

Scientific Article

Evaluation of Conformity and Homogeneity Indices Consistency Throughout the Course of Head and Neck Cancer Treatment With and Without Using Adaptive Volumetric Modulated Arc Radiation Therapy



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Abstract

Purpose: Conformity indices (CI) and homogeneity indices (HI) are important tools for evaluating treatment plan quality. In this study, we evaluate the consistency of these indices with respect to anatomic changes undergone by patients.

Methods and Materials: Fifty-five patients with advanced head and neck cancer were treated with simultaneous integrated boost volumetric modulated arc therapy. The initial plan (iplan) then was projected on the new computed tomographs (CT) and 2 adaptive plans (Aplans) for each patient were performed on the new CTs. A comparison of CI and HI between the iplan, hybrid plan (Hplan), and Aplan was performed.

Results: There was a significant weight loss ($P < .001$) between CT1, CT2, and CT3, where the median weight at CT1 was 75.78 (68.95-83.42) kg, and 74.88 (68.35-82.2) kg at CT2 and 73.1 (67.6-80.7) kg at CT3. Also, gross tumor volume (GTV) showed significant decrease at CT1, CT2, and CT3. The initial GTV was 32.3 (21-58.6) cc and 28.24 (15.85-48.63) cc at CT2 and 25.12 (14.1-42.2) at CT3. In addition, there was a significant decrease in left parotid volume after 10 and 20 fractions; the median left parotid gland volume at CT1 was 31.04 (26.34-36.27) cc, then was 25.84 (19.19-28.59) cc after 10 fractions and 19.5 (13.53-22.25) cc after 20 fractions; the median right parotid volume at CT1 was 29.81 (24.6-38.75) cc and 22.38 (18.19-30.12) cc at CT2, then the volume fell to 17.74 (13.41-22.66) cc at CT3. Also, a significant increase in dose to organs at risk were noticed at Hplans, the median dose for brain stem at iplan was 5156 (4561-5324) cGy then increased to 5321 (4688-5545) cGy at Hplan1 then increased again to reach 5401 (4821-5812) cGy at Hplan2. The CI showed regression at Hplan1 and Hplan2 and then improvement at Aplan1 and Aplan2. The HI also showed regression in its value at the Hplans and then improved at the Aplans.

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Conclusions: Based on the results, we conclude that anatomic changes such as weight loss greatly affect the quality of plan, and with Aplans, we maintained the quality of plan by sustaining the values of CI and HI as in the iplan

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Introduction

Radiation therapy (RT) is the treatment modality for locally advanced head and neck cancer with or without chemotherapy. Intensity modulated radiation therapy (IMRT) is the most common treatment modality for head and neck cancer; it provides significant advantages compared with 3-dimensional conformal radiation therapy in organs at risk (OARs) sparing and target coverage.¹

Intensity modulated radiation therapy sculpts dose on the target and reduces dose to the nearby organs, resulting in a steep dose gradient at the region between the target and the nearby organs.²

Although IMRT improves target coverage and results in good organs sparing, patients can experience anatomic changes such as weight loss and tumor shrinkage through treatment sessions, which may severely effect dose delivery to the target and surrounding tissues.³

The quality of any plan can be measured by different tools—one of those tools is the dose volume histogram, which is used to evaluate dose delivered to the target and OARs. Other tools for plan evaluation are conformity index (CI) and homogeneity index (HI), where CI measures the conformation of dose on target and the volume of surrounding tissue that is covered by the reference dose.

