



Predictors of Mucositis in Oropharyngeal and Oral Cavity Cancer in patients treated with volumetric modulated radiation treatment: a Dose-Volume Analysis

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Background



Patient-reported Measurements of Oral Mucositis in Head and Neck Cancer Patients Treated With Radiotherapy With or Without Chemotherapy

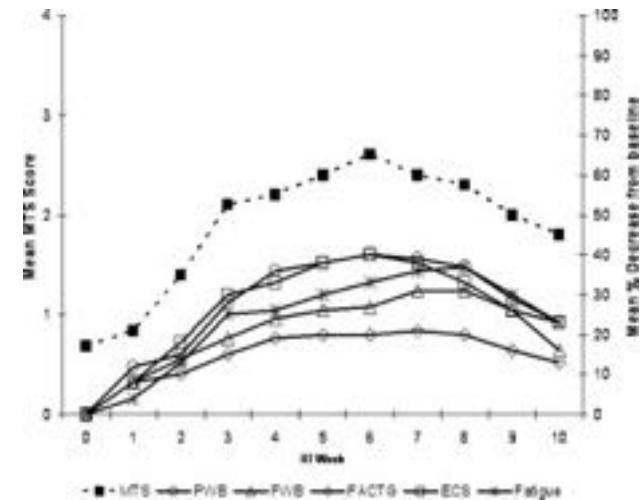
Demonstration of Increased Frequency, Severity, Resistance to Palliation, and Impact on Quality of Life

Elting L.S. et al. Cancer, 2008

In 40-80% of patients undergoing radiotherapy and/or chemotherapy for head and neck cancer, mucositis affects quality of life and compliance to treatment.

Factors related to RT:*

- Site of disease (especially *Oral Cavity and Oropharynx*)
- Treated volume
- Total dose and Fractionation
- Overall treatment time
- Chemotherapy



Relation between mean mouth and throat soreness score (left vertical axis) and mean percentage decrease in quality of life score (right vertical axis) during RT

Background



Multi-institutional comparison of volumetric modulated arc therapy vs. intensity-modulated radiation therapy for head-and-neck cancer: a planning study

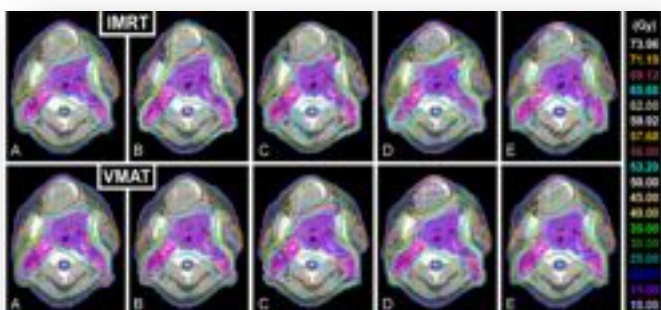


Figure 1. Dose distributions in a transverse slice for IMRT and VMAT plans of all participating institutes. Dose distributions in a transverse slice for IMRT and VMAT plans prepared by the participating institutes. A to E: OARs are depicted with a thick solid line and cavity (brown), parotid glands (orange) and spinal cord (blue).

In the era of dose painting IMRT, it becomes crucial to spare healthy structures to improve the patient's QoL

