3. A comparison between the original plan and the perturbed dose evaluation

Average perturbed $D_{98\%}$ dose to the CTV relative to the original plan dose were 99.4% and 97.8% with PTV-based and robust optimization, respectively. The variation of $D_{98\%}$ of the CTV changed from 2.0 cGy versus 0.0 cGy to 2.6 cGy versus 2.5 cGy for the PTV-based and the robust optimization plans, respectively. Average perturbed $D_{2\%}$ dose to the left and right carotid arteries relative to the original plan dose were 104.6% versus 104.0% and 105.3% versus 103.5% with PTV-based and robust optimization, respectively. The variation of $D_{2\%}$ of the left carotid artery changed from 13.2 cGy versus 7.8 cGy to 23.4 cGy versus 16.5 cGy for the PTV-based and the robust optimization plans, respectively. The variation of $D_{2\%}$ of the right carotid artery changed from 17.2 cGy versus 19.6 cGy to 25.2 cGy versus 22.8 cGy for the PTV-based and the robust optimization plans, respectively. Average perturbed $D_{2\%}$ dose to the spinal cord relative to the original plan dose were 107.8% and 103.0% with PTV-based and robust optimization, respectively. The variation of $D_{2\%}$ of the spinal cord changed from 4.9 cGy versus 4.0 cGy to 8.3 cGy versus 5.3 cGy for the PTV-based and the robust optimization plans, respectively.

## 4. Discussion

We investigated the photon robust optimization method for larynx cancer patient and evaluated the plan robustness with perturbed doses shifted from isocenter. The robust optimization plans were also compared with the PTV-based optimization plans for CTV dose coverage, OAR doses, HI, CI, and MU. Doses to the CTV and carotid arteries exhibited a statistically significant difference between the PTV-based and robust optimization plans. The $D_{98\%}$ dose to the CTV using the robust optimization plan was higher than that for the PTV-based optimization plan. In this study, the PTV-based optimization plan was prescribed at a dose of $D_{50\%}$ to the PTV. In contrast, the robust optimization plan was prescribed at a dose of $D_{98\%}$ to the CTV. That is, the normalized target was different for each optimization plan. For an appropriate comparison, we should have renormalized the $D_{98\%}$ dose of the CTV covered by the PTV-based optimization. The $D_{2\%}$ doses to the left and right carotid arteries in the robust optimization plans were significantly lower than

**Table 3**
Doses to the CTV and OAR, HI, CI, and MU using PTV-based and robust optimization plans.

| | PTV-based plan | robust plan | *p*-value |
|---|---|---|---|
| CTV: $D_{98\%}$ (cGy) | 194.8 ± 2.0 (191.0–198.0) | 200.0 ± 0.0 (200.0–200.0) | 0.002* |
| CTV: $D_{50\%}$ (cGy) | 202.1 ± 1.9 (200.0–207.0) | 206.1 ± 1.4 (204.0–209.0) | 0.002* |
| CTV: $D_{2\%}$ (cGy) | 208.8 ± 1.7 (206.0–212.0) | 211.6 ± 2.2 (209.0–216.0) | 0.025* |
| carotid artery_left: average dose (cGy) | 88.1 ± 9.0 (81.0–105.0) | 82.6 ± 6.5 (75.0–93.0) | 0.006* |
| carotid artery_left: $D_{2\%}$ (cGy) | 121.2 ± 13.2 (98.0–147.0) | 108.7 ± 7.8 (99.0–123.0) | 0.004* |
| carotid artery_right: average dose (cGy) | 92.9 ± 13.6 (81.0–125.0) | 86.5 ± 13.0 (74.0–118.0) | 0.002* |
| carotid artery right: $D_{2\%}$ (cGy) | 127.0 ± 17.2 (111.0–168.0) | 116.0 ± 19.6 (100.0–169.0) | 0.004* |
| spinal cord: average dose (cGy) | 33.7 ± 5.2 (26.0–42.0) | 32.0 ± 4.4 (24.0–38.0) | 0.254 |
| spinal cord: $D_{2\%}$ (cGy) | 42.2 ± 4.9 (34.0–48.0) | 39.6 ± 4.0 (32.0–47.0) | 0.152 |
| HI | 0.069 ± 0.016 (0.043–0.099) | 0.056 ± 0.011 (0.044–0.077) | 0.160 |
| $CI_{95\%}$ | 1.801 ± 0.355 (1.282–2.564) | 1.713 ± 0.366 (1.249–2.433) | 0.125 |
| $CI_{80\%}$ | 2.988 ± 0.581 (1.907–4.175) | 2.784 ± 0.551 (1.939–3.879) | 0.020* |
| $CI_{50\%}$ | 5.276 ± 1.004 (3.484–7.265) | 4.688 ± 0.864 (3.484–6.640) | 0.004* |
| MU | 308.5 ± 43.6 (238.3–394.8) | 260.1 ± 14.7 (235.0–287.1) | 0.004* |

