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Research Letter

A Dosimetric Comparison of Oral Cavity Sparing in the Unilateral Treatment of Early Stage Tonsil Cancer: IMRT, IMPT, and Tongue-Deviating Oral Stents

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Abstract

Introduction: Tongue-deviating oral stents (TDOS) are commonly used during unilateral neck radiation therapy to reduce unnecessary dose to nontarget oral structures. Their benefit in the setting of highly conformal treatment techniques, however, is not defined. The goal of this study was to investigate the potential benefit of TDOS use on dosimetric parameters in unilateral intensity modulated radiation therapy (IMRT) and intensity modulated proton therapy (IMPT).

Methods: A total of 16 patients with T1-2 tonsil cancer treated at a single institution were selected, of which 8 were simulated/treated with a TDOS and 8 without a TDOS. All received definitive unilateral IMRT to a dose of 66 Gy in 30 fx. IMPT plans were generated for each patient for study purposes and optimized according to standard institutional practice.

Results: For IMRT plans, the presence of a TDOS (vs without) was associated with a significantly lower oral mucosa mean dose (31.4 vs 35.3 Gy; $P = .020$) and V30 (42.7% vs 57.1%; $P = .025$). For IMPT plans, the presence of TDOS (vs without) was not associated with any improvement in oral mucosa mean dose (18.3 vs 19.9 Gy; $P = .274$) or V30 (25.0% vs 26.2%; $P = .655$). IMPT plans without TDOS compared with IMRT plans with TDOS demonstrated reduced oral mucosa mean dose ($P < .001$) and V30 ($P < .001$).

Conclusion: The use of a TDOS for the unilateral treatment of well-lateralized tonsil cancers was associated with oral mucosa sparing for IMRT, but not for IMPT. Moreover, mucosa sparing was improved for IMPT plans without a TDOS compared to IMRT plans with a TDOS.

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Data sharing statement: All available data can be obtained by contacting the corresponding author.

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Introduction

Unilateral radiation therapy (RT) is an established treatment option for well-lateralized early stage tonsil cancers.[1] Although tongue-deviating oral stents (TDOS) are used at some centers to decrease normal mucosa dose and reduce treatment-related oral toxicity, their dosimetric and clinical benefits are not clearly defined.[2,3] Moreover, any potential benefits of a TDOS may diminish with highly conformal radiation planning techniques such as intensity modulated RT (IMRT) and intensity modulated proton therapy (IMPT). The goal of this study was to investigate the dosimetric effect of TDOS use on normal oral structures during unilateral IMRT or IMPT for early stage tonsil cancer.

Methods and Materials

Between 2008 and 2013, 97 patients with T1-2, N0-3 (American Joint Committee on Cancer, 7th edition) nonmetastatic tonsil cancer at a single institution were treated with unilateral IMRT to a dose of 66 Gy in 30 fx. Seventy-one cases were simulated/treated without a TDOS and 26 with a TDOS. A total of 16 patients (8 with a TDOS and 8 without a TDOS) were randomly selected for inclusion in this dosimetric analysis. There was no difference in stage distribution between the 16 selected patients and the larger 97-patient cohort (χ^2 $P = .961$ and $P = .132$ for T-stage and N-stage, respectively). All IMRT plans were designed using static field IMRT with all normal tissues met per institutional guidelines. IMPT