Different formulas can be used for calculating the CI: (1) $CI_{\text{RTOG}} = V_{\text{RI}}/TV^4$, where V_{RI} is volume of reference isodose and TV is target volume; (2) $CI = TV_{\text{RI}}/V_{\text{RI}}$, developed by Lomax et al⁵ is the healthy tissue CI, where TV_{RI} is target volume covered by reference isodose; (3) conformity number (CN) = $(TV_{\text{RI}})^2/(TV \cdot V_{\text{RI}})$, developed by Van't Riet et al,⁶ introduces the conformal number, which is the formula used in our study and referred to as the CI; (4) other formulas for calculating CI were introduced by Lefkopoulos et al⁷ and Baltas et al.⁸

The HI describes how the prescribed dose is homogeneous inside the target. Different formulas can be used

to represent HI: (1) $HI_{\text{RTOG}} = I_{\text{max}}/RI$, where I_{max} is the maximum dose inside target and RI is the reference isodose⁴; (2) lesion under dosage factor = lesion volume (LV) $<_{\text{RI}}/LV$, developed by Lefkopoulos et al, in which they refer to the HI as the lesion under dosage factor, where $LV <_{\text{RI}}$ is lesion volume receiving isodoses less than the reference isodose and LV is lesion volume⁹; (3) $HI = ((D_2 - D_{98})/D_p) \cdot 100$, developed by Wu et al, where D_2 and D_{98} are the minimum dose to 2% and 98% of the target, respectively, and D_p is the prescribed dose¹⁰; (4) $HI = D_5/D_{95}$, developed by Semerenko et al, where D_5 and D_{95} represent minimum dose to 5% and 95% of the target volume, respectively.¹¹

In our study, we evaluated anatomic changes occurring in patients during the course of radiation therapy, where the patients underwent repeated CT scans at week 2 and week 4, and the effect on the CI and HI for the initial plans (iplans), hybrid plans (Hplans), and adaptive plans (Aplans).

Methods and Materials

Fifty-five patients with advanced head and neck cancer were treated with volumetric modulated arc therapy in concurrent with chemotherapy. A contrast-enhanced CT simulation was performed on all patients using a GE CT scanner (GE Revolution EVO, GE Health Care, Japan Corporation) with 2.5 mm slice thickness. Also, contrast-enhanced magnetic resonance imaging or positron emission tomography were performed and fusion with CT simulation images was achieved to ensure precise determination of the gross tumor volume (GTV) and high-risk areas. Targets and OARs were contoured by an oncologist using Monaco treatment planning system (5.1.1). iplans were made by a physicist using simultaneous integrated boost volumetric modulated arc therapy plans with doses of 66 Gy and 69.96 Gy in 33

Table 1 Weight loss, tumor and parotids volume change through 20 treatment sessions

| | CT1 (endpoints median, 25th-75th) | CT2 (endpoints median, 25th-75th) | P value, CT1 vs CT2 | CT3 (endpoints median, 25th-75th) | P value, CT2 vs CT3 |
|---------------------------|-----------------------------------|-----------------------------------|---------------------|-----------------------------------|---------------------|
| Weight (kg) | 75.78 (68.95-83.42) | 74.88 (68.35- 82.2) | | 73.1 (67.6-80.7) | < .001 |
| GTV volume (cc) | 32.29 (21.04-58.61) | 28.24 (15.85-48.63) | < .001 | 25.1 (14.1-42.2) | < .001 |
| Left parotid volume (cc) | 31 (26.3-36.3) | 25.8 (19.2-28.6) | < .001 | 19.5 (13.5-22.3) | < .001 |
| Right parotid volume (cc) | 29.8 (24.6-38.6) | 22.4 (18.2-30.1) | < .001 | 17.7 (13.4-22.7) | < .001 |

Abbreviations: CT1 = initial computed topography scan; CT2 = second computed topography scan; CT3 = third computed topography scan; GTV = gross tumor volume.

fractions (200 and 212 cGy per fraction) for PTV primary and 59.4 Gy in 33 fractions (180 cGy per fraction) for high-risk lymph nodes and 54.78 Gy in 33 fractions (166 cGy per fraction) for low-risk lymph nodes.

The plans were then approved by oncologists before treatment using a dose volume histogram and dose for OARs that met dose constraints showed in the Supplementary Material E1 (Table). After 10 treatment sessions, patients underwent a new contrast-enhanced CT simulation, fusion between the initial CT and second CT was performed, and new contouring of targets and OARs was performed by the same oncologist.

