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Advances in Radiotherapeutic Management of Oral Cancer

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Overview

Cancers of the oral cavity and oropharynx include very diverse cancers of varying histologies arising from many subsites of oral cavity i.e., the lips, buccal mucosa, upper and lower gingiva, hard palate, oral tongue, floor of the mouth and 4 subsites of oropharynx i.e., the tonsillar area, base of tongue, soft palate and posterior pharyngeal wall. Because of diversity of subsites and histology of oral cancers showing their own unique spread patterns, management of each cancer is quite varied. Associated morbidities of each cancer and treatment involve very important functions governing the good quality of life and survival such as speech, eating, breathing and appearance. The overall management goals for these patients are to achieve the highest cure rates at the lowest cost in terms of functional and cosmetic morbidity. The achievement of these goals requires specific multidisciplinary expertise in the close interaction and cooperation.

1. Primary tumors

Limited size lesions(T1, T2) generally can be controlled equally well by either surgery or radiotherapy alone. Large lesions(T3, T4), if resectable with an acceptable surgical morbidity, are generally best controlled by surgery followed by RT in which the basic target volume for RT is formulated as if no surgery had been performed. Advanced unresectable tumors are treated with RT including brachytherapy and sometimes in combination with chemotherapy. For selected cases, chemoradiotherapy is used for organ preservation and surgery held in reserve for salvage of recurrence.

2. Lymph nodes

Clinically negative necks should be electively treated if the likelihood of occult metastatic disease is significant. This risk is significant for all primary sites in the oral cavity and oropharynx with the exception of the lips, hard palate and upper alveolar ridge. Bi-

Table 1. Therapeutic approaches in H/N cancer

Established	Investigational
Definitive surgery(S)	Induction chemotherapy and S or RT
Definitive radiotherapy(RT)	Induction chemotherapy with curative RT
Surgery and preop. or postop. RT	(organ preservation)
Definitive RT. S for salvage of recurrence	Concurrent chemoradiotherapy
Altered fractionation RT	Altered fractionation RT
Concurrent chemoradiotherapy	S or RT and adjuvant chemotherapy
Palliative radiation therapy	RT with hyperthermia or with radiosensitizers
Palliative chemotherapy	3D conformal RT
	Immunobiologic therapy
	Chemoprevention

lateral neck should be treated if the primary was arised from a midline structure i.e., base of tongue, palate, pharyngeal wall etc. If nodal metastases are present on one side of the neck, contralateral neck should be electively treated. Frequently the mode of treatment selected for the primary influences the treatment applied to the nodes. RT with 50 Gy in 5 weeks has been very effective in preventing relapse in N0. N1 disease can be treated with surgery or radiotherapy. Palpable disease is boosted upto 70 Gy with electron or brachytherapy. N2 or N3 disease, if resectable, is best treated by neck dissection followed by irradiation. In this case, gross tumor bed has to be boosted. Because of high risk of subsequent distant metastasis in these patients, patients can be placed on chemotherapy trial. Advanced unresectable nodal disease heralds a poor prognosis and such patients should be enrolled in investigative protocols whenever feasible.

3. Recurrent disease

If local recurrences occur after primary radiotherapy, they can often be successfully treated with salvage surgery, resulting in similar overall survival rates. But salvage of surgical recurrences by radiotherapy is less effective than is surgical salvage of radiation failures.

General Principles in Radiotherapy for Oral Cancer

1. Target volume and dose

The primary target volume for standard radiotherapy for oral cancer typically includes the gross primary tumor and enlarged neck nodes and the secondary target volumes with submandibular, jugular, posterior neck nodes and LN groups at a risk of 10–15% for subclinical metastasis. Most often, shrinking field technique is applied and 50 Gy in 5 weeks for large fields including subclinical disease, and 70–75 Gy for gross disease are needed. In postop. cases, the surgical bed of primary tumor and involved node are included as primary targets. After 50 Gy for large fields, primary targets are boosted upto 60 Gy when resection margins are free. When resection margin contains tumor, primary targets should be boosted upto 65–70 Gy.

