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ORIGINAL ARTICLE

CT-based dose recalculations in head and neck cancer radiotherapy: comparison of daily dose recalculations to less time-consuming approaches

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Abstract

Background The goal of this study was to investigate if daily dose recalculations are necessary or if less time-consuming approaches can be used to identify dose differences to the planned dose in patients with head and neck cancers (H&N).

Methods For 12 H&N patients treated with helical tomotherapy, daily dose calculations were performed retrospectively. Four different summation doses (SuDo) were calculated: DayDo (daily dose calculation), MVCTx2, MVCTx5, and MVCTx10 (dose calculations every second, fifth, and tenth fraction). Dose recalculations were depicted on the last contoured mega voltage CT (MVCT). The DayDo was compared to the planned dose and to the less time-consuming SuDo scenarios. The doses were assessed for the planning target volume (PTV) and the organs at risk (OARs): mandible (mand), spinal cord (SC), spinal cord +5 mm (SC+5 mm), parotid glands (PG).

Results The ipsilateral PG, contralateral PG, and PTV volume decreased by –22.5% (range: –34.8 to 5.2%), –19.5% (–31.5 to 15.8%), and –2.6% (–16.7 to 0.2%), respectively. There was a significant median mean dose (Dmean) dose difference for DayDo compared to the planned dose for PG total of 1.9 Gy (–3.3 to 7.3 Gy). But less time-consuming SuDo compared to DayDo showed statistically significant but not clinically relevant (<2%) dose differences for several organs. Hence the small dose difference to the gold standard (DayDo), we recommend dose recalculations every fifth MVCT in order to identify the occurrence of dose differences compared to the planned dose.

Conclusion Daily dose calculations are the most precise to assess dose differences between actual and planned dose. Dose recalculations on every fifth MVCT (i. e., weekly control CTs) are an applicable and time-saving way of identifying patients with significant dose differences compared to the planned dose.

Keywords MVCT cancers · Adaptive radiotherapy · Helical tomotherapy · IGRT · IMRT

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CT-basierte Dosisneuberechnung bei der Strahlentherapie von Kopf-Hals-Tumoren: Vergleich der täglichen Dosisneuberechnung mit weniger zeitaufwändigen Ansätzen

Zusammenfassung

Hintergrund Ziel dieser Studie war es, zu untersuchen, ob die tägliche Dosisneuberechnung (DayDo) nötig ist und ob weniger zeitaufwendige Dosisberechnungen geeignet sind, um Dosisunterschiede bei der Planungsdosis von Patienten mit Kopf-Hals-Tumoren (H&N) zu identifizieren.

Methoden Insgesamt 12 H&N-Patienten wurden mittels Tomotherapie bestrahlt und tägliche Dosisberechnungen wurden retrospektiv durchgeführt. Es wurden 4 verschiedene Szenarien (SuDo) berechnet: DayDo (tägliche Dosisberechnung), MVCTx2, MVCTx5 und MVCTx10 (Dosisberechnungen jede zweite, fünfte und zehnte Fraktion). Die Dosis-Neuberechnungen wurden auf dem letzten MVCT dargestellt. Die tägliche Dosisberechnung wurde mit der Planungsdosis und den weniger zeitaufwendigen Szenarien verglichen. Des Weiteren wurden die Volumenveränderungen im Verlauf der Strahlentherapie erfasst. Bestimmt wurden die Dosen für das Zielvolumen (PTV) und für die Risikoorgane (OARs): Unterkiefer (mand), Rückenmark (SC), Rückenmark +5 mm (SC+5 mm) und Ohrspeicheldrüsen (PG).

