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Short communications and technical notes

Investigating the feasibility of using Ethos generated treatment plans for head and neck cancer patients

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ABSTRACT

The Varian Ethos treatment platform is designed to automatically create complex RT treatment plans, reducing both workload and operator variability in plan quality. The aim of this study is to evaluate the quality of Ethos-generated head and neck (H&N) treatment plans.

Ethos plans were created for ten previous H&N patients and these were compared with the original clinical plans generated in Eclipse. Ethos automatically creates several plans with different field arrangements for each patient. All plans were compared quantitatively using: dose-volume metrics; dose conformity; dose heterogeneity and monitor units (MU). In addition, two H&N Oncologists assessed the clinical acceptability of the Ethos plans.

Consultant 1 judged there to be at least three clinically acceptable Ethos plans for 9 out of 10 patients reviewed. Consultant 2 approved of at least two Ethos plans for 5 out of 5 patients reviewed. The Ethos plans' average dose metrics were comparable to the clinical plans. The average plan MU was similar for Eclipse and Ethos VMAT plans. The average plan MU for Ethos IMRT plans was larger with respect to all VMAT plans.

The Ethos Treatment Planning system is capable of automatically creating good quality treatment plans for a range of H&N cancer patients.

Introduction

The fundamental principle of Radiotherapy treatment has never changed: deliver an efficacious dose to the treatment target, whilst minimising the dose to surrounding healthy tissue and organs at risk (OARs). Radiotherapy treatment planning systems (TPSs) are a vital component in adherence to this principle. Most TPSs can produce highly complex intensity modulated radiotherapy (IMRT) and volumetric modulated arc therapy (VMAT) treatment plans, which can effectively 'sculpt' high dose envelopes to target volumes. These highly conformal dose distributions have the added benefit of minimising the dose to surrounding healthy tissue, thus reducing the risk of harmful side effects. The complex dose distributions are created by the linear accelerator (linac) continually modulating multi-leaf collimator (MLC) positions for IMRT. As well as MLC motions, the dose rate and gantry speed are continually changing for VMAT deliveries.

The TPS utilises computational algorithms to optimise & calculate the dose distribution, based on some initial dose requirements from the operator (inverse planning). Most TPSs still require an operator to manually 'drive' the optimisation process. This involves the operator assigning weighted dose objectives to planning target volumes (PTVs) and OARs. The more weight assigned to an objective, the higher its priority. This process is generally iterative and relies on trial-and-error so it can often be difficult and time consuming to create a high quality treatment plan.

oART – Online adaptive radiotherapy, DIR – Deformable image registration, IOE – Intelligent optimisation engine, DSI - Dice similarity index

Varian Medical Systems (VMS Palo Alto, California, USA) has recently released a new treatment planning and delivery platform called Ethos [1].

The on-line adaptive radiotherapy (oART) process involves creating a new treatment plan for every treatment session in order to account for patients' internal anatomy at time of treatment [2–4]. The new planning image is acquired using the linac's CBCT system, which is then registered to the original planning image in order to create a synthetic CT. AI-based or deformable image registration (DIR) structures are then automatically contoured onto the synthetic CT. An adaptive IMRT or VMAT

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plan is then automatically created using Ethos' proprietary intelligent optimisation engine (IOE). The IOE effectively replaces the planning operator by driving the photon optimisation (PO) algorithm, using an input of pre-set dose constraints. The IOE then controls and monitors the optimisation by trying different dose objectives and weights until a suitable solution is found.

The IOE is also used in the initial treatment planning of both ART and image-guided radiotherapy (IGRT) patients. The IOE's automatic capabilities offer the opportunity to reduce both inter- and intra-operator variability in plan quality for a given patient group. The automatic optimisation process is typically much quicker than a manual operator, thus there is potential to save time and staff resources. These benefits can only be attained if the Ethos system can provide treatment plans of comparative quality to clinically accepted plans created using conventional TPSs. Other groups have investigated the efficacy of Ethos generated treatment plans for pelvis sites [2,5–6].

The primary aim of this study is to assess the feasibility of using Ethos auto-generated treatment plans for head and neck (H&N) cancer patients. This assessment involved retrospectively comparing a range of Ethos IMRT & VMAT plans with clinically treated reference VMAT plans.

Materials and methods

A total of 10 previous H&N patients were selected for this study (Table 1). The Ethos default beam geometry treatment plans were generated for all 10 patients. For bilateral patients (N = 5), this resulted in five Ethos treatment plans: 7, 9 & 12 equidistantly spaced field IMRT plans and 2 and 3 full arc VMAT plans. In addition to the five 'bilateral' plans, the lateral patients had two additional plans: a lateral 7 field IMRT plan, and a partial 2 arc VMAT plan.

