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Automatic treatment planning improves the clinical quality of head and neck cancer treatment plans

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A B S T R A C T

Background: Treatment plans for head and neck (H&N) cancer are highly complex due to multiple dose prescription levels and numerous organs at risk (OARs) close to the target. The plan quality is inter-planner dependent since it is dependent on the skills and experience of the dosimetrist. This study presents a blinded prospective clinical comparison of automatic (AU) and manually (MA) generated H&N VMAT plans made for clinical use.

Methods: MA and AU plans were generated for 30 consecutive patients in Pinnacle® using the IMRT optimisation module and the new Autoplan module, respectively. The plan quality was blindedly compared by three senior oncologists and the best plan was selected for treatment of the patient. Planning time was measured as the active operator time used. The plan quality was analysed with DVH metrics and the dose delivery accuracy validated on the ArcCheck phantom.

Results: For twenty-nine out of the thirty patients the AU plan was chosen for treatment. Target doses were more homogeneous with the AU plans and the OAR doses were significantly reduced, between 0.5 and 6.5 Gy. The average operator time spent on creating a manual plan was 64 min which was halved by Autoplan. The AU plans were more modulated as illustrated by an increase in MUs, which might cause the slightly lower pass rate of 97.7% in the ArcCheck measurements.

Conclusions: Target doses were similar between MA and AU plan, while AU plans spared all OAR considerably better than the MA plans.

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1. Introduction

Radiotherapy of head and neck (H&N) cancer is challenging due to complex shaped targets situated close to numerous radiosensitive organs at risk (OARs). Thus, a high quality H&N plan is conformal, has homogeneous target doses according to prescription and as low doses to OAR’s as possible with a proper balance between target coverage and OAR doses. The plan quality has been shown to directly affect treatment outcome in clinical trials, which in itself has created a new era of quality assurance [1,2].

Obtaining high quality plans is a demanding task. A high quality treatment plan relies on the skills and experience of the dosimetrist, which can vary greatly. Even for the most experienced dosimetrist, time pressure to deliver a clinically applicable dose plan may result in treatment plans of inferior quality than desired. With several OARs in play in the head and neck region, there may be a tendency to focus more on specific OARs and thereby disregarding the importance of other risk organs during the optimisation process. This results in plans with acceptable target coverage and adequate sparing of e.g. the spinal cord and parotids, but for which e.g. the oral cavity and constrictor muscles are irradiated to higher levels than necessary [3]. This is not necessarily due to lack of skills or experience of the dosimetrist, but merely due to the ability to focus on only a limited number of objectives at a time.

The user-dependant variation of plan quality can be improved by applying specific guidelines which define the minimum standards for dose targets and OARs [4]. Such guidelines can to some extent reduce the overall variation of the dosimetrist-dependant plan quality, but they do not guide the dosimetrist towards the

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optimal plan for the specific patient – more towards as guideline acceptable level.

Recently, new techniques have been applied for head and neck treatments such as Volume modulated arc therapy (VMAT) [5], Tomotherapy [6] and proton therapy [7]. These technical developments have increased the degrees of freedom compared to intensity modulated radiotherapy (IMRT) and thereby made it possible to improve the plan quality. Various approaches have been made for an automatic search for the optimal patient plan such as atlas-based planning (RapidPlan [8]), ideal dose distribution estimation (PlanIQ [9] and Erasmus-iCycle [10]), and template-based optimisation as used in AutoPlanning (AP) provided by Pinnacle3 [11,12].

In a previous study, we retrospectively evaluated a research version of Autoplan in seven field step and shoot IMRT (ssIMRT) plans for H&N treatment. The results were promising based on DVH analysis as well as within a blinded clinical plan evaluation [12]. Since the study was made as a retrospective study, the plans delivery were not dosimetrically validated, and the plans were ssIMRT and not VMAT which is the current clinical standard in our department.

This prospective study presents a blinded comparison study of automatic and manually generated H&N VMAT plans made for clinical use utilizing the clinically released version of Autoplan. Finally, the dosimetric accuracy and deliverability of the generated plans were validated.

2. Material and methods

All patients (n = 30) referred to curative H&N radiotherapy in August and September 2015 were included prospectively. The demographics (Table 1) are representative for the general entry of head and neck patients in the cancer centre, though with slightly more unknown primary tumours and less oral cavity tumours. No patients were censored from the study.