Ergebnisse Das Volumen der ipsi- und kontralateralen PG sowie das PTV sanken um –22,5 % (Spanne –34,8–5,2 %), –19,5 % (Spanne –31,5–15,8 %) bzw. –2,6 % (Spanne –16,7–0,2 %). Es gab eine statistisch signifikante Dosisdifferenz der medianen Dmean beider PG zusammen um 1,9 Gy (Spanne –3,3–7,3 Gy). Für verschiedene OARs existierten für die weniger zeitaufwändigen Szenarien im Vergleich zur DayDo zwar statistisch signifikante, aber klinisch nicht relevante Dosisunterschiede (<2 %). Aufgrund der klinisch irrelevanten Unterschiede sind Dosisberechnungen jedes fünften MVCT ein einfaches und zeitsparendes Verfahren, um Dosisunterschiede zwischen Planungsdosis und wirklicher Dosis festzustellen.

Schlussfolgerung Tägliche Dosisneuberechnung ist die genaueste Methode, um Dosisunterschiede zwischen Planung und tatsächlicher Dosis zu ermitteln. Aber Dosisberechnung jedes fünften MVCT ist ein zeitsparendes und einfaches Verfahren, um Dosisunterschiede zwischen Planungsdosis und wirklicher Dosis festzustellen.

Schlüsselwörter Kopf- und Halstumore · Adaptive Strahlentherapie · Helikale Tomotherapie · IGRT · IMRT

Background

Radiotherapy (RT) is a very important part of the treatment of patients with head and neck (H&N) cancer. Helical tomotherapy (HT) achieves steep dose gradients between the planning target volume (PTV) and normal tissue(organs at risk-OAR). This is especially beneficial in patients with H&N cancers [1–5].

During the course of treatment, H&N patients often undergo soft tissue changes due to weight loss and consequential volume reductions of OARs and gross tumor volume (GTV)/PTV [6, 7]. Furthermore, daily setup errors occur in all patients. Accordingly, there can be insufficient PTV coverage or overdosing of OARs [8–14]. These inaccuracies are especially critical in patients with H&N cancers, since PTV and OARs such as parotid glands or spinal cord are in very close anatomic proximity. Replanning at some point during the course of treatment (adaptive radiotherapy, ART) shows a positive effect regarding the sparing of OARs, but is still time consuming and therefore not feasible to be performed on a daily basis for every patient [11, 15–19].

The aim of our study was to assess if daily dose recalculations are necessary in order to predict, at any given point, the need for ART, or if less time-consuming approaches can be used. We aimed to test if less time-consuming approaches can be used, for example, if the dose can be recalculated on a CT performed every second or every fifth treatment day.

Materials and methods

Twelve postoperative H&N cancer patients were included in the present study—six of them with hypopharyngeal (HPC) and the other six with oropharyngeal (OPC) cancer. The characteristics of these patients are shown in Table 1.

Treatment planning and delivery

All patients were treated with a helical tomotherapy (HT) Hi·Art machine (Accuracy Inc., Madison, WI, USA) in our institution. A two-layer thermoplastic head mask (BrainLAB AG, Feldkirchen, Germany) was used for immobilization.

Prior to their treatment, a planning kilovoltage CT (kVCT) scan (Somatom Emotion 16, Siemens, Erlangen, Germany) was performed in the treatment position with an axial slice thickness of 3 mm. Organs at risk (OARs), gross tumor volume (GTV), clinical target volume (CTV), and planning target volume (PTV) were manually contoured on the kVCT system (Eclipse Treatment Planning

Table 1 Patient characteristics

Patient	Age[a]	Sex	Tumor	Loc	TNM Classification	Chemotherapy	Boost	Fractions	PTV dose (Gy)	Total Boost dose (Gy)
1	76	M	HPC	R	pT2, pN2, M0, R0	No	SB	32	50	64
2	54	M	HPC	R	pT2, pN2b, M0, R0	Mitomycin C	SIB	32	54.4	70.4
3	64	M	OPC	L	pT1, pN2b, M0, R0	Cisplatin	SB	32	50	64
4	59	M	OPC	L	pT3, pN2, M0, R1	Cisplatin	SB	33	50	66
5	53	M	OPC	L	pT2, pN2b, M0, R0	Cisplatin	SIB	32	54.4	70.4
6	58	F	HPC	R	pT2, pN0, M0, R1	No	SB	34	50	68
7	62	M	HPC	R	pT1, pN2b, M0, R0	Cisplatin	SIB	32	50	64
8	67	M	OPC	L	pT4a, pN2b, M0, R1	No	SIB	32	54.4	70.4
9	59	F	OPC	R	pT2, pN2b, M0, R0	No	SB	32	50	64
10	63	M	OPC	R	pT1, pN2a, M0, R0	No	SIB	33	54	66
11	61	M	HPC	R	pT2, pN2c, M0, R0	Cisplatin	SIB	35	50.4	70
12	75	M	HPC	L	pT2, pN0, M0, R0	No	SIB	30	54	64.2

