EVALUATION OF SPECIMEN BASED AND PATIENT BASED RESECTION MARGINS IN HEAD AND NECK MALIGNANCIES

By

DR. FESLI LATHEEF

DISSERTATION SUBMITTED TO

SRI DEVARAJ URS ACADEMY OF HIGHER EDUCATION AND RESEARCH,

KOLAR, KARNATAKA

In partial fulfillment of the requirements for the degree of

MASTER OF SURGERY
IN
OTORHINOLARYNGOLOGY

Under the guidance of

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2022

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The Institutional Ethics Committee of Sri Devaraj Urs Medical College, Tamaka, Kolar has examined and unanimously approved the Synopsis entitled **"Evaluation of Specimen based and Patient based Resection Margins in Head and Neck Malignancies"** being investigated by Dr.FESLI LATHEEF, Dr. S. M. Azeem Mohiyuddin & Dr. Manjula K[1] in the Departments of ENT & Pathology[1] at Sri Devaraj Urs Medical College, Tamaka, Kolar. **Permission is granted by the Ethics Committee to start the study.**

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Dr. FESLI LATHEEF

LIST OF ABBREVIATIONS

SCC	Squamous Cell Carcinoma
AJCC	American Joint Committee of Cancer
CECT	Contrast Enhanced Computed Tomography
NACT	Neoadjuvant chemotherapy
RT	Radiotherapy
CT	Chemotherapy
ENE	Extra Nodal Extension
KPS	Karnofsky Performance Status
EORTC	European Organization for Research and Treatment of Cancer
BFF	Before formalin fixation
AFF	After formalin fixation
DOI	Depth of Invasion
HPR	Histopathological resection.

ABSTRACT

BACKGROUND: Surgery is the main modality of treatment in head and neck malignancies. Close or positive margins of resection result in microscopic disease being left behind and carry poor prognosis. Owing to complex anatomy and proximity to vital structures wide margins may not be always possible in this cases it has been a controversy weather to harvest a cut margin for histopathology from the patient site (defect) or from specimen site .This study was taken up to address the above controversy involves histopathological evaluation of a full thickness wedge of resection from the defect (patient site) for distance tumor as well as microscopic disease clearance in 60 patients undergoing surgery for oral cancer with or without extension to pharynx and staged T2 to T4a.

OBJECTIVES:

1. To evaluate full thickness slice from the visible closest margin of resection for microscopic disease both from specimen as well as defect in the patient (tumor bed) during resection of primary tumor in head and neck surgeries.
2. To document the distance from margin of primary tumor to closest margin of resection before and after formalin fixation in head and neck squamous cell carcinoma.

METHODS: A full thickness slice of tissue was harvested from the margin closest to the tumor both from specimen as well as patient defect site. The distance from the visible margin of tumor to the margin of resection was measured in millimeters intraoperatively, and after resection (Before Formalin Fixation (BFF)) and by

histopathology (After formalin fixation (AFF)). The shrinkage of the margin at the surface as well as depth in the muscle along with the third dimension (deepest part) was evaluated during histopathological examination and disease clearance was documented. The patients having Positive or close margins were analyzed with regard to the subsite were the primary tumor was located and Oncological outcome with regard to locoregional control.

RESULTS:

Majority of our study subjects had tumors involving buccal mucosa 61.7% and oral tongue 16.7% and majority of the patients in our series had locally advanced disease. In our study 1 patient had positive margin and 18 patients had close margins on histopathology. 2 patients had specimen site positive margin and none of the patients had positive margin in (defect) patient site. In our study 33.3% of patients had metastatic cervical lymph nodes and 10% of patients had extra nodal spread. Among 18 patients with close margins, 31.6% patients recurred whereas among patients with adequate margins only 17.5% recurred. Majority of the patients (92%) had tumors with depth of invasion ≥5mm and 25.5% recurred and only 7.7% recurred among patients with depth of invasion <5mm.

1. **CONCLUSION**: A margin of at least 1cm from outmost part of the tumor to the line of resection before formalin fixation and at least 5mm after formalin fixation is considered adequate in most regions involving squamous cell carcinoma of head and neck. Adequate margins of resection ensure better locoregional control.

2. While evaluating margins of resection for disease clearance, it would be safer to evaluate a full thickness slice of tissue from the specimen (closest margin from the tumor) along with a full thickness slice from the adjoining the defect (patient site). This is all the more important at depth in the muscle tissue.

KEYWORDS:

Head and Neck squamous cell carcinoma, Margins of resection, Close margins, Patient and Specimen site margin, Shrinkage on formalin fixation, recurrence, locoregional control.

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INTRODUCTION

INTRODUCTION

Head and neck malignancies constitute the sixth cause of cancer-related deaths worldwide. Majority of the head and neck malignancies (90%) are squamous cell carcinoma. 30% of all cancers in our country are head and neck malignancies with prevalence of oral cancer and most prevalent cancer in kolar is oral cancer with an incidence of 29.66% mainly due to addiction to chewable carcinogens like tobacco quid and arecanut and 80% of our patients present with locally advanced disease requiring multimodality treatment consisting of surgery followed by radiotherapy or radiotherapy and chemotherapy.[1,2]

Since surgery in the form of composite resection is the first step in treatment of the malignancies, adequate margins of resection are mandatory. The loco regional control and intensity of adjuvant treatment are directly dependent on resection margins which are usually 1cm away from visible margin of tumor and at least 1 plane deeper more in tongue. However, the complex anatomy, proximity to important structures, difficult access, and diluted margins due to earlier chemotherapy or radiation, can sometimes compromise the margins resulting in microscopically positive or close margins which can adversely affect the outcome[3].

It has been common practice by surgeons to harvest a cut margin wherever the resection goes closest to the tumor and evaluate this cut margin as well as the specimen by either frozen section or conventional histopathology. However, the reporting of the resection margins has always been an area of controversy. This is because the visible tumor margin on the surface mucosa or skin may be unreliable as the tumor can extend beyond it sub mucosal or along the muscles. Tissues also undergo shrinkage on formalin fixation for histopathological examinations. This further complicates the status of resection margins. The muscle deep to the tumor can retract or shrink much more than the epithelium. This causes discrepancy

between surgical findings and histopathological reports and can affect the further management. Close margins require aggressive adjuvant treatment in form of Chemotherapy + Radiotherapy and also adversely affect locoregional control[3,4].

Due to the above reasons, it has always been controversial whether to harvest a cut margin from the defect (patient site) or from the resected specimen. The cut margin based on epithelial extent of tumor may not represent the deeper muscular margin. There are ongoing studies in premier institutions in various countries in this regard.

This study which involves evaluation of a full thickness wedge of resection from the defect (patient site) and the resected specimens wherever the resection is closest to the tumor and may contribute in addressing this controversy as to where the cut margins should be from. It will also throw light on the extent of tissue shrinkage on formalin fixation and the discrepancy between epithelial and deeper muscular margins. It may help contribute to future protocols with regard to resection margin control and there by contribute to better outcome in these locally advanced cancers.

RESEARCH HYPOTHESIS

Resected Margins from patient site is more representative of microscopic clearance particularly when it involves muscular tissue compared to resected margin from patient site.

RESEARCH QUESTION

Will margin of resection from specimen site be more representative than resected margins from patient site with regard to microscopic tumor clearance particularly it involves muscular tissue?

AIMS & OBJECTIVES

OBJECTIVES OF THE STUDY

1. To evaluate full thickness slice from the visible closest margin of resection for microscopic disease both from specimen as well as defect in the patient (tumor bed) during resection of primary tumor in head and neck surgeries.

2. To document the distance from margin of primary tumor to closest margin of resection before and after formalin fixation in head and neck squamous cell carcinoma.

REVIEW OF LITERATURE

REVIEW OF LITERATURE

Carcinoma is derived from a Greek word meaning crab and the latinised form is “cancer”. Another terminology for cancer was malignancy from its Latin roots malignus and genus meaning endangering harm. Cancer was used to characterize abnormal growths of cells which result in the invasion of normal tissue or spread to the organs.

Head and Neck cancer is highly prevalent in India and around one lakh deaths occur per year in our country due to squamous cell carcinoma of head and neck and around 2 lakh new cases are diagnosed every year in India.[1]

About 30% of all the cancers in our country are Head and Neck Malignancies, the most common among them is oral cancers. An increased trend is seen in morbidity and mortality rates of squamous cell carcinoma (SCC) of oral cavity in industrialized areas. Head and neck is the 6th most common cancer worldwide with high prevalence in South Asia and most prevalent cancer in Kolar is oral cancer with an incidence of 29.66% of total.[1,2]

The main causative factors for head and neck squamous cancer in the country are chewable carcinogens, smoking and alcohol mostly affecting the oral cavity and pharynx and the sites of oral cavity involving are buccal mucosa, lower alveolus, upper alveolus, hard palate, floor of mouth, retromolar trigone, gingivo buccal sulcus and some of these subsites involve underlying bone and the soft tissue is very thin comprising of mucosa and periosteum[1,2,3].

Since majority of patients are presenting in late stage with locally advanced disease, treatment comprises of composite resection with atleast 1cm visible margin from all sites and at least 1 plane deeper from base of tumor. However in certain subsites the complex anatomy

and presence of bone under the mucosa and periosteum present difficulties in achieving adequate margins. Microscopic disease can also contribute to this problem.[4,5]

Removal of all tumor cells at both macro- and microscopic levels is the ultimate goal of any onco-surgeon treating Squamous Cell Carcinoma (SCC). One of the main goals of treatment of SCC of buccal mucosa is resection with a minimum of a 5 mm margin after formalin fixation of surrounding normal tissue, the violation of which has been consistently correlated with poor prognosis.[6]

Adjuvant treatment is planned according to various features like lymphovascular spread, perineural spread, positive margins [7.] Adequate three-dimensional clearance is mandatory to have good outcome as well as to plan the adjuvant treatment. Where ever margins are positive or extra nodal spread from lymph nodes are present adjuvant treatment in the form Radiotherapy with chemotherapy is given. In rest of the patients with T3 or T4 disease, adjuvant treatment is only Radiotherapy.[7,8] Patients with close margins or positive margins of resection have poor prognosis compared to those with negative margin of resection.

EMBRYOLOGY

The stomatodeum bounded by brain above and pericardial sac below becomes apparent at 4th week of intrauterine life. The breakdown of bucco-pharyngeal membrane causes mouth to become continuous with the developing pharynx.

Mesodermal condensation in lateral wall and floor of the pharynx gives rise to branchial arches which differentiate to produce cartilaginous bar, branchial musculature and branchial arch artery with each arch receiving an afferent and efferent nerve supply, post and

pretrematic nerve supply. [9]

The mandibular process arising from the lateral aspects of developing head fuse by the 6th week in midline and the maxillary process arising as buds from mandibular processes, grow forwards and meet with lower end of nasal septum and its contralateral side in the midline. Fusion of maxillary processes separates primitive nasal cavity from primitive oral cavity.[10]

ORAL CAVITY – ANATOMY[11]

Oral cavity is the uppermost part of digestive tract.

The oral extends from the mucocutaneous junction of the lips, the vermilion border extending.

POSTERIORLY: SUPERIORLY - The junction of hard and soft palate

LATERALLY - Anterior fauces

INFERIORLY - Junction of the anterior two-thirds and posterior third of the tongue[11]

The various anatomical sites within the oral cavity as described by the American Joint Committee for Cancer staging[12] are:

- Lip
- Tongue (Anterior 2/3rd)
- Floor of mouth
- Gingiva - Upper alveolus and Lower alveolus
- Buccal mucosa
- Retromolar trigone
- Hardpalate

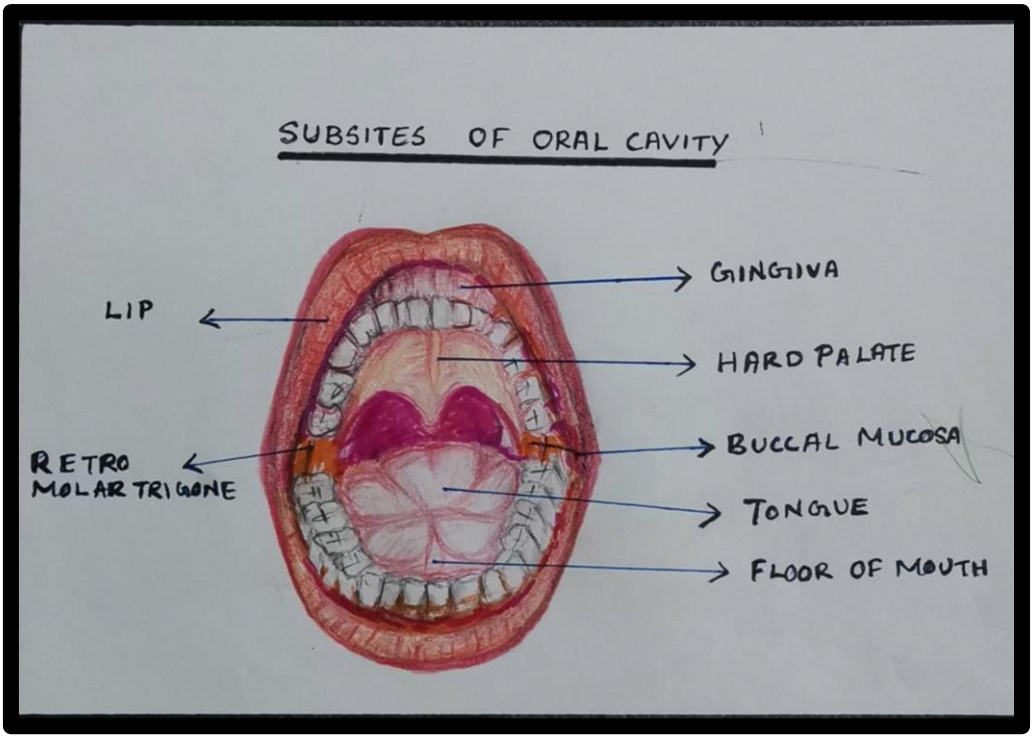


Fig 1: - Oral cavity - subsites

Lip: The lip begins at the vermilion border of the skin. The vermilion surface is that portion of the lip that comes into contact with the opposing lip. It is divided into an upper and lower lip, which join at the commissures of the mouth.

