

Evaluating the impact of anatomical changes on dose distributions in head and neck cancer

Aleksandra SOBAJTIS^{1,D,*}, Paweł KUKOŁOWICZ^{2,D}, Beata IWANOWSKA-CHOMIAK^{1,B}

¹Medical Physics Department, University Hospital Zielona Góra, Poland

²Medical Physics Department, Maria Skłodowska-Curie National Research Institute of Oncology, Warsaw, Poland

*Corresponding author: Aleksandra Sobajtis; aleksandra.sobajtis@gmail.com

(received 12 May 2023; revised 6 August and 6 September 2023; accepted 6 September 2023)

Abstract

Introduction: Thanks to modern IGRT procedures, it is possible to track changes in the patient's anatomy and thus calculate the dose distribution for the current anatomical conditions of the patient. This allows the scheduled dose to be compared with the delivered dose. In the case of large discrepancies, it is possible to improve the treatment plan. Radiotherapy, during which the treatment plan is modified, resulting from changes in anatomy, is referred to as adaptive radiotherapy.

Material and methods: This study was performed for 30 patients with H&N cancer at the University Hospital in Zielona Góra. All patients were treated with VMAT. The Simultaneous Integrated Technique was used. In each treatment session, set-up verification was performed. Alternating every other day, the CBCT and two orthogonal portal images were made, and position correction prior to each session was performed. For all patients, new planning CT was made after the 11th and 22nd treatment sessions. Dose distributions with the initial plan on CT11 and CT22 were calculated. The initial dose-volume histograms DVH0 were compared with dose-volume histograms DVH11 and DVH22 calculated on CT11 and CT22.

Results: We compared the dose distribution in the CTVs and in the most important organs at risk obtained for initial anatomy and dose distributions calculated with the initial plan on the CTs performed after the second and the fourth week of irradiation. The differences between mean doses and V95% to GTV obtained for the initial CT and two other CTs were small. For a few CTs, the values of V95% were smaller by more than 5% points. In most patients, the mean dose in salivary glands increased during treatment.

Conclusions: Anatomical changes occurring during radiotherapy in patients with head and neck cancers have little influence on the dose deposited in the Clinical Target Volume. Adaptive therapy may be of particular importance if relapse occurs and re-irradiation.

Keywords: head and neck cancer; dose volume histogram; adaptive radiation therapy; image-guided radiation therapy.

Introduction

In the 21st century, radiotherapy has changed in an extraordinary way. Nowadays, 2D and 3D-conformal radiotherapy is seldom used. Intensity Modulated Radiation Therapy (IMRT) and the more sophisticated version of the IMRT, Volumetric Modulation Radiotherapy (VMAT), are gradually replacing the older techniques. This change is primarily due to the better dose distributions obtained with IMRT.¹ However, the most important change in radiotherapy concerns a very wide use of different imaging methods in the preparation and monitoring of the treatment.²

The increasingly better quality of Cone Beam Computerized Tomography (CBCT) and greater access to computed tomography enabled the monitoring of changes in patient's anatomy during radiotherapy. Access to modern imaging methods made it possible to adjust the treatment plan to the patient's current anatomy.^{3,4} This technique is called the Adaptive Radiation Therapy (ART). There are two different approaches to adaptive therapy: Offline ART and Online ART.^{5,6} The first one is based on the out-of-room replanning using updated CT images for planning or images from the CBCT. The second ART technique is based on selecting the plan from a library that matches better to the current anatomy (anatomy-of-the-day) or, quite new, based on daily re-

optimization (replanning) with the CBCT images obtained just before irradiation.⁷ Each of the adaptive irradiation techniques has its advantages and disadvantages. All techniques are quite time-consuming and costly, but some preliminary clinical studies revealed that IMRT or VMAT with replanning may improve prognosis, decrease toxicity and improve quality of life.⁸

Of particular interest is the application of these techniques to patients with head and neck cancers. This is because, for these patients, the long, multi-week treatment combined very often with chemotherapy leads to significant anatomical changes. However, these changes are rather slow, which is beneficial from the point of view of offline adaptation techniques. The changes are well visible on CBCT images used for daily set-up control, which facilitates the decision to change the treatment plan.⁹ This makes the replanning technique relatively simple and effective. In this work, we evaluate the changes in dose distribution obtained for a group of 30 head and neck cancer patients irradiated with VMAT according to prospective 3-phase radiation therapy protocol if plans would not be adapted to actual anatomy.

Material and methods

This prospective study was performed for 30 patients with H&N cancer. All patients included in the study were treated with VMAT in the Eclipse v.13.6 treatment planning system using the AAA calculation algorithm. The 14 patients were treated in combination with chemotherapy. Before treatment planning tomography was performed, each patient had a thermoplastic mask immobilizing the head in order to ensure good reproducibility of the position. Patients were placed in the supine position with a headrest. The Simultaneous Integrated Technique was used. The high-risk target, which was the GTV with a 3 mm margin, was irradiated to 63-70 Gy. The low-risk target CTV2 with a 3 mm margin was irradiated to 59.4-66 Gy. The low-risk target CTV3 with a 3 mm margin was irradiated to 54-56 Gy. The dose objectives for Organs at Risk (OARs) are presented in **Table 1**.