An Hplan1 which is an iplan with the same beams arrangement and treatment parameters was projected on the second CT. The treatment isocenter was placed using radiopaque markers and according to bony landmarks. Patients then underwent another contrast-enhanced CT scan at week 4 and the iplan then projected on CT2 (referred to as Hplan2) with same procedures mentioned above.

Aplans were also generated on CT1 and CT2, where the process of an Aplan was performed at the end of sessions 10 and 20 (repeating CT, contouring and adaptive planning were done in the same day after the end of the 10th and 20th sessions in the weekend, so the patient would start with the Aplan the next week for 11th and 21st sessions) considering the anatomic changes, and a new plan approval was performed by the radiation oncologist.

Results

All patients showed a decrease in weight: the median weight was 75.78 (68.95-83.42) kg at CT1, 74.88 (68.35-82.2) kg at CT2, and 73.1 (67.6-80.7) kg at CT3.

The gross tumor showed a decrease in volume throughout the treatment sessions: the median GTV was 32.3 (21-58.6) cc at CT1, 28.24 (15.85-48.63) cc at CT2, and 25.12 (14.1-42.2) cc at CT3 Table 1. shown the volumetric changes of targets and parotid glands during 20 treatment sessions.

Skin separation was measured for different sections of interest in the x and y direction of the axial CT image, where the same points in CT1, CT2, and CT3 at which the measurements were made were marked according to bony anatomy.

The median skin separation at the isocenter was 13.42 (12.32-14.55) cm for the iplan, 13.1 (12.04-14.28) cm at Hplan1, and 12.86 (11.58-14) cm at Hplan2 Table 2. shows the skin separation change measured from the center of several organs throughout the treatment course.

The goal from Hplans is to measure the stability and feasibility of dosimetric properties at iplan for targets and OARs during radiation therapy sessions. Considering the anatomic changes that had been observed in almost all cases during radiation therapy treatment sessions, continuing use of the initial treatment plan could lead to unreal dose distribution throughout treatment sessions

Table 2 Skin separation change measured from center of several organs

| | CT1 (skin separation endpoints median, 25th-75th) (cm) | CT2 (skin separation endpoints median, 25th-75th) (cm) | CT3 (skin separation endpoints median, 25th-75th) (cm) | P value, CT1 vs CT2 | P value, CT2 vs CT3 |
|--------------------------------------|--|--|--|---------------------|---------------------|
| At isocenter in x direction | 13.42 (12.3-14.6) | 13.1 (12.0-12.3) | 12.9 (11.6-14) | < .001 | < .001 |
| At center of brain stem in x axis | 14.1 (13.8-14.7) | 14.1 (13.7-14.5) | 14 (13.6-14.4) | < .001 | < .001 |
| At center of brain stem in y axis | 21.5 (20.7-22.3) | 21.3 (20.6-22.2) | 21.3 (20.5-22) | < .001 | < .001 |
| At center of spinal cord in x axis | 13 (11.8-14.1) | 12.7 (11.6-13.7) | 12.4 (11.1-13.4) | < .001 | < .001 |
| At center of spinal cord in y axis | 16.2 (15-17.1) | 15.9 (14.7-16.8) | 15.6 (14.6-16.8) | < .001 | < .001 |
| At center of mandible in x axis | 15 (12.9-15.9) | 14.6 (12.3-15.6) | 14.2 (12.1-15.2) | < .001 | < .001 |
| At center of mandible in y axis | 19.3 (17.6-21) | 19 (17.2-20.6) | 18.9 (16.6-20.3) | < .001 | < .001 |
| At center of left parotid in x axis | 14.8 (13.9-15.7) | 14.3 (13.5-15.1) | 13.9 (13-14.6) | < .001 | < .001 |
| At center of right parotid in x axis | 14.8 (13.9-15.7) | 14.3 (13.5-15.1) | 13.9 (13-14.6) | < .001 | < .001 |

Abbreviations: CT1 = initial computed topography scan; CT2 = second computed topography scan; CT3 = third computed topography scan.