All treatment plans were exported back to Eclipse in order to compare them side-by-side with the reference Eclipse VMAT plan. Two H&N consultants reviewed the Ethos plans - consultant 1 (C.1) reviewed all 10 patients, consultant 2 (C.2) reviewed 5. For each plan review, the consultant would make a binary decision as to whether the plan was clinically acceptable or not. Prior to consultant reviews, the Ethos plans' dose constraints were assessed. If an Ethos plan failed to meet a dose constraint that the reference plan successfully met, then the plan was automatically rejected.

The Ethos plans were also quantitatively compared to their respective Eclipse plans using dose volume histogram (DVH) metrics, Homogeneity Index (HI) [7], Dice Similarity Index (DSI) [8], 50 % & 20 % isodose volumes, and monitor units (MU).

The DVH metrics compared in this study are a sub-set of the typical important H&N clinical goals. This sub-set does not include optical structures, as all 10 patients' PTVs were sufficiently distant from these structures that they received clinically negligible doses.

The Homogeneity Index, HI, is defined in ICRU-83 [7]:-.

$$HI = \frac{D_2 - D_{98}}{D_p} \quad (1)$$

Where D_2 and D_{98} represent the PTV doses received by 2% and 98% of the PTV volume respectively. D_p is the prescribed PTV dose.

The Dice Similarity Index, DSI, was used in this study as a measure of PTV dose conformity. In general terms the DSI, for two volumes A & B, is defined as:-.

$$DSI = 2\frac{A \cap B}{A + B} \quad (2)$$

A value of 1 represents complete overlap and a value of 0, no overlap at all. For the patients' high-dose PTV (PTVHD), the two volumes used to calculate the DSI were the PTV and the isodose surface representing 95% of the dose prescribed to the high dose PTV.

The medium- and low-dose PTVs (PTVMD and PTVLD) abut the high-dose PTV, so the difference of the 95% and 107% isodose surfaces was calculated, where the percentages are relative to the prescribed dose for the given PTV. The volumes calculated in this way were used together with the relevant PTV to calculate the DSI. This conformity metric was chosen for its ability to assess conformity for lower level PTVs. The quantitative metrics were all averaged over all applicable patients, for each plan type (Eclipse and Ethos).

All plans were generated using Ethos TPS v2.1 or Eclipse v16.1. Both planning systems utilised AcurosXB v16.1 for the dose calculation (dose to medium), as well as using the same photon optimisation algorithm (PO v16.1). All reference plans were created by three dosimetrists, who had at least 32 months of work experience in treatment planning. All plan optimisation objectives were inserted 'manually' i.e. Eclipse's Knowledge-Based planning algorithm, RapidPlan, was not used.

Results

Plan reviews

In total, sixty Ethos treatment plans were generated. Table 1 shows the consultant review results.

C.1 judged there to be at least three clinically acceptable Ethos plans for 9/10 patients. C.1 did not find any of the Ethos plans acceptable for patient 10 (Fig. 1). Overall 80% of the Ethos-generated plans were deemed clinically acceptable by C.1. For bilateral and lateral patients, C.1 approved of 65% and 91% of Ethos plans respectively. C.1 deemed 89% of Ethos IMRT plans clinically acceptable. The percentage of clinically acceptable VMAT plans for C.1 was 68%.

C.2 approved of at least two Ethos plans for 5/5 patients reviewed. With the exception of patient 10, C.2 deemed a minimum of four Ethos plans clinically acceptable. Overall 72% of the Ethos-generated plans were deemed clinically acceptable by C.2. For bilateral and lateral patients, C.2 approved of 67% and 79% of Ethos plans respectively. C.2 determined that 94% of Ethos IMRT plans were clinically acceptable.

Table 1
Consultant plan review results. The green and red dots represent 'clinically acceptable' and 'not clinically acceptable' respectively. The patient rows with 2 dots indicate that both consultants reviewed the patient, with consultant 1's dot always on LHS. The patient rows with 1 dot indicate that only consultant 1 reviewed the patient. Patients 3–5 & 7–8 had lateralised sites and thus two extra Ethos plans were generated.

