Dosimetric and radiobiological comparison of helical tomotherapy, forward-planned intensity-modulated radiotherapy and two-phase conformal plans for radical radiotherapy treatment of head and neck squamous cell carcinomas

¹S CHATTERJEE, FRCP, FRCR, FHEA, ¹N WILLIS, DCR(T), ²S M LOCKS, BSc, MIPEM, ²J H MOTT, MIPEM, PhD and ¹C G KELLY, FRCP, FRCR

¹Northern Centre for Cancer Care and ²Regional Medical Physics Department, Freeman Hospital, Newcastle upon Tyne, UK

Objectives: The usual radical radiotherapy treatment prescribed for head and neck squamous cell carcinoma (HNSCC) is 70 Gy (in 2 Gy per fraction equivalent) administered to the high-risk target volume (TV). This can be planned using either a forward-planned photon-electron junction technique (2P) or a single-phase (1P) forward-planned technique developed in-house. Alternatively, intensity-modulated radiotherapy (IMRT) techniques, including helical tomotherapy (HT), allow image-guided inversely planned treatments. This study was designed to compare these three planning techniques with regards to TV coverage and the dose received by organs at risk.

Methods: We compared the dose–volume histograms and conformity indices (CI) of the three planning processes in five patients with HNSCC. The tumour control probability (TCP), normal tissue complication probability (NTCP) and uncomplicated tumour control probability (UCP) were calculated for each of the 15 plans. In addition, we explored the radiobiological rationality of a dose-escalation strategy.

Results: The CI for the high-risk clinical TV (CTV1) in the 5 patients were 0.78, 0.76, 0.82, 0.72 and 0.81 when HT was used; 0.58, 0.56, 0.47, 0.35 and 0.60 for the single-phase forward-planned technique and 0.46, 0.36, 0.29, 0.22 and 0.49 for the two-phase technique. The TCP for CTV1 with HT were 79.2%, 85.2%, 81.1%, 83.0% and 53.0%; for single-phase forward-planned technique, 76.5%, 86.9%, 73.4%, 81.8% and 31.8% and for the two-phase technique, 38.2%, 86.2%, 42.7%, 0.0% and 3.4%. Dose escalation using HT confirmed the radiobiological advantage in terms of TCP.

Conclusion: TCP for the single-phase plans was comparable to that of HT plans, whereas that for the two-phase technique was lower. Centres that cannot provide IMRT for the radical treatment of all patients could implement the single-phase technique as standard to attain comparable TCP. However, IMRT produced better UCP, thereby enabling the exploration of dose escalation.

Received 12 April 2010
Revised 20 August 2010
Accepted 24 August 2010

DOI: 10.1259/bjr/53812025

© 2011 The British Institute of
Radiology

Background

Radiotherapy for head and neck squamous cell carcinoma (HNSCC) entails delivering a high radiation dose (70 Gy in 2 Gy fraction equivalent) to the high-risk area and a prophylactic dose to the cervical nodal chain at lower risk. Treating complex planned target volumes (PTV) while sparing adjoining organs at risk (OAR) can be challenging [1]. The benefits of linear accelerator-based intensity-modulated radiotherapy (IMRT) in improving PTV conformity [2], and normal tissue complication probability (NTCP) by sparing OAR have been well documented. Several publications have addressed the benefits of IMRT in reducing xerostomia after radiotherapy [3–14].

The development and commercial release of the helical tomotherapy (HT) system by Mackie et al (Tomotherapy Inc., Madison, WI) introduced advanced helical IMRT delivery techniques in combination with integrated image-guidance capability [15, 16], providing image-guided IMRT. Helical tomotherapy techniques have been assessed against linear accelerator-based IMRT in head and neck cancers and have been found to produce better homogeneity and normal tissue sparing [17, 18]. The adoption of this new technology is limited by the additional resources required, by the need for clinicians to find extra time for outlining target volumes and by the increased physics time required for the complex planning and quality assurance needed for these inverse-planned techniques [19].

Conventionally, head and neck cancers have been treated with a two-phase technique requiring a junction between a lateral photon field covering the anterior part of the target volume and, during the second phase of treatment, a matched lateral electron field covering the

Address correspondence to: Dr Sanjoy Chatterjee, Northern Centre for Cancer Care, Freeman Hospital, Freeman Road, Newcastle upon Tyne, NE3 2JZ, UK. E-mail: sanjoy.chatterjee@nuth.nhs.uk

Table 1. Site, stage and treatment details of the five cases

Case number	Primary site	Stage (TNM)	Prescribed dose for PTV1 (i.e. high-risk volume) (Gy in 30 fractions)	Prescribed dose for PTV2 (i.e. prophylactic volume) (Gy in 30 fractions)
1	Base of tongue	T3N2b	65.1	54
2	Soft palate	T1N0	65.1	54
3	Neck node with unknown primary site in head and neck	Multiple neck nodes bilaterally Tx N2c	65.1	54
4	Base of tongue	T2N2a	65.1	54
5	Tonsil	T4N2b	65.1	54

PTV, planning target volume.

posterior part of the target volume. Mismatch at this junction can lead to overdosage or underdosage, and to a decrease in dose homogeneity in an important area of the treatment volume, including diseased cervical nodes.

