Squamous Cell Carcinoma of the Oral Cavity: Radio therapeutic Considerations

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Ochsner Health Systems
### Association of Postoperative Radiotherapy With Survival in Patients With N1 Oral Cavity and Oropharyngeal Squamous Cell Carcinoma

- NCDB review 2004 – 2013
- 2251 pts. pT1N1 or T2N1 oral cavity and oropharynx
- No adverse features (positive margins, ECE, lympho-vascular invasion)
- No chemotherapy
- 1467 pts. Oral cavity cancer (727 no PORT, 740 PORT)
- 790 pts. Oropharyngeal cancer (341 no PORT, 449 PORT)
- Survival primary endpoint

Chen M, et.al. JAMA Otolaryngol Head Neck Surg 2016,

### Oral Cavity
- PORT associated with improved survival
- Age >70, pT2, decreased performance status associated with decreased survival
  - 5 yr. survival PORT 60.8% vs 52.0% without PORT

### Oropharyngeal Cancer
- PORT associated with improved survival
- pT2, decreased performance status associated with decreased survival
  - 5 yr. survival PORT 86.3% vs 78.8%

Chen M, et.al. JAMA Otolaryngol Head Neck Surg 2016,
Association of Postoperative Radiotherapy With Survival in Patients With N1 Oral Cavity and Oropharyngeal Squamous Cell Carcinoma

Table 3. Cox Models Predicting Hazard of Mortality Stratified by Tumor Stage

<table>
<thead>
<tr>
<th>Site by T Category</th>
<th>PORT</th>
<th>HR (95% CI)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>All</td>
<td>No</td>
<td>1 [Reference]</td>
<td></td>
</tr>
<tr>
<td>Oral cavity SCC</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>pT1</td>
<td>Yes</td>
<td>0.80 (0.60-1.07)</td>
<td>.14</td>
</tr>
<tr>
<td>pT2</td>
<td>Yes</td>
<td>0.64 (0.43-0.96)</td>
<td>.03</td>
</tr>
<tr>
<td>Oropharyngeal SCC</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>pT1</td>
<td>Yes</td>
<td>0.66 (0.35-1.24)</td>
<td>.20</td>
</tr>
<tr>
<td>pT2</td>
<td>Yes</td>
<td>0.56 (0.32-0.95)</td>
<td>.03</td>
</tr>
</tbody>
</table>

Abbreviations: HR, hazard ratio; PORT, postoperative radiotherapy; SCC, squamous cell carcinoma.

* Models are adjusted by sex, age group, race, comorbidities, site, insurance, income, educational level, and hospital type.

Chen M, et al. JAMA Otolaryngol Head Neck Surg 2016,
**Adjuvant Radiotherapy in Head and Neck Cancer**

**Combined Chemoradiotherapy**

- **RTOG 95-01 & EORTC 229311**

  Significantly improved survival in EORTC 53% vs. 40% with trend in RTOG 56% vs. 47%

Risk Stratification of Patients with Oral Cavity Squamous cell Carcinoma and Contralateral Neck Recurrence following Radical Surgery

Tongue Cancer
Independent Factors for contralateral neck recurrence.
- Poor Differentiation
- Perineural invasion
- Level IV or V metastasis

Liao, et. al, Ann Surg Oncol, 2009, 16:159
Identification of High-Risk Subgroups of Patients with Oral Cavity Cancer: Postoperative Adjuvant Radiotherapy or Chemo-Radiotherapy

- 2002 – 2013, 567 patients Oral cavity cancer
- 138 (24%) received postoperative radiotherapy – 60 – 66 Gy, 2d, 3d or IMRT
- 127 (22%) received postoperative chemo-radiotherapy, weekly cisplatin
- 5 yr overall survival Stage I, II, III, IVA, IVB 79.7%, 70.8 %, 65.8%, 49%, and 17.7%, respectively
- PRM and ECE were major risk factors
- T4, Positive nodes, margin of ≤ 5 mm, tumor depth of ≥ 1 cm, LVI, perineural invasion and poor differentiation minor risk factors

Chen, et al, Medicine 2016, 95:1

Identification of High-Risk Subgroups of Patients with Oral Cavity Cancer: Postoperative Adjuvant Radiotherapy or Chemo-Radiotherapy

192 pts. with 2 minor risk factors but no major risk factors

<table>
<thead>
<tr>
<th></th>
<th>LRC (surgery +CCRT)</th>
<th>LRC (surgery +XRT)</th>
<th>LRC (surgery)</th>
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<tbody>
<tr>
<td>DFS</td>
<td>76.7%</td>
<td>75.4%</td>
<td>66.3%</td>
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<tr>
<td>OS</td>
<td>69.8%</td>
<td>62.1%</td>
<td>48.6%</td>
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</tbody>
</table>