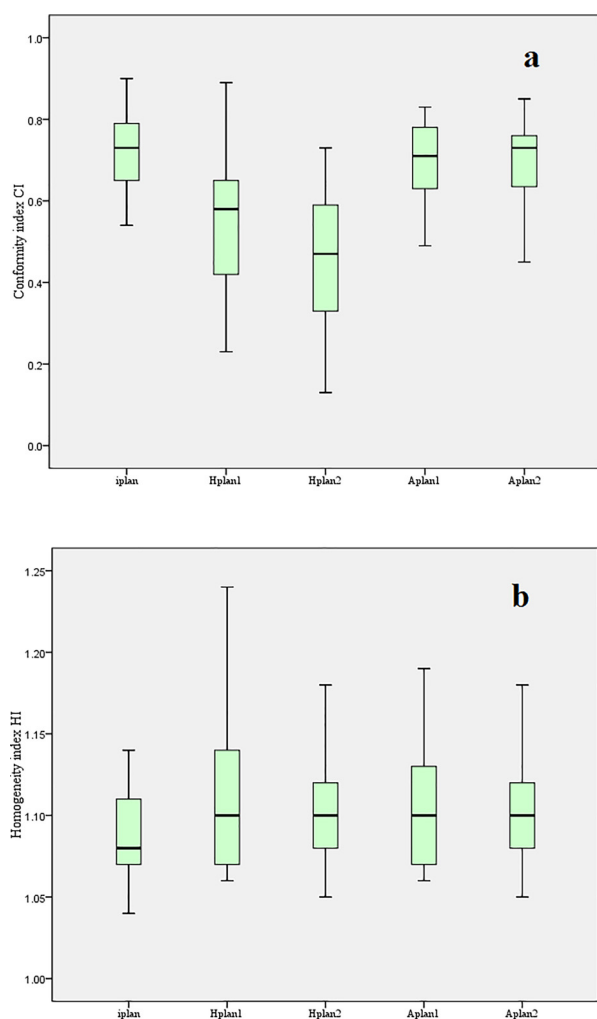


Fig. 1 A, Conformity index and B, Homogeneity index changes for initial plan, hybrid plans, and adaptive plans. *Abbreviations:* Aplan1 = adaptive plan 1; Aplan2 = adaptive plan 2; CI = conformity index; HI = homogeneity index; Hplan1 = hybrid plan 1; Hplan2 = hybrid plan 2; iplan = initial plan.

and eventually imprecise dose delivery to the organs and can delivered dose exceeds their tolerance. Taking the spinal cord, for example, the median maximum dose at iplan was 4113 (3845-4115) cGy, then rose to 4390 (4154-4587) cGy at Hplan1 and increased to 4598 (4291-4959) cGy at Hplan2. Another example is the maximum dose to brain stem; there was a significant increase in maximum dose at Hplan1 compared with iplan, and also at Hplan2 compared with Hplan1. The median maximum dose at iplan

was 5156 (4561-5324) cGy reached to 5321 (4688-5545) cGy at Hplan1 then increased to 5401 (4821-5812) cGy at Hplan2. The dosimetric variations for some organs during radiation therapy session showed in the Supplementary Material E2 (Figure). Approximately all OARs showed significant increase in dose delivery at Hplan1 and Hplan2. Supplementary Material E3 (Table) revealed dose changes for organs during radiation therapy sessions.

With the significant changes in patients' anatomy and dosimetric changes during RT sessions relative to dosimetric results of iplan, an Aplan strategy was used during RT sessions considering the changes mentioned above.