Many centres in the UK continue to treat head and neck cancers with this technique. At the Northern Centre for Cancer Care, Newcastle upon Tyne, UK, all patients requiring radical radiotherapy for HNSCC are treated using either helical tomotherapy or a field-in-field forward-planned single-phase linear accelerator-based method. This study compared the dosimetric and radiobiological aspects of three different planning techniques: a forward-planned photon-electron junction technique (2P), a single phase (1P) forward-planned technique developed in-house and HT.

Materials and methods

Treatment planning

HT plan

Five patients who had HT treatment for HNSCC were identified. The primary site, TNM stage and dose prescribed to the different PTVs are described in Table 1. All patients were immobilised using a custom-made beam directional shell (BDS) made of polyethylene terephthalate glycol (PTEG). Contrast-enhanced CT localisation scans covering the vertex to the upper thorax were acquired using a Somatom Sensation Open widebore CT scanner (Siemens, Concord, CA) 40 s after the injection of 70 ml iohexol (Omnipaque; GE Healthcare, Waukesha,

Figure 1. (a) Lateral opposed beams for the first phase of the two-phase treatment (forward planned) (fields 1 and 2). (b) In order to maintain safe cord dose, the posterior neck electron boost field is matched to the anterior photon field. (c) Anterior split neck field for prophylactic lower neck. The dotted lines inside the fields represent the outlined planning target volume (PTV)1 (high dose: red) and PTV2 (prophylactic dose: purple).

Figure 2. (a) A typical segmented field. Note the position of the multileaf collimators (arrow), which have been taken out into the high-dose planning target volume to ensure homogenous dose distribution. Note the shielding of the cord. (b) Complex forward-planned field in field technique can produce an acceptable dose distribution without the necessity to junction electron fields to photon fields.

WI). Images were reconstructed with a 3-mm slice thickness and exported to Oncentra MasterPlan.

The details of our HT planning technique have been discussed in another paper published by our group [20]. In summary, gross tumour volumes (GTVs), clinical target volumes (CTVs), PTV and OAR were outlined by a consultant clinical oncologist using a local protocol. A high-risk CTV (CTV1), comprising the gross primary tumour with adequate margin and the entire involved cervical node level was outlined first, followed by a lower-risk CTV2, which included the uninvolved cervical nodal stations. A 3-mm margin was added to the CTV to get the PTV. OAR that were routinely outlined included the spinal cord, brain stem, bilateral parotids, mandible and larynx. This planning was followed by the creation of additional “dummy volumes” by the planning physicist and dosimetrist in order to achieve an optimised HT plan. HT calculates the multileaf collimator (MLC) position every 7 degrees of rotation, providing very conformal isodose distributions [12, 13, 21, 22]. All five patients were treated on an optimised HT plan.

For the purposes of this study, two further plans using forward-planned techniques were created for each patient, using the same PTVs.

Two-phase plans

Plan 1 was a two-phase plan designated “Conventional”. Two lateral photon fields (Field 1 and 2 in Figure 1a) were used in the first phase to treat the PTV of the primary tumour and upper neck. The lower neck treatment was planned by using a half beam anterior asymmetric field matched on to Fields 1 and 2 (Figure 1b). The lower neck (prophylactic dose) field was “split” to block the spinal cord, larynx and trachea (Figure 1c), unless such an arrangement impeded the dose received by the PTV, in which case the lateral fields were extended to cover the inferior aspect of the PTV, accepting compromise on the dose distribution. In order to achieve the dose specified for the PTVs without compromising spinal cord tolerance, the treatment was carried out in two phases, requiring a junction between a lateral photon field covering the anterior part of the target volume and a matched lateral electron field covering the posterior part of the target volume administered during phase 2 (Table 1).