Group averages with ranges in parentheses are shown (n = 10). *The Wilcoxon signed-rank test resulted in a statistically significant difference ($p < 0.05$). HI, homogeneity index; CI, conformity index; MU, Monitor unit.

**Table 4**
Doses for the CTV and OAR for each plan at offset locations using PTV-based and robust optimization plans.

| | PTV-based plan | robust plan | *p*-value |
|---|---|---|---|
| CTV: $D_{98\%}$ (cGy) | 193.7 ± 2.6 (185.0–199.0) | 195.6 ± 2.5 (188.0–200.0) | < 0.001* |
| CTV: $D_{50\%}$ (cGy) | 201.1 ± 1.8 (196.0–207.0) | 205.7 ± 1.7 (202.0–209.0) | < 0.001* |
| CTV: $D_{2\%}$ (cGy) | 209.8 ± 2.8 (205.0–218.0) | 211.4 ± 2.7 (206.0–216.0) | 0.003* |
| carotid artery_left: average dose (cGy) | 89.5 ± 13.3 (72.0–130.0) | 83.2 ± 9.7 (69.0–110.0) | < 0.001* |
| carotid artery_left: $D_{2\%}$ (cGy) | 126.8 ± 23.4 (92.0–177.0) | 113.0 ± 16.5 (88.0–159.0) | < 0.001* |
| carotid artery_right: average dose (cGy) | 94.3 ± 16.6 (74.0–140.0) | 86.9 ± 14.6 (69.0–134.0) | < 0.001* |
| carotid artery_right: $D_{2\%}$ (cGy) | 133.7 ± 25.2 (96.0–190.0) | 120.1 ± 22.8 (91.0–184.0) | < 0.001* |
| spinal cord: average dose (cGy) | 34.5 ± 6.0 (23.0–50.0) | 32.7 ± 6.5 (21.0–66.0) | 0.002* |
| spinal cord: $D_{2\%}$ (cGy) | 45.5 ± 8.3 (30.0–69.0) | 40.8 ± 5.3 (30.0–52.0) | < 0.001* |

Group averages with ranges in parentheses are shown (n = 10). *The Wilcoxon signed-rank test resulted in a statistically significant difference for all the all parameter ($p < 0.05$).

those in the PTV-based optimization plans, respectively. The maximum $D_{2\%}$ dose to the CTV using the robust optimization plan was 108%, and the hotspots were confined within the CTV, which may be preferable clinically. A higher dose to the CTV and lower dose to the OAR are advantageous in radiation therapy. The conventional PTV-based optimization plan for VMAT resulted in plans that achieved uniform doses to the PTV while minimizing the doses to sensitive structures. The robust optimization plan which uses the minimax optimization method to minimize the objective function tends to have a lower dose the edge of PTV compared to the PTV-based optimization plan. In addition, the robust optimization plan which directly defines the prescribed dose to the CTV rather than the PTV can potentially reduce the dose to normal tissues even under a nominal scenario, compared to the PTV-based optimization plan which irradiates the entire PTV. Therefore, $CI_{80\%}$, $CI_{50\%}$ and doses to the OARs for the robust optimization plans were better than those for the PTV-based optimization plan. The robust optimization plan was approximately 50 MU lower compared to the corresponding PTV-based optimization plan. The reduced MU may decrease the risk of secondary cancer [22].