In each treatment session, set-up verification was performed. Alternating every other day, the CBCT and two orthogonal portal images were made, and position correction prior to each session was performed. The image matching was made on bones. The spinal cord and jaw were used. The set-up correction procedure was performed by radiation therapists. In case of doubts related to the matching of images, the medical physicist and radiotherapist were informed, who made the final decision.

For all patients new planning CT was made after the 11th and 22nd treatment sessions. For patients who had a significant change in body weight before a new CT, a new immobilization mask was prepared. New CT images were overlaid on the original CT. Translations and rotations were used to match the images. The area of interest for rigid fusion includes the spine, skull bones, and mandible. Next, the ROI images (images containing all areas of interest, i.e. target volumes with margins and critical organs) were propagated from the initial CTs to the new set of images. The new set of ROI images ROI11 and ROI22 were obtained. An experienced specialist in radiotherapy checked all propagated contours and, if needed, adjusted to the actual anatomy.

Dose distributions with the initial plan on CT11 with ROI11 and CT22 with ROI22 were calculated. The dose distribution was recalculated without optimizing the treatment plan for the new ROI. The initial dose-volume histograms DVH0 were compared with dose-volume histograms DVH11 and DVH22 calculated on CT11 and CT22. For OARs, the comparison was described in terms of the objectives given in **Table 1**. For GTVs and CTVs both Intermediate-Risk and Low-Risk dose changes were also evaluated in terms of the V95% and the mean dose.

Table 1. Objectives for Organs at Risk

Organ at risk	Max dose (D_{max})	Mean dose
spinal cord	< 50 Gy	-
brain stem	< 54 Gy	-
jaw	< 72 Gy	-
parotid glands	-	< 25 Gy

Results

In **Figure 1**, the V95% for GTV for each patient calculated on CT0, CT11 and CT22 are presented. Never the V95% for GTV calculated on CT11 and CT22 is larger than on CT0. For some patients, the GTV V95% decreases by more than 5%. Such big changes were obtained for 2 patients on CT11 and for 6 patients on CT22.

In **Figure 2**, the mean doses to GTV calculated on CT0, CT11 and CT 22 are presented. For 4 CTs (2 on CT11 and 2 on CT22), the mean dose to GTV was larger than the mean dose to GTVs on CT0. In one patient for one CT the mean dose has increased by more than 5%.

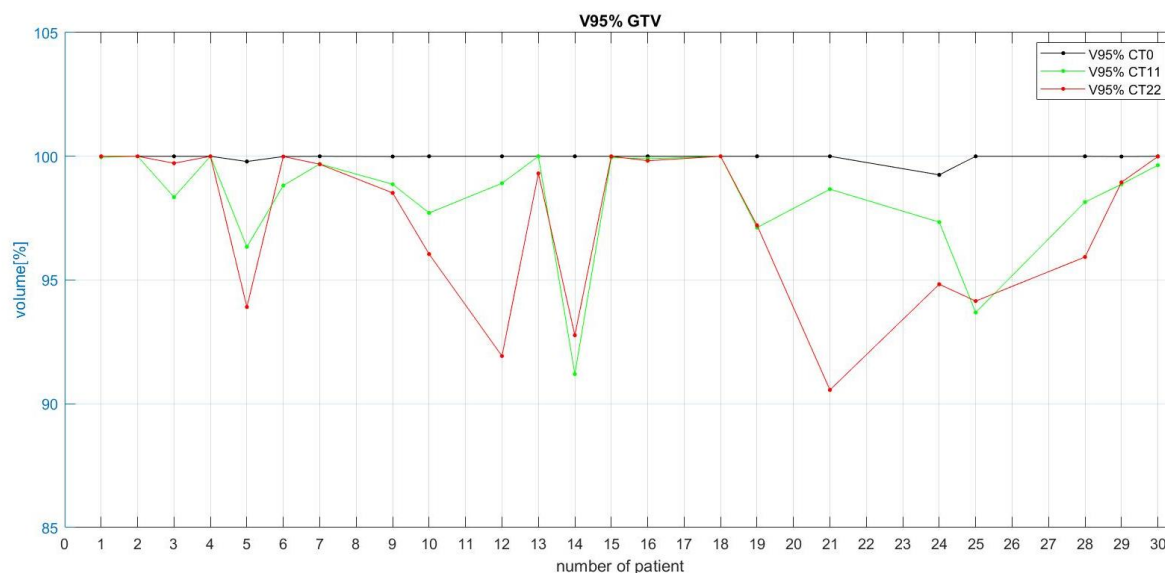


Figure 1. Changes of the V95% to GTV.