Using Aplans, we found that the median maximum dose to spinal cord significantly ($P < .001$) decrease by 6.5% at Aplan1 compared with iplan and by 2.3% ($P < .001$) at Aplan2 compared with Aplan1.

For Mandible, the median maximum dose at iplan was 6814 (6500-6952) cGy and for Aplan1 the value is decreased to 6633 (6286-6802) cGy then decreased again at Aplan2 to reach 6600 (6157-6781) cGy. In general, with Aplans the dose to all organs was significantly decreased (Supplementary Material E4 (Table)), except for parotid glands where the median mean dose was insignificantly increased at Aplan1 compared with iplan and then significantly increased at Aplan2 compared with Aplan1. A dosimetric comparison between iplan, Aplan1 and Aplan2 for some OARs showed in the Supplementary Material E5 (Figure).

The CI was calculated for PTV_p using the equation $CI = (TV_{RI})^2 / (TV \cdot V_{RI})$, where the 95% isodose for our plan is the reference isodose. The CI ranges from 0 to 1, where CI equal to 1 is referred to as the optimal plan in which all target volume is covered with reference isodose and no parts of the surrounding tissue are covered by reference isodose, and values <1 represents less conformity of the dose where either a part of the target is not covered by the reference isodose or the reference isodose volume is large and covers the target volume as well as parts of the surrounding tissues. The HI was calculated for PTV_p using the equation $HI = D_5 / D_{95}$; where HI equal to 1 is optimal, and HI values >1 indicate the plan has less homogeneity. Fifty-one of 55 patients showed a decrease in CI at Hplan1 compared with iplan ($P < .001$). The CI continued to decrease significantly ($P < .001$) at Hplan2, where 50 out of 55 patients showed decrement in CI compared with Hplan1.

For Aplan1, there was no significant change ($P = .12$) in CI value compared with iplan (55% of patients showed

Table 3 Conformity index and homogeneity index for iplan, Hplans, and Aplans

| Endpoint (mean \pm SD) | iplan | Hplan1 | Hplan2 | Aplan1 | Aplan2 |
|--------------------------|------------------|------------------|------------------|-----------------|------------------|
| CI | 0.715 \pm 0.08 | 0.544 \pm 0.17 | 0.443 \pm 0.17 | 0.694 \pm 0.1 | 0.673 \pm 0.14 |
| HI | 1.09 \pm 0.03 | 1.13 \pm 0.1 | 1.12 \pm 0.09 | 1.06 \pm 0.02 | 1.08 \pm 0.02 |

Abbreviations: Aplan1 = adaptive plan 1; Aplan2 = adaptive plan 2; CI = conformity index; HI = homogeneity index; Hplan1 = hybrid plan 1; Hplan2 = hybrid plan 2; iplan = initial plan; SD = standard deviation.