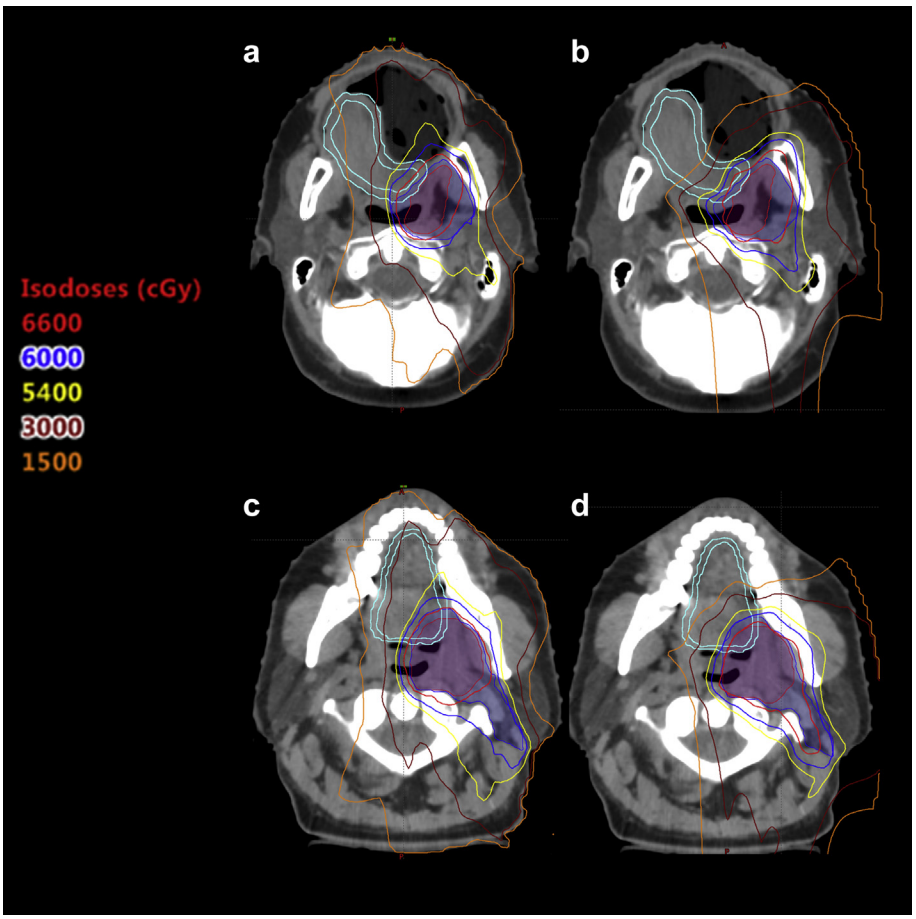

Figure 1 Representative plans. The top panels show a patient with a left T2N1 tonsil cancer and a tongue-deviating oral stents (TDOS), planned with intensity modulated radiation therapy (IMRT) (panel a) and intensity modulated proton therapy (IMPT) (panel b). The bottom panels show a patient with a left T2N1 tonsil cancer and no TDOS, planned with IMRT (panel c) and IMPT (panel d). Representative mucosa contours, clinical target volume (CTV)_66, CTV_60, and CTV_54 are shown in cyan, red, blue, and yellow color wash, respectively.

plans were generated for each patient for study purposes and optimized according to standard institutional practice[4] with 3 fields (posterior anterior, posterior oblique, and anterior oblique) and multifield robust optimization (3 mm isocenter shifts, 12 plan perturbations, range uncertainty of +/− 3.5%). For study purposes, normal structures of interest including the tongue (oral tongue and base of tongue) and oral mucosa (3 mm surface thickness for mucosa covering tongue, soft palate, hard palate, floor of mouth, inner lips, and buccal surfaces) were generated according to published guidelines[5] (Fig 1 and Fig E1). Dosimetric parameters were extracted and compared including the mean dose, V30 (the percent volume of tissue receiving at least 30 Gy, previously demonstrated to correlate with grade 3+ mucositis), and D3cc (the minimum dose to a 3 cc volume of normal tissue receiving the highest dose, felt to correlate with risk of mucosal ulceration).[6,7] Data analysis was performed using STATA/IC statistical software (version 12.1; STATA, College Station, TX). Statistical tests were 2-sided with $\alpha = 0.05$ for statistical significance.

Results

Patient and tumor characteristics by TDOS group are summarized in Table 1. There were no differences in target structure volumes or coverage between groups (Table 2). The presence of a TDOS (vs without) was associated with a significantly lower oral mucosa mean dose (31.4 vs 35.3 Gy; $P = .020$) and V30 (42.7% vs 57.1%; $P = .025$) for IMRT plans, although no difference was seen for IMPT plans (mean dose of 18.3 vs 19.9 Gy, $P = .274$; V30 of 25.0% vs 26.2%, $P = .655$) (Table 3). An intergroup comparison was performed to evaluate the difference between IMRT plans in patients with a TDOS and IMPT plans in patients without a TDOS. Even without a TDOS, IMPT plans demonstrated reduced oral mucosa mean dose ($P < .001$) and V30 ($P < .001$) compared with IMRT plans with a TDOS (Table 4).

Table 1 Patient and tumor characteristics by presence of a TDOS

	TDOS absent	TDOS present
	n = 8	n = 8
Age		
Median (years)	52.5	58.5
Sex		
Male	5	5
Female	3	3
HPV status		
Positive	8	7
Unknown	0	1
Smoking status		
Never	4	5
Former	4	3
T stage		
T1	6	6
T2	2	2
N stage		
N0	3	1
N1	3	4
N2	2	2
N3	0	1
Year of treatment		
Median	2010	2011
Range	2008-2013	2008-2013
Group stage, AJCC 7		
I	6	5
II	2	2
III	0	1
Tumor laterality		
Left	4	2
Right	4	6

Abbreviations: AJCC = American Joint Committee on Cancer; HPV = human papillomavirus; TDOS = tongue-deviating oral stents.

Discussion

In this single institution dosimetric analysis of unilateral RT for well-lateralized early stage tonsil cancer, we demonstrate (1) improved oral mucosa sparing for IMRT plans with a TDOS compared with no TDOS, (2) no difference in oral mucosa dose for IMPT plans regardless of TDOS status, and (3) improved oral mucosa sparing for IMPT plans without a TDOS compared with IMRT plans with a TDOS.