M male, *F* female, *HPC* hypopharyngeal carcinoma, *OPC* oropharyngeal carcinoma, *Loc* localization, *R* right, *L* left, *SB* sequential boost, *SIB* simultaneous integrated boost
[a]Age at therapy begin

System, Varian Medical Systems, Palo Alto, CA, USA) and exported to the tomotherapy planning software (TomoTherapy Planning Station, version 4, Accuracy Inc., USA).

The tumor clinical target volume (CTV) was defined as the gross tumor volume (GTV) delineated on pretreatment CT and/or MRI plus a safety margin of 10 mm including postoperative changes. The elective nodal CTV was defined according to the literature [20, 21]. A safety margin of 5 mm was applied from the CTV to the planning target volume (PTV). All patients were treated five times per week. Dose prescriptions to the PTV are depicted in Table 1.

Dose constraints for the OARs were set to <25 Gray (Gy) for mean dose (Dmean) of the parotid glands and to <35 Gy and <45 Gy for the maximum doses (Dmax) of the SC and SC+5 mm, respectively.

Prior to each treatment, patients underwent daily megavoltage computed tomography (MVCT) scans. The MVCT was performed in coarse mode, with a slice thickness of 6 mm and a mean beam energy of 0.75 MeV. To correct setup errors, daily MVCT scans were automatically fused to the planning kVCT by choosing the available bone and tissue algorithm provided by TomoTherapy. Every automatic registration was reviewed by an experienced therapist and corrected manually prior to each fraction.

Dose recalculations

The TomoTherapy software can generate a "merged image" in which the corrected setup errors of the given day are already included. The daily dose recalculations were performed on this merged MVCT with the TomoTherapy Planned Adaptive software (Accuracy Inc., USA.). Dose recalculations were performed with a dose grid solution and voxel size of 2 × 2 × 3 mm. Daily dose recalculations were not combined with daily recontouring of GTV and OAR. The daily dose recalculation of course takes the soft tissue changes into account, but a structure set is not needed in order to perform the recalculation of the actual delivered dose. The daily recalculated dose distributions were rigidly summed up to generate different "summation doses" (SuDo). We projected the SuDo dose recalculations onto the last MVCT. The daily recalculated dose summation (DayDo) describes the actual dose received by the patients during treatment course and acts as the gold standard for the comparison to all other scenarios.

Further, we decided not to compare doses calculated on MVCTs to doses calculated on kVCT (i.e., the initial planned dose), as MVCT dose calculations could be prone to inaccuracies of up to 5% [22, 23]. We choose the dose on the first MVCT multiplied by the number of treated fractions (first MVCT) as a surrogate for the "initial plan."

We compared five different scenarios (four summation dose scenarios and the planned dose scenario):

1. SuDo every fraction (DayDo)
2. SuDo every second fraction (MVCTx2)
3. SuDo every 5th fraction (MVCTx5)
4. SuDo every 10th fraction (MVCTx10)
5. planned dose (1st MVCT)

To compare the different SuDo to each other and to the planned dose, they were multiplied to the total number of fractions for each patient. For the approaches 2, 3, and 4, the calculated SuDo were each multiplied by 2, 5, and 10, respectively.