Single-phase plan

This technique has been in use since 2002 at our institution, having been introduced and developed by the authors (CGK) before our department’s acquisition of IMR-capable technology. The technique has recently

Table 2. Radiobiological parameters used to calculate the normal tissue complication probability (based on Emami et al [24])

Model parameter OAR	Parotid	Larynx	Larynx	Mandible	Spinal cord
TD50	46	80	70	72	66.5
m	0.18	0.075	0.17	0.1	0.175
n	0.7	0.11	0.08	0.07	0.05
α/β	3	3.8	3.8	3.5	2
End point	Xerostomia	Necrosis	Oedema	Limited joint function	Myelitis/necrosis

TD50: tolerance doses for 50% complication probability; m is the slope of the complication probability vs dose curve; n is the volume dependence parameter, which is large when a fraction of the organ can be damaged without destroying the whole organ function; α/β denotes fraction sensitivity.

Table 3. Isodose coverage and CI

Case number	Planning technique	PTV1 (Gy)			PTV2 (Gy)			PTV1 CI
		Max	Min ^a	Mean	Max	Min	Mean	
1	Tomotherapy	67.9	44.8	64.6	65.8	52.9	56.3	0.78
	Single-phase	70.4	41.0	64.4	70.1	36.5	59.5	0.58
	Two-phase	71.3	30.2	60.8	70.3	22.4	41.3	0.46
2	Tomotherapy	69.6	43.0	64.9	66.1	38.6	56.3	0.76
	Single-phase	72.6	25.6	64.9	68.2	7.1	56.6	0.56
	Two-phase	73.0	29.2	63.5	77.1	17	63.1	0.36
3	Tomotherapy	67.7	58.8	64.9	66.4	42.7	57.1	0.82
	Single-phase	69.3	59.9	66.3	68.7	35.3	60.2	0.47
	Two-phase	70.0	61.1	66.0	70.8	41.4	64.7	0.29
4	Tomotherapy	66.6	45.8	62.9	64.9	45.6	54.4	0.72
	Single-phase	66.2	43.9	62.4	66.8	29.4	54.0	0.35
	Two-phase	71.5	5.4	63.2	70.5	6.5	60.1	0.22
5	Tomotherapy	68.1	53.0	64.7	63.8	50.8	54.6	0.81
	Single-phase	72.0	30.6	65.3	70.0	31.8	55.6	0.60
	Two-phase	73.1	22.4	62.4	71.2	10.6	53.8	0.49

PTV, planning target volume.

^aNote the low minimum dose achieved with the two-phase techniques. The area of low dose was noted in the posterior aspect of level V lymph node stations, which were outlined by the clinicians, extending up to the trapezius muscles. With a junction of anterior split neck and lateral fields, a clinical decision was taken such that coverage of the high-risk area was not compromised. With the anterior neck fields, it was therefore not possible to plan a higher dose to the lower posterior neck in certain cases.

been modified to allow differential dose prescription to different regions of the PTV. The plan created using this technique involved multiple segmented photon fields and enabled adequate coverage of the PTV in a single phase without compromising the dose to the spinal cord or brain stem. The position of the isocentre was chosen such that it fell within the high-dose PTV. Depending on the shape of the high-dose PTV, the position of the isocentre was adjusted in the supero-inferior, lateral and anteroposterior directions. Moving the isocentre in the superior direction allowed for better, more homogeneous coverage inferiorly. The position of the isocentre was adjusted anteriorly such that there was adequate coverage of level IIB lymph nodes without beam entry through the spinal cord (Figure 2a). The lateral position was restricted such that the isocentre needed to be at least 1.8 cm from the MLC bank to account for accurate calculation using the beam information available. Four gantry angles (typically at 50°, 310°, 130° and 230°)

corresponding to two anterior oblique and two posterior oblique angles were set to cover the PTV. If required, a floor twist was added to the posterior oblique fields to enable adequate dose coverage inferiorly without entering through the shoulders. The spinal cord and brain stem were fully shielded on the posterior obliques. These gantry angles were offset slightly to the right or left cervical nodal chains, according to the requirement for more dose. Figure 2b shows the field arrangements for the single-phase plan.

Dose calculation algorithm and dose grid

The forward-planned two-phase and single-phase techniques were calculated using Oncentra Masterplan (OMP) software. In OMP, we used the "Pencil Beam" algorithm with a calculation grid of 0.5 cm. The tomotherapy plans were produced using a "Fine" grid and the "Convolution/Superposition" calculation algorithm.