All patients followed the standard process of radiotherapy planning, i.e.: immobilisation, CT simulation (slice thickness of 3 mm and in plane voxel size of 1 mm × 1 mm), contouring by a radiologist and oncologist before the dosimetrist created a MA VMAT plan and an AU VMAT plan. Treatment planning was performed in accordance with the Danish Head and Neck Cancer Group’s guidelines (DAHANCA – Version 2013 ver. 2.0 [13]) and each dose plan included up to three dose levels of 66 Gy (PTV1), 60 Gy (PTV2) and 50 Gy (PTV3) in 33 or 34 fractions. All plans used the simultaneous integrated boost technique and a full 360 degree VMAT arc for bilateral targets and a 200–220 degree VMAT arc for unilateral targets.

The MA plans were optimised according to standard clinical practice, with a script template for optimisation objectives. Manual adjustment of the template predefined objective values were performed a minimum of 3 times guided by the patient-specific possibilities as determined by the dosimetrist.

The AU plans were created by the Autoplan software available in Pinnacle3 version 9.10, using settings shown in Table 2. The spinal cord and brain stem had higher priority than the target coverage (non-compromise); and the remaining OARs were automatically prioritised according to the proportion of overlap with the target (high if <25% overlap, medium if 25–50% overlap and low if >50% overlap). After AU optimisation, a minor manual fine-tuning of the plans was performed for all plans. No direct comparisons between the two plans were performed before both plans were finalised, however the bias of the same dosimetrist making both plans was minimised by one half of patients having the MA plans created first and for the other half of the patients having the AU plan was created first. Dose calculation was performed with the Pinnacle3 collapsed cone algorithm with a dose grid resolution of 3 mm and a control point spacing of 2 degrees.

The planning techniques were blinded before MA and AU plans were presented at the daily clinical radiotherapy conference. Clinical evaluation was performed based on isodoses shown on
axial images, DVHs, and a protocol compliance scorecard derived from the DAHANCA guidelines. Plan selection was performed by three senior H&N oncologists and overviewed by oncologists of other treatment sites, medical physicists and RTTs.

To supplement the clinical evaluation, the operator time for the dosimetrist was recorded, and delivery accuracy of the plans was validated on an ArcCheck phantom using the pass rate of a gamma evaluation (3% of max measured dose, 3 mm).

Quantitative dosimetric evaluation of the treatment plans was performed on Dose Volume Histograms (DVHs) extracted from the planning system. The average DVH was calculated for each type of treatment plan as the average of the patient-specific DVH values at each dose level. The DVH analysis was performed for all target volumes as well as for the parotid glands, submandibular glands, the mandible, oral cavity, lips, larynx, thyroid, brain stem, and spinal cord. To evaluate radiation dose to the remaining healthy tissue, a DVH evaluation of all healthy tissues was performed. In contrast to the previous DVH evaluations, this evaluation was performed in absolute volume to compensate for a difference of the CT scanned volume of each patient (relative values would depend on the scanned volume).

The mean OAR doses and target conformity index (CI = D95%/D prescription) and homogeneity index (HI = D2/D prescription) were calculated.

### 2.1. Statistics

Differences were tested using Wilcoxon matched-pair signed-rank with a significance level of 5%. To indicate dose regions in the DVHs for which statistically significant differences exist, a Wilcoxon matched-pair sign rank probability curve was calculated as in Bertelsen et al. [5].

### 3. Results

In 29 of the 30 plans, the AU plan was chosen for clinical application (p < 0.001).

All plans adhered to the critical objectives for targets and critical OAR (spinal cord and brain stem).

In terms of target coverage, the AU plans had a higher mean dose to all three PTVs. However, the D2 was lower for the AU plans.

The HI showed that each dose plateau was more homogenous for the AU plans compared to MA. The HI of the AU plans was more than twice that of AU plans.

### 4. Discussion

In 29 of the 30 patients the AU plan was selected. In most cases, the plan selection was straightforward with the AU plans clearly superior in the dose range 10–45 Gy for all organs. Average DVH are shown in Fig. 1 for six of the OAR and in Fig. 2 for four ring structures surrounding the targets. During the clinical plan evaluation, the general impression was that the AU plan was visually more conform, spared OAR better and had steeper dose fall away from the targets. The irradiation of OARs was in particular reduced for the submandibular glands. In Fig. 3 a screen dump of a representative patient is shown. Here the sparing of the right submandibular gland, the extended oral cavity and the spinal cord is mainly seen for the dose spillage iso-dose curves of 40 and 30 Gy.

The only manual plan selected for clinical use was a non-typical H&N case for a thyroid cancer involving level VII lymph nodes. That is, the plan included a relatively large volume of lung tissue, which was irradiated to a lesser degree by the manually created plan.

Compared to the MA plans, a larger degree of MLC modulation was observed for the AU plans which are reflected in an increased number of monitor units in the AU plans. The pass rate was 97.7% in AU plans compared with 98.4% for MA plans assessed by ArcCheck measurements (Table 5). The average beam-on-time of was 4 s longer in the AU plans. Mean operator time spent on MA was more than twice that of AU plans.