All SuDo are depicted on the last MVCT in order to have the "final anatomy" at the end of treatment. The OARs and PTV were re-contoured on this MVCT by an experienced radiation oncologist.

Table 2 Dose difference between planned dose and DayDo

Structure	Dose parameter	Absolute dose difference (Gy)[a]
Spinal cord	Max dose	0.03 (–4.0; 6.8)
	Dose 1cc	0.4 (–4.1; 2.5)
	Dose 0.1cc	–0.5 (–0.5; 2.7)
Spinal cord +5 mm	Max dose	–1.2 (–6.9; 8.3)
	Dose 1cc	–0.06 (–5.5; 8.0)
PG total	Mean dose*	1.9 (–3.3; 7.3)
	Dose 1cc	–0.8 (–5.2; 3.1)
Mandible	Max dose	–0.7 (–8.7; 1.2)
	Mean dose	–0.2 (–4.9; 3.6)
	Dose 1cc	–0.5 (–5.1; 2.8)
PTV	Max dose	–0.6 (–3.0; 1.3)
	Min dose	2.4 (–12.6; 13.2)
	Mean dose	0.05 (–0.3; 1.0)
	Dose 1cc	–0.02 (–1.1; 1.0)

[a]median (min; max)
*indicates statistical significance with p-value <0.05

The relative dose differences (in %) between the less time-consuming SuDo (MVCTx2, x5, and x10) compared to the actual dose (DayDo) were assessed using the following formula:

$$\Delta\text{Dose} = \frac{(\text{SuDo} - \text{DayDo})}{\text{DayDo}} \times 100$$

For evaluation purposes, all SuDo and the 1st MVCT dose—i. e., the planned dose—were exported to the Eclipse planning system using DICOM-Export. We assessed the volume changes for the PTV, ipsilateral- and contralateral parotid gland (ipsilateral PG, contralateral PG), both parotid glands (PG total), mandible, spinal cord (SC), and spinal cord +5 mm (SC+5 mm). For the PG we assessed the mean dose (Dmean) and dose to 1 cm^3 (D1cc); for the SC and SC+5 mm the maximum dose (Dmax), D1cc, and the dose to 0.1 cm^3 (D0.1cc). For the mandible we assessed Dmean, Dmax, and the minimum dose (Dmin), and for the PTV Dmin, Dmax, Dmean, and D1cc were assessed.

The statistical analyses were performed with IBM SPSS Statistics 23.0 (SPSS Inc., NY, USA) and Windows Excel 2013 (Microsoft, Redmond, WA, USA). For description purposes, the median values with min and max for dose difference are reported. The assessment of statistical significance was performed by using the Wilcoxon signed rank test. Furthermore, to determine the existence of a correlation between the volume changes and dose changes, the Spearman's correlation coefficient was used. All statistical tests were performed two sided and a p-value of 0.05 (5%) was considered to indicate statistical significance.

Results

Comparison of planned dose vs. applied dose

There was a significant relative volume change during the course of treatment, with –22.1% (range –34.8 to 5.2%) and –19.5% (–31.5 to 15.8%) for the ipsilateral and contralateral PG, respectively. On average, a daily volume decrease of 0.7%/d for the ipsilateral and 0.6%/d for the contralateral PG was calculated. During the course of treatment, the PTV volume decreased by 2.6% (–16.7 to 0.2%), with a mean calculated volume decrease of 0.1% per day. Furthermore, there was a statistically significant correlation for the volume losses of the ipsilateral and contralateral PG ($p = 0.002$) during the course of treatment. No significance was detected between the volume losses of PG total and the PTV. No volume changes were detected in the SC or the mandible between the first and the last MVCT.

Table 2 depicts the dose differences between the planned dose (1st MVCT) and the DayDo. Only the PGs showed a significant dose difference between planned dose and DayDo ($p = 0.04$), with a dose difference of more than 4 Gy in 33% of our patients. No significant differences were measured between the planned dose and the DayDo for the PTV, spinal cord, the SC+5 mm, and the mandible. There was no statistically significant correlation between the volume loss and the dose differences.