Table 4. Parotid and spinal cord doses for the different planning techniques

Case number	Technique	Right parotid mean dose (Gy)	Left parotid mean dose (Gy)	Spinal cord max. dose (Gy)	Brain stem max. dose (Gy)
1	Tomotherapy	26.41	25.64	26.55	28.90
	Single-phase	64.17	64.42	48.35	42.65
	Two-phase	66.57	65.70	47.49	49.70
2	Tomotherapy	39.67	25.62	25.66	31.31
	Single-phase	64.31	54.74	50.60	51.11
	Two-phase	62.65	61.61	49.43	48.84
3	Tomotherapy	29.89	22.19	25.23	28.95
	Single-phase	54.47	45.78	49.45	44.61
	Two-phase	62.74	61.83	54.66	45.02
4	Tomotherapy	30.02	26.63	19.85	23.69
	Single-phase	59.64	54.80	50.42	44.71
	Two-phase	60.60	58.93	44.77	40.92
5	Tomotherapy	na ^a	26.5	21.8	29.4
	Single-phase	na ^a	62.8	48.5	43.7
	Two-phase	na ^a	62.7	46.6	42.1

^aIntraparotid lymph node, hence the parotid gland is included in the planned target volume.

Table 5. Integral dose for each case using the different planning techniques

Case no.	Two-phase plan	Single-phase plan	Tomotherapy
	Integral dose (kg.Gy)	Integral dose (kg.Gy)	Integral dose (kg.Gy)
1	4514.4	6654.2	5924.7
2	3912.4	3972.4	3182.7
3	6160.4	6521.4	6184.5
4	4436.0	5325.0	4502.5
5	6002.6	7397.8	6460.5

Radiobiology calculation using BIOPLAN [23]

BIOlogical evaluation of PLANs (BIOPLAN) was conceived and developed as a PC-based software that allows the user to evaluate and compare treatment plans in terms of the biological responses of tissues—both tumour and the OAR—to irradiation. In this study, BIOPLAN was used to calculate tumour control probability (TCP) using the Poisson model and NTCP using the Lyman–Kutcher model. Dose–volume histogram (DVH) data were extracted from the treatment planning system (TPS) and pasted into a Microsoft Excel spreadsheet, which was pre-written by staff at the Regional Medical Physics Department (RMPD), in order to parse the data as required by BIOPLAN then re-export in ASCII format ready to be picked up by the BIOPLAN software. BIOPLAN contains a library of model NTCP parameters; for this study, the NTCP was calculated as described by Emami et al [24] and by Burman et al [25] (Table 2).

An estimate of the tumour clonogenic cell density is required to calculate TCP. $TCP = e^{-sf \cdot m}$, where sf is survival fraction and m is clonogenic cell number. Bentzen and Thames [26] estimated the number of clonogens for a large series of patients with squamous cell carcinoma of the oropharynx as being between 1.8×10^3 and $6.6 \times 10^5 \text{ cm}^{-3}$. Other investigators have reported similar values [27]. To assist us in picking a realistic value from within this range, we used BIOPLAN to calculate a clonogenic cell density, assuming an 80% cure probability for a T1 squamous cell carcinoma. These densities were applied to each case, thereby ranking them according to their stage and grade; this provided us with the required densities for the high- and low-dose PTVs.

From the plotted TCP and NTCP (total) data, an uncomplicated tumour control probability (UCP) was calculated as a function of the prescribed dose. $UCP = TCP(1 - NTCP_{Tot})$. UCP values provide an objective function that denotes the biological benefit that could be provided by that particular treatment plan, depending on the TCP and NTCP values. By displacing a vertical line on the plot for TCP and NTCP values in BIOPLAN, the coordinates of the intersecting points on the curves were displayed in the adjacent text boxes, thereby enabling us to calculate an UCP value for a prescribed dose. This tool has helped to predict the outcomes of different prescribing regimes, including those postulated for dose escalation within the UK Clinical Research Network VortigERN study [28].

Conformity index

To analyse the conformity of the 95% isodose to the PTV, CIs were calculated for all plans in all five patients. CI was calculated for each of the plans using the following

formula [29]: $CI = PTV(\text{enclosed by 95\% isodose})^2 / PTV(\text{total volume}) \times \text{volume enclosed by 95\% isodose}$.

The 95% isodoses for the high- and low-dose PTVs are different. We calculated the CI values for the high-dose PTV (65 Gy) so that a unique value of the 95% isodose could be used.

Results

Table 3 shows the maximum, minimum and mean dose achieved in each case using the three different planning techniques. The HT technique produced the most homogenous treatment plans with adequate PTV coverage, although the single-phase technique plans covered the PTV adequately in almost all cases. The PTV coverage and CI were better for the single-phase plans than for the two-phase technique.

Similarly, HT plans were better in sparing the parotid glands and other OAR, followed by the single-phase plans, then the two-phase plans. Table 4 shows the DVH data for the OAR. Dose to the spinal cord and brain stem was similar for the two forward-planned techniques, but the HT plans provided significantly lower doses.