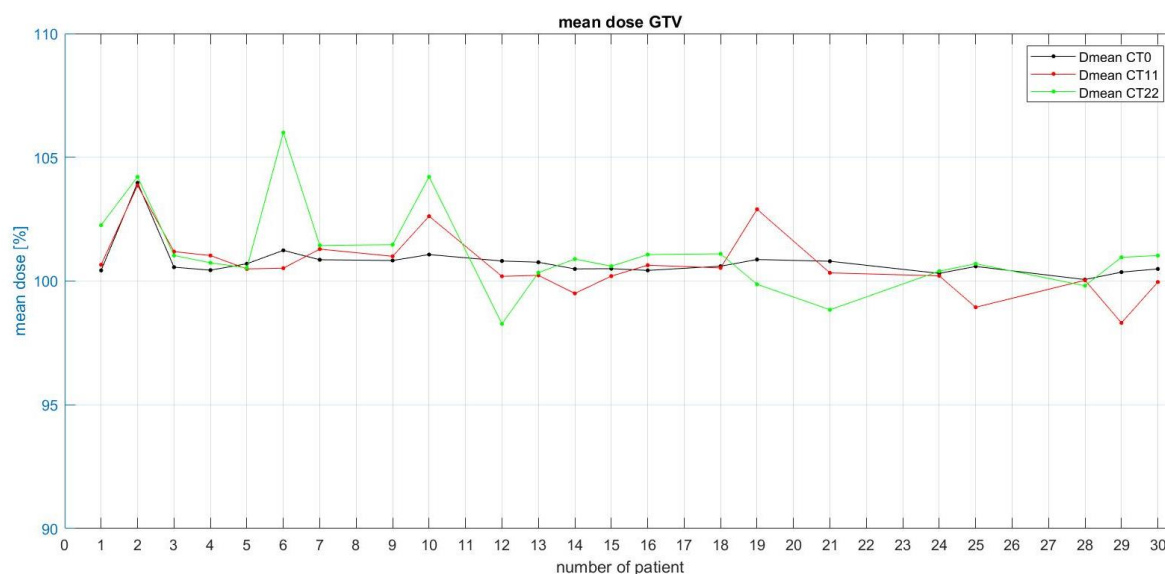


Figure 2. Changes of the mean dose to GTV.

The results of changes of the V95% for CTVs are presented in **Figure 3**. In none of the analyzed cases V95% has increased. The V95% for CTVs Intermediate-Risk was smaller than the initial one on 4 CTs. In two cases, the V95% decreased by 8% points.

In **Figure 4**, the changes of the mean doses delivered to the CTV Intermediate-Risk are presented. The changes of the mean

dose to CTV Intermediate in 26 cases did not exceed 2 Gy. We may conclude that very similar mean doses were delivered for the entire treatment.

During the V95% analysis for CTVs Low-risk, deviations of no more than 5% were obtained (**Figure 5**). It should be noted that the V95% decreased a little in time.

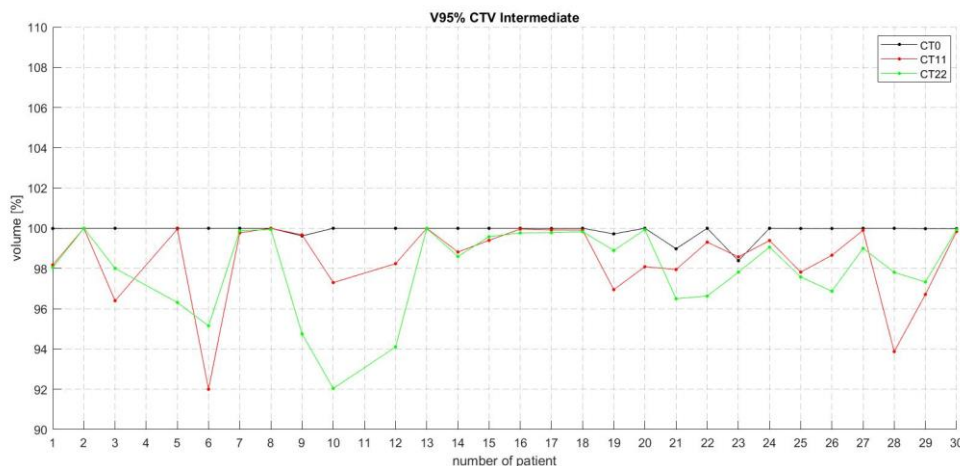


Figure 3. Changes of the V95% to intermediate risk CTV.

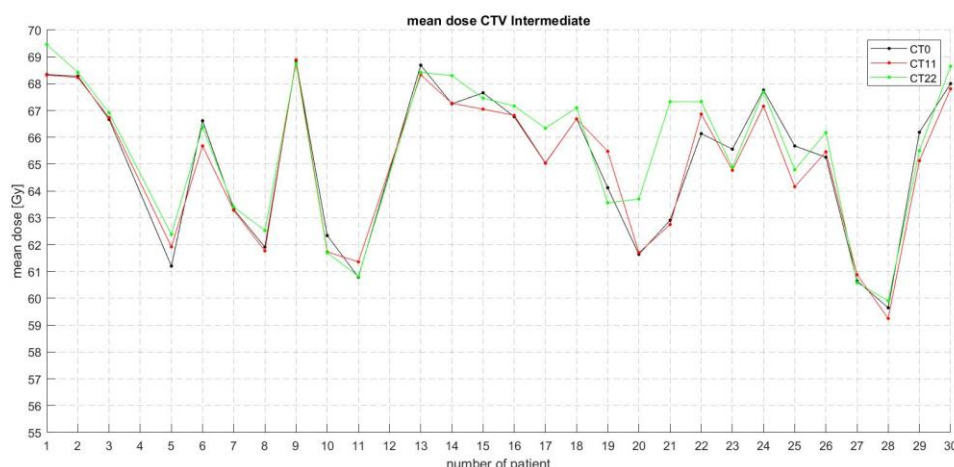


Figure 4. Changes of the mean dose to intermediate risk CTV.