			Ethos - IMRT				*Ethos - VMAT*		
Patient	**Site**	**Fractionation**	**7 Fields**	**9 Fields**	**12 Fields**	**7 Fields (Lat)**	**2 Arcs**	**3 Arcs**	**2 Arcs (Lat)**
1	Oropharynx	65 Gy in 30 #	🟢🟢	🟢🟢	🟢🟢	*N/A*	🟢🔴	🟢🟢	*N/A*
2	Oropharynx	65 Gy in 30 #	🟢	🟢	🟢	*N/A*	🟢	🔴	*N/A*
3	Parotid Right (Lat)	66 Gy in 33 #	🟢	🟢	🟢	🟢	🟢	🟢	🟢
4	Tongue Left (Lat)	60 Gy in 30 #	🟢🟢	🟢🟢	🟢🟢	🟢🟢	🟢🔴	🟢🟢	🔴🔴
5	Parotid Right (Lat)	24 Gy in 12 #	🟢🟢	🟢🟢	🟢🟢	🟢🟢	🟢🟢	🟢🟢	🔴🔴
6	Larynx	70 Gy in 35 #	🟢🟢	🟢🟢	🟢🟢	*N/A*	🔴🔴	🟢🟢	*N/A*
7	Parotid Left (Lat)	60 Gy in 30 #	🟢	🟢	🟢	🟢	🟢	🔴	🟢
8	Parotid Right (Lat)	66 Gy in 33 #	🟢	🟢	🟢	🟢	🟢	🟢	🟢
9	Oral Cavity	60 Gy in 30 #	🔴	🟢	🟢	*N/A*	🔴	🟢	*N/A*
10	Larynx	65 Gy in 30 #	🔴🟢	🔴🟢	🔴🔴	*N/A*	🔴🔴	🔴🔴	*N/A*

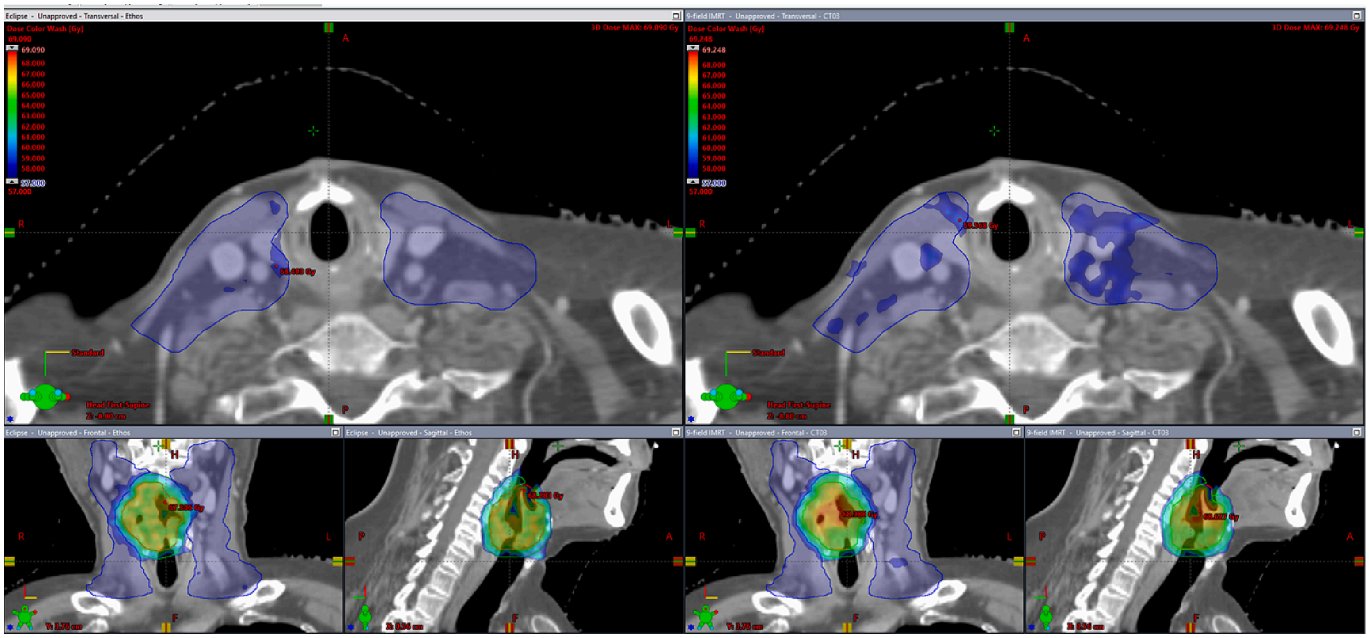

Fig. 1. Ethos plan evaluation example. Patient 10 (Larynx) 9-field IMRT plan (RHS) being assessed next to reference Eclipse plan. PTVLD (54 Gy in 30 #) shown in both plans. Doses of 57 Gy and above displayed.

The acceptable percentage rate for Ethos VMAT plans was 42%.