The ventral and lateral surfaces are in continuity with the floor of mouth, having a lining mucosa with non-keratinizing stratified squamous epithelium. The dorsum and tip of tongue are lined by specialized gustatory mucosa, with a thick, primarily keratinized epithelium.

Anterior 2/3rd of the tongue: It is the freely mobile part of the tongue that extends from the tip anteriorly to the line of circumvallate papillae posteriorly. Inferiorly it extends up to the junction of the floor of the mouth at the under-surface of the tongue. It is composed of four areas: the lateral borders, the tip, the ventral surface and the dorsum.

Buccal mucosa: It is the mucous membrane lining of the inner surface of the cheek and lips

from the line of contact of the lips to the line of attachment of mucosa to the alveolar ridge (upper and lower) and to the pterygomandibular raphe.

Lower alveolar ridge: Mucosa lining the alveolar process of the mandible from line of insertion in buccal sulcus to floor of mouth mucosa. Posteriorly up to the ascending ramus of the mandible.

Upper alveolar ridge: Mucosa lining the alveolar process of the maxilla, extending from the line of attachment in the upper gingivo-buccal sulcus to the hard palate. Posterior margin extending up to superior end of pterygopalatine arch.

Retromolar gingiva (Retromolar trigone): This is a triangular area over the ascending ramus of the mandible lined by mucosa. Anterior border is formed by lower last molar tooth and apex is at maxillary tuberosity.

Floor of the mouth: This is a semilunar space over the base of tongue muscles i.e. mylohyoid and hyoglossus muscles, extending from the inner surface of the mandibular alveolar ridge to the ventral surface of the tongue. Lower part of anterior pillar of the tonsil forms the posterior boundary. It is divided into two sides by the frenulum of the tongue and contains opening of the submandibular and sublingual salivary gland ducts.

Hard palate: Area between the two-upper alveoli, lined by mucous membrane, formed by palatine process of maxilla. It extends from the inner surface of the superior alveolar ridge to the posterior edge of the palatine bone.

ORAL CAVITY – BLOOD SUPPLY

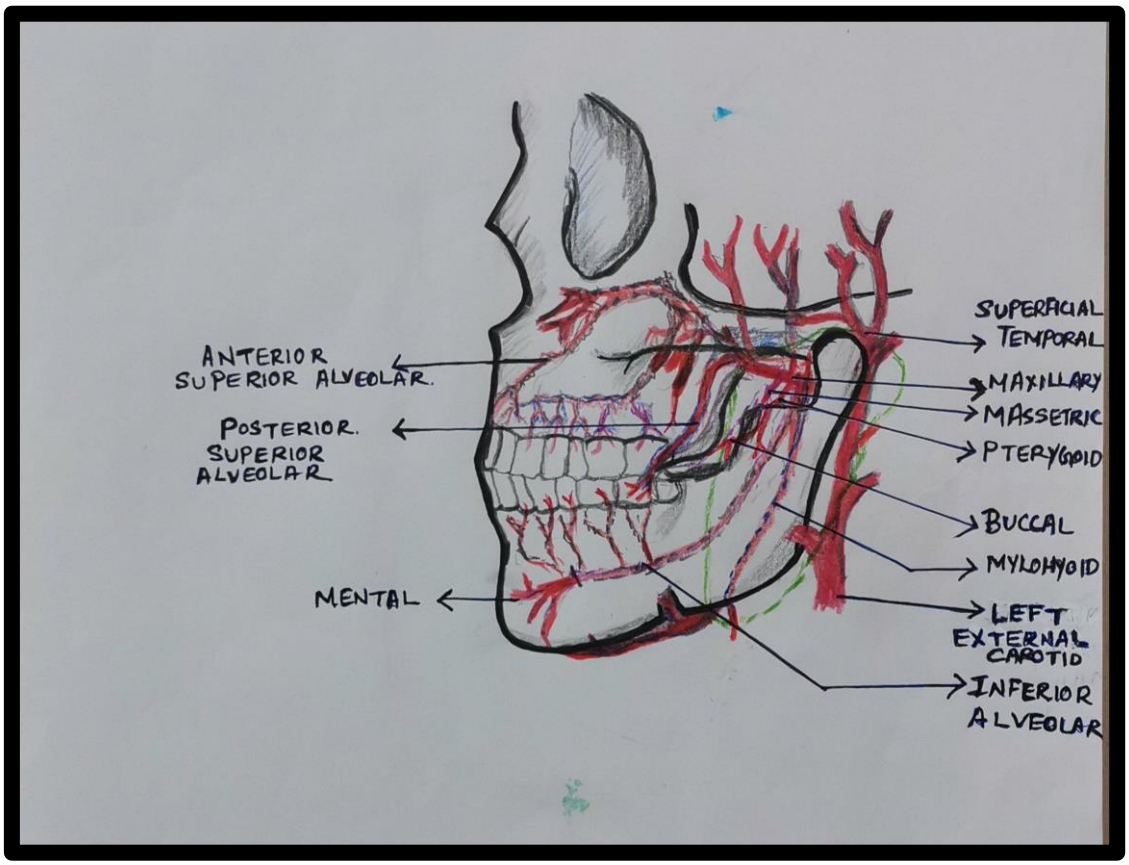


Fig 2: Oral cavity – Blood supply

Branches of external carotid artery provide blood supply to oral cavity. Lingual arteries provide blood supply to the tongue. The lips, buccal mucosa and alveolar ridges receive its blood supply from facial arteries, internal maxillary and inferior alveolar arteries. Palate and upper alveolus are supplied by greater palatine arteries.[9]

ORAL CAVITY – NERVE SUPPLY

The sensory nerve supply to oral cavity is provided by sensory component of second and third division of trigeminal nerve, through superior and inferior alveolar and lingual nerves. Special senses of taste and secretomotor fibres to the salivary glands are provided through chorda tympani nerve traversing along the lingual nerve. Motor control of the lips and cheek

is provided by the facial nerve. The hypoglossal nerve is the motor nerve for the intrinsic and extrinsic muscles of the tongue. The movements of the medial and lateral pterygoid muscles and their actions are controlled by the motor components of the second and third divisions of the trigeminal nerve.[13]

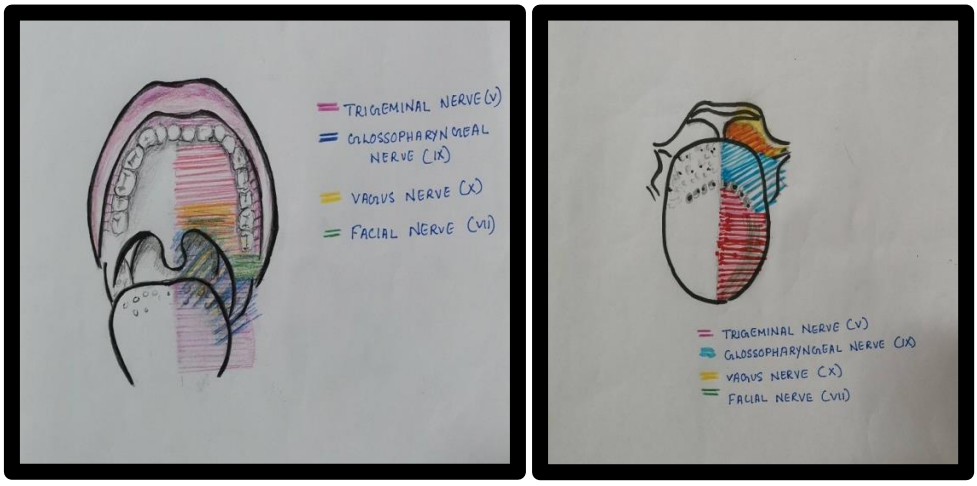


Fig 3: Nerve supply of Oral cavity

HISTORY OF LYMPHATIC SYSTEM

Gaspero Aselli, professor of anatomy and surgery from Italy made the first description of lymphatic systems in 1662. William Hunter, William Cruikshank, and William Hewson in London precisely described the anatomy and physiology of the lymphatics in 1786 in their monograph by Cruikshank.[14]

Sappey, further described the anatomical understanding of the lymphatic system and his diagrams of lymphatic flow are used even today. During this time, Virchow and other researchers advocated that lymph nodes were a barrier to cancer spread and that cancer progressed sequentially from a primary tumor to regional lymph nodes and then to systemic sites.

Radical surgical procedures, including Crile's radical neck dissection, were developed in response to this belief.

DEVELOPMENT OF LYMPHATIC SYSTEM

First evidence of lymphatic system in intrauterine life is appearance of structures known as lymph sacs which are closely related to veins. First to appear is jugular lymph sacs which are two in number. Others are two posterior lymph sacs, one retroperitoneal lymph sac and one cisterna chyli.

According to Sabin (1916) lymph sac develops as outgrowth of endothelium of veins and lymph vessels sprout in a radiating manner and primary connections with veins are lost.[9] According to Huntington (1911) and McClure (1915) all lymph vessels are originally formed as clefts in the mesenchyme exactly as blood vessels. Lymph nodes develop as aggregation of cells in mesenchymal strands surrounded by plexus of lymph vessels. Around each nodule vessels are transformed to lymph sinus.

LYMPH NODE GROUPS[13]

Level I: Contains the submental (Ia) and submandibular (Ib) triangles. It is bounded by the anterior belly and the posterior belly of the digastric muscle, and the hyoid bone inferiorly, and the body of the mandible superiorly.

Level II: Extends from the level of the skull base superiorly to the hyoid bone inferiorly and contains the upper jugular lymph nodes. In anterior triangle of neck (from a vertical line dropped from angle of mandible to posterior border of sternocleidomastoid). It is further divided into IIa (anterior) and IIb (posterior) by spinal accessory

Level III: Contains the middle jugular lymph nodes from the hyoid bone superiorly to the level of the lower border of the cricoid cartilage inferiorly, midline to posterior border of sternocleidomastoid.

Level IV: Contains the lower jugular lymph nodes. It extends from the level of the cricoid

cartilage superiorly up to the clavicle inferiorly in anterior triangle of neck (IVa and IVb).

Level V: Contains the lymph nodes in the posterior triangle, which are bounded by the anterior border of the trapezius muscle posteriorly, by the posterior border of the sternocleidomastoid muscle anteriorly and by the clavicle inferiorly. It is divided into Va and Vb by inferior belly of omohyoid.

Level VI: Contains the lymph nodes of the anterior central compartment from the hyoid bone superiorly to the suprasternal notch inferiorly. On each side, the medial border of the carotid sheath forms the lateral boundary.

Level VII: Contains the lymph nodes inferior to the suprasternal notch in the superior mediastinum.[13]

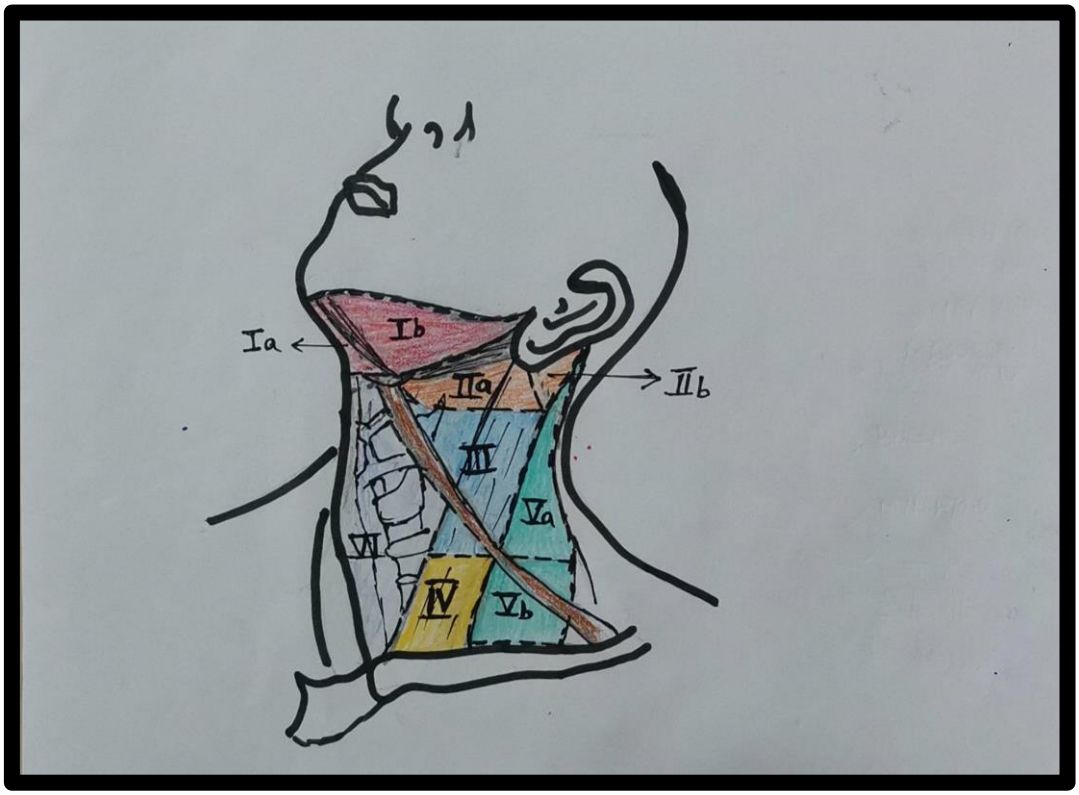


Fig 4: Levels of Lymph nodes in Neck

ORAL CAVITY CANCER EPIDEMIOLOGY:

According to history, man has always been trying to conquer malignant diseases. However, it still remains a major cause of death and morbidity. It is estimated that about nine million new cancers are diagnosed every year in the world. Worldwide estimate of oral cancer detection each year is 4,05,000 cases with 2/3rd occurring in developing countries.[15]

India, Sri Lanka, Pakistan, Bangladesh, Hungary & France have the highest rates with the India accounting for 30% of newly detected cases.[14] The estimated number of new cancers in India is about seven lakhs, and about 3.5 lakhs people die of cancer every year.[15]

According to the cancer registry of Kidwai Memorial Institute of Oncology, Bangalore, Karnataka, on an average, about 5000 new cancers are registered per year.[2,17] Oral cancer ranks among the top three in India. Age adjusted rates of oral cancers in India is 20 per 100,000 population and accounts for over 30% of all cancers in the country.[18]

Carcinoma of buccal mucosa accounts for 40% of oral cancers in South East Asia.[2] 85% cases occur >50 years of age, except in developing countries where onset can be earlier due to tobacco and pan chewing habits. Floor of mouth cancer accounts for 18-33% of oral cancers and seen more frequently in men in 6th-7th decade. 22-39% of oral carcinomas arise in the tongue, most commonly in middle 1/3rd and in the lateral aspect.[9]

Retromolar trigone incidence in oral cancers is 6-7% and is more common in males. Incidence of carcinoma in upper alveolus is 3.5 – 6.5% & hard palate is 1 – 3%. Oral cancers are more common in males except in hard palate carcinomas where pre-ponderance in females is more due to reverse smoking in certain area. Lower alveolar cancers account for 7.5 – 17.5 % of oral cancers.[9]

However, in Kolar region carcinoma of buccal mucosa is the most common malignancy.[2] It is more prevalent in women due to addiction to tobacco quid chewing. In India, patients present in advanced stage and both buccal mucosa and lower alveolus will be involved making it difficult to identify the epi-centre or starting point of tumour. Such tumours involving the buccal mucosa and lower alveolar complex have been nick named **"**Indian oral cancer**"** and are high volume disease.