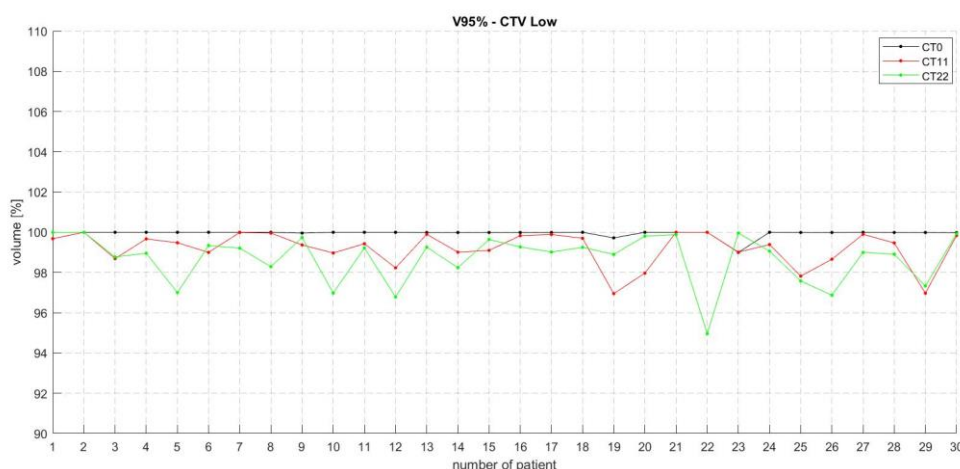


Figure 5. Changes of the V95% to low risk CTV.

The most important critical organs are the spinal cord and brainstem. In the case of the spinal cord, exceeding the tolerance dose may lead to the development of persistent and progressive post-porous myelopathy, while exceeding the tolerance dose for the brainstem to necrosis or permanent cranial neuropathy. In **Figure 6**, the maximum doses to spinal cord obtained for CT0, CT11 and CT22 are presented.

In 25 cases the maximum doses to spinal cord obtained for CT11 and CT22 were larger than for CT0 (**Figure 6**). The average difference for each analyzed patient between the maximum dose to the spinal cord for CT11 and CT22 in relation to CT0 was 13.73 Gy and 17.69 Gy, respectively (for the same patient). For none of the patients the tolerance dose to the spinal

cord exceeded 50 Gy, which is the tolerance dose for this organ. However, for 6 patients the maximum doses calculated for CT22 were very close to 50 Gy.

In 11 cases, the maximum brainstem doses obtained for CT11 and CT22 were higher than for CT0, and lower than for CT0 in 7 cases (**Figure 7**). For none of the patients the brainstem doses were larger than 55 Gy. However, for 2 patients the maximum doses calculated for CT22 were very close to 54 Gy. It should be emphasized that, as in the case of the spinal cord, although the doses of tolerance have not been exceeded, the information about the dose increase may be important in the case of recurrence and the decision of re-irradiation.

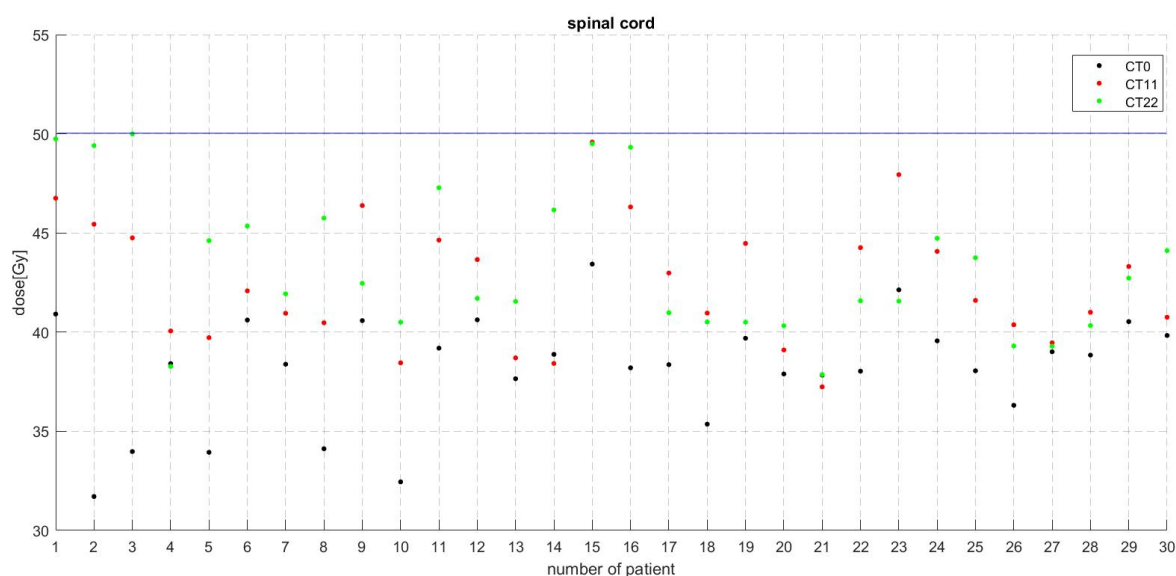


Figure 6. The maximum doses to spinal cord obtained for CT0, CT11, and CT22. The blue line represents the tolerance dose.