The CIs for each of the plans are shown in Table 3. This confirms the superior conformity of the 95% isodose to the target for HT plans, followed by single-phase and two-phase plans. The integral dose calculated for each of the techniques is shown in Table 5. These calculations show that the single-phase plans delivered a higher integral dose than did the HT and two-phase plans.

HT plans were best in achieving adequate TCP and lowest NTCP in all cases (Tables 6 and 7). The single-phase plans had TCP values that were comparable with those of the HT plans. The slightly higher TCP values for Case 2 may be caused by “hot spots” above 107% within the CTV, which would have driven up the calculated TCP in marginal cases

Table 6. TCP for GTV and CTV1 (high-risk) using the three planning techniques

Patient	Volume	Two-phase %	Single-phase %	Tomotherapy %
1	GTV	74.4	86.0	88.5
	CTV1	38.2	76.5	79.2
2	GTV	93.0	93.6	92.8
	CTV1	86.2	86.9	85.2
3	GTV	80.2	92.0	90.4
	CTV1	42.7	73.4	81.1
4	GTV	91.8	90	90.6
	CTV1	0	81.8	83.0
5	GTV	65.1	78.5	77.4
	CTV1	3.4	39.8	53.0

CTV, clinical target volumes; GTV, gross tumour volumes; TCP, tumour control probability.

Table 7. NTCP for different OAR

Case number	Organ (endpoint)	Two-phase %	Single-phase %	Tomotherapy %
1	Left parotid (xerostomia)	92.9	81.3	0.4
	Right parotid (xerostomia)	95.5	94.5	1.3
	Mandible (joint function)	1.4	4.0	5.8
	Spinal cord (myelitis)	43.1	66.7	0.0
	Left parotid	99.5	99.0	0.3
2	Right parotid	99.7	98.9	0.4
	Mandible	10.9	13.5	0.8
	Spinal cord	39.8	72.0	0.0
	Larynx (necrosis)	3.1	0.0	0.0
	Larynx (oedema)	47.3	3.6	1.2
3	Left parotid	96.8	78.2	0.2
	Right parotid	97.9	99.0	21.5
	Mandible	3.5	0.4	0.1
	Spinal cord	22.6	72.3	0.0
	Left parotid	97.3	39.6	0.0
4	Right parotid	98	80.2	1.4
	Mandible	1.3	0.4	0.1
	Spinal cord	77.3	72.6	0.0
	Larynx	0.0	0.0	0.0
	Larynx	10.5	8.5	1.4
5	Left parotid	100.0	48.7	3.2
	Right parotid	100.0	100.0	100.0
	Mandible	100.0	100.0	100.0
	Spinal cord	39.7	58.2	0.0

NTCP, normal tissue complication probability; OAR, organs at risk.

of good overall dose coverage. Conventional two-phase plans had the least TCP and the highest NTCP values.

Figure 3 shows the UCP values for Case 4, representing the therapeutic indices for the three plans. It is clear from the UCP plots that the HT plan has the highest UCP resulting from much lower NTCP values.

Dose escalation

With the possibility of increased therapeutic index with HT treatment, we explored the TCP values that could be achieved with dose escalation. The Royal Marsden Hospital has explored the dose-escalation schedule for squamous cell carcinomas of the hypopharynx [30], whereas we used a similar dose-escalation protocol for oropharyngeal primaries within the VortigERN study

[28]. None of the five cases described here were re-planned to the escalated dose using HT. However, we used BIOPLAN software to calculate the UCP, TCP and NTCP values for the GTV and parotid glands when prescribing a dose of 67.2 Gy in 28 fractions to the tumour, thereby delivering a 9% increase in dose to the primary tumour based on a tumour α/β of 10 and late effects α/β of 3. Table 8 confirms the raised UCP values for HT plans using 67.2 Gy in 28 fractions and provides theoretical confirmation of the possible benefits of dose escalation.

Discussion

It is clear that HT plans provide the best conformity of the three techniques. Previous studies have demonstrated the superiority of inverse-planned IMRT techniques in the

Figure 3. Comparison of tumour control probability (TCP), normal tumour complication probability (NTCP) and generation of uncomplicated tumour control probability (UCP) for Case 4. The NTCP_{Tot} denotes the average NTCP probabilities for the different organs at risk.