ETIOLOGY:

The cause of oral cancer is yet to be completely understood. Several risk factors have been implicated.

SMOKING:

Tobacco is smoked more commonly in the form of cigarette and bidi. Some smoke a chutta (a cigar) with the burning end inside the mouth. Chemical carcinogens in the burning tobacco or repeated thermal injury are agents, which are risk factors for oral cancer. Risk increases with the amount smoked and with the total cumulative lifetime smoking years. Tobacco is smoked commonly in the form of bidi, a type of cheap cigarette made by rolling a rectangular dried piece of tendu leaf (Diospyros melanoxylon). As compared with cigarette smoke, bidi smoke has high content of several toxic agents such as carbon monoxide, ammonia, hydrogen cyanide, phenol and carcinogenic hydrocarbons.

The other ways of smoking tobacco are clove-flavored cigarette, various forms of pipes (wooden, clay, metal), the hookah (the Hubble bubble or water pipe), cheroots (or chuttas) and dhumtis. Tobacco may be used in raw or as processed mixtures and as a pyrolised form. The raw forms are used with lime and with areca nut (Mawa-smokeless tobacco).

Khaini is a mixture of freshly powdered tobacco and slaked lime; a quid of the mixture. It is kept for hours in the lower gingivolabial sulcus and sucked, which is risk factor for khaini cancer (squamous cell carcinoma of the lower lip). The processed forms, for example zarda, gutkha, and Manipuri tobacco are industrial products. The pyrolised (roasted) forms of tobacco (mishri, bajjar, etc) are used as dentifrice. Oral use of snuff is also practised in specific areas. Brings about hyperacetylation and hypomethylation of histones which silences tumour suppressor genes.[19]

Spirits: - Consumption of calvados {a pot distilled spirit}

Sepsis: - Septic and decayed teeth.

Sharp teeth: - Poor oral hygiene, faulty restorations, and ill-fitting dentures.

Spices

Syphilis

Betel quid chewing habit:

The quid consists of a betel leaf wrapped around an arecanut, which is high in tannin, quick lime and tobacco. Oral cancer develops at the site where quid is habitually kept. Smoking along with betel quid chewing enhances the risk of oral cancer by 20 to 30 times. This is most common risk factor for oral cancer in our region.

Fig 5: Betel leaves coated with slaked lime

Snuff dipping and other tobacco products

Fig 6: showing various forms of tobacco consumption

Alcohol:

Alcohol consumption has a synergistic local effect of dissolving the carcinogen in the sump area of the mouth and a systemic downward effect on the immune system. Alcoholics often have nutritional problems. Brings about hypermethylation of histones.[9]

Industrial chemicals

Viruses: Herpes simplex virus and the Human papilloma virus (subtype 16)

Immune status: - Immune deficiency due to low cell mediated immunity.

Genetic factors: - Most sporadic tumours are the result of a multi-step process of accumulated genetic alterations. These alterations affect the epithelial cell behaviour by the loss of chromosomal heterozygosity. This in turn leads to a series of events progressing to the eventual stage of invasive squamous cell carcinoma. The corresponding genetic alterations are reflected in the clinical and microscopic pathology from hyperplasia to invasiveness of the tumour. Over expression of p53, p16 and other tumor suppressor genes may predispose to development of cancer and recurrence following treatment. Overexpression of c-erbB-2 has shown correlation with nodal disease and metastasis and worsened survival.

The syndromes that are characterized by mutagen sensitivity, including Xeroderma pigmentosum, Fanconi's anemia and Ataxia telangiectasia have all been associated with oral cavity cancers. Other relevant genetic markers may include inducibility of cytochrome p450 enzyme system.[20]

Social status: - Related to social habits and to low socio-economic status

Cirrhosis of liver

Diet

Occupation: Employment in textile industries

PRE-MALIGNANT CONDITIONS:

Definition: A morphologically altered tissue in which cancer is more likely to occur than in its apparently normal counterparts.

Leukoplakia:

Definition: It is defined as a clinical white patch in the oral mucosa that cannot be characterized clinically or pathologically as any other disease and cannot be scraped out.

Rates of malignant transformation ranges from less than 1% to 17.5%. [21]

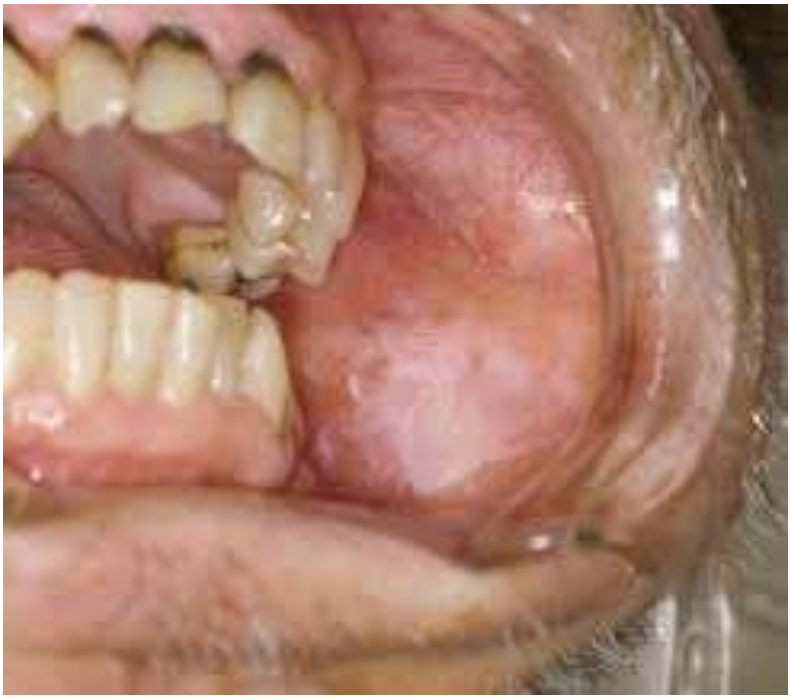


Fig 7:- Leukoplakia of buccal mucosa

Types of Oral Leukoplakia[21]

According to Sugar L and Banoczy J:

Leukoplakia simplex – White, homogeneous keratinised lesion, shows lowest frequency of malignancy.

Leukoplakia verrucosa – White, verrucous lesion with wrinkled surface, exhibits the highest rate of association with carcinoma.

Leukoplakia erosiva – White, lesion with erythematous areas, erosions, fissures, exhibit the highest rate of association with carcinoma.

According to Lindberg (clinical types):

Homogeneous: White patch with a variable appearance, smooth or wrinkled; smooth areas may have small cracks or fissures. It shows lowest frequency of malignancy.

Speckled or nodular: White patches with erythematous base or nodular excrescences. It shows highest rate of association with carcinoma.

According to Burkhardt (microscopic types):

Plain form, corresponding clinically to leukoplakia simplex.

Papillary endophytic, corresponding clinically to erosive leukoplakia.

Papillomatous exophytic, corresponding clinically to verrucous leukoplakia.

Proliferative verrucous leukoplakia:

It is high-risk type of leukoplakia. It has a tendency to be extensive or multifocal. Verrucous carcinoma evolves from this form of leukoplakia. They are associated with a high risk for malignant transformation and dysplasia.[21]

Erythroplakia:

These are oral mucosal lesions that appear as red, velvety plaques that cannot be clinically or pathologically ascribed to any other pre-determining condition. About 30-40% of erythroplakia exhibits either carcinoma or severe epithelial dysplasia.

Fig 8: Image showing erythroplakia of buccal mucosa

Melanoplakia

Oral Submucous fibrosis

Sideropenic dysphagia

Oral lichen planus: Rate of malignant transformation is about 4%. [22]

Discoid lupus erythematosus Hyperkeratosis Dyskeratosis congenital Syphilis

REGIONAL LYMPH NODES:

The involvement of the lymph nodes in metastatic deposits is always associated with a worse prognosis, approximately 50% worse than for the patients with equivalent tumours with no lymph node involvement.

PATTERN OF CERVICAL LYMPH NODE METASTASIS

The capacity for metastatic spread can be regarded as the single most important characteristic feature of a malignant tumor. The first step in the metastatic process is breach of the basement membrane at the site of primary tumor. This occurs through hydrolytic enzymes

secreted by tumor like the urokinase type plasminogen activator, collagenase and stereomelysins.[13] The enzymes degrade the basement membrane proteins such as collagen IV, laminin and proteoglycans which allow the spread of tumor cells.[22]

The lymphatic spread provides the main mode of spread beyond the primary site of origin for squamous cell carcinoma of head and neck region. The tumor cells disseminate as emboli through the lymphatic system. The tumor emboli are carried to the afferent lymphatic vessels of first level of lymph nodes. The tumor cells then localize first in the sub capsular sinus then progressively grow to replace the cortex and medulla. Eventually tumor invades the capsule of the node heralding extra capsular spread.[24] The extra capsular spread may occur in much smaller lymph nodes where tumor emboli first lodge in the capsular lymphatic sinuses and focal destruction of capsular collagen by type I Collagenase.

As the first level of lymph nodes is replaced by metastatic tumor, afferent lymph flow is deflected carrying tumor cells to the second and third level of nodes. Increasing obstruction in the lymphatics and intra nodal sinuses eventually may lead to reversal of lymphatic flow and retrograde spread of tumor cells to unpredictable nodal groups.

Lympho-hematogenous spread can occur by tumor cells invading blood vessels within the lymph node or by invading small lymphatic-venous communication. Once the tumor cells arrive at draining lymph node, they can proliferate, die, remain dormant or enter the blood circulation through blood vessels in the node. The pattern of lymphatic spread follows a predictable pattern. In general, well-localized tumors spread to ipsilateral first or second echelon lymph nodes[23,24].

The patients with clinically positive nodes in the ipsilateral neck are at risk for contralateral lymph node metastasis. This shunting occurs mainly through anastomotic channels

decussating in the midline at the submental and submandibular triangles.

The Lindberg study defined the nodal groups at most risk for each primary and the pattern of subclinical microscopic metastasis follows a similar distribution.[23] Carcinoma located anteriorly within the oral cavity spreads most commonly to the submental and submandibular lymph nodes, followed by the upper jugular nodes. The posteriorly located oral carcinoma is more likely to spread to the upper jugular nodes and less frequently spread to the submandibular nodes. Shah reported a comprehensive histopathological study, which confirmed Lindberg's clinical findings.[24] The level I, II and III were at highest risk for metastasis from oral cavity cancer. Thus, first echelon of lymph nodes for oral cavity lies in level I, particularly level Ib (sub-mandibular) for buccal mucosa and lower alveolar complex.

The incidence of lymph node metastasis that can be detected clinically is about 60%. The overall incidence of occult metastasis in patients with clinically negative neck node is around 30%. The relative risk of nodal metastasis depends on site, size, thickness, histological features and the immunological and biological factors of the primary tumour.[22] Poorer the differentiation the more likely the tumour metastasize early. The tumour with infiltrative margin is more likely to metastasize than those with pushing margin.

Table 1:- The following table describes the lymph node levels and the nodes that are at greatest risk of harboring metastases from different primary sites.[25]

Lymph node group	Primary site
Level 1A	Floor of mouth, anterior 2/3 tongue, anterior part of mandibular ridge, lower lip.
Level 1B	Oral cavity, anterior nasal cavity, soft tissue of the mid face, submandibular gland.
Level II	Oral cavity, Anterior Nasal cavity, Nasopharynx, Oropharynx, Hypo pharynx, Supra glottic larynx, Parotid.
Level III	Oral cavity especially tongue, Nasopharynx, Oropharynx, Hypo pharynx, Supra glottic larynx, thyroid.
Level IV	Hypopharynx, Thyroid, Larynx, Cervical oesophagus.
Level V	Nasopharynx, Oropharynx, Cutaneous structures of the posterior scalp and neck.
Level VI	Thyroid gland, Glottic and subglottic Larynx, apex of Pyriform fossa, Cervical oesophagus.

Lymph node levels that are at greatest risk of harboring metastases from different primary

DISTANT METASTASIS:

Distant metastasis is a rare clinical presentation, involving less than 10% of patients. The lungs are the most common sites of distant metastases; skeletal and hepatic metastases occur less often. Mediastinal lymph node metastases are considered distant metastases.

TNM CLASSIFICATION[12]

Primary Tumour (T) - AJCC 8th EDITION

TX - Primary tumour cannot be assessed

Tis - Carcinoma in situ

TI – Tumour <2cm , < 5 mm depth of invasion (DOI) DOI is depth of invasion.

T2 - Tumour < 2 cm, DOI > 5 mm and <10 mm or tumour > 2 cm but < 4 cm, and < 10 mm DOI

T3 – Tumour >4 cm or any tumour> 10 mm DOI

T4 - Moderately advanced or very advanced local disease

T4a - Moderately advanced local disease (lip) Tumour invades through cortical bone or involves the inferior alveolar nerve, floor of mouth, or skin of face (i.e., chin or nose) (oral cavity) Tumour invades adjacent structures only (e.g., through cortical bone of the mandible or maxilla, or involves the maxillary sinus or skin of the face)

Note: Superficial erosion of bone/tooth socket (alone) by a gingival primary is not sufficient to classify a tumour as T4.