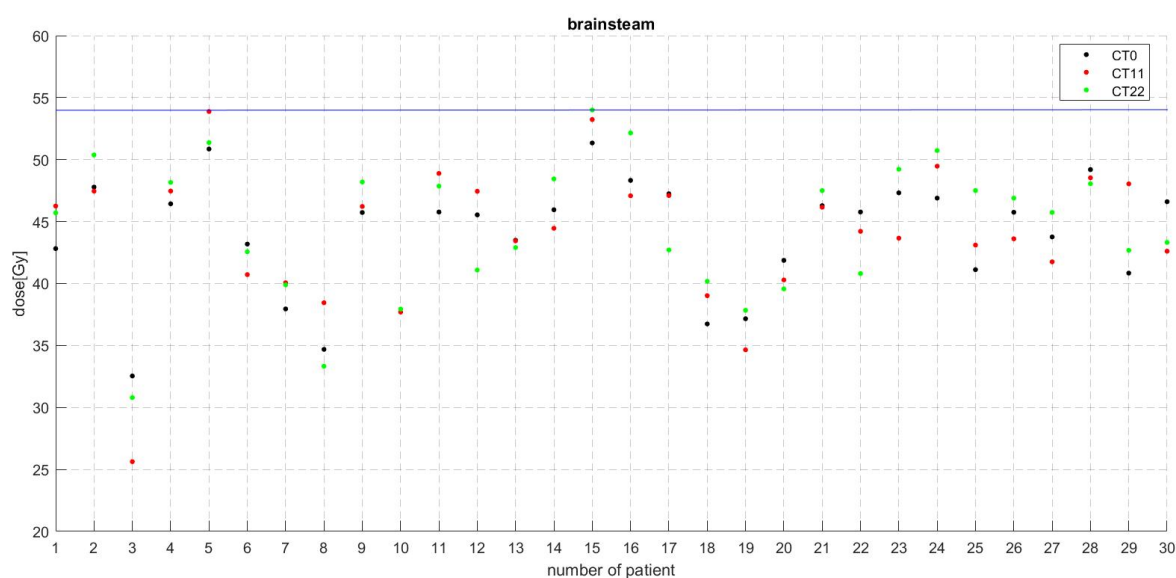


Figure 7. The maximum doses to brainstem obtained for CT0, CT11, and CT22. The blue line represents the tolerance dose.

In **Figures 8** and **9** the mean doses for salivary gland left and right for three CTs are presented.

For 15 patients for both salivary glands the doses for CT22 were the largest one. The changes in the anatomy led to an increase in dose. Only for some patients was it possible to keep the mean dose for salivary glands smaller than 25 Gy. For all

patients but one, the mean dose to the left or right salivary gland for at least one CT was larger than 30 Gy. The dose increase in the salivary glands during treatment is of particular importance because the doses received by the salivary glands are in an area of the strong relationship between dose and normal tissue complication probabilities.¹⁰