External beam RT provides the most common form of treatment and interstitial brachytherapy or surface mold or intraoral cone therapy can be utilized for a boost therapy for gross tumor. Interstitial brachytherapy or intraoral cone therapy alone can be utilized for a definitive radiotherapy for selective small lesions. When adequate resection is not feasible, afterloading catheters can be implanted into tumor bed for iridium-192 loading in post-op. 3–4 days to deliver 30–40 Gy if post-op external RT is planned, 55–65 Gy if no post-op external RT is feasible. Post-op RT should not be delayed beyond 6 weeks after surgery.

The most popular brachytherapy technique for oral cancer includes afterloading Ir-192 temporary implants and iodine-125 permanent implants. Recently high dose rate(HDR) Ir-192 brachytherapy has gained its popularity because of its superiority with regard to radiation protection considerations. Yet, clinical data for HDR brachytherapy for H/N cancer is still very limited.

Table 2 shows local control rates and survival data for patients with squamous cell carcinoma in the oral cavity and oropharynx treated with definitive RT. While the local control rates are excellent for the small lesions, there is obviously a need for improvement in radiotherapy for larger lesions.

2. Complications

Majority of patients experience moderate degree of oral mucositis and rarely it interrupts the treatment with proper oral care. Standard RT volume for oral cancer includes parotid and submandibular glands bilaterally and this causes permanent xerostomia in most of cases. Soft tissue or bone necrosis can occur in less than 10% of patients and a boost with interstitial brachytherapy may increase the incidence of these complications.

Table 2. Representative local control rates and survival for patients with squamous cell carcinoma of oral cavity and oropharynx

Stage by site	Local control(%)	Survival(%)
Oral cavity		
Oral tongue		
T1	80 - 90	75 - 80
T2	60 - 85	40 - 60
T3	30 - 50	20 - 30
T4	25 - 45	10 - 15
Floor of mouth		
T1	75 - 85	70 - 85
T2	60 - 80	50 - 60
T3	30 - 50	15 - 40
T4	5 - 30	5 - 20
Oropharynx		
Base of tongue		
T1	80 - 95	65 - 85
T2	60 - 75	40 - 55
T3	40 - 65	15 - 20
T4	30 - 50	5 - 20
Tonsil/tonsillar fossa		
T1	75 - 95	65 - 85
T2	60 - 80	55 - 60
T3	35 - 70	20 - 40
T4	20 - 30	10 - 15
Soft palate		
T1	90 - 100	90 - 95
T2	75 - 85	65 - 75
T3	60 - 70	30 - 40
T4	25 - 35	10 - 15

Advances in Radiotherapy

New or advanced technology for planning and delivery of radiation may bring drastic changes in the way radiation therapy is provided for H/N cancer. We expect 3D conformal RT and intensity modulated RT to improve the outcome of H/N cancer but clinical data is rather slow to come because of diversity of cancers in this region and its anatomic complexity.

Improvement in our understanding of radiobiology for acute and late responding tissues to radiation has stimulated numerous trials of altered fractionation schemes comparing to the conventional RT and in H/N cancer, altered fractionation schemes appears to be superior to conventional RT.

HDR brachytherapy is a new technology and prospective studies for optimum dose fractionation schedule for oral cancer are awaited to evaluate its efficacy.

Researches for predictive assay for radiosensitivity of individual tumor or to look for potential markers that may guide how to deliver RT on a more individualized basis are on going.

Clinical trial with concurrent chemoradiotherapy showed somewhat improved outcome in H/N cancer.

In spite of promising results of laboratory works with radiosensitizers and protector, yet, human trials for radiation sensitizer and protector did not reveal positive results.

Research for chemoprevention to prevent subsequent second cancer is on-going.

1. Altered fractionation schemes

Based on different radiobiologic principles on tumor tissue and on normal tissue, hyperfractionation, accelerated fractionation, concomitant boost with accelerated fractionation or continuous hyperfractionated accelerated RT have been tried. The current trials of altered fractionation scheduled RT for H/N cancer have reported consistently somewhat improved outcome.

2. CT-simulation and Virtual simulation

This simulation technology improves the accuracy of the target coverage and helps to minimize the inclusion of the critical structures like the parotid glands from the treatment volume. This technology is not only the essential step for 3D conformal therapy but also, very useful for 2D conventional RT.