Comparison of the DayDo scenario to less time-consuming scenarios

Fig. 1 depicts the relative dose difference between the less time consuming SuDo compared to DayDo. For the Dmax of the SC there was a statistically significant dose difference for MVCTx2 compared to DayDo. Regardless of this, the dose difference between each SuDo and DayDo of the SC Dmax was below –1.5%. For the Dmax of the SC+5 mm, the relative dose differences between the SuDo and DayDo was below –0.5%. There was a statistically significant difference for MVCTx10 Dmean of the mandible but the relative dose differences for each SuDo compared to DayDo were small (<0.5%). The ipsilateral and contralateral PG showed only a median dose difference for Dmean of ±1%. For the PTV there were only small median dose differences for Dmean between DayDo and the different SuDo of below –0.5%.

Table 3 depicts the median absolute dose differences between the different SuDo and DayDo. Less time-consuming SuDo scenarios showed statistically significant median dose differences for MVCTx2 (SC Dmax), for MVCTx5 (SC+5 mm Dose1cc) and for MVCTx10 (SC+5 mm Dose1cc) as compared to DayDo. Furthermore, statistically significant dose differences between DayDo and the different SuDo occurred for the mandible, con-

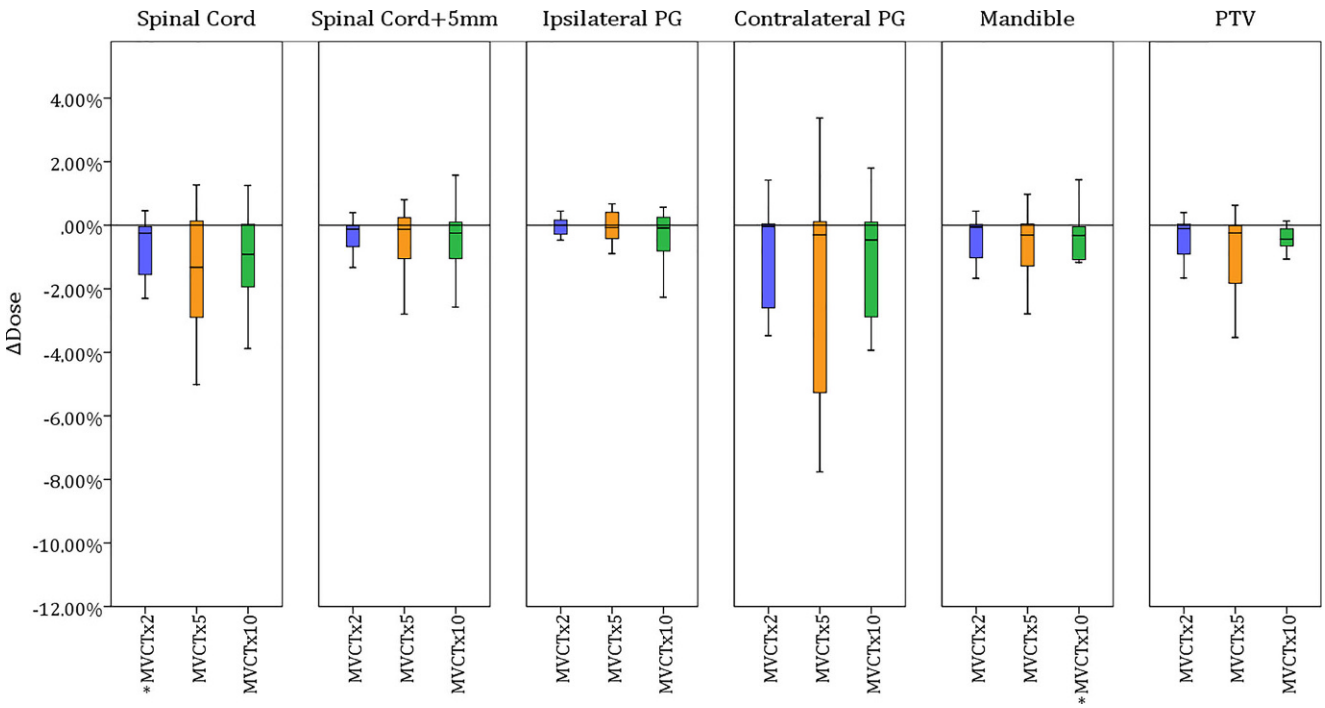

Fig. 1 Relative dose differences of the less time-consuming summation dose scenarios compared to DayDo. The figure depicts the relative dose differences between DayDo and MVCTx2 (*blue*), MVCTx5 (*orange*), and MVCTx10 (*green*). A zero percent on the y axis would mean the DayDo and the depicted SuDo scenario are identical, i.e., 0% difference. For spinal cord and spinal cord +5 mm the Dmax, for the parotid glands (*PG*), mandible, and planning target volume (*PTV*) the Dmean is shown (*indicates results with a statistically significant difference)