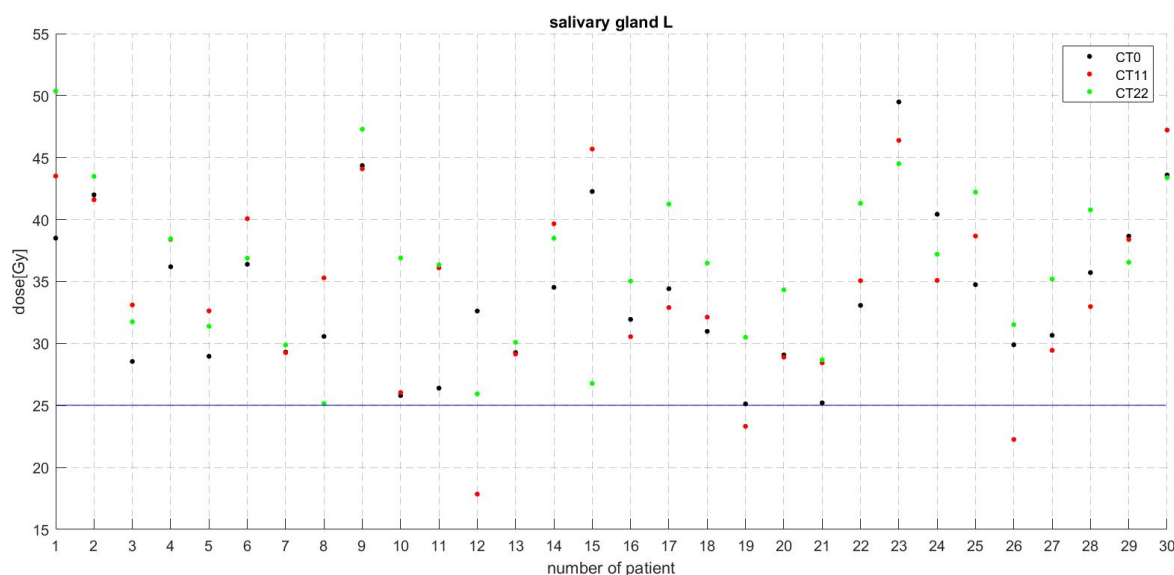


Figure 8. The mean doses to left salivary gland obtained for CT0, CT11, and CT22. The blue line represents the tolerance dose.

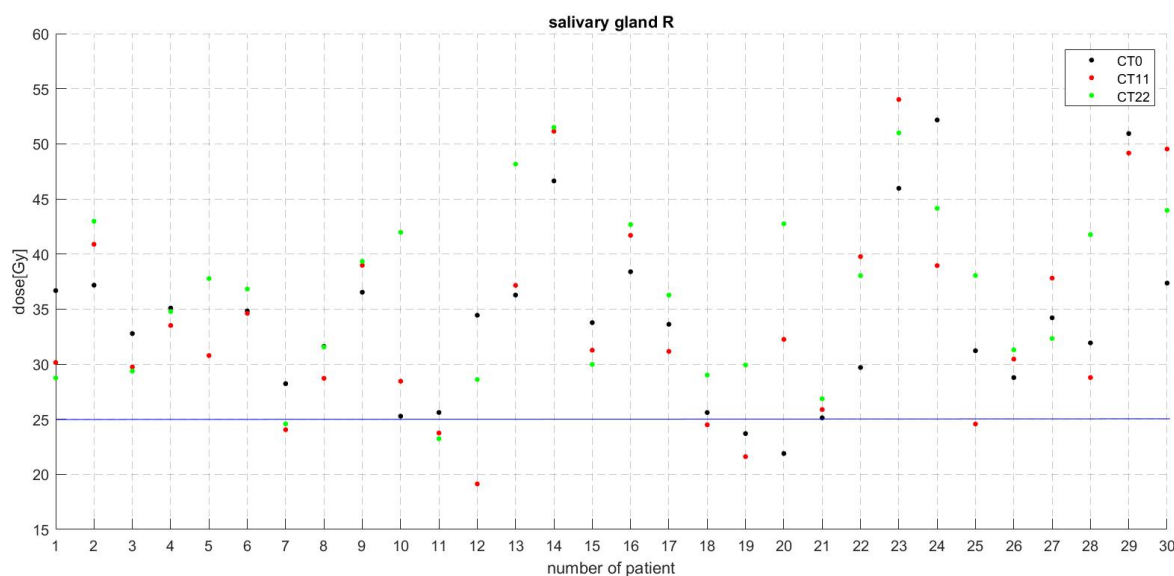


Figure 9. The mean doses to right salivary gland obtained for CT0, CT11, and CT22. The blue line represents the tolerance dose.

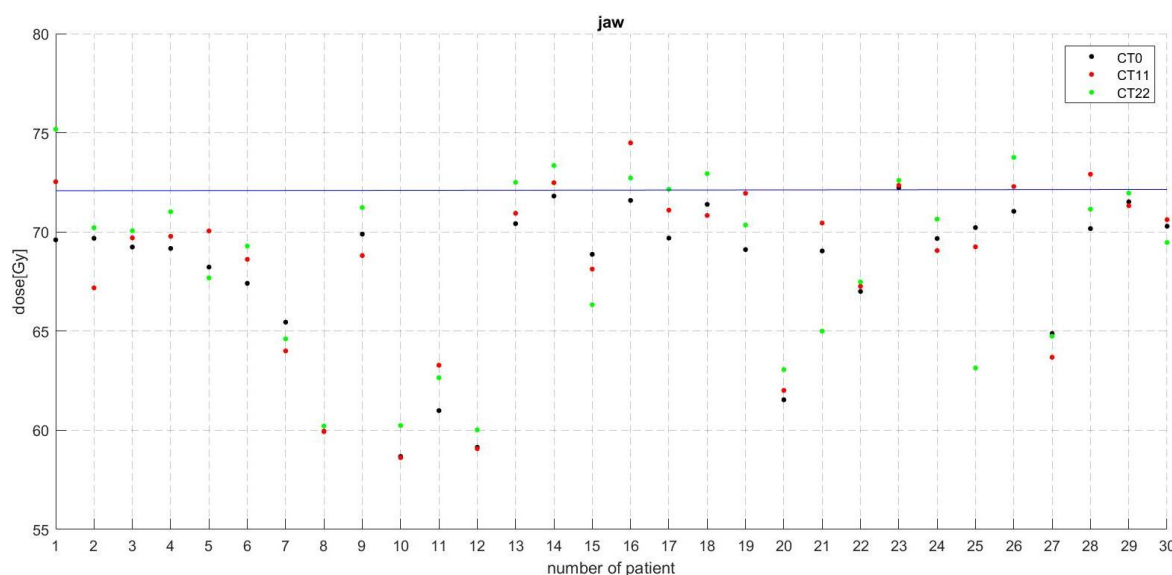


Figure 10. The maximum doses to the jaw obtained for CT0, CT11, and CT22. The blue line represents the tolerance dose.