Table 8. TCP and NTCP values for GTV and parotids with a dose escalation to 67.2 Gy in 28 fractions

	Case 1	Case 2	Case 3	Case 4	Case 5
GTV	91.8 (88.5)	95.1 (92.8)	93.3 (90.4)	94.9 (90.6)	94.05 (77.4)
Left parotid	0.7 (0.4)	0.5 (0.3)	0.3 (0.2)	0.1 (0.0)	1.12 (3.2)
Right parotid	2.4 (1.3)	0.8 (0.4)	33.3 (21.5)	3.6 (1.4)	na ^a (100)
UCP	88.91 (87.01)	93.35 (92.1)	64.54 (70.89)	90.97 (85.5)	92.04 (90.0)

GTV, gross tumour volumes; NTCP, normal tissue complication probability; TCP, tumour control probability.

^aIntraparotid lymph node, hence the parotid gland is included in planned target volume.

treatment of head and neck tumours [31, 32]. This study compares HT treatment to the conventional two-phased photon electron junction technique and a forward-planned single-phase field-in-field photon-only technique. The latter is a safe technique that is easy to implement, is within the tolerance limits of the spinal cord and could be considered for routine use for all non-inverse-planned IMRT head and neck cases. This single-phase technique has the added advantage of reliable and reproducible dosimetric verification checks, which may be difficult to achieve in a two-phased photon electron junction approach. The DVH analysis and TCP values reported here indicate that the single-phased techniques provide better conformity than do the two-phased techniques. This single-phased technique can therefore be implemented by centres that lack the resources necessary to implement inverse-planned IMRT techniques for all the head and neck cancer cases. The disadvantages of the single-phase technique include higher doses to the OAR, including the parotid glands, when compared with HT.

Comparison of the NTCP data confirms the superiority of the HT technique in reducing the NTCP and improving the UCP. The high UCP values provided by HT make dose-escalation techniques possible, and the TCP and NTCP values confirm the possibility of improved outcomes. Centres using inverse-planned IMRT techniques should explore such dose escalation within a controlled trial setting. At the Royal Marsden Hospital, a Phase 1 study for patients with hypopharyngeal cancer has been conducted, in which the PTV1 (high dose) was treated with a dose of 67.2 Gy in 28 fractions and the PTV2 (prophylactic dose) with 56 Gy in 28 fractions [30]. In the VortigERN study, a 5-mm isotropic margin was outlined around the GTV (both primary and nodal) to create a PTV3. For dose escalation in the oropharynx, consideration needs to be given to the pharyngeal constrictor muscles, the temporo-mandibular joint and the muscles of mastication. These were outlined in the VortigERN study to evaluate the feasibility of future Phase 1 and Phase 2 clinical studies. We are exploring the doses to these extra OAR in another in-house study.

Cold spots will rapidly drive down the TCP, which cannot be rescued by hotspots at different locations in the PTV. It is interesting to note that although HT treatment might be expected to deliver a higher integral dose per plan, the single-phased technique actually seemed to have a higher integral dose. Although the concepts of higher integral dose [33, 34] and second malignancies are debatable, this study highlights the fact that current forward-planned techniques may not be delivering lower integral dose than inverse-planned HT techniques in complex head and neck treatment plans.

It is worth noting that recent QUANTEC publications [35–37] have described a predictive model based on pooled data from multiple studies. The tolerances described in these papers are slightly different to those discussed by Emami et al [24]. Although the possible limitations of QUANTEC studies have been highlighted [35], the new data may well be more accurate clinically. We did not base our calculations on these new values, although we understand that they could provide changed NTCP values for the DVH generated in the plans. This could well be a limitation of our study. On the other hand, we tried to keep our calculations pure and used BIOPLAN to calculate the NTCP values as described by Sanchez-Nieto and Nahum [23]. In addition, it is worth noting that the HT plans were calculated using a different planning algorithm and grid than that used for the forward-planned techniques. This could mean that the DVH could have had some inherent differences originating from the differences in planning systems.

In conclusion, while confirming the superiority of HT plans in treating head and neck tumours, our study establishes the role of a single-phase photon-only technique in this context. This technique could be used as a standard technique for managing head and neck tumours in departments that lack the resources necessary to implement inverse-planned approaches for all patients.