T4b - Very advanced local disease Tumour invades masticator space, pterygoid plates, or skull base and/or encases the internal carotid artery

Regional Lymph Nodes (N) AJCC 8TH EDITION

NX - Regional lymph nodes cannot be assessed

N0 - No regional lymph node metastasis

NI - Metastasis in a single ipsilateral lymph node, 3 cm or smaller in greatest dimension ENE(-)

N2 - metastasis in a single ipsilateral node larger than 3 cm but not larger than 6 cm in greatest dimension and ENE(-); or metastases in multiple ipsilateral lymph nodes, none larger

than 6 cm in greatest dimension and ENE(-); or in bilateral or contralateral lymph nodes, none larger than 6 cm in greatest dimension, and ENE(-)

N2a - metastasis in a single ipsilateral node larger than 3 cm but not larger than 6 cm in greatest dimension, and ENE(-)

N2b - metastasis in multiple ipsilateral nodes, none larger than 6 cm in greatest dimension, and ENE(-)

N2c - metastasis in bilateral or contralateral lymph nodes, none larger than 6 cm in greatest dimension, and ENE(-)

N3 - metastasis in a lymph node larger than 6 cm in greatest dimension and ENE(-); or metastasis in any node(s) and clinically overt ENE(+)

N3a - metastasis in a lymph node larger than 6 cm in greatest dimension and ENE(-) N3b - metastasis in any node(s) and clinically overt ENE(+).

Histological Grade (G)

GX Grade cannot be assessed

G1 Well differentiated

G2 Moderately differentiated

G3 Poorly differentiated

Residual tumour (R)

Rx Presence of residual tumour cannot be assessed

R0 No residual tumour

R1 Microscopic residual tumour

R2 Macroscopic residual tumour

Table 2: Stage grouping

Stage 0	T0	N0	M0
Stage I	T1	N0	M0
Stage II	T2	N0	M0
Stage III	T3	N0	M0
	T1	N1	M0
	T2	N1	M0
	T3	N1	M0
Stage IV A	T4a	N0	M0
	T4a	N1	M0
	T1	N2	M0
	T2	N2	M0
	T3	N2	M0
	T4a	N2	M0
Stage IV B	Any T	N3	M0
	T4b	Any N	M0
Stage IV C	Any T	Any N	M1

AJCC staging of oral cavity squamous cell carcinoma

GENERAL PRINCIPLES FOR SELECTION OF TREATMENT:

All patients with T3 and T4 tumors requires multimodality treatment

- **Surgery → RT/CT +RT**

In very advanced tumours requires

- **Neoadjuvant chemotherapy (NACT) → surgery → Adjuvant treatment (radiotherapy (RT)** or **chemotherapy (CT) +RT)**

Only or selected T2 tumors can have single modality treatment either

- **Surgery or Radiotherapy alone.**

  However when there are positive margins they all required post operative chemotherapy with radiotherapy.

T4 SCC's are further divided into:

T4a (resectable) & T4b (unresectable) by AJCC 2002 AJCC 8th edition has classified T4a as moderately advanced local disease and T4b as very advanced local disease.

Studies have shown that not all T4b tumors is unresectable and that some of these patients can be offered surgery as the primary treatment rather than just palliation. Those tumors involving skull base or with encasement of carotid artery are excluded. Better reconstruction options in recent times have allowed to reduce the morbidity associated with such radical surgeries.

Advantages of surgery compared to radiation therapy offering similar cure rates:

1- Limited amount of time exposed to treatment

2- Treatment time is shorter

3- Risk of immediate & late radiation sequelae are avoided

4- Irradiation is reserved for subsequent head & neck primary tumour which may not be suitable for surgery

MALIGNANT CONDITIONS OF ORAL CAVITY[22]

Squamous cell carcinoma: It is the preponderant epithelial malignancy of the oral cavity.

Variants of squamous cell carcinoma:

- Verrucous carcinoma: It is a low-grade highly well differentiated carcinoma with keratinising exophytic or warty appearance. The cellular response is usually prominent.
- Sarcomatoid carcinomas / Pseudosarcoma/Pseudosarcomatous squamous carcinoma / pleomorphic carcinoma / metaplastic carcinoma / epidermoid carcinoma- spindle cell variant
- Adenosquamous cell carcinoma
- Adenoid squamous cell carcinoma
- Basaloid squamous carcinoma
- Basal cell carcinoma
- Lymphoepithelioma
- Malignant oral salivary gland tumors
- Adenoid cystic carcinoma
- Adenocarcinoma
- Mucoepidermoid carcinoma
- Melanoma of oral cavity

To determine the nature of lesion, nature of abnormal tissue (cyst, granulomas) and to establish the diagnosis which are suspicious of malignancy can be confirmed on biopsy

BIOPSY

Biopsy is the removal of tissue from a living person for microscopic examination to confirm or to establish the diagnosis of the disease. The term was coined by Ernst Henry, a French dermatologist in 1879. This procedure is used in all tissues of the body, including oral cavity.

Various types of biopsies are as follows

1. Excisional Biopsy
2. Punch Biopsy
3. Wedge biopsy
4. Needle Biopsy
5. Imprint Cytology
6. Shave Biopsy
7. Fine Needle Cutting Biopsy
8. Exfoliative cytology

TUMOUR THICKNESS AND DEPTH OF INVASION

Tumour thickness is defined as the vertical extent of the tumour from point of maximum projection to maximum infiltration in a perpendicular fashion. It was Breslow, who established a strong link between tumour thickness (TT) and both tumour-free survival and metastasis in patients with cutaneous melanoma. Following Breslow's hypothesis, Other authors demonstrated the relationship between lymph-node involvement and tumour thickness to oral cavity malignancy.[28] Since then, many studies have been carried out to test

this relationship. These studies have shown that tumour thickness is an important predictor for lymph-node involvement in OSCC. Many authors have also found that the thickness of the tumour correlates better with survival and involvement of the lymph nodes than does its superficial diameter.[28] However later studies showed that the exophytic growth of the tumour should not be considered, as it does not represent the overcoming of tissue resistance. The space left by the ulcerated tumour should be given importance, because it represents tissue destroyed by the downwards growth of the tumour. As a result, Tumour depth was introduced as a better predictive marker for lymph node metastasis. Tumour depth is defined as the infiltrative portion of the tumour which extend below the Basement membrane of mucosa.[29]

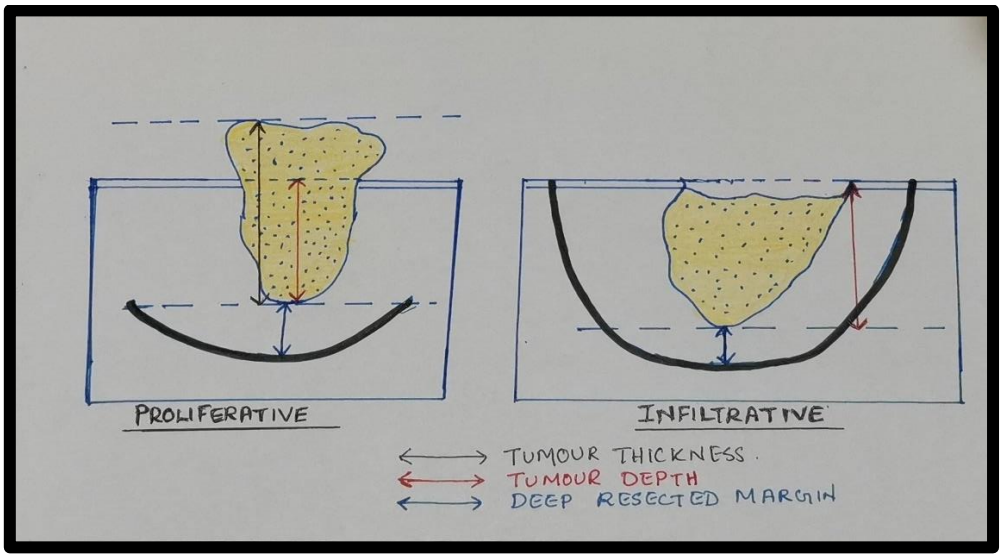


Fig 9: Showing tumour thickness and tumour depth

Primary tumour thickness and depth of invasion have been used as a predictor for lymph node metastasis in oral tongue cancer. Depth of tumour invasion is considered as an independent predictor for cervical lymph node metastasis. Infiltration depth was defined as the maximum depth of tumour infiltration (millimetres) below the Basement Membrane of mucosa. In case of ulcerated or exophytic tumours, the reconstructed mucosal surface was used.[30]

In a meta-analysis by Pentenero et al, where over 50 studies were included, comparing depth of invasion and tumour thickness in predicting nodal involvement and prognosis in oral squamous cell carcinoma, depth of invasion proved to be a better predictor of cervical metastasis and over-all prognosis.[31] Depth of invasion is known to be a better predictor for nodal status, because it compensates for exophytic growth or tissue destruction by the tumour. Also, studies have shown that tumour located more towards the midline i.e. lower alveolus, floor of mouth and tongue, showed a higher tendency to throw cervical metastasis.[32]

One of the Literature showed, cervical lymph node metastasis is the single most important prognostic factor in the management of patients with oral cavity squamous cell carcinoma and that factors such as primary site and depth of invasion of tumour are best predictors of nodal metastasis.

These patients are at a higher risk for locoregional recurrences requiring adjuvant therapy. Because adjuvant therapy may induce severe toxic effects, it is important to find a reliable method to help identify such high-risk patients immediately post-surgery.

It takes 10^{11} cells to produce a mass that is palpable. Due to likelihood of occult nodal metastasis, prophylactic or elective surgical neck dissection is done in oral cancer patients; particularly those involving sites that tend to metastasise early.

But identification of metastatic positive lymph nodes is based on both the quality of neck dissection (i.e. nodal yield- number of total nodes/neck specimen) by the surgeon and level of scrutiny by the pathologist. As both poor neck dissection or failure to identify positive nodes could possibly downstage the disease.

Cervical lymph nodal metastasis has a significant impact on the prognosis in patients with

carcinomas of the head and neck. Lymph node metastasis reduces the survival by almost 50%. The frequency of lymphatic spread of squamous cell carcinoma is very high and even patients with no palpable lymph nodes have occult metastasis. The incidence of occult lymph-node metastasis in early-stage tumours (primary site T- categorization T1 or T2) has been reported to be between 27% and 40%. Step serial sectioning of lymph-node will help to identify micro-metastasis.[33,34]

Level I is the most common site for nodal metastasis from oral cancers (100%), followed by level II (32%), level III (16%), and level IV (8%).[9] Though there are multimodality treatment options, the prognosis is usually poor. The presence of occult lymph node metastasis of oral tongue followed by buccal carcinoma, is observed more often than in any other cancer of the oral cavity.[35] Literature shows an overall 5-year survival rate of 65%, even though the tumour stage distribution remained the same compared to the preceding 10-year period.[36] Survival was better related to a more aggressive treatment of the neck even in early tumour stages and to adjuvant radiotherapy in advanced tumour stages.

The presence of extra capsular spread reduces the chances of cure by 50%. As mentioned earlier the site, size, differentiation of tumour, perineural invasion, perivascular invasion, inflammatory response and DNA content predicts aggressiveness of cervical lymph node metastasis.[37]

In recent AJCC staging, extra capsular spread from lymph nodes makes the staging N3b. In the current literature, there are multiple retrospective studies correlating primary site and depth of invasion of oral cavity squamous cell carcinoma to cervical lymph node to that of prognosis. However, there is paucity in literature regarding the correlation between tumor volume and recurrence and between tumor volume and lymph node metastasis in oral cancer.

SURGICAL MARGINS[11]

The aim of surgical resection is adequate clearance of the tumour. Inadequate clearance of tumour results in increased local recurrence and decreased long term prognosis.

Increase in margin of resection in head and neck region leads to potentially increased deficit in function and cosmesis. Resection of margins up to 2 cm have been advocated by some authors. But even with such large margin of resection significant morbidity was observed even after resection of small tumours. One centimetre 3D-resection margins have been demonstrated as acceptable when dealing with oral and oropharyngeal tumours(1.5cm). 1 cm surgical margins were adopted, keeping in mind the shrinkage of the specimen that occurs following resection and fixation, Therefore atleast 5mm pathological margins (AFF) has been advised for all oral cavity cancers. The confounding factor that was considered when discussing surgical margins was the resecting modality that used. The 5 mm was taken as a cut-off point for 'clear' margins as arbitrarily as an acceptable margin of resection. Some authors advocate 3 mm as an acceptable histological margin when considering the need for adjunctive treatment. It is very important to reassess margins visually and on palpation during tumour resection. Adjuncts to assess margin status include intra-operative tissue staining and ultrasound for deep margins and mucosal staining for mucosal margins. Reconstructive considerations should not influence the tumour resection if the resection of a tumour is with curative intent.

The definition of a positive margin ranges from invasive tumour at the margin, tumour within 1 mm, and tumour within 5 mm microscopically. The UK Royal College of Pathologists have issued guidelines suggesting clear margins if the histological clearance is > 5 mm, close margins if 1–5 mm and positive margins if < 1 mm.

The incidence of positive margins for tumours of the oral cavity has demonstrated higher than other head and neck malignancies, due to its complex anatomy and 3D shape. Large

tumours, perineural spread, vascular permeation, a non-cohesive invasive front or cervical metastasis are all associated with a greater risk of failing to achieve clear margins. These features suggest that close or involved margins potentially reflect a more aggressive tumour. The incidence of close or involved margins following tumour resection may be greater than 60% depending on tumour site and size. Invariably it is the deep margin that is close or positive. The close deep margins do not necessarily require adjunctive treatment. Frozen sections are not routinely used by many surgeons**,** due to increased cost and unavailability to reliably prevent positive final margins, failure to influence 5-year survival or primary failure rates and difficulty in identifying the biopsy site should the result be positive. Ninety-nine percent of American Head and Neck surgeons routinely use frozen section intraoperatively, however over reliance on frozen section may result in under treatment of tumours.

For bony resection of 1 cm margin should be achieved. It has been demonstrated that it is unusual for extension of tumour in bone to exceed the overlying soft tissue extension, consequently the bony resection should be dictated by the extent of soft tissue disease.