No patient had a jaw tolerance dose exceeded during the evaluation of the primary treatment plan (**Figure 10**). However, for 9 patients, for at least CT11 or CT22, maximum doses were larger than 72 Gy. In only one patient the dose to jaw reached 75 Gy.

Discussion

Inherent changes in the anatomy of head and neck cancer patients influence dose distribution. The influence of anatomy changes is more important for VMAT techniques for which dose distribution is very conformal and has steep dose gradients. According to the protocol used in our hospital for all patients, new optimized treatment plans were prepared after the second and fourth week of treatment. However, in this work, we present what would happen if new plans were not prepared. In this work we compared the dose distribution in the CTVs and in the most important organs at risk obtained for initial anatomy and dose distributions calculated with the initial plan on the CTs performed after the second and the fourth week of irradiation. There were three CTVs: the High-Risk CTV, which in our work was identified with GTV, the Intermediate-Risk CTV, and the Low-Risk CTV. Most commonly, the mean doses to GTV increased, but at the same time the values of V95% decreased. The differences between mean doses and V95% to GTV obtained for the initial CT and two other CTs were small. For a few CTs, the values of V95% were smaller by more than 5% points. Because the differences in dose distribution were rather small and because the mean doses were not smaller, they were even little larger it seems that the probability of local control should not be deteriorated by anatomical changes. The idea of radiotherapy is to deposit a strictly defined dose in the area of GTV and CTV. Theoretical studies indicate that the effect of

radiotherapy, unless the dose distribution in CTV is very heterogeneous, is related to the average dose. Lower doses are deposited in the PTV, but the PTV area is only created to ensure proper dose distribution in the CTV area. In conclusion, the changes of anatomy should not deteriorate the local control (within the parotid glands). For patients irradiated with adaptive radiotherapy techniques some previous studies reported favorable clinical outcomes.¹¹⁻¹³ Our results confirmed these conclusions. We showed that an adaptation of the plan is not necessary to maintain the local control as for the initial plan.

The significant influence of anatomy changes on dose distribution, which may be considered clinically important, was observed for salivary glands. In most patients, the mean dose in both left and right salivary glands increased during the assessment of the plans obtained after transferring the dose distribution from the original plan to two successive CT scans performed during treatment. The dose increase is caused by the changes in the spatial orientation and shift of the salivary gland with respect to CTV and the change in the volume of the salivary glands. Typically, salivary glands move superiorly and medially. Castelli and co-workers, in the prospective study for 15 patients with locally advanced unresectable Head&Neck Cancer estimated the difference between the planned dose and actually delivered dose. An overdose in the salivary gland was observed for 9 patients. The average mean dose increase was 3.7 Gy. The estimated increase in complication probability was about 8%. In our group of patients, the dose increase was observed for 26 patients with an average increase of 5.1 Gy.¹⁴⁻¹⁶

The maximum doses to the spinal cord increased for each of 30 patients. Usually, the maximum dose for the third CT was larger. The mean dose increased on the average of 5.1 Gy. However, the maximum dose never exceeded the tolerance dose

of 50 Gy. The information about dose increase may be important in case of re-irradiation. Similar results were reported by Loo. We obtained similar results for the brainstem. For some patients, the dose increased. However, never the tolerance dose was exceeded.

Our prospective study changed the policy in our department. For all Head&Neck patients, after the second and fourth week of treatment, new planning CTs and new plans are made. As we have already written, new immobilization masks were prepared for some patients. The decision whether to continue treatment with a new plan was made by a medical doctor. This procedure has now been accepted and implemented. The question is whether it is appropriate to use this method for all patients. On the one hand, there are reports indicating that such adaptive treatment makes it possible to reduce the dose in the salivary glands.¹⁴ On the other hand, it would be much better to address this complicated procedure to patients for whom adaptive radiotherapy would significantly improve dose distribution. The other question is, what is the optimal number and time of replanning? This aspect of adaptation is also not clear.¹⁷ Some hopes can be associated with a wider use of CBCT image

information. Unfortunately, the quality of CBCT images is not good enough for the delineation of the salivary glands, which are important organs at risk for this group of patients. However, it can be expected that technological development will lead to significant improvements in image quality, which will allow adaptive therapy to be used only for selected patients.

Conclusions

Anatomical changes occurring during radiotherapy in patients with head and neck cancers have little influence on the dose deposited in the Clinical Target Volume. At most of the patients, doses absorbed by the salivary glands increase, which may significantly increase the risk of xerostomia. A significant effect of the use of adaptive therapy is greater protection of critical organs, which may be particularly important in the event of relapse and planned re-radiation.

The study was approved by the Ethical Committee at the Regional Medical Chamber in Zielona Góra.