Dose metrics and indices

The average DVH metrics are shown in Table 2. The Ethos plans have a lower maximum plan dose on average, with respect to the clinical plans. The Ethos plans' average target coverage values (D99%) are also marginally better than the Eclipse plans. The Ethos plans tend to result in a higher D2% for the high dose PTV. However, D2% is comparable for Ethos and Eclipse plans for medium and low dose PTVs. The average maximum dose to the brainstem is slightly higher for the Ethos plans compared with the Eclipse plan. It should be noted that this average increase is a small fraction of typical brainstem dose tolerances for H&N radiotherapy treatments with 30 or more fractions. The average maximum dose to the spinal cord is comparable for all plan types. The average mean dose to larynx and oral cavity are again slightly higher for the Ethos plans. All other OAR average DVH metrics are comparable. The Ethos IMRT plans generally offer better target coverage than their VMAT counterparts. This is most pronounced for the low dose PTVs, which typically are the largest PTVs in a given treatment plan.

The PTV dose homogeneity for the Ethos plans is on average very similar (or slightly better) than the reference plan. The conformity of the dose to the PTVs (using DSI as a metric) is similar for all plan types, for both the high dose and low dose PTVs. The Ethos IMRT plans typically produce a DSI value very similar to the Eclipse plan for the medium dose PTV, indicating comparable conformity. The Ethos generated VMAT plans typically result in a significantly inferior conformity value with respect to the Eclipse plan. The average 50 % isodose volume is very slightly larger for the Ethos plans. The average 20 % isodose volume is comparable for all plan types.

The average MU for all VMAT plans are comparable. The average MU for the Ethos IMRT plans is significantly higher when compared to the Ethos and Eclipse VMAT plans.

Discussion

The results in Table 1 indicate that the Ethos generated viable plans for most patients. As C.2 only reviewed 5/10 patients, it is important to consider the plan review results for each consultant separately.

It is encouraging that C.1 approved of at least three Ethos plans for 9/10 patients. For C.2, there were at least two acceptable Ethos plans for each of the 5 patients that they reviewed.

Patient 10 was a particularly interesting case, as C.1 and C.2 disagreed on the clinical acceptability of the Ethos 7 and 9 field IMRT plans. It should be noted that there were also consultant 'disagreements' for patients 1 & 4, but these patients had a minimum of 4 other Ethos plans that both consultants agreed were acceptable. The primary reason that consultant 1 rejected the two IMRT plans for patient 10 was due to the large amount of 'high dose splash' (>57 Gy) received by the PTV54 (Fig. 1). Both the 7 and 9 field IMRT plans met all the same dose constraints as the Eclipse plan.

The ratio of unacceptable plans to acceptable is higher for the VMAT plans compared with the IMRT plans. The main reason for an Ethos VMAT plan to be rejected by a consultant was target coverage, particularly the lower dose PTVs. At this point it is still unknown why the Ethos TPS tends to generate VMAT plans with inferior target coverage compared with the IMRT plans. All default Ethos plans use the same optimisation objectives via the IOE. Perhaps the PO algorithm finds more optimal solutions with IMRT sliding window MLC motions. Assuming this variation in 'plan quality' between VMAT and IMRT is consistent for all H&N plans, it may be prudent to strongly consider generating only IMRT treatment plans for all future H&N patients. It should be noted that Ethos IMRT plans typically result in significantly higher MU compared to VMAT. This suggests these plans may be more complex to deliver and may initially require additional quality assurance checks.

The average DVH metrics for all patients are comparable for all plan types. The target coverage tends to be slightly superior for the Ethos plans when compared with the reference plan. This may be due to the targets' lower-limit planning directives in the H&N RT Intents. They were deliberately designed to be strict (in order to match with what we typically expect in Eclipse-generated plans). In general, the Ethos 2-arc VMAT plans' low PTV dose coverage is inferior to the rest of the plans.

Conclusion

The Ethos TPS is capable of automatically creating good quality treatment plans for a range of H&N cancer patients, without user

Table 2
Average values of important H&N DVH metrics and plan indices for all H&N plan types[1]. High dose (HD), medium dose (MD), and low dose (LD) PTV dose metrics are included. DX% (%) represents the minimum dose received (normalised to the prescription dose) by X % of the volume in question.