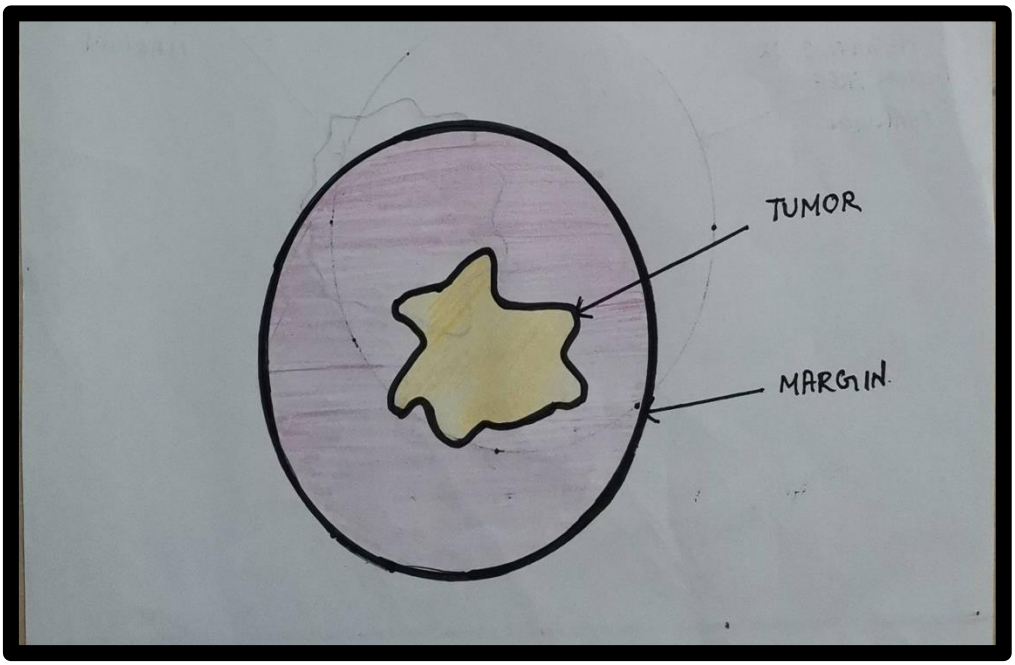


Fig 10 – Diagramatic representation of resection of margin

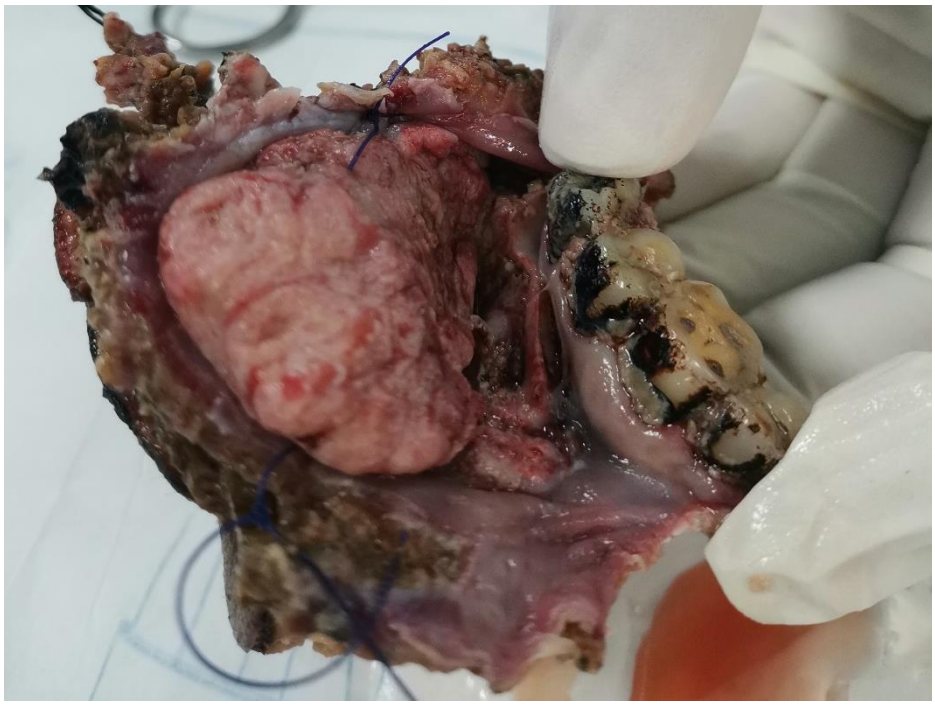


Fig 11:- Image showing resection of Margin.

BUCCAL MUCOSA- The primary tumour should be resected with a 1 cm margin, and up to 2 cm if skin is involved. Facial access incisions (upper or lower lip splits) may be required to facilitate access, particularly in patients with concurrent oral submucous fibrosis. The buccinator muscle is included as the deep margin in very few cases.

FLOOR OF MOUTH- Surgical resection with a 3-dimensional 1 cm margin should be achieved if surgery is the preferred treatment modality. Even in the best surgeons' hands positive or close margins may be seen in up to 47% of resections, despite the use of intraoperative frozen section. Possible reason explaining such a high incidence of positive margins is the infiltrative nature of many floor-of-mouth tumours. Further resection is advocated if margins are positive. So, 1 cm margins, though considered by most surgeons to be adequate, extended 2 cm margins have been advocated by some. Many patients require

rim or segmental resection of the mandible because of the early extension of floor-of-mouth tumours into the tongue or mandible,104 and resection of the floor of mouth in majority of cases will involve resection of part of the submandibular ducts.

TONGUE- Resection of the tumour with 1 cm margin in three dimensions should be obtained if surgery is the treatment of choice. Ultrasonography can aid in assessment of surgical clearance, particularly to assess the deep margin. Frozen section is not routinely used in many centres. Even with apparently adequate margins during surgery, 10% of resections may demonstrate histologically positive margins. Resection of tongue tumours using a 'compartmental' approach as adopted by musculoskeletal oncology surgeons has been advocated, with improved outcomes with this technique.

RETROMOLAR TRIGON- Resection should be achieved with a 1 cm margin in all planes. The incidence of positive margins following resection of retromolar tumours is higher than other oral sites.

HARD PALATE- Similar to other subsites a surgical clearance of 1 cm in three dimensions is required. Small tumours may be approached per orally, however larger tumours may require an upper cheek flap or midfacial degloving to augment access.

UPPER AND LOWER ALVEOLUS- Carcinoma involving the mandibular alveolus invariably requires some degree of bone resection, with only 6–7% requiring soft tissue resection. Small alveolar carcinomas with no clinical evidence of significant bone involvement may be resected via per oral approach with a marginal mandibulectomy, aiming

for 1 cm soft tissue and bony margin. Larger tumours with obvious bone involvement require segmental resection and extraoral access incisions.

TYPES OF RESECTION MARGINS[38]

Based on structure of tissue (anatomically) three types of resection of margins.

1.Mucosal Margins -The rim of mucosa around the tumour removed along with complete tumour removal.

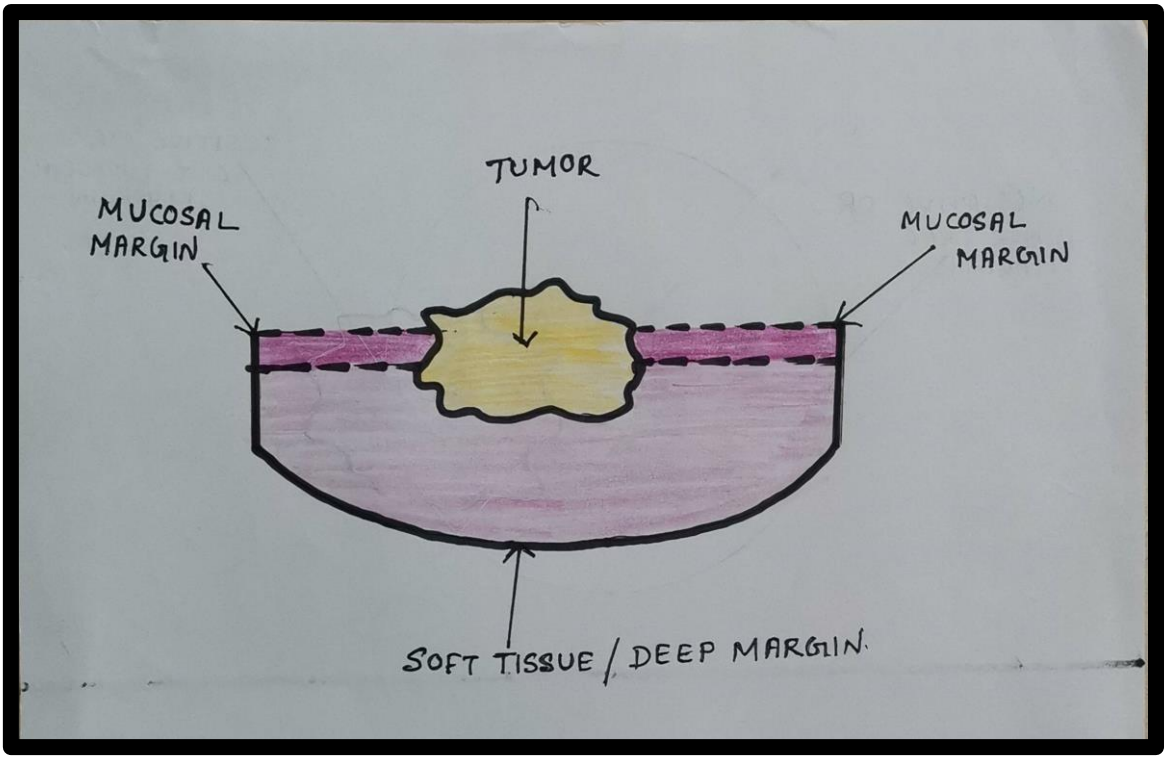


Fig 12- Diagramatic representation of Mucosal and Soft tissue margins

2.Soft-tissue or Deep Margins – Three – Dimensional resection of complete removal of tumour with excision of tumour along with cuff of normal soft tissue in and around the tumour. Soft tissue or deep margin or base include muscle, adipose tissue, neurovascular and connective tissue components. Some of the studies showing recurrences involving deep resection margins are more frequent.

3.Osseous Margins – Along with tumour cut edge of bone is removed. In case of jaw bone involvement tumour is resected with surrounding bone.

There are two major approaches to the sampling of margins. In the **(1)** specimen driven approach, margin clearance is assessed from en bloc resection specimens. In the **(2)** defect-driven approach, the tumor bed is sampled after the primary resection. Studies have shown that the most relevant margins are those derived from the resection specimen[1].

Most studies classify margins as either (1) positive, tumor cut through i.e. invasive carcinoma at the margin (2) close i.e. within one high power field or (3) negative margin, with varying definitions of close and negative while commonly mentioning a measurement of > 5 mm to define margin adequacy or clear margin on microscopic evaluation . Using the following criteria, clear margin (5 mm from the nearest surgical margin), close (1–5 mm), and involved (<1 mm), their results demonstrate that surgical margin status did not have an independent predictive effect on disease specific survival[.3,4,5]

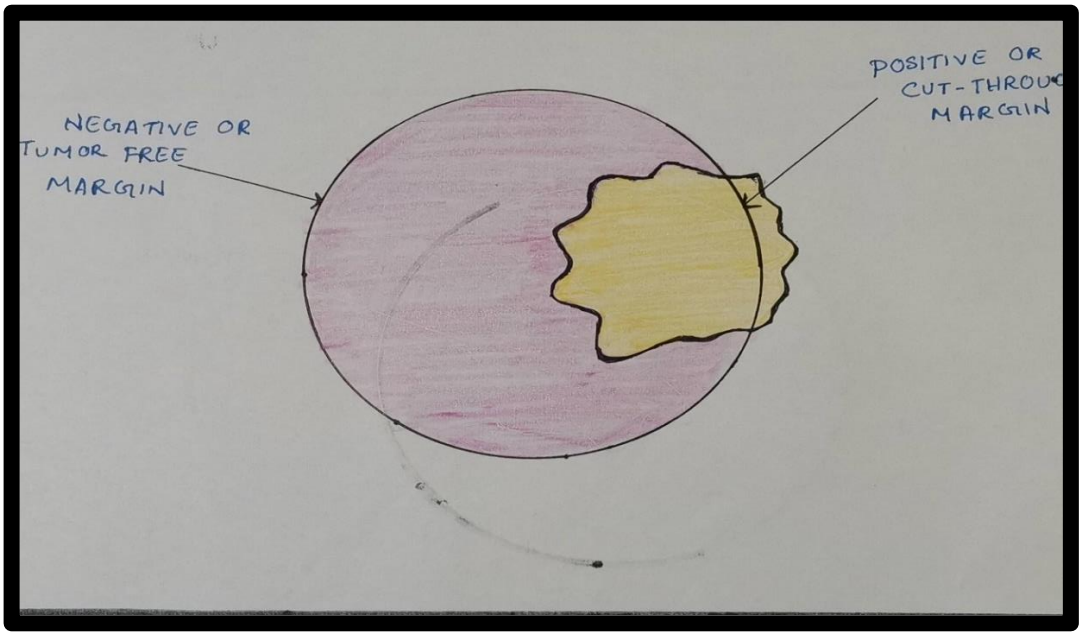


Fig 13-schematic diagram showing positive and negative margins

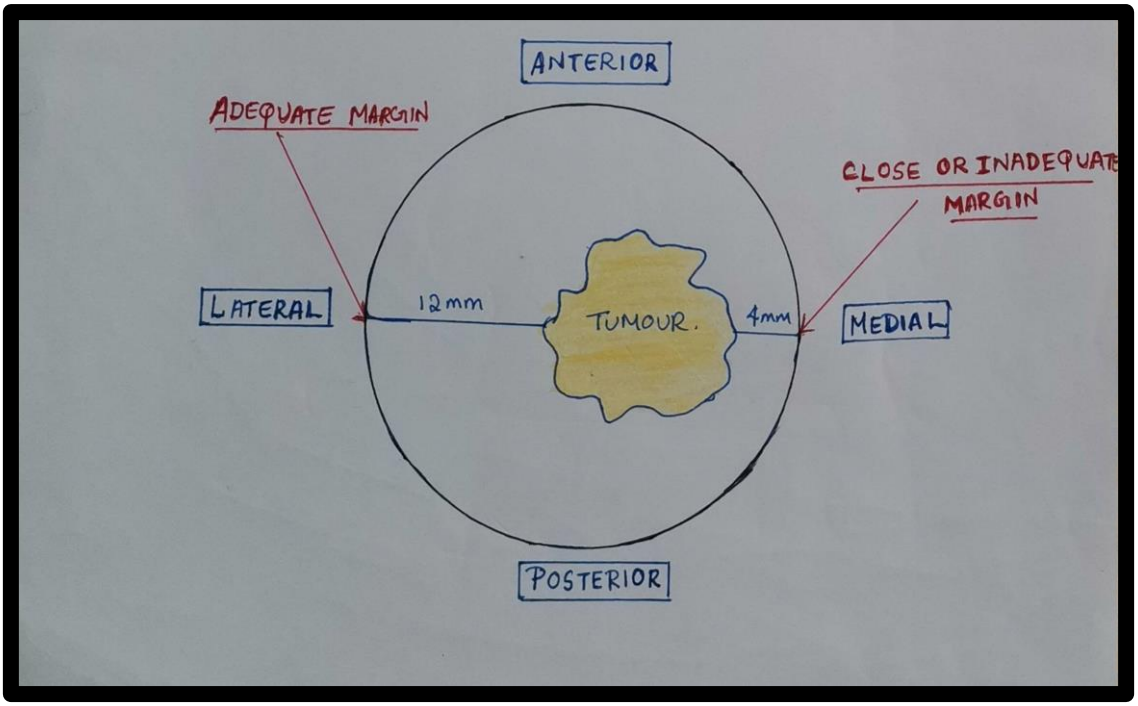


FIG 14:- Schematic diagram showing the concept of adequate and inadequate or close margins

EFFECT OF FORMALIN FIXATION ON RESECTION OF MARGIN[39,40]

Formalin fixation causes shrinkage of surgical margins and result in underestimation of tumour -free margins. Marked shrinkage of mucosal margin was seen in patients with SCC of the tongue and buccal mucosa after resection. Shrinkage was not affected by age, gender and site. 30% shrinkage of soft tissue occurs after formalin fixation due to contraction of actin myosin due to use of cautery in muscle much more than epithelial margin or due to the possibility of tissue under tension reduces in dimension after or on surgical release from the surrounding tissue.

