

## Radiation Therapy for Oral Cavity Cancer

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### General Management

The choice of treatment modality, either single or in combination, depends on the stage and tumor size and relevant patients factors such as toxicities, performance status, comorbid disease, and convenience.

For early stage cancer, T1 or T2 lesions, control rate of either modality, surgery or radiation is generally same. However, usually, the choice of initial treatment is surgical resection in many institutions. Main cause of these clinical practices are required time of courses of radiation and moreover, the risk of associated xerostomia, osteoradionecrosis may render radiation therapy a less attractive choice of single modality therapy for early stage lesions. Nevertheless, for patients having high risk of surgery or in whom surgical approach result in significant functional loss, radiation therapy offers a good alternative for definitive treatment for early lesion of oral cavity. For advanced disease, combined treatment approach is preferred. Postoperative radiation therapy had preponderance data and preferred practice of pattern. Furthermore, there are emerging data for selected high risk patients, addition of concurrent chemotherapy during radiation therapy may improve treatment outcome.

Historically brachytherapy and intraoral cone therapy has played an important role for oral cavity cancer as a boost treatment after external radiation therapy or as a sole treatment in early stage lesions. Now steady advancement of highly conformal radiation therapy technique such as IMRT (intensity modulated radiation therapy) or Tomotherapy has contributed to less frequent practice of brachytherapy or intraoral cone therapy.

### Radiation Therapy

#### 1. General principle

For early lip, oral tongue, and floor of mouth tumors, ac-

ceptable local control has been achieved with brachytherapy alone or combination with brachytherapy and external beam radiation. Decroix and Ghossein reported recurrence rate after radium implant or implantation plus external radiation therapy was 14% and 22% for T1 and T2 lesions respectively. The Royal Marsden Hospital reported 5 years local control rate approximately 90% for T1,T2 lesions. Other retrospective series suggested that control rates at the primary site in oral cavity cancer treated with brachytherapy alone or combination of brachytherapy plus external radiation ranged from 70% to 95%. Intraoral cone therapy like brachytherapy is a localized radiation technique that has been used to boost dose to primary sites. Either technique for the boosting primary tumor resulted in improved outcome compared to high dose external beam radiation therapy alone. As with specialized procedure and technique, skill and experiences of the radiation oncologist is of critical importance to the successful delivery and outcome of interstitial radiation or intraoral cone therapy.

The outcome for advanced lesions of the oral cavity (T3, T4) are less satisfactory with either surgery or radiation alone. Adjuvant radiation therapy can be delivered to preoperatively or postoperatively. Although each strategy has potential advantages and disadvantage, postoperative radiation therapy is generally preferred. Postoperative radiation therapy carries the advantage of no radiation dose limitation, no delay in the implementation of surgical resection and complete pathologic staging of the tumor. However, postoperative wound complication may delay the radiation therapy and regional hypoxia that can accompany the postoperative stage may diminish the effectiveness of radiation therapy compared to that achievable under of full oxygenation.

#### 2. Role of adjuvant radiation

Adjuvant radiation therapy is commonly recommended for advanced lesion to enhance the likelihood of locoregional tumor control.

Mishra et al conducted phase III study of surgery with or without adjuvant radiation therapy within 6 weeks after surgery. They reported a 30% absolute improvement in disease free survival, although there was no difference in overall survival with the use of adjuvant radiation therapy.

### 3. Role of neoadjuvant radiation therapy

At least two randomized trial were conducted neoadjuvant chemotherapy before surgery for T2-4/N0-2 oral cavity carcinoma. There were no difference of survival but did on the potential improving respectability and reducing the need for adjuvant radiation therapy postoperatively. Preoperative chemoradiation has been studied prospectively by Mohr et al for 268 patients with T2-4/N0-3 oral cavity and oropharyngeal carcinoma to either preoperative chemoradiation with cisplatin versus surgery alone. The result of this study revealed an improvement in overall survival and local control with use of preoperative therapy. This regimen, however, has not shown common adoption on other centers around the world. The main cause of poor adoption of preoperative chemoradiation would be fear of possible increased wound complication induced by radiation therapy.

### 4. Recent radiation therapy technique(IMRT and adaptive radiation therapy by image guidance)

In recent year, there has been increasing use of IMRT for the treatment of head and neck cancer. With the regard to oral cavity cancer, IMRT offers the opportunities to diminish normal tissue damage including salivary gland (xerostomia) and to the mandible. Reduced dose to the salivary gland less than 26-24 Gy through IMRT remarkably improved postradiation salivary function. In light of the steep dose gradients of IMRT plan, successful delivery of IMRT is dependent on accurate and reproducible localization and immobilization during IMRT procedure. Recently several image guided localization system is used to enhance daily treatment precision for IMRT including tomotherapy or through treatment room imaging, thereby allowing image guided adaptive radiation therapy and daily set-up verification.

### 5. Radiation dose and fractionation

For postoperative therapy, dissected tissue that harbored original tumor should generally receive on the order of 60 Gy. However, for close or positive margin or extracapsular nodal extension, 4 to 6 Gy localized boost should be considered. If there is gross residual disease, focal boost upto 70 Gy is advisable. Region of less risk (i.e., clinically or pathologically uninvolved area) should receive 50–54 Gy.

When definitive radiation is used for oral cavity cancer, boosting primary site with brachytherapy or intraoral, submental cone therapy can result in increased tumor control and decreased complication, particularly osteoradionecrosis.

RTOG 90-03 altered fractionation randomized clinical trial demonstrated hyperfractionated radiation and concomitant boost therapy increased disease free survival in almost head and neck sites. However, oral cavity primary cancer constituted a minority of cases enrolled in these studies.

### 6. Concurrent chemoradiotherapy

Several recent studies focused on the use of chemoradiation in the patients with high risk pathologic features following surgery. Cooper et al reported the results of a randomized study in North America comparing radiation alone (60–66 Gy) to chemoradiation (same radiation dose plus three cycles of 100 mg/m<sup>2</sup> cisplatin) in patients with high risk pathologic features (two or more involved lymph node, microscopically involved margin, extracapsular extension of nodal disease). This study demonstrated benefit in locoregional control and disease free survival rate for chemoradiation arm. Parallel study in Europe by Bernier et al showed superior local control, progression free survival and survival on the chemoradiation arm. These two studies suggested that addition of chemoradiation following surgery may be beneficial in selected good performance status patients with high risk groups, although with increased toxicities profiles.

### 7. Importance of dental care for oral cavity cancer

Dentition in poor condition should be identified and considered for extraction to minimize the subsequent risk of osteoradionecrosis. Specifically, those teethes that will reside within high dose radiation volume that demonstrated significant periodontal disease, advanced caries, abscess formation, in state of disrepair and impacted teeth and marginal teeth should be extracted. Even teeth condition is adequate in pre-radiation period, radiation can induce several chronic effects in oral cavity and impair bone healing and diminished the capacity for successful recovery following trauma or oral surgery. Also radiation to the major salivary gland changes the nature of saliva, which creates an environment to predispose dental caries that increase the risk of osteoradionecrosis. During courses of radiation therapy, simple technique such as the use of dental mold to absorb electron backscatter can diminish hot spot mucositis. Attention to oral hygiene with frequent dental follow-up and cleansing, daily fluoride therapy, flossing, and brushing should be integral component of education and postradiation care in oral cavity cancer patients.