		Ethos - IMRT			*Ethos VMAT*			
	Ref. Eclipse	**7 Fields**	**9 Fields**	**12 Fields**	**7 Fields (Lat[5])**	**2 Arcs**	**3 Arcs**	**2 Arcs (Lat[5])**
Max. Dose (%)	107.6	106.4	106.5	106.2	106.2	106.9	106.9	107.4
PTVHD[2] – D99% (%)	94.6	95.4	95.6	95.5	95.4	95.0	94.8	95.4
PTVHD[2]– D50% (%)	100	99.9	99.9	99.9	99.9	99.9	100.0	99.9
PTVHD[2] – D2% (%)	102.9	103.8	103.6	103.5	103.2	103.5	103.5	103.2
PTVMD[3] – D99% (%)	96.2	98.0	98.0	98.0	*N/A*	98.3	98.3	*N/A*
PTVMD[3] – D50% (%)	102.8	103.8	103.6	103.6	*N/A*	103.9	103.8	*N/A*
PTVMD[3] – D2% (%)	108.6	107.9	107.7	108.0	*N/A*	108.1	108.0	*N/A*
PTVLD – D99% (%)	96.0	97.4	97.6	97.6	97.3	95.4	96.1	95.1
PTVLD – D50% (%)	100.8	101.1	100.8	100.8	100.6	101.3	100.9	100.3
PTVLD – D2% (%)	107.8	107.1	107.1	107.1	107.6	107.4	106.9	107.9
Brainstem[4] – Max. Dose (Gy)	17.7	20.3	20.4	20.1	15.6	20.0	19.4	13.2
Spinal Cord[4] – Max. Dose (Gy)	33.2	35.0	31.5	28.9	23.9	34.9	34.8	29.7
Mandible – Max. Dose (Gy)	63.8	61.6	61.7	61.2	63.2	62.5	61.6	64.7
Left Cochlea - Mean dose (Gy)	6.8	3.9	3.8	3.9	10.3	4.7	4.9	5.5
Right Cochlea - Mean dose (Gy)	6.8	4.0	4.1	4.4	6.0	4.5	4.3	5.3
Larynx - Mean dose (Gy)	34.2	36.4	35.0	36.6	34.9	39.1	39.7	31.4
Oesophagus - Mean dose (Gy)	16.2	17.9	17.3	17.3	16.5	16.5	16.2	13.7
Oral Cavity - Mean dose (Gy)	19.3	22.4	22.5	21.8	14.2	23.8	22.8	14.8
Left Parotid - Mean dose (Gy)	18.0	18.7	18.5	18.1	10.9	18.5	18.5	10.9
Right Parotid - Mean dose (Gy)	18.7	19.1	19.5	18.3	10.7	19.3	18.9	9.7
Trachea - Mean dose (Gy)	19.3	19.9	19.5	19.6	21.2	18.9	19.0	19.3
PTVHD – HI[2,98]	0.07	0.07	0.07	0.07	0.07	0.08	0.08	0.08
PTVMD – HI[2,98]	0.11	0.09	0.09	0.09	*N/A*	0.09	0.09	*N/A*
PTVLD – HI[2,98]	0.11	0.10	0.09	0.09	0.10	0.11	0.10	0.12
PTVHD – DSI[95]	0.87	0.88	0.88	0.88	0.90	0.88	0.89	0.91
PTVMD – DSI[95-107]	0.59	0.59	0.60	0.61	*N/A*	0.51	0.53	*N/A*
PTVLD – DSI[95-107]	0.81	0.80	0.80	0.81	0.78	0.81	0.82	0.80
50 % isodose volume (cc)	1282.8	1358.9	1332.5	1303.7	1004.41	1293.0	1253.7	960.9
20 % isodose volume (cc)	3320.36	3355.44	3308.59	3260.71	3004.82	3491.16	3412.71	2889.57
Monitor Units	536.0	1082.8	1248.9	1357.5	901.9	572.9	562.4	458.6

Footnotes 1, 2, 3, 4 and 5 here
[1]Average values acquired by including all patients applicable for the dosimetric quantity considered e.g. patient 5 only had Brainstem and Spinal cord contoured, patient 3 does not have a right parotid, etc. Therefore for all average values shown, N $\leq$ 10.
[2]Note that not all patients had a defined PTVMD.
[3]PTVHD for each of the ten patients: (1 $\times$ 70 Gy, 2 $\times$ 66 Gy, 3 X 65 Gy, 3 $\times$ 60 Gy, and 1 $\times$ 24 Gy).
[4]The maximum Brainstem and Spinal cord values for patient 5 are not included in the average calculation as their fractionation regime is significantly different to the other nine.
[5]The lateralised Ethos plans are only available for lateral site patients. I.e. N $\leq$ 5.

intervention. The Ethos generated plans also reduce operator variability. The Ethos IMRT plans are generally of better quality compared to the Ethos VMAT plans.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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