References

1. Gupta T, Sinha S, Ghosh-Laskar S, et al. Intensity-modulated radiation therapy versus three-dimensional conformal radiotherapy in head and neck squamous cell carcinoma: long-term and mature outcomes of a prospective randomized trial. *Radiat Oncol.* 2020;15(1):218. <https://doi.org/10.1186/s13014-020-01666-5>
2. Thorwarth D, Muren L. Imaging science and development in modern high-precision radiotherapy. *Phys Imaging Radiat Oncol.* 2019;12:63-66. <https://doi.org/10.1016/j.phro.2019.11.008>
3. van Beek S, Jonker M, Hamming-Vrieze O, et al. Protocolised way to cope with anatomical changes in head & neck cancer during the course of radiotherapy. *Tech Innov Patient Support Radiat Oncol.* 2019;12:34-40. <https://doi.org/10.1016/j.tipsro.2019.11.001>
4. Davis AT, Palmer AL, Nisbet A. Can CT scan protocols used for radiotherapy treatment planning be adjusted to optimize image quality and patient dose? A systematic review. *Br J Radiol.* 2017;90(1076):20160406. <https://doi.org/10.1259/bjr.20160406>
5. Noble DJ, Yeap PL, Seah SYK, et al. Anatomical change during radiotherapy for head and neck cancer, and its effect on delivered dose to the spinal cord. *Radiation Oncol.* 2019;130:32-38. <https://doi.org/10.1016/j.radonc.2018.07.009>
6. Green OL, Henke LE, Hugo GD. Practical Clinical Workflows for Online and Offline Adaptive Radiation Therapy. *Semin Radiat Oncol.* 2019;29(3):219-227. <https://doi.org/10.1016/j.semradonc.2019.02.004>
7. Moazzezi M, Rose B, Kisling K, et al. Prospects for daily online adaptive radiotherapy via ethos for prostate cancer patients without nodal involvement using unedited CBCT auto-segmentation. *J App Clin Med Phys.* 2021;22(10):82-93. <https://doi.org/10.1002/acm2.13399>
8. Castelli J, Simon A, Lafond C, et al. Adaptive radiotherapy for head and neck cancer. *Acta Oncologica.* 2018;57(10):1284-1292. <https://doi.org/10.1080/0284186X.2018.1505053>
9. Srivastava R, Sharma PK, Das KJM, Manjhi J. A hybrid approach for head and neck cancer using online image guidance and offline adaptive radiotherapy planning. *J Radiother Pract.* 2019;18(3):271-275. <https://doi.org/10.1017/S146039691800078X>
10. Beetz I, Schilstra C, van der Schaaf A, et al. NTCP models for patient-rated xerostomia and sticky saliva after treatment with intensity modulated radiotherapy for head and neck cancer: The role of dosimetric and clinical factors. *Radiation Oncol.* 2012;105(1):101-106. <https://doi.org/10.1016/j.radonc.2012.03.004>
11. Surucu M, Shah KK, Roeske JC, Choi M, Small W Jr, Emami B. Adaptive Radiotherapy for Head and Neck Cancer. *Technol Cancer Res Treat.* 2017;16(2):218-223. <https://doi.org/10.1177/1533034616662165>
12. Zhao L, Wan Q, Zhou Y, Deng X, Xie C, Wu S, et al. The role of replanning in fractionated intensity modulated radiotherapy for nasopharyngeal carcinoma. *Radiation Oncol.* 2011;98:23-27. <https://doi.org/10.1016/j.radonc.2010.10.009>

13. Chen AM, Daly ME, Cui J, Mathai M, Benedict S, Purdy JA. Clinical outcomes among head and neck cancer patients treated with intensity-modulated radiotherapy, with and without adaptive replanning. *Head Neck*. 2013;36(11):1541-1546. <https://doi.org/10.1002/hed.23477>
14. Castelli J, Simon A, Louvel G, Henry O, Chajon E, Nassef M, et al. Impact of head and neck cancer adaptive radiotherapy to spare the parotid glands and decrease the risk of xerostomia. *Radiat Oncol*. 2015;10:6. <https://doi.org/10.1186/s13014-014-0318-z>
15. Lee C, Langen KM, Lu W, Haimel J, Schnarr E, Ruchala KJ, et al. Assessment of parotid gland dose changes during head and neck cancer radiotherapy using daily megavoltage computed tomography and deformable image registration. *Int J Radiat Oncol Biol Phys*. 2008;71(5):1563-1571. <https://doi.org/10.1016/j.ijrobp.2008.04.013>
16. Bhides SA, Davies M, Burke K, et al. Weekly volume and dosimetric changes during chemoradiotherapy with intensity-modulated radiation therapy for head and neck cancer: a prospective observational study. *Int J Radiat Oncol Biol Phys*. 2010;76(5):1360-1368. <https://doi.org/10.1016/j.ijrobp.2009.04.005>
17. Avgousti R, Antypas C, Armpilia C, et al. Adaptive radiation therapy: When, how and what are the benefits that literature provides? *Cancer Radiother*. 2022;26(4):622-636. <https://doi.org/10.1016/j.canrad.2021.08.023>