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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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

Trotti A et al. Radiother Oncol, 2003
In the era of dose painting IMRT, it becomes crucial to spare healthy structures to improve the patient’s QoL.
Background

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

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Department of Radiation Oncology, University of Michigan, Ann Arbor, MI

CONCLUSIONS

We estimate that the addition of concurrent chemotherapy to radiation for HNSCC increases the BED for mucositis by 8 Gy_{10}, 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
The purpose of the present study was to analyze **Predictors of Acute Mucositis** in oropharyngeal and oral cavity cancers after VMAT +/- Chemotherapy

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**Study Design**

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

<table>
<thead>
<tr>
<th>Factors</th>
<th>%</th>
<th>No. Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Site of disease</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oral Cavity</td>
<td>50</td>
<td>25</td>
</tr>
<tr>
<td>Oropharynx</td>
<td>50</td>
<td>25</td>
</tr>
<tr>
<td>T-stage</td>
<td></td>
<td></td>
</tr>
<tr>
<td>T1</td>
<td>10</td>
<td>5</td>
</tr>
<tr>
<td>T2</td>
<td>34</td>
<td>17</td>
</tr>
<tr>
<td>T3</td>
<td>18</td>
<td>9</td>
</tr>
<tr>
<td>T4</td>
<td>38</td>
<td>19</td>
</tr>
<tr>
<td>Neck nodes positive</td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>18</td>
<td>9</td>
</tr>
<tr>
<td>Unilateral</td>
<td>26</td>
<td>13</td>
</tr>
<tr>
<td>Bilateral</td>
<td>56</td>
<td>28</td>
</tr>
</tbody>
</table>

**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

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*

*Bhide S.A. et al. 2010
Results

New proposed Oral Mucosa dose constraints Predictors of Mucositis ≥ G2 (RTOG/EORTC)

## Results

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

<table>
<thead>
<tr>
<th>Variable</th>
<th>P-value</th>
<th>(95% CI)</th>
<th>Odds Ratio</th>
<th>% Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Concomitant Chemotherapy</strong></td>
<td>0.006</td>
<td>0.1 - 1.2</td>
<td>5</td>
<td>50 %</td>
</tr>
<tr>
<td><strong>Total OM:</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$D_{\text{mean}} \geq 50$ and $D_{\text{max}} \geq 65$</td>
<td>0.02 - 0.04</td>
<td>0.1 - 1.3</td>
<td>3.75</td>
<td>38 - 40%</td>
</tr>
<tr>
<td><strong>Ratio total OM/OM out of PTVs:</strong></td>
<td>0.03</td>
<td>0.8 - 1.8</td>
<td>2.6</td>
<td>35%</td>
</tr>
<tr>
<td>$\geq 2.5$</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>OM out of PTVs:</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$V_{45} &gt; 40$, $V_{50} &gt; 30$, $V_{55} &gt; 20$</td>
<td>0.04 - 0.009 - 0.003</td>
<td>0.5 - 2.3</td>
<td>4.85</td>
<td>8 - 22%</td>
</tr>
</tbody>
</table>

**Abbreviations:** OM=Oral Mucosa; CI=confidence interval; PTVs=planning target volumes; $D_{\text{mean}}$=mean dose; $D_{\text{max}}$=maximum dose; $V_{45}$=volume % of oral mucosa exposed to at least 45 Gy; $V_{50}$=volume % of oral mucosa exposed to at least 50 Gy; $V_{55}$=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!