References

1. Widesott L, Pierelli A, Fiorino C, Dell'oca I, Broggi S, Cattaneo GM, et al. Intensity-modulated proton therapy versus helical tomotherapy in nasopharynx cancer: planning comparison and NTCP evaluation. *Int J Radiat Oncol Biol Phys* 2008;72:589–96.
2. Lee N, Puri DR, Blanco AI, Chao KS. Intensity-modulated radiation therapy in head and neck cancers: an update. *Head Neck* 2007;29:387–400.
3. van Rij CM, Oughlane-Heemsbergen WD, Ackerstaff AH, Lamers EA, Balm AJ, Rasch CR. Parotid gland sparing IMRT for head and neck cancer improves xerostomia related quality of life. *Radiat Oncol* 2008;3:41.
4. Rudat V, Münter M, Rades D, Grötz KA, Bajrovic A, Haberkorn U, et al. The effect of amifostine or IMRT to preserve the parotid function after radiotherapy of the head and neck region measured by quantitative salivary gland scintigraphy. *Radiother Oncol* 2008;9:71–80.
5. Ortholan C, Chamorey E, Benezery K, Thariat J, Dassonville O, Poissonnet G, et al. Modeling of salivary production recovery after radiotherapy using mixed models: determination of optimal dose constraint for IMRT planning and construction of convenient tools to predict salivary function. *Int J Radiat Oncol Biol Phys* 2009;73:178–86.
6. Chao KS, Majhail N, Huang CJ, Simpson JR, Perez CA, Haughey B, et al. Intensity-modulated radiation therapy reduces late salivary toxicity without compromising