Table 3 Dose differences in Gy between less time-consuming SuDo and DayDo

Structure	Dose parameter	Absolute dose differences to DayDo (in Gy)[a]		
		MVCTx2	MVCTx5	MVCTx10
Spinal Cord	Dmax	–0.1* (–2.3; 0.2)	–0.49 (–3.7; 0.6)	–0.31 (–2.3; 0.5)
	Dose 1cc	–0.09 (–1.2; 0.2)	–0.33* (–2.6; 0.7)	–0.40* (–3.7; 0.3)
Spinal cord +5 mm	Dmax	–0.06 (–0.8; 0.2)	–0.07 (–1.6; 0.4)	–0.13 (1.4; 1.0)
	Dose 1cc	–0.04 (–1.0; 2.8)	–0.52* (–2.0; 0.6)	–0.47* (–2.8; 0.5)
Ipsilateral PG	Dmean	0.00 (–0.7; 0.2)	–0.01 (–1.5; 0.6)	–0.05 (–0.7; 0.3)
	Dose 1cc	0.00 (–1.2; 0.2)	–0.05 (–2.6; 0.8)	–0.13 (–1.3; 0.2)
Contralateral PG	Dmean	–0.01 (–1.1; 0.4)	–0.01 (–2.4; 1.0)	–0.17 (–1.2; 0.03)
	Dose 1cc	–0.06 (–1.9; 0.5)	–0.11 (–4.1; 1.2)	–0.66* (–2.1; 0.6)
Mandible	Dmean	–0.03 (–1.1; 0.2)	–0.07 (–2.4; 0.4)	–0.20* (–1.2; 0.1)
PTV	Dmean	–0.07 (–1.0; 0.3)	–0.16 (–2.1; 0.4)	–0.28 (–1.0; 0.1)
	Dmax	0.00 (–0.1; 0.8)	0.03 (–0.4; 0.2)	0.01 (–0.4; 0.9)
	Dmin	–0.04 (–1.5; 0.1)	–0.20* (–3.4; 0.3)	–0.18* (–2.3; 1.0)
	Dose 1cc	0.01 (–0.1; 0.2)	–0.03 (–0.3; 0.3)	–0.03 (–0.3; 1.3)

[a]median (min; max)
*indicates statistical significance with p-value <0.05

tralateral PG, and PTV. Overall, median dose differences of the OARs and PTV for all SuDo compared to DayDo were below 1 Gy.

Discussion

In this study a significant volume change was shown for the ipsilateral and contralateral parotid gland (–22.1% and –19.5%) and the PTV (–2.6%) during therapy. A significant correlation between the shrinkage of both parotid glands during the course of treatment was shown. Several authors have published similar results with a significant decrease in

volume of the parotid glands [6, 19, 24–27] or PTV [19, 24, 26] during the course of treatment.