THERAPEUTIC MODALITIES FOR ORAL CANCER[13]

The factors that influence the choice of initial treatment are those related to the characteristics of the primary tumour (tumour factors), those related to the patients (patient factors) and those related to the treatment delivery team (physician factors).

PHYSICIAN FACTORS:

Surgery

Radiotherapy

Chemotherapy

Combined modality treatment

Dental

Rehabilitation services

Prosthetics

Support services

Photodynamic therapy

Immunotherapy

Gene therapy

Most therapies other than surgery are not known to be effective against large tumours. Therefore, the most promising results may be obtained with therapy of non metastatic tumor in an adjuvant setting after surgical removal of the primary tumour.

TUMOUR FACTORS:

- Site
- Size (T stage)
- Location (anterior versus posterior)
- Proximity to bone (mandible)
- Lymph node metastasis
- Previous treatment
- Histology (type, grade, depth of invasion)

PATIENT FACTORS:

- Age
- General medical condition
- Tolerance
- Occupation
- Acceptance and compliance with regards to treatment
- Lifestyle (smoking, drinking, tobacco chewing)
- Socio-economic consideration
- Nutrition

CLASSIFICATION OF NECK DISSECTION

1991 classification

1. Radical neck dissection

2. Modified radical neck dissection

3. Selective neck dissection.

a) Supraomohyoid

b) Lateral

c) Posterolateral

d) Anterior

4. Extended neck dissection.

2001 CLASSIFICATION BY THE COMMITTEE FOR HEAD AND NECK SURGERY AND ONCOLOGY OF THE AMERICAN ACADEMY OF OTOLARYNGOLOGY - HEAD AND NECK SURGERY (AAO-HNS)

1. Radical neck dissection
2. Modified radical neck dissection
3. Selective neck dissection:
4. Extended Neck dissection

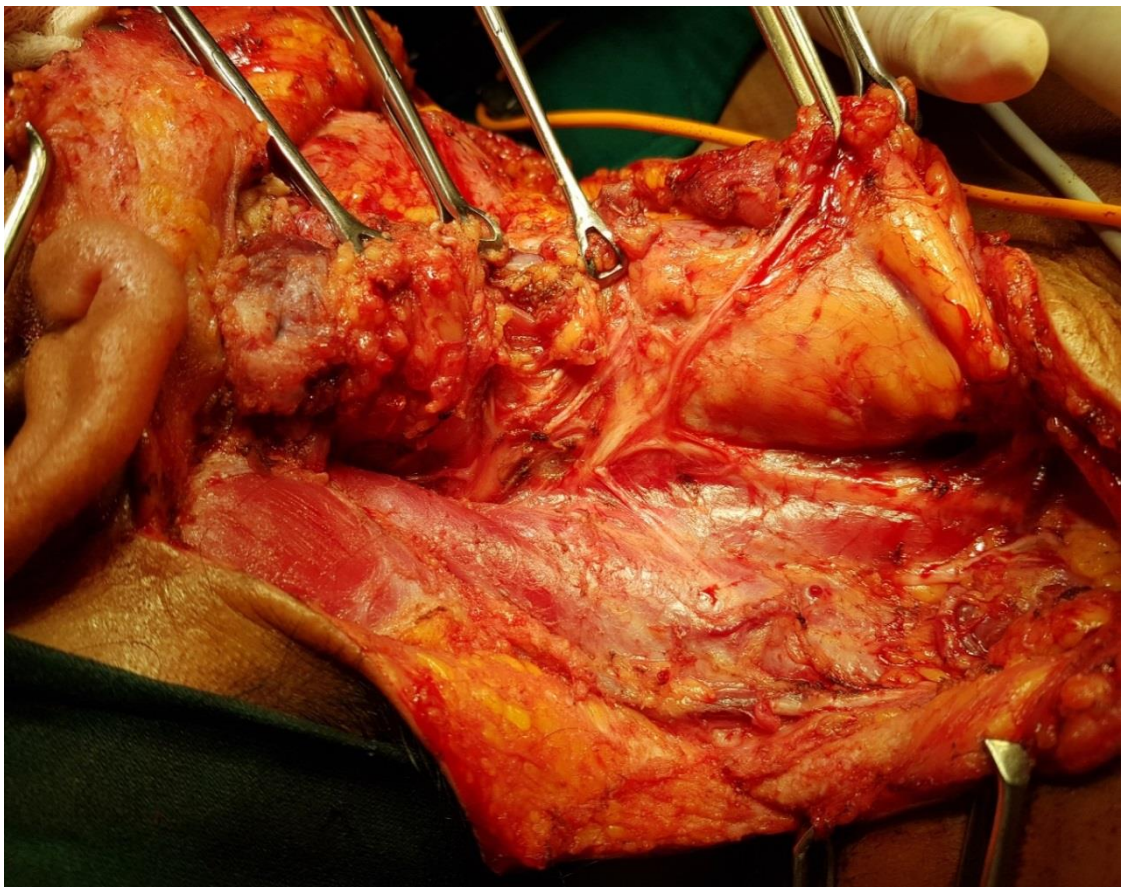


Fig 15: Modified Radical Neck dissection

RECONSTRUCTION[43]

Oro-mandibular reconstruction continues to be one of the most challenging areas of head and neck reconstruction. Reconstruction of resulting defect can be done by the following methods:

1.a) Split thickness skin grafts

b) Full thickness skin grafts

2. Mucous membrane flaps

3. Tongue flaps

a) Posteriorly based lateral tongue flap

b) Posteriorly based bilateral tongue flap

c) Anteriorly based ventral tongue flap

4. Masseter flap

5. Nasolabial flap

6. Medial based delto-pectoral flap

7. Forehead flap

8. Sternocleidomastoid myocutaneous flap

9. Trapezius

10. Platysma myocutaneous flap

11. Pectoralis major myocutaneous flap

12. Latissimus myocutaneous flap

13.Costochondral grafts

14.Osteo-myocutaneous flap-fifth rib with pectoralis major myocutaneous flap-Spine of scapula with trapezius

15. Free osteo-cutaneous groin Map

16. Free osteo-cutaneous fibula flap

17. Scapular Osseo-cutaneous flap

18. Radial forearm flap (microvascular free flap)

19. Radial forearm free osteo-cutaneous flap

20. Free fibula and osseo-integrated implants

21. Anterolateral thigh free flap

Whenever possible, immediate single stage reconstruction is preferred over laved reconstruction, when the former can be achieved with acceptable success rates and low morbidity. Immediate restoration of the mandible prevents the development muscle contracture and restores mandibular form. Delayed reconstruction interferes with the radiotherapy and later healing[41,43].

The bone to mucosa relationship of the periosteum of the alveolar ridge and gingival mucosa most difficult to duplicate and is necessary for wearing dentures. Preservation of chewing, provision of a base for dental appliances and preservation of a normal appearing lower third of the face are achieved by preservation of the buccal sulcus and the oral floor, which are all essential reasons for maintenance or restoration of the mandibular contour.

QUALITY OF LIFE[42]

The surgical resection of tumor involving the oral cavity has been associated with significant destruction of normal anatomy, functional deficits and suboptimal reconstruction. Historically, disease-free survival, overall survival and tumour response rates were the traditional outcome measures used to judge efficacy of treatment. Although these traditional outcomes have been helpful to clinicians, they affect some of the most basic functions of life.

Despite the most aggressive treatment regimen, there has been little change in overall survival rates for patients with head and neck cancer. With this has come a greater awareness of the functional impact of surgical resection on patient's function.

Quality of life is the term used to describe the non-traditional outcome measures of functional status and psychological wellbeing.

Different dimensions of quality of life

1. Functional status
2. Physical complaints
3. Psychological distress
4. Social interactions

The unique attributes of the head and neck surgery and its role in speech, swallowing and deglutition as well as the cosmetic appearance allows for social interaction. Mandibular resection has always been associated with some of the functional deficits.

Different quality of life scales are used to evaluate functional status in cancer patients. They include:

1) Karnofsky Performance Scale[43]
2) The Sickness Impact Profile.
3) The University of Washington Quality of Life Scale.
4) The Head & Neck Cancer Specific Quality of Life Instrument.[43]

1) Karnofsky Performance Scale:

The AJCC strongly recommends recording of KPS (The Karnofsky Performance Status) along with standard staging information." David A. Karnofsky devised KPS in 1948, which provides a uniform, reliable and objective assessment of an individual's functional status.

Karnofsky Scale: Criteria of Performance Status (PS)

100 Normal; no complaints; no evidence of disease.

90 Able to carry on normal activity; minor signs or symptoms of disease.

80 Able to carry on normal activity with effort; some signs or symptoms of disease

70 Cares for self; unable to carry on normal activity or do active work.

60 Requires occasional assistance but is able to care for most of own needs.

50 Requires considerable assistance and frequent medical care.

40 Disabled; requires special care and assistance.

Diagnosis and treatment of depression also aid in symptom control and improved quality of life.

MATERIAL & METHODS

MATERIALS AND METHODS

TYPE OF STUDY

STUDY DESIGN: Prospective Analytical study

SOURCE OF DATA:

Patient The study was done in 60 patients who underwent surgery for squamous cell carcinoma of oral cavity with or without extension to pharynx (head and neck) staged T2 to T4 according to AJCC classification 2018 in the department of Otorhinolaryngology at R.L.Jalappa.Hospital & Research Centre, Tamaka, Kolar from December 2019 to July 2021 after fulfilling the inclusion criteria.

SAMPLE SIZE:

Sample size was calculated using the prevalence of squamous cell carcinoma that is 82.7% based on a study "Clinicopathological study of surgical margins in squamous cell carcinoma of buccal mucosa"[40].

$$n = \frac{Z^2_{1-\alpha/2}\, p(1-p)}{d^2}$$

Where,

p : Expected proportion

d : Absolute precision

1- α/2 : Desired Confidence level

P = 82.7%

d = absolute precision at 10%

n = 54.9

Due to sample loss because of nonresponse and nonavailability of participants during the study period for any of the following stages of the current study i.e. clinical examination, histopathological examination and other laboratory investigations therefore extra 10% was added to the sample (ie,55). Hence total **sample size** was **60.**

METHODOLOGY

- Patient who were planned for surgery for biopsy proven Squamous Cell Carcinoma of Head and Neck in the Department of Otorhinolaryngology at R.L.Jalappa.Hospital & Research.Centre, Tamaka, Kolar from December 2019 till July 2021 were taken up for the study. Patients who fulfilled the inclusion criteria and after taking informed consent was included in the study and who underwent the standard treatment for head and neck squamous cell carcinoma staged T2 – T4 which includes surgery followed by adjuvant treatment in the form of radiotherapy or radiotherapy + chemotherapy.

INCLUSION CRITERIA

1. Patients between 30 to 70 years age, with biopsy proven Squamous cell carcinoma of Oral cavity with or without extension to pharynx (Head and neck) and staged T2 to T4, undergoing curative treatment by composite resection and adjuvant treatment.

EXCLUSION CRITERIA

1 Patients with severe trismus.

2 Oral cancers with N3 lymph nodes.

3 Patients with locoregional recurrence.

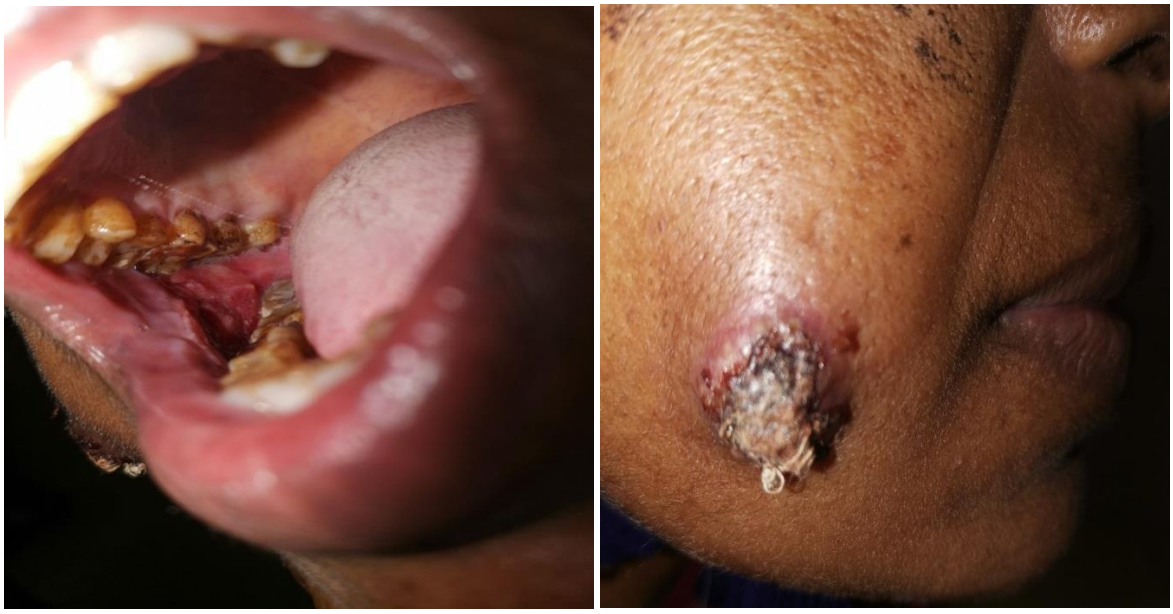
4 Patients operated for head and neck tumors or radiated earlier.