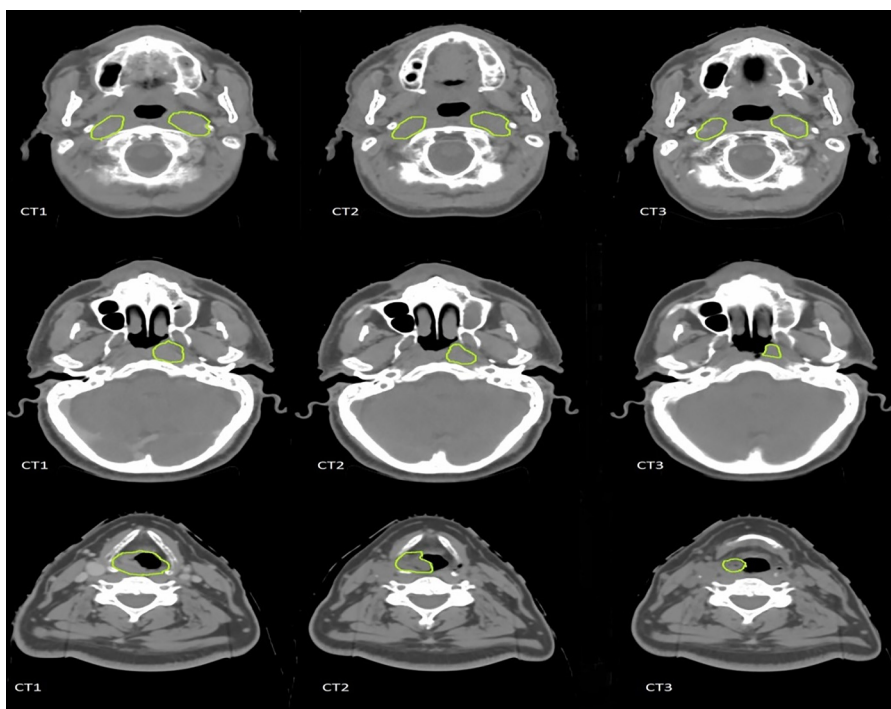


Fig. 2 Transverse computed tomography images for 3 patients demonstrates gross tumor volume reduction before radiation therapy treatment, week 10 and week 20, respectively. *Abbreviations:* CT1 = initial computed tomography scan; CT2 = second computed tomography scan; CT3 = third computed tomography scan.

improvement in CI and 44% showed regression of CI, and 1% showed approximately the same CI compared with iplan). Also, Aplan2 showed a nonsignificant change in CI value ($P = .22$) compared with Aplan1. Figure 1.A shows CI change for iplan, Hplans, and Aplans. The HI in Hplan1 showed significant regression ($P < .001$; 86% patients showed regression in HI) compared with iplan. Comparing Hplan1 and Hplan2, HI showed regression in its value at Hplan2 ($P = .026$).

In comparing iplan and Aplan1, it can be seen that HI showed significant regression ($P < .001$) in value compared with iplan (but its value improved compared with

Hplan1). Also, for HI at Aplan2 compared with Aplan1, there was no significant change ($P = .44$) in its value. Figure 1.B shows HI value for iplan, Hplans and Aplans, respectively. Table 3. shows a comparison of CI and HI for iplan, Hplan1, Hplan2, Aplan1, and Aplan2.

Discussion

Many studies have addressed the anatomic and dosimetrical changes in patients during the course of radiation therapy treatment of head and neck cancer, but no study

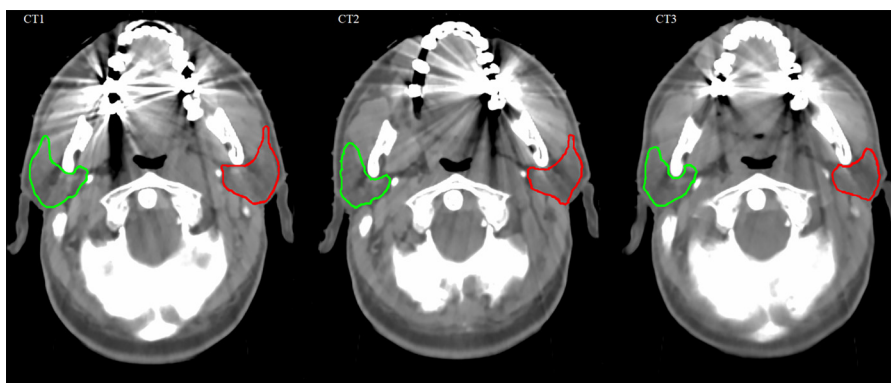


Fig. 3 Transverse computed tomography images shows parotid glands volume change before and during radiation therapy treatment sessions. *Abbreviations:* CT1 = initial computed tomography scan; CT2 = second computed tomography scan; CT3 = third computed tomography scan.

has evaluated the anatomic changes and their effect on CI and HI, which are important parameters to evaluate the quality of any treatment plan.