Oral mucositis is a common acute side effect of radiation to the oropharynx and is associated with severe pain, the use of narcotic pain medications, decreased oral nutrition and hydration, increased resource utilization, and decreased quality of life.[8-11] Despite advances in supportive care measures and radiation treatment techniques, mucositis remains an important dose-limiting toxicity. In unilateral head and neck radiation treatments, IMPT has demonstrated dramatic sparing of midline and contralateral structures and lower rates of oral mucositis compared with unilateral IMRT.[12-14]

Although a TDOS displaces normal tissue away from the target, downsides include time needed for stent fabrication, difficulty in coordinating dental consultation with radiation simulation and start date, and patient discomfort and distress with use in the setting of mucositis.[15,16] This report demonstrates that the dosimetric benefits of IMPT in the unilateral treatment of tonsil cancers may outweigh benefits of TDOS use. It may thus be reasonable to forego TDOS in this scenario. Although clinical correlation was not performed in this dosimetric analysis (given the post hoc nature of IMPT plans), both

Table 2 Mean volume and dosimetric parameters for target by treatment modality and presence of a TDOS

	IMRT			Proton		
	TDOS absent	TDOS present	*P*	TDOS absent	TDOS present	*P*
Target volumes						
Total CTV (cm^3)	153.0	153.3	.986	153.0	153.3	.986
CTV_high (cm^3)*	61.0	55.5	.549	61.0	55.5	.549
CTV_low (cm^3)†	91.9	97.7	.754	91.9	97.7	.754
Overlap with oral mucosa						
CTV_high (cm^3)*	0.86	0.95	.739	0.86	0.95	.739
CTV_low (cm^3)†	1.64	1.86	.598	1.64	1.86	.598
CTV_high coverage						
V100 (%)‡	98.3	98.0	.818	98.5	98.5	1.000
V95 (%)	99.9	100.0	.644	99.8	100.0	.243
V105 (%)	11.4	7.9	.683	9.9	9.5	.879
CTV_low coverage						
V100 (%)	98.1	99.3	.250	99.2	99.0	.679
V95 (%)	99.9	99.9	.880	99.9	99.9	.937

Abbreviations: CTV = clinical target volume; IMRT = intensity modulated radiation therapy; TDOS = tongue-deviating oral stents.
* CTV_high includes 66 Gy volumes.
† CTV_low includes 54-60 Gy volumes.
‡ V100% is defined as the percent of the target receiving 100% of the prescribed dose.

Table 3 Mean dosimetric parameters for oral mucosa and tongue by treatment modality and presence of a TDOS

	IMRT			IMPT		
	TDOS absent (n = 8)	TDOS present (n = 8)	*P*	TDOS absent (n = 8)	TDOS present (n = 8)	*P*
Oral mucosa						
mean (Gy/Gy [RBE])	35.3	31.4	.020	19.9	18.3	.274
V30 (%)*	57.1	42.7	.025	26.2	25.0	.655
D3cc (Gy)†	61.9	61.2	.746	56.8	59.6	.463

Abbreviations: IMPT = intensity modulated proton therapy; IMRT = intensity modulated radiation therapy; RBE = relative biological effectiveness; TDOS = tongue-deviating oral stents.
* V30 is defined as the percent of the structure receiving at least 30 Gy.
† D3cc is defined as the minimal dose to the hottest 3cc of tissue.

Table 4 Mean dosimetric parameters for IMRT with TDOS group vs IMPT without TDOS group

	IMRT with TDOS (n = 8)	IMPT without TDOS (n = 8)	*P*
Oral mucosa			
mean (Gy)	31.4	19.9	<.001
V30 (%)*	42.7	26.2	<.001
D3cc (Gy)†	61.2	56.8	.233

Abbreviations: IMPT = intensity modulated proton therapy; IMRT = intensity modulated radiation therapy; TDOS = tongue-deviating oral stents.
* V30 is percent of the structure receiving at least 30 Gy.
† D3cc is defined as the minimal dose to the hottest 3cc of tissue.

mean dose and V30 to the oral mucosa have been identified as important predictors for mucositis.[17]

There are several limitations to this study. First, although the IMRT plans were generated before the start of each patient's treatment, the post hoc IMPT plans were created for comparative purposes, with potential for selection, dosimetric, and optimization bias. Still, extensive effort was made to generate IMPT plans according to institution standards and with the same constraints used for the initial IMRT plans. Second, although this study includes a relatively small number of patients, a cohort of 16 (with 32 separate radiation plans) was felt to be of sufficient size for this dosimetric comparison. Third, each patient underwent a single planning simulation with decision for or against TDOS made by the treating physician. The TDOS and no TDOS groups were thus made up of distinct patients without any formal matching of clinical characteristics. Although the groups were relatively

balanced with regards to overall clinical target volume, tumor stage, and target coverage, the high-dose clinical target volume was slightly larger in the no-TDOS cohort, which introduces the possibility for selection bias.

Conclusions

The use of a TDOS for the unilateral treatment of well-lateralized tonsil cancers was associated with oral mucosa sparing for IMRT but not for IMPT. The routine use of TDOS with IMPT in this scenario may thus be unnecessary.

Supplementary Materials

Supplementary material for this article can be found at https://doi.org/10.1016/j.adro.2020.08.007.

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