5 Patients with distant metastases

A full thickness slice of tissue was harvested from the margin closest to the tumor both from specimen as well as patient defect site and was analyzed by histopathology for presence of tumor cells as well as actual distance from the tumor margins to the cut margin.

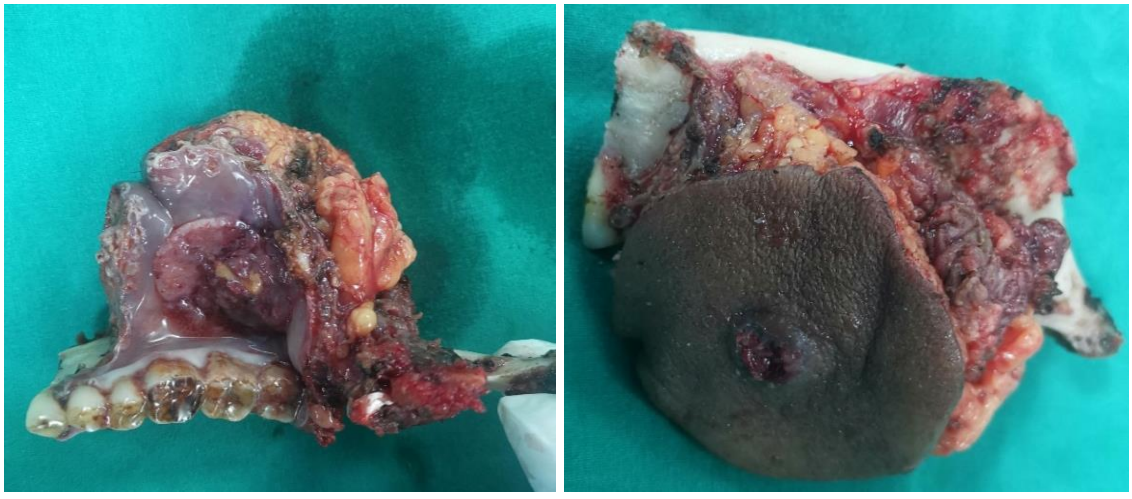
A section was taken from muscular or submucosal plane (also in this cut margins) to correlate between epithelial margins and deeper margin. The distance from the visible margin of tumor to the closest margin of resection was measured by a sterile scale and documented both before and after formalin fixation. Detailed histopathological examination was done both on the resected specimen as well as the cut margin from both specimen as well as resected site and the reliability of the cut margin between the specimen and patient site was evaluated and the surgical defect of patient was reconstructed in the same sitting followed by adjuvant treatment based on the histopathology report in the form of radiotherapy or radiotherapy + chemotherapy and patient was followed up for minimum of 6 months after completion of treatment to monitor for locoregional control for recurrence or second primary or distant metastases.

An attempt was made to evaluate the reliability of the cut margins between the specimen site and patient (defect) site and an observation was made regarding the shrinkage of tumor size as well as the tumor free margin following formalin fixation also an attempt was made to correlate the epithelial margin with deeper muscular or sub epithelial margin.



A) Intra oral lesion **B) Extra oral lesion**

Fig 16– locally advanced tumor of buccal mucosa (Preoperative)



A) Mucosal aspect **B) External aspect**

Fig 17:- Locally advanced tumor of buccal mucosa showing enbloc resection

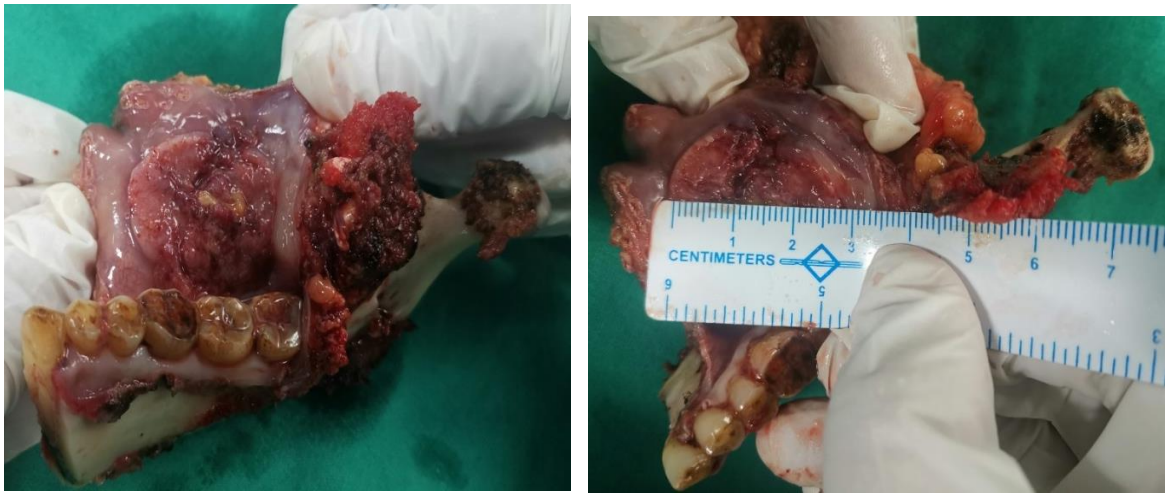


Fig 18:- Measurement of tumor dimensions before formalin fixation.

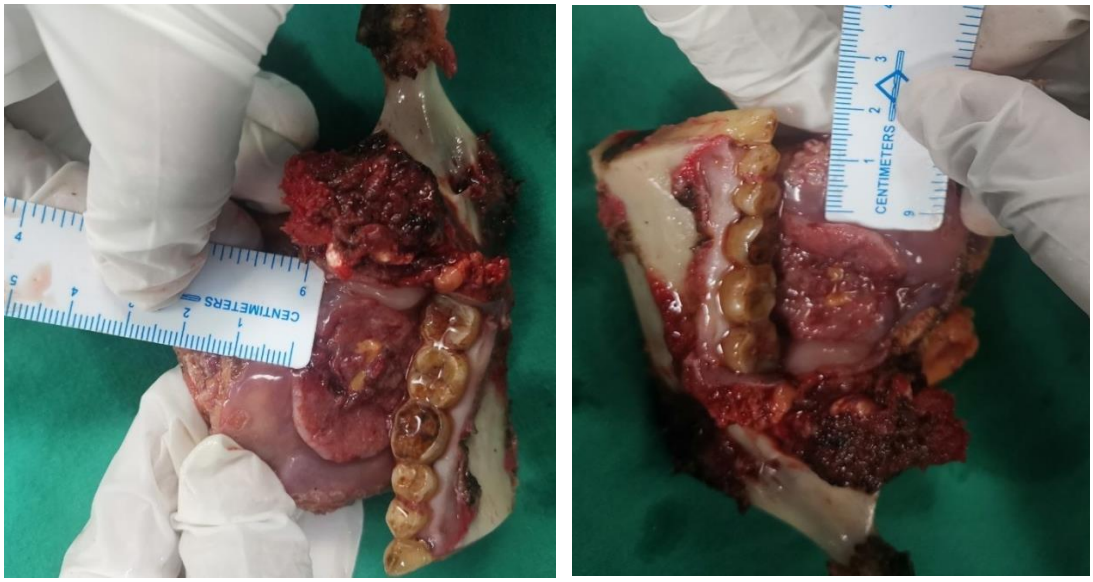


Fig 19:- Measurement of margins of resection before formalin fixation (buccal mucosa)

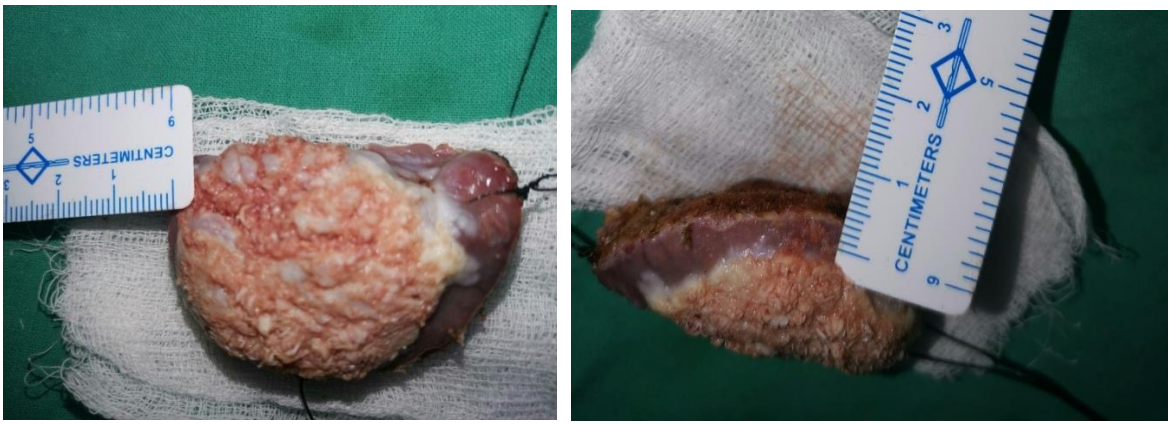


Fig 20:- Measurement of margins of resection before formalin fixation (tongue)

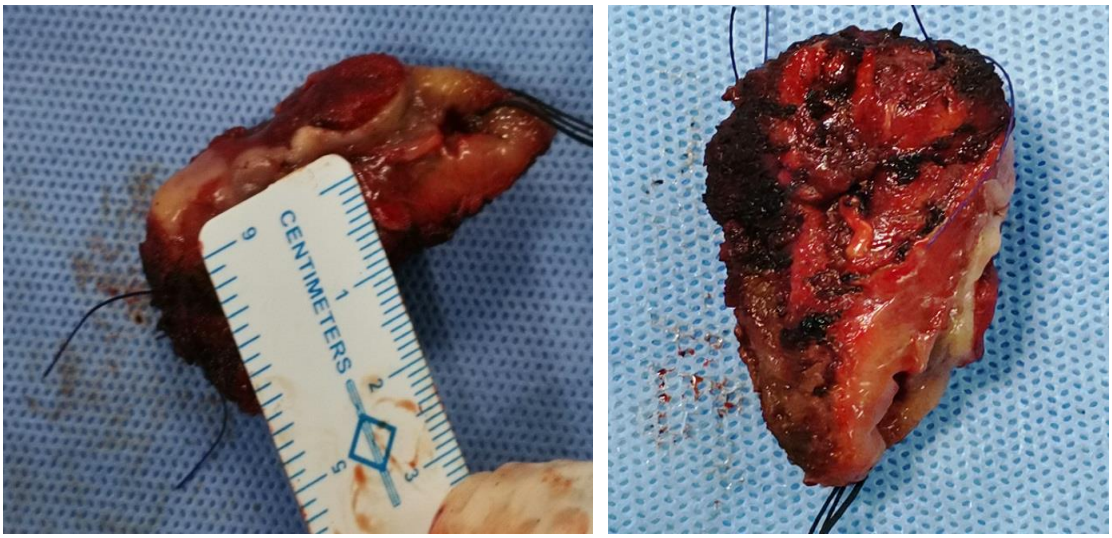


Fig 21 A)Measurement of tumor thickness and distance from deep margin B)Deep Margin of resection of tumor (third dimension)

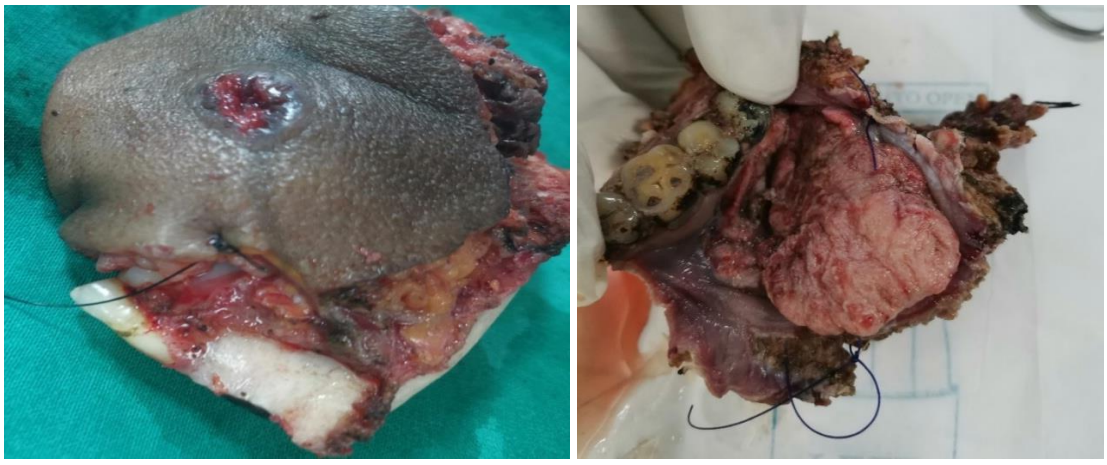


Fig 22:- Marking the closest margin of specimen with a stitch (for refernce during histopathology)

STATISTICAL ANALYSIS

Data was entered into Microsoft excel data sheet and was analyzed using SPSS 22 version software. Categorical data was represented in the form of Frequencies and proportions. **Chi-square test or Fischer's exact test** (for 2x2 tables only) was used as test of significance for qualitative data.