3. 3-D Conformal therapy and Intensity modulated radiotherapy

Recent developments on 3-dimensional RT planning computer, CT-simulator and computer controlled medical accelerators equipped with multi-leaf

collimators and on-line electronic portal image verification systems enable the delivery of 3-D conformal therapy. 3-D conformal RT provides a signigicant advantage in normal tissue sparing as well as tumor coverage in the target volume. 3D conformal therapy trial for H/N cancer reported a significant reduction in the degree of xerostomia. Dose escalation study to improve the local control is yet to come.

4. Concurrent Chemoradiotherapy

5. Radiation sensitizer and protector

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구강암에 대한 수술적 치료의 역할

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서 론

소화기관이 처음 시작하는 입술에서 부터 상·하치주, 구강저, 혀의 앞2/3, 경구개부, 구후치 삼각부, 볼점막 등을 포함하는 구강에 발생하는 암은 몇가지 특징이 있다. 대부분 편평상피암(95%)이며 이들의 3/4이 전체 구강 표면적의 1/10에 해당하는 구강저, 혀의 측면, 구후치 삼각부에서 주로 발생한다. 구순암은 다른 나라의 보고와는 다르게 발생빈도가 적다. 또한 구강에 발생하는 암은 쉽게 환자 자신이 발견할 수 있는 데도 불구하고 진단이 늦어지는 경우가 많다.

두경부의 모든 암에 대한 치료법은 일반적으로 수술, 방사선치료, 항암화학요법 등을 단독 혹은 병용하여 사용하게 된다. 구강암 치료의 궁극적 목표는 암의 완전한 치유, 구강의 형태와 기능 보존, 치료 후유증의 최소화, 그리고 이차 원발암의 예방에 있다. 그러나 구강암은 치료후유증으로 발성, 저작, 연하 및 미용적 장애를 초래하는 경우가 많아 암종자체의 특성, 환자의 상태와 생활습성, 의료진의 수준과 협동성 등을 고려하여 환자 개개인에게 맞는 신중한 치료법의 선택이 필요하다. 특히 수술적 치료는 가장 중요한 치료역활을 담당하지만 다른 치료법에 비하여 장점과 단점을 동시에 갖고 있는 침습적 방법이어서 세심한 절제부위의 결정과 재건방법의 선택이 없으면 많은 합병증, 후유증과 재발을 남기게 된다.

수술적 치료의 역사적 배경

두경부 수술은 쉽게 접근할 수 있는 입술과 혀의 작은 병변에서 부터 사실상 시작되었다고 하여도 과언이 아니다. Marchetti(1664)는 소작술로 혀암종을 절제하였고, Heister(1743)는 혀암의 수술시 정상경계를 포함하여 절제한 것을 처음 보고하였다. Cloquet(1827), Regnoli(1838)는 설골상부 접근법으로 혀를 절제하였으며, Roux(1836)는 정중 하악절개접근법을 소개하였다. Butline(1885)는 혀의 수술법을 분류하였고 경부피판을 고안하고 구강병변과 동시에 하악임파절을 제거하였다.

Polya(1902)는 처음 두경부 임파계에 대한 연구를 보고하였고, George Crile(1906)은 최근의 경부곽청술과 동일한 개념의 radical neck dissection과 13%의 사망율을 보고하여 두경부암 수술의 전환점을 만들었다. Semken(1927)은 제한적 경부청소술을 제안하였고 Ward, Grant(1932)는 composite(commendo) operation 을 시작하였다.

Hayes Martin(1957)은 두경부암 수술법을 체계적으로 정리 기술하였다. Ariyan(1979)이 대흉근피부피판술, Yang(1981)이 전완유리피판술을 개발하여 두경부재건술에 획기적인 전기를 마련하였다.

치료법 선택의 고려점

구강암의 초기 치료법의 선택에 고려하여야 할 요인은 1) 원발 종양의 특성, 2) 환자의 특징, 3) 의료진의 수준과 협동성 등이 있다. 구강암 자체가 치료법 선택에 미치는 요인으로는 원발장소, 크기, 위치, 뼈의 근접도, 경부 임파절 전이, 과거 치료력, 조직학적 분류 등이 있다. 환자의 나이, 전신 상태, 인내성, 직업, 이해도, 생활습관, 사회 경제적 상태 등을 고려하여야 한다.