As discussed above, all patients showed significant decreases in weight throughout the course of treatment; this agrees with a study by Baker et al which revealed that all head and neck cancer patients exhibited decreases in weight through the course of radiation therapy or chemoradiotherapy.¹² Another study by Vangelov and Smees showed a significant decrease in weight for patients with advanced oropharynx cancer, whether using reactive tubing feeding or not.¹³

Another study result showed that gross tumor and PTV_p volumes significantly decreased at week 2 and week 4 of the treatment session (as shown in Fig. 2); this agrees with many studies showing significant decrease in tumor volume for patients of head and neck cancer treated with RT.^{14,15}

Both parotids in our study showed significant decreases in their volume during treatment sessions (Fig. 3). Streejeev et al studied parotid volume changes during radical chemotherapy with IMRT of locally advanced head and neck cancer, where all patients underwent CT simulation before RT treatment followed by weekly CT scans from week 1 to week 6; the study showed significant right and left parotid volume reduction.¹⁶ Additional studies have shown significant parotid gland shrinkage through the course of RT.¹⁷⁻¹⁹

The average skin separation measured at different centers of OARs showed a significant decrease throughout treatment sessions, with the most significant decreases observed at the center of the parotids (Supplementary Material E6 (Figure)). A study by Fung et al included 30 patients with nasopharyngeal cancer and established an adaptive RT strategy considering the anatomic changes in patients during treatment, showing significant decreases in neck volume by 2.85%, 7.76%, and 11.54% at week 9, 19, and 29, respectively.²⁰

For Hplans, a decrease in CI values was observed, which can be attributed to 2 factors. The first factor is shrinkage in GTV (which will lead to shrinkage of PTV_p), which makes the 95% isodose volume much larger than PTV_p volume, meaning that it will cover all PTV_p volume and the healthy tissue surrounding PTV_p. This led to increase dose to parotid glands, where parotid glands were shifted toward the nonconformed PTV_p dose. The second factor is the variation in target position between CT scans which leads to a shift in isodose volume position relative to the PTV_p position, so that a part of the reference dose volume will cover the nearby tissue and miss part of PTV_p (this led to significant increase in dose delivered to all OARs), thus decreasing the CI value (Supplementary Material E7 (Figure)).

In the Aplans, we consider the anatomic changes, and thus tend to maintain the CI value as in the iplan. Despite the CI improvement in the Aplans compared with the

Hplans, it is still slightly less than the iplan value. This is mainly due to parotid gland volume shrinkage and its shift toward the high dose region of the PTV_p, saving the parotid gland (while covering the target with 95% isodose) becomes harder to achieve by the planning system. This tends to increase the dose from beams that are far from the parotids, which influences the dose conformity, meaning there will be shrinkage in dose in the contact region between the parotid and the target.

The HI in the Hplans showed significant regression in comparison with the iplan. This can be explained by decreased skin separation due to weight loss such that the treatment beams face less attenuation while traveling toward the target, resulting in the generation of hot spots in the target and these hot spots mean that OARs near the target will receive higher doses than they received at iplan. We showed a hot spot generated in mandible as a result of dose inhomogeneity at Hplan1 and Hplan2 [Supplementary Material E8 (Figure)].

Conclusions

With crucial anatomic changes during the radiation therapy course, Aplans at the 10th and 20th treatment sessions for patients with head and neck cancer proved to be a very useful way to maintain or improve the values of CI and HI (guaranteeing the consistency and quality of the RT plan throughout the entire treatment course). Furthermore, this technique of 2 Aplans should be established as a treatment protocol for head and neck cancer patients. In summary, the study shows that repeat treatment planning performed after 10 and 20 fractions were associated with measurable decrements in CI and HI and that these decrements were better corrected by adaptive planning rather than hybrid planning.

According to our article there is a significant dosimetric finding which can be translated to clinical decrement in acute and late toxicity. We hypothesize that adaptive planning of head and neck cases can be further studied in future prospective trials comparing clinical findings.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at [doi:10.1016/j.adro.2022.100905](https://doi.org/10.1016/j.adro.2022.100905).

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