		VMAT average \pm 1 SD*	IMRT average \pm 1 SD*	Average difference \pm 1 SD* (VMAT – IMRT)	p-value (Wilcoxon's signed-rank test) [†]
PTV _{boost}	D _{95%}	1.37 \pm 0.08	1.45 \pm 0.11	-0.08 \pm 0.09	.001
PTV _{total}	D _{95%}	1.50 \pm 0.09	1.62 \pm 0.10	-0.12 \pm 0.07	< .001
Normal tissue	V _{100%} (cm ³)	5050 \pm 750	5050 \pm 750	-20 \pm 260	ns.
	V _{100%} (cm ³)	4050 \pm 630	3970 \pm 590	-80 \pm 160	ns.
	V _{100%} (cm ³)	2830 \pm 510	2860 \pm 480	30 \pm 150	ns.
Spinal cord	D _{max} (Gy)	45.1 \pm 3.5	46.6 \pm 3.0	-1.5 \pm 23	.001
	D _{1%} (Gy)	43.4 \pm 3.7	44.4 \pm 3.5	-0.9 \pm 22	.005
	D _{mean} (Gy)	29.3 \pm 4.4	29.8 \pm 3.6	-0.5 \pm 24	ns.
Brain stem	D _{max} (Gy)	46.4 \pm 5.4	47.1 \pm 4.7	-0.7 \pm 46	ns.
	D _{1%} (Gy)	43.8 \pm 5.8	44.0 \pm 5.5	-0.2 \pm 49	ns.
	D _{mean} (Gy)	13.6 \pm 3.6	14.5 \pm 4.3	-1.0 \pm 24	ns.
Parotid gland ipsilateral	V _{100%} (cc)	42.9 \pm 15.6	50.3 \pm 20.0	-7.4 \pm 14.0	< .001
	V _{100%} (cc)	30.0 \pm 14.6	35.9 \pm 18.6	-5.9 \pm 11.2	< .001
Parotid gland contralateral	D _{mean} (Gy)	28.0 \pm 7.5	31.1 \pm 9.1	-3.1 \pm 5.1	< .001
	V _{100%} (cc)	31.0 \pm 7.1	34.5 \pm 6.8	-3.5 \pm 3.6	< .001
Submandibular gland contralateral [‡]	D _{mean} (Gy)	22.0 \pm 2.9	23.3 \pm 2.8	-1.3 \pm 1.5	< .001
	V _{100%} (cc)	88.1 \pm 15.3	90.8 \pm 13.5	-2.7 \pm 6.9	ns.
Oral cavity	V _{100%} (cc)	16.4 \pm 21.4	21.8 \pm 27.3	-5.5 \pm 8.5	.020
	D _{mean} (Gy)	53.0 \pm 5.9	54.2 \pm 6.1	-1.2 \pm 3.8	.027
	V _{100%} (cc)	79.8 \pm 22.9	86.3 \pm 15.7	-6.5 \pm 10.2	.011
Larynx	V _{100%} (cc)	40.6 \pm 22.0	48.8 \pm 23.3	-8.2 \pm 12.4	.002
	D _{mean} (Gy)	36.7 \pm 7.8	39.4 \pm 7.3	-2.7 \pm 2.8	< .001
	V _{100%} (cc)	75.4 \pm 24.7	79.1 \pm 21.6	-3.8 \pm 6.7	.012
Pharyngeal constrictor ^{††}	V _{100%} (cc)	54.1 \pm 27.4	58.2 \pm 26.5	-4.1 \pm 9.3	ns.
	D _{mean} (Gy)	45.5 \pm 5.3	46.5 \pm 4.4	-1.0 \pm 1.5	.004
	V _{100%} (cc)	78.7 \pm 24.5	81.5 \pm 20.0	-2.8 \pm 15.2	ns.
Mandible ^{†††}	V _{100%} (cc)	58.7 \pm 29.4	57.5 \pm 25.5	1.2 \pm 19.9	ns.
	D _{mean} (Gy)	47.1 \pm 5.3	46.9 \pm 3.8	0.2 \pm 2.7	ns.
	V _{100%} (cc)	74.0 \pm 13.1	78.2 \pm 11.8	-4.2 \pm 8.4	.025
Effective delivery time ^{††††}	V _{100%} (cc)	25.7 \pm 15.0	30.1 \pm 16.2	-4.4 \pm 5.1	< .001
	D _{mean} (Gy)	48.6 \pm 5.5	50.3 \pm 5.7	-1.7 \pm 1.7	< .001
Effective delivery time ^{†††††}	(minsec)	5:54 \pm 1:05	13:15 \pm 1:08	-7:21 \pm 1:55	< .001
MLUs	-	643 \pm 111	828 \pm 149	-185 \pm 129	< .001

Background



MUCOSITIS VERSUS TUMOR CONTROL: THE THERAPEUTIC INDEX OF ADDING CHEMOTHERAPY TO IRRADIATION OF HEAD AND NECK CANCER

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CONCLUSIONS

We estimate that the addition of concurrent chemotherapy to radiation for HNSCC increases the BED for mucositis by 8 Gy₁₀, corresponding to three or four additional 2-Gy fractions. This estimate is strongly dependent on the assumed relationship between BED and mucositis, but within the range

Study Design

The purpose of the present study was to analyze **Predictors of Acute Mucositis** in oropharyngeal and oral cavity cancers after VMAT +/- Chemotherapy