Three of the 30 patients had critical OAR adjacent to the PTV1 (high dose target) which required more operator time for both the MA and AU plans resulting in a relatively large variation in operator time.

### Table 3

<table>
<thead>
<tr>
<th>Organ</th>
<th>Unit</th>
<th>Autoplan Mean</th>
<th>Autoplan STD</th>
<th>Manual Mean</th>
<th>Manual STD</th>
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<td>2.1</td>
<td>25.0</td>
<td>2.3</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>CT3</td>
<td>Gy</td>
<td>31.2</td>
<td>2.3</td>
<td>32.5</td>
<td>2.4</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

All doses are normalised to prescription dose (68, 66, 60 or 50 Gy). * Conformity index calculated from the full PTV.
Fig. 1. Mean DVH of six OAR for all 30 patients. Red line is MA plan and blue line is AU plan. The grey $p$-value curve illustrates dose regions from around 10 to 45 Gy where AU plans significantly spare the organs more. The mean dose reductions for these six organs are between 2 to 5 Gy. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)
Fig. 2. Mean DVH of four ring-ROI’s for all 30 patients. Black line is MA plan and dotted line is AU plan. Red line is MA plan and blue line is AU plan. The grey $p$-value curve illustrates where the AU and MA plans are significantly different.

Fig. 3. Screen dump comparison of a representative patient. Iso-dose curves are 105% (green), 100% (blue) and 95% (yellow) for the three dose prescriptions (68 Gy, 60 Gy and 50 Gy). Dose spillage iso-dose curve are 40 and 30 Gy. The GTV tumour and GTV lymph node are shown in red and orange. CTV1 is shown in light orange, with corresponding PTV1 in colourwash purple. Colourwash blue and light blue represent PTV2 and PTV3. The contour of the extended oral cavity is brown. The right submandibular gland and spinal cord are shown in green and the PRV spinal cord in light brown. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)
plan is then created by comparing targets and OAR anatomy with approaches. One being the atlas based model, where a group of targets set to "none compromise" the max dose could exceed the tolerance slightly for patients with targets close to the OAR. This was done to reduce the mean CTV1 dose to match the prescription dose within ±1%, as recommended within the DAHANCA guidelines. The "need" of an additional constraint on the high dose volume seems related to the difference between dose prescription doses for HPV positive tumours [17,18]. This is desired because the treatment dose could be lowered and hence the toxicity could be reduced and potentially improving the quality of life for the patients. With Autoplan the dose reduction to the OAR is around 10%, which is roughly the same dose reduction the HPV positive de-escalation trials are aiming for. The benefit of the Autoplan, however, is for all H&N cancer patients and comes with no higher risk of recurrences, since the target doses are maintained, hence, AU can be perceived as "free of charge".

Another benefit of AU planning is in the adaptive radiotherapy setting. In this study replanning, during treatment, was necessary for 3 out of the 30 patients. Autoplan was also used to create the new plans; however they were not included in the analysis. The plans showed similar sparing of OAR and were substantially quicker to produce compared to conventional manual replans.

The AU plans achieve improved planned dose distributions, compared to MA, by adding more MLC modulation which can be observed by an average increase of 75 MU per plan in this study. This propagates into a slightly lower pass rate measure on the ArcCheck phantom, however all plans were clinically acceptable. Comparison to other TPS (Monaco or Eclipse) the number of MU used by Autoplan for head and neck is still low [19–21].

In Autoplan the prioritisation of OAR only has four levels (low, medium, high, non-compromise), which for some specific patients will be too low and therefore it can be difficult to find the appropriate compromise between target and multiple OARs. The automatic nature of Autoplan makes manual interaction time-consuming and therefore, a generic template is of vital importance.

5. Conclusion

In conclusion, the Autoplan-generated treatment plans were selected in 29 of 30 cases for clinical treatment of head and neck cancer when selected blindly head-on with the standard manual planning method. The target coverage was similar with maintained treatment doses while average OAR mean doses were reduced between 0.5 and 6.5 Gy. The manual time spent on planning was reduced by a factor of two and the delivery of the AU plans was of high clinical quality, though the pass rate was slightly lower compared to MA plans. From these results, AU planning has now been implemented as the clinical standard of head and neck treatment in our centre.
Authors’ contributions

CRH and AB collected data, performed the data analysis and drafted the manuscript. IH helped create plans and collect the data. RZ, NG, JJ and JGE did the blinded clinical evaluation of the manual and automated optimised plans. CRH, AB and CB conceived the study. All authors read and approved the final manuscript.

Competing interests

The authors declare that they have no competing interests.

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