- tumor control in patients with oropharyngeal carcinoma: a comparison with conventional techniques. *Radiother Oncol* 2001;61:275–80.
7. Daly ME, Lieskovsky Y, Pawlicki T, Yau J, Pinto H, Kaplan M, et al. Evaluation of patterns of failure and subjective salivary function in patients treated with intensity modulated radiotherapy for head and neck squamous cell carcinoma. *Head Neck* 2007;29:211–20.
 8. Saarilahti K, Kouri M, Collan J, Hämäläinen T, Atula T, Joensuu H, et al. Intensity modulated radiotherapy for head and neck cancer: evidence for preserved salivary gland function. *Radiother Oncol* 2005;74:251–8.
 9. Marzi S, Iaccarino G, Pasciuti K, Soriani A, Benassi M, Arcangeli G, et al. Analysis of salivary flow and dose-volume modeling of complication incidence in patients with head-and-neck cancer receiving intensity-modulated radiotherapy. *Int J Radiat Oncol Biol Phys* 2009;73:1252–9.
 10. Eisbruch A, Kim HM, Terrell JE, Marsh LH, Dawson LA, Ship JA. Xerostomia and its predictors following parotid-sparing irradiation of head-and-neck cancer. *Int J Radiat Oncol Biol Phys* 2001;50:695–704.
 11. Lee NY, de Arruda FF, Puri DR, Wolden SL, Narayana A, Mechalakos J, et al. A comparison of intensity-modulated radiation therapy and concomitant boost radiotherapy in the setting of concurrent chemotherapy for locally advanced oropharyngeal carcinoma. *Int J Radiat Oncol Biol Phys* 2006;66:966–74.
 12. Rusthoven KE, Raben D, Ballonoff A, Kane M, Song JJ, Chen C. Effect of radiation techniques in treatment of oropharynx cancer. *Laryngoscope* 2008;118:635–9.
 13. Vergeer MR, Doornaert PA, Rietveld DH, Leemans CR, Slotman BJ, Langendijk JA. Intensity-modulated radiotherapy reduces radiation-induced morbidity and improves health-related quality of life: results of a nonrandomized prospective study using a standardized follow-up program. *Int J Radiat Oncol Biol Phys* 2009;74:1–8.
 14. Huang K, Xia P, Chuang C, Weinberg V, Glastonbury CM, Eisele DW. Intensity-modulated chemoradiation for treatment of stage III and IV oropharyngeal carcinoma: the University of California – San Francisco experience. *Cancer* 2008;113:497–507.
 15. Mackie TR. History of tomotherapy. *Phys Med Biol* 2006;51:R427–53.
 16. Beavis AW. Is tomotherapy the future of IMRT? *Br J Radiol* 2004;77:285–95.
 17. Sheng K, Molloy JA, Read PW. Intensity-modulated radiation therapy (IMRT) dosimetry of the head and neck: a comparison of treatment plans using linear accelerator-based IMRT and helical tomotherapy. *Int J Radiat Oncol Biol Phys* 2006;65:917–23.
 18. van Vulpen M, Field C, Raaijmakers CP, Parliament MB, Terhaard CH, MacKenzie MA, et al. Comparing step-and-shoot IMRT with dynamic helical tomotherapy IMRT plans for head-and-neck cancer. *Int J Radiat Oncol Biol Phys* 2005;62:1535–9.
 19. Murthy V, Gupta T, Kadam A, Ghosh-Laskar S, Budrukhar A, Phurailatpam R, et al. Time trial: a prospective comparative study of the time-resource burden for three-dimensional conformal radiotherapy and intensity-modulated radiotherapy in head and neck cancers. *J Cancer Res Ther* 2009;5:107–12.
 20. Chatterjee S, Mott JH, Smyth G, Dickson S, Kelly GC. Clinical challenges in the implementation of a tomotherapy service for head and neck cancer patients in a regional UK radiotherapy centre. *Br J Radiol* 2011;84:358–66.
 21. Mackie T, Balog J, Ruchala K, Shepard D, Aldridge S, Fitchard E, et al. Tomotherapy. *Semin Radiat Oncol* 1999;9:108–117.
 22. Mackie TR, Kapatoes J, Ruchala K, Lu W, Wu C, Olivera G, et al. Image guidance for precise conformal radiotherapy. *Int J Radiat Oncol Biol Phys* 2003;56:89–105.
 23. Sanchez-Nieto B, Nahum AE. BIOPLAN: software for the biological evaluation of radiotherapy treatment plans. *Med Dosim* 2000;25:71–6.
 24. Emami B, Lyman J, Brown A, Coia L, Goitein M, Munzenrider JE, et al. Tolerance of normal tissue to therapeutic irradiation. *Int J Radiat Oncol Biol Phys* 1991;21:109–22.
 25. Burman C, Kutcher GJ, Emami B, Goitein M. Fitting of normal tissue tolerance data to an analytic function. *Int J Radiat Oncol Biol Phys* 1991;21:123–35.
 26. Bentzen SM, Thames HD. Tumor volume and local control probability: clinical data and radiobiological interpretations. *Int J Radiat Oncol Biol Phys* 1996;36:247–51.
 27. Webb S, Evans PM, Swindell W, Deasy JO. A proof that uniform dose gives the greatest TCP for fixed integral dose in the planning target volume. *Phys Med Biol* 1994;39:2091–8.
 28. UK Clinical Research Network: Portfolio Database. [Cited Jan. 4, 2010] MREC No: 08/H0907/127, UKCRN ID 7341. Chatterjee S (Chief investigator). VortigERN: variation of radiotherapy target volume definition, dose to organs at risk (OAR) and clinical target volumes using anatomic (CT) vs. combined anatomic and molecular imaging (PET-CT): intensity modulated radiotherapy delivered using a tomotherapy Hi Art machine. Available from: <http://public.ukcrn.org.uk/search/StudyDetail.aspx?StudyID=7341>.
 29. Feuvret L, Noël G, Mazon JJ, Bey P. Conformity index: a review. *Int J Radiat Oncol Biol Phys* 2006;64:333–42.
 30. Guerrero Urbano T, Clark CH, Hansen VN, Adams EJ, A'Hern R, et al. A phase I study of dose-escalated chemoradiation with accelerated intensity modulated radiotherapy in locally advanced head and neck cancer. *Radiother Oncol* 2007;85:36–41.
 31. Sheng K, Molloy JA, Larner JM, Read PW. A dosimetric comparison of non-coplanar IMRT versus helical tomotherapy for nasal cavity and paranasal sinus cancer. *Radiother Oncol* 2007;82:174–8.
 32. Longobardi B, De Martin E, Fiorino C, Dell'oca I, Broggi S, Cattaneo GM. Comparing 3DCRT and inversely optimized IMRT planning for head and neck cancer: equivalence between step-and-shoot and sliding window techniques. *Radiother Oncol* 2005;77:148–56.
 33. Hall EJ, Wu CS. Radiation-induced second cancers: the impact of 3D-CRT and IMRT. *Int J Radiat Oncol Biol Phys* 2003;56:83–8.
 34. Nguyen F, Rubino C, Guerin S, Diallo I, Samand A, Hawkins M, et al. Risk of a second malignant neoplasm after cancer in childhood treated with radiotherapy: correlation with the integral dose restricted to the irradiated fields. *Int J Radiat Oncol Biol Phys* 2008;70:908–15.
 35. Marks LB, Yorke ED, Jackson A, Ten Haken RK, Constone LS, Eisbruch A, et al. Use of normal tissue complication probability models in the clinic. *Int J Radiat Oncol Biol Phys* 2010;76:S10–9.
 36. Bentzen SM, Constone LS, Deasy JO, Eisbruch A, Jackson A, Marks LB, et al. Quantitative analyses of normal tissue effects in the clinic (QUANTEC): an introduction to the scientific issues. *Int J Radiat Oncol Biol Phys* 2010;76:S3–9.
 37. Deasy JO, Moiseenko V, Marks L, Chao KS, Nam J, Eisbruch A. Radiotherapy dose-volume effects on salivary gland function. *Int J Radiat Oncol Biol Phys* 2010;76:S58–63.