In the present study the PTV was always sufficiently covered. The dose difference between DayDo and the planned dose regarding the PTV (mean dose) was very small (0.05 Gy) and thus not clinically relevant. However, with regard to OARs and especially the PGs, a significant dose difference between the actual and the planned Dmean (1.9 Gy) was detected. Several authors have described similar results in definitive RT for patients with H&N cancers [11, 18, 28]. Hunter et al. [18] treated in their prospective study 18 patients with stage III–IV OPC with definitive IMRT with a prescription dose of 70 Gy. They calculated the actual delivered dose on daily cone beam CT scans (CBCT) through deformable image registration (DIR) and compared the cumulative delivered dose to the planned dose. They reported an increase in PG dose of 0.92 Gy during the course of treatment. 11% of the parotid glands showed an increase of more than 4 Gy. In this study, in 33% of the patients a dose difference of more than 4 Gy appeared for the PGs between the actual and planned dose. Hermans et al. [28] treated 27 patients, 20 having different types of H&N cancer and 7 having nasopharyngeal cancer (NPC), with volumetric modulated radiotherapy (VMAT) in their department. Dose recalculations and summations were performed on weekly kVCTs. They reported a significant dose difference to the planned dose for the cumulative PG Dmean by 1.1 Gy for the NPC patients. The highest dose differences were between the mean PG doses at the last weeks of the treatment (weeks 5, 6, 7) and the planned dose. Regarding the other H&N cancer patients, no significant differences were described. In contrast to our results, Ho et al. [17] reported a non-significant dose difference between the planned and delivered contralateral PG Dmean and SC Dmax of 0.2 Gy and 1.1 Gy in a study of ten patients receiving a 65 Gy IMRT. They recalculated and summed up the weekly doses and depicted them on the performed CBCT. Inconclusive data are available on dose improvement by ART and on which patients should undergo ART [11, 13, 17, 24, 29]. One of the main impediments in defining the best approach for ART is the time consumption of daily dose recalculations.

To our knowledge, this is the first study that analyzed the accuracies of less time-consuming approaches as compared to the daily dose (gold standard). In the present study we showed that there were only small median differences (<2%) for the OARs and PTV between the DayDo and the different SuDo. There were some statistically significant differences between the DayDo and the other SuDo scenarios (Table 3), but with a mean dose difference below 1 Gy, they are not clinically relevant in most of the cases. A higher frequency of dose recalculations is closer to DayDo (for e. g., for ipsilateral and contralateral PG), but since the absolute difference is very low, dose recalculations every fifth fraction are applicable. Nonetheless, there are some exceptions. We would recommend patients with doses that are close to the tolerance dose of the OARs to be monitored more closely. In these cases, we recommend daily or every-second-day recalculations to observe whether dose differences occur.

In our study, we showed an applicable way of identifying patients in whom dose differences occur, especially when daily deformable image registration is not implemented in the hospital and thus daily calculations are not feasible during routine treatment. Prospective clinical trials have to be conducted to prove that the patients identified with our recalculations will benefit using ART.

The retrospective design, heterogeneity of our patients (PTV dose variation 64.0–70.4 Gy), and the small sample size constitute limitations of our work. Furthermore, the dose recalculations (DayDo and different SuDo) are rigidly depicted on the last contoured MVCT. However, from our point of view, the methods used in our study to reflect the actual dose (DayDo) and the different SuDo were applicable and similar methods have been used by several authors to compare the actual dose to the planned dose [26, 28, 30].

Conclusion

A statistically significant increase in dose to the parotid glands compared to the planned dose was shown. However, adequate PTV coverage was given at any time. Daily dose recalculations are the most precise procedure to assess dose differences between the actual and the planned dose.

In our opinion, dose recalculations at every fifth (MV)CT, with only a median difference (<2%) to the gold standard (DayDo), are a sufficient and time-saving way to identify patients in whom dose differences appear and ART should be performed.

Conflict of interest S. Kampfer received 2015 a professional fee from Accuray. S. Wagenblast, K.J. Borm, S.E. Combs, S.U. Pigorsch, and M.-N. Duma declare that they have no competing interests.

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