Patient setup error and organ motion may lead to a delivered dose distribution that deviates from the planned dose distribution [23]. The robust optimization plan exhibited a lower variation of the CTV, carotid arteries, and spinal cord doses compared to the PTV-based optimization plan. The CTV $D_{98\%}$ is commonly used clinical parameter to describe the minimum dose to the clinical target. The CTV $D_{98\%}$ is expected to withstand the positioning errors throughout the treatment course. Perturbed dose evaluation reduced the dose to the CTV and increased the dose to the OARs compared with the original plans. The carotid arteries are located in the path of the opposed-lateral beams and may receive radiation doses equivalent to that prescribed to the CTV. It is known that incidences of stroke and other cerebrovascular events are increased in neck radiotherapy for cancer [24,25]. These adverse effects of radiation on the vasculature are observed within the first year after completion of radiation therapy. A long history of head and neck irradiation (> 6 years) is the only significant risk factor for disease progression. The tolerance dose at the conventional fractionation for the spinal cord is well-established at approximately 50 Gy [26]. Values in excess of 60 Gy lead to a serious condition called chronic progressive radiation myelopathy. In the VMAT plan, allowance for an increased dose to the spinal cord potentially results in a decreased dose to the carotid arteries. The spinal cord constraints should be stringent values for a maximum dose of < 45 Gy in a 2 Gy/fraction [4]. Our results show that the $D_{2\%}$ dose to the spinal cord was very small and spared a dose to the carotid arteries. (e.g., 39.6 cGy × 35 fractions = 1396 cGy).

In this study, treatment planning and perturbed dose evaluation were only considered for interfractional motion of a rigid body. It should be noted that the shape of the body may be deformed from weight loss. Further studies will be pursued to investigate the influence of deformation and daily changes in the position of anatomic structures on dose distribution. It should be stressed that this study considered a maximum dose variation in the worst scenario under only one fraction. Mathematical calculations of the probability distribution should be considered for the number of fractions because day-to-day setup variations were random. To establish the robustness settings for an adequately robust treatment, appropriate CTV coverage for a given population-based distribution of systematic and random setup errors should be investigated [27]. Another example of a robust optimization method is probabilistic optimization, which is based on a priori knowledge or image feedback from patient treatment [28,29]. Probabilistic and robust optimization plans produce steeper isodose lines around the CTV to reduce the dosage to the OAR in the case of overlap with the original PTV of the target, but not with the CTV. The motion of the larynx during swallowing is 20–25 mm in the superior-inferior direction and 3–8 mm in the anterior-posterior direction, respectively [30]. Intrafraction motion cannot be considered using daily image guidance. Swallowing should be prevented during the acquisition of the planning CT scan, to reduce systematic errors. Radiation therapy oncology group trials recently reported the use of reduced PTV margins using daily image guidance for target localization. Although a 3 mm expansion of the PTV near the carotid arteries could reduce the carotid arteries dose, the risk of tumor recurrence due to contouring errors and organ motion might be increased. Target delineation error is an important issue in radiation oncology for image guidance radiotherapy [31]. We use daily cone-beam computed tomography (CBCT) for daily image guidance and instructed the patients not to swallow during treatment. Further research is aimed at determining each user-defined error scenario to achieve an optimal solution to ensure that clinical objectives are met in the worst-case scenario using daily CBCT.

## 5. Conclusions

We compared a robust optimization plan with a corresponding PTV-based optimization plan in VMAT larynx cancer patients. The robust optimization plan yielded higher doses compared to the CTV and more spared dose to the carotid artery compared to the PTV-based optimization plan. The robust optimization plan also exhibited lower MUs compared to the PTV-based optimization plan. With respect to the perturbed evaluation, the doses to the carotid arteries and spinal cord showed less variation with the robust optimization plan compared to the PTV-based optimization plan. The former lead to a reduction of the dose to the carotid arteries compared with the PTV-based optimization plan, without compromising coverage of the CTV.

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## Conflict of interest

None.

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