Chen, et al, Medicine 2016, 95:1
Identification of High-Risk Subgroups of Patients with Oral Cavity Cancer: Postoperative Adjuvant Radiotherapy or Chemo-Radiotherapy

179 pts. with at least 3 minor risk factors and/or one major risk factor

LRC
- surgery +CCRT – 70.1%
- surgery +XRT – 48.7%
- surgery – 46.0%

DFS
- surgery +CCRT – 39.8%
- surgery +XRT – 24.8%
- surgery – 29.7%

OS
- surgery +CCRT – 53.3%
- surgery +XRT – 31.3%
- surgery – 44.2%

Chen, et al, Medicine 2016, 95:1

Morbidity of (Chemo)Radiotherapy

**Acute**
- Mucositis
- Radiation Dermatitis
- Dysphagia
- Xerostomia
- Dysgeusia

**Chronic**
- Dysphagia
- Xerostomia
- Dental Caries
- Osteoradionecrosis
- Dysgeusia
- Trismus
- Lymphedema
- Voice and Speech difficulties
Organ Preservation ≠ Function Preservation

- Complications of therapy
  - Dysphagia, aspiration, stricture, PEG dependence, ORN
  - Analysis of 3 RTOG CRT trials (99-11, 97-03, 99-14)
  - 43% of patients experienced severe late toxicity

![Table 1: Types of Late Toxicity Events Seen by Trial](image)

**Improving Late Side Effects**

- IMRT - Volumetric- Modulated Arc Therapy (VMAT)
- Cytoprotective drugs
  - Amifostine
  - Pilocarpine
- Submandibular gland transfer
- Acupuncture
- Photobiomodulation / Low Level Laser Therapy
Beyond mean pharyngeal constrictor dose for beam path toxicity in non-target swallowing muscles: Dose–volume correlates of chronic radiation-associated dysphagia (RAD) after oropharyngeal intensity modulated radiotherapy

MD Anderson Head and Neck Cancer Symptom Working Group

Radiotherapy and Oncology 118, 2016
**Dental Caries**

Rare < 30 Gy, 2-3x increased 30 – 60 Gy, 10x increased risk > 60 Gy

- Retraction of gingiva, circumferential decay
- Demineralization, generalized erosions, worn occlusal surfaces

**Photobiomodulation**

- Low level laser 600 – 1000cm nm, 5 – 150 W/ cm², applied for 30 – 60 seconds (intra- orally and extra oral)
- Cytochrome C oxidase in the mitochondrial results in increase ATP production
- Short transient burst of reactive oxygen species, mitigate radiation induced in injury.
- Significantly reduces inflammation, decreases cells migrating to the area
- Helps to prevent fibrosis, decreases fibroblasts and macrophages and collagen deposition and rebuilding
**Photobiomodulation**

**Mucositis Study Group of the Multinational Association of Supportive Care in Cancer/International Society of Oral Oncology (MASCC/ISOO)**

**Recommendation**
Low level laser 650 nm, 40 mW, 2 J/cm² for prevention of oral mucositis in stem cell transplant patient with or without TBI

**Suggestion**
Low level laser for prevention of mucositis in patients undergoing radiotherapy without chemotherapy for head and neck cancer.

Migliorati, et.al, Support Care Cancer, 2013, 21:333

**Photobiomodulation**

**Oral Mucositis**
- Extra oral – lips, cheeks, neck
- Intra oral – mucosal surface

**Xerostomia**
- Extra oral – major salivary glands
- Intra oral – 6 pts major, minor glands
Photobiomodulation
Prevention of Xerostomia

• Prospective study - Sao Paulo, Brazil
• 23 pts. Head and neck cancer chemoradiotherapy (66 – 70 Gy 3D with weekly cisplatin)
• 13 pts. Intraoral and extra oral laser
• 10 pts with supportive care
• Measured salivary flow rate


<table>
<thead>
<tr>
<th>Mean Salivary Flow Rate</th>
<th>Laser</th>
<th>Control</th>
<th>p-value</th>
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<tr>
<td>Unstimulated sialometry</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>N0</td>
<td>0.480</td>
<td>0.400</td>
<td>0.081</td>
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<tr>
<td>N30</td>
<td>0.257</td>
<td>0.113</td>
<td>0.0143</td>
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<tr>
<td>Stimulated sialometry</td>
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<tr>
<td>N0</td>
<td>0.717</td>
<td>0.587</td>
<td>0.0771</td>
</tr>
<tr>
<td>N30</td>
<td>0.463</td>
<td>0.213</td>
<td>0.0131</td>
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