50 pts were selected according to Inclusion Criteria:

- 1) *Age >18 years*
- 2) *Histologically proven carcinoma of the oropharynx and oral cavity*
- 3) *No dysphagia prior of RT*
- 4) *Radical and adjuvant treatment with VMAT (RapidArc -Varian Medical System-Palo Alto - CA)*

Patients and Treatment

	Factors	%	No. Patients
Site of disease	Oral Cavity	50	25
	Oropharynx	50	25
T-stage	T1	10	5
	T2	34	17
	T3	18	9
	T4	38	19
Neck nodes positive	None	18	9
	Unilateral	26	13
	Bilateral	56	28
Level nodal irradiation	IA		
	Unilateral	12	6
	Bilateral	28	14
	IB		
	Unilateral	26	13
	Bilateral	56	28
	II		
	Bilateral	82	41
	III		
	Bilateral	82	41
Level nodal irradiation	IV		
	Bilateral	82	41
	V		
	Unilateral	26	13
	Bilateral	56	28

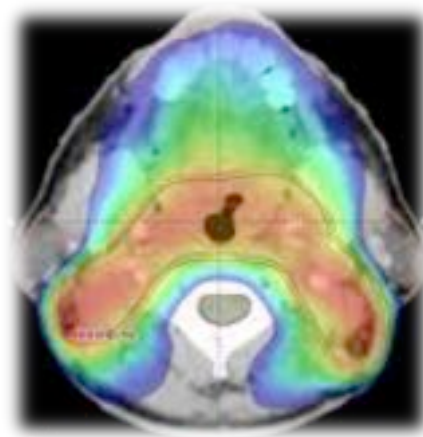
Radiation Treatment	Definitive	50	25
	Adjuvant	50	25
Chemo	Cisplatin - weekly	20	13
	Cisplatin - 3-weekly	40	20
	None	40	20

Radical setting:

- 70 Gy (33-35 fr) PTV(T)
- 59.94 - 63 Gy PTV(HR)
- 54.45 - 58.1 Gy PTV(LR)

Postoperative setting:

- 60 Gy Surgical Bed
- 54 Gy Nodes



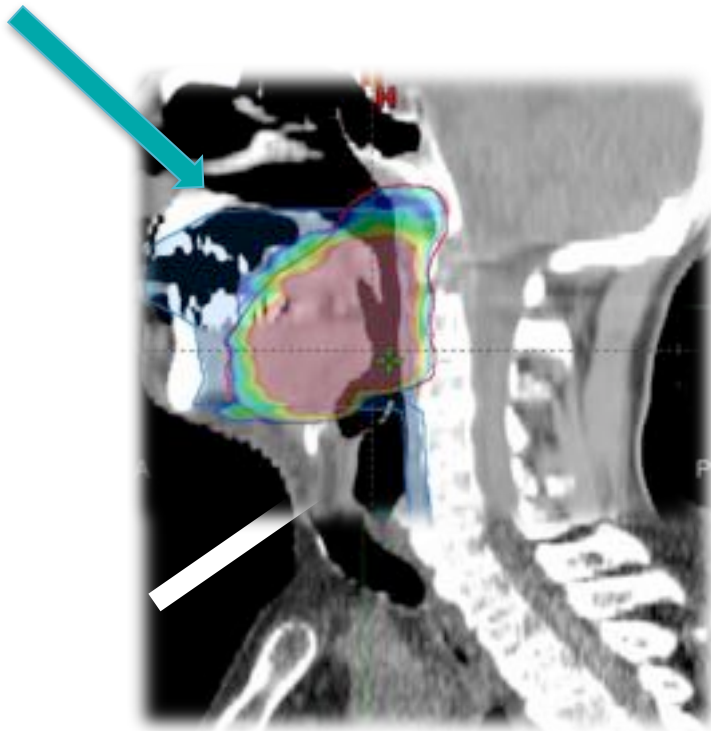
Cisplatin 100 mg/m² q21:

- ECOG – PS 0-1
- Age ≤ 70 y
- Locally advanced

Cisplatin 30 mg/m² qw:

- ECOG - PS 2
- Age ≤ 70 y
- Locally advanced

Methods



CT-Planning

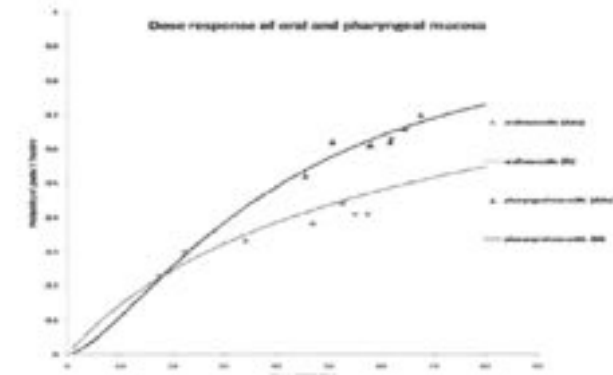
Limits

- **Superiorly:** Hard Palate
- **Inferiorly:** Cricoid Cartilage
- **Anteriorly:** Buccal Mucosa around the teeth
- **Posteriorly:** The posterior pharyngeal wall

Oral Mucosa minus target PTVs

Mucositis Evaluation

- 1) EORTC/RTOG radiation morbidity score system
- 2) Weekly transoral inspection of the oral cavity and the visualized oropharynx
- 3) No endoscopy to score the degree of mucositis
- 4) Observer-assessed dysphagia was used as a surrogate for pharyngeal mucositis



Observer-assessed acute swallowing symptoms (such as burning, dysphagia, and pain) were a surrogate of pharyngeal mucositis extension*

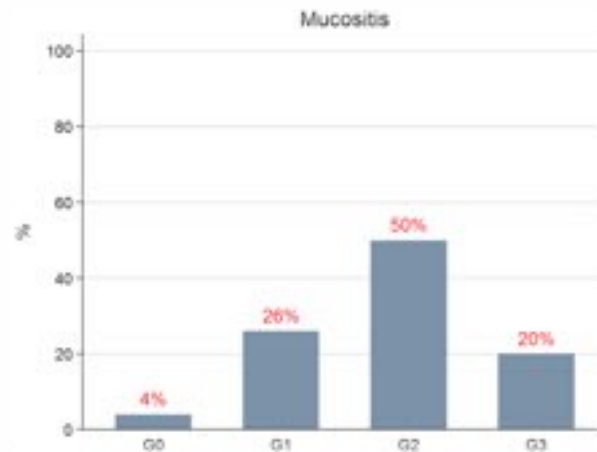
Results

ORIGINAL ARTICLE

Predictors of mucositis in oropharyngeal and oral cavity cancer in patients treated with volumetric modulated radiation treatment: A dose-volume analysis

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Parameters	Dose Constraints
Total Oral Mucosa	Mean dose ≥ 50
	Dmax ≥ 65
Oral Mucosa minus target planning target volumes	V45 Gy > 40 %
	V50 Gy > 30 %
	V55 Gy > 20 %

New proposed Oral Mucosa dose constraints **Predictors of Mucositis $\geq G2$** (RTOG/EORTC)

Results

Risk of grade ≥ 2 Mucositis according to EORTC/RTOG scale after Oral Mucosa Re-contouring

Variable	P-value	(95% CI)	Odds Ratio	% Risk
Concomitant Chemotherapy	0.006	0.1 - 1.2	5	50 %
Total OM: <i>Dmean</i> ≥ 50 and <i>Dmax</i> ≥ 65	0.02 - 0.04	0.1 - 1.3	3.75	38 - 40%
Ratio total OM/ OM out of PTVs: ≥ 2.5	0.03	0.8 - 1.8	2.6	35%
OM out of PTVs: <i>V45</i> > 40 , <i>V50</i> > 30 , <i>V55</i> > 20	0.04 - 0.009 - 0.003	0.5 - 2.3	4.85	8 - 22%

Abbreviations: OM=Oral Mucosa; CI=confidence interval; PTVs=planning target volumes; Dmean=mean dose; Dmax=maximum dose; V45=volume % of oral mucosa exposed to at least 45 Gy; V50=volume % of oral mucosa exposed to at least 50 Gy; V55=volume % of oral mucosa exposed to at least 55 Gy

Conclusions

*New **Constraints** were found, useful for clinical practice*

*The parameters analyzed were used to develop a multivariate **Model Predicting Moderate-Severe Mucositis***

It is necessary to validate clinical application in prospective analyses

THANKS FOR ATTENTION!