Continuous data was represented as mean and standard deviation. **Independent t test** was used as test of significance to identify the mean difference between two quantitative variables.

Graphical representation of data: MS Excel and MS word was used to obtain various types of graphs

P value (Probability that the result is true) of <0.05 was considered as statistically significant after assuming all the rules of statistical tests.

Statistical software: MS Excel**,** SPSS version 22 **(**IBM SPSS Statistics, Somers NY, USA) was used to analyze data.

RESULTS

RESULTS

Table 3:- Distribution of subjects according to age.

AGE	FREQUENCY	PERCENT
<40yrs	4	6.7
41-50yrs	18	30.0
51-60yrs	27	45.0
61-70yrs	6	10.0
>70yrs	5	8.3
Total	60	100.0

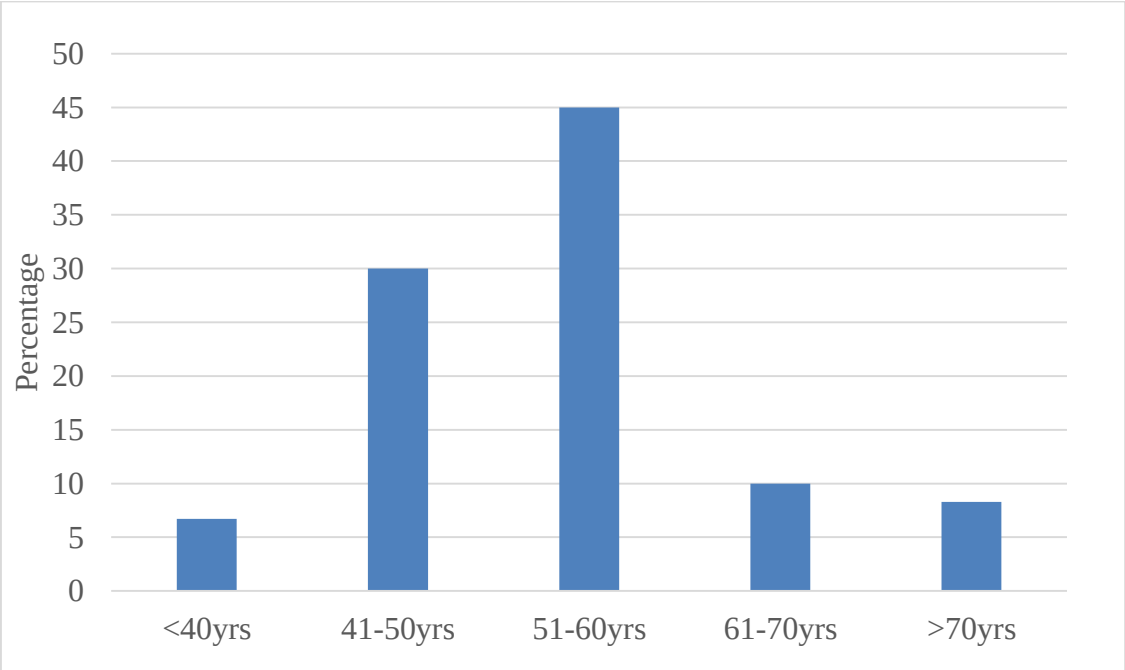


Figure 23:- Graph showing Distribution of subjects according to age.

Majority of our study subjects were between the age group of 40 to 60 years

Table 4:- Distribution of subjects according to sex.

SEX	FREQUENCY	PERCENT
Female	47	78.3
Male	13	21.7
Total	60	100.0

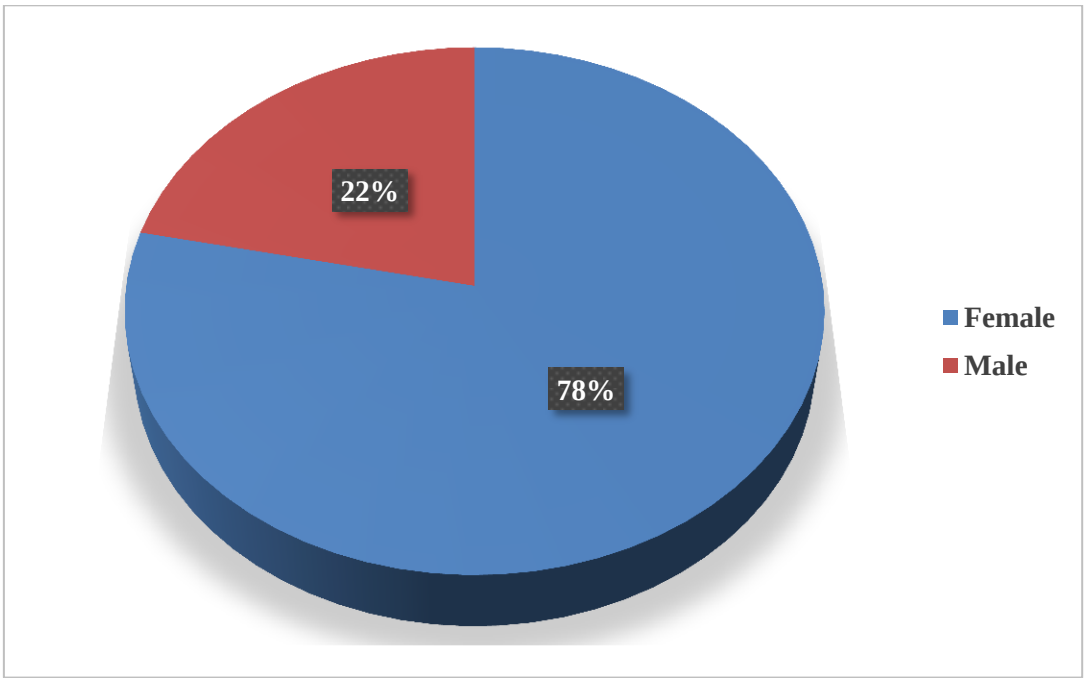


Figure 24:- Distribution of subjects according to sex.

In our study, majority of the patients were females (78%) and 22% were males.

Table 5:- Distribution of subjects according to site of lesion

SITE OF PRIMARY TUMOR	FREQUENCY	PERCENT
Lower Alveolus	4	6.7
Buccal Mucosa	37	61.7
Lower GBS	9	15.0
Tongue	10	16.7
Total	60	100.0

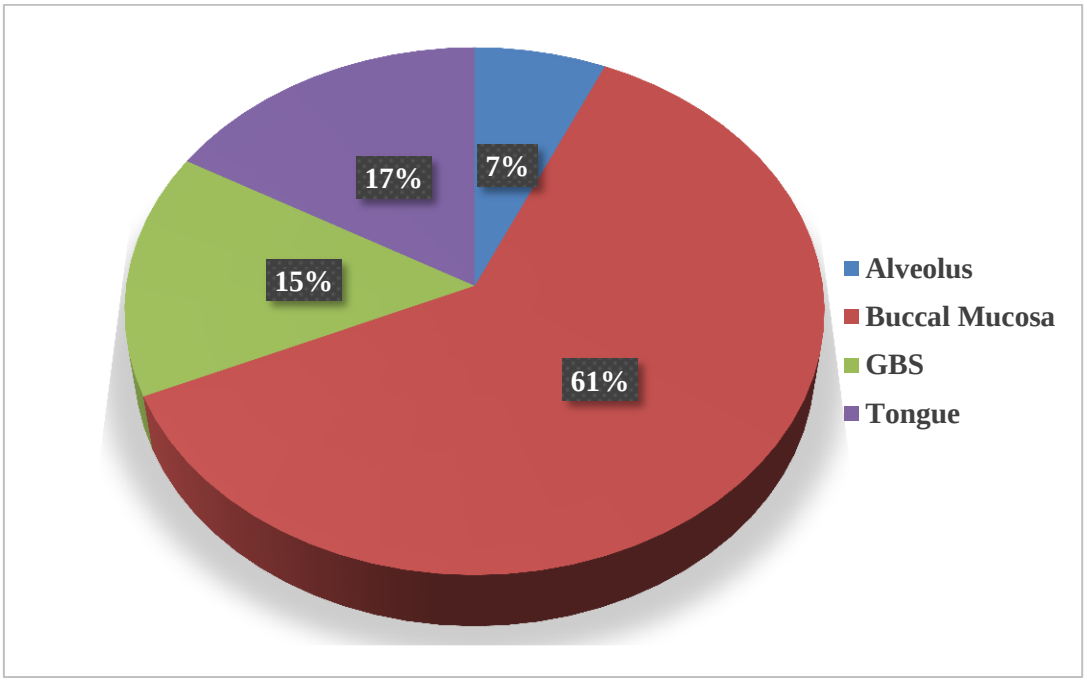


Figure 25:- Distribution of subjects according to site of lesion

Table 6:- Distribution of subjects according to nodal status.

NODAL STATUS	FREQUENCY	PERCENT
Negative	40	66.7
Positive	20	33.3
Total	60	100.0

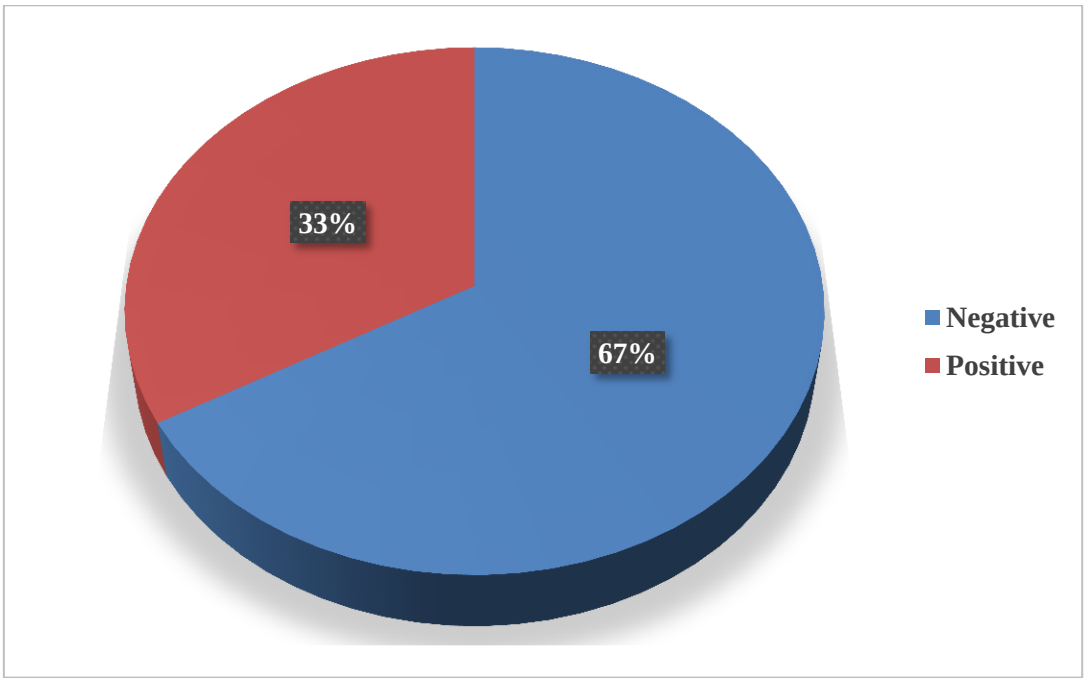


Figure 26:- Distribution of subjects according to nodal status.

Table 7:- Frequency Distribution of Extra nodal, Extra capsular invasion, Perineural invasion Among subjects.

ADVERSE HISTOPATHOLOGICAL FACTORS	FREQUENCY	PERCENT
Extra nodal and Perineural invasion	4	6.7
Extra capsular invasion	2	3.3

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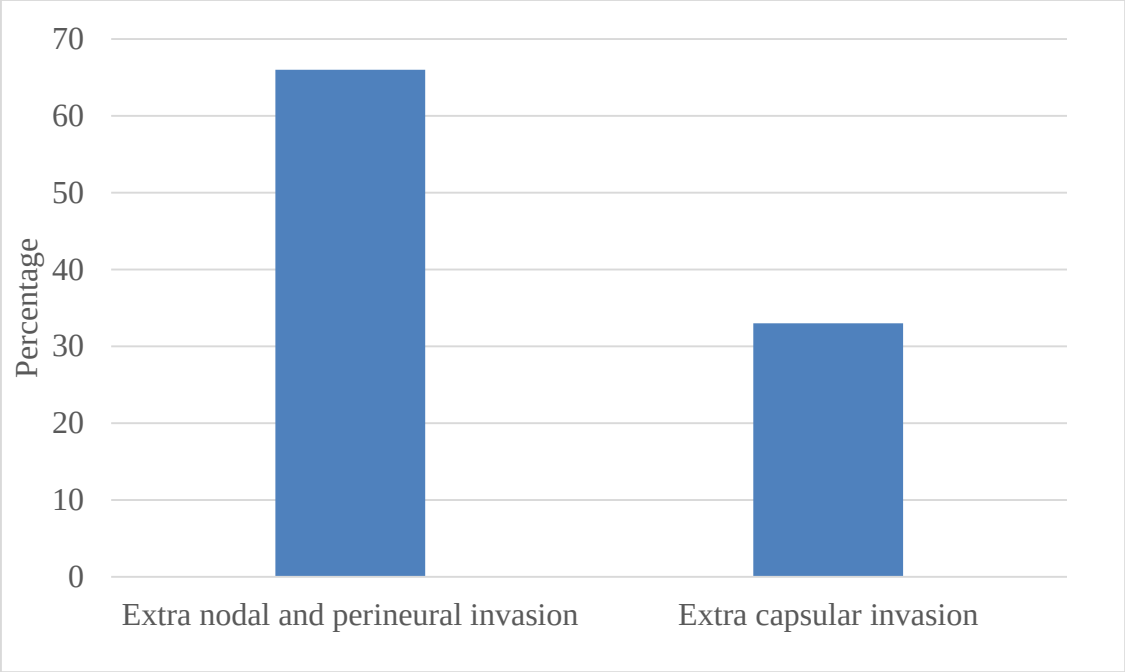

Figure 27:- Graph showing Frequency Distribution of Extra nodal, Extra capsular invasion, Perineural invasion Among subjects

Table 8:- Distribution of subjects according to depth of invasion

DEPTH OF INVASION	FREQUENCY	PERCENT
<5mm	5	8.3
≥5mm	55	91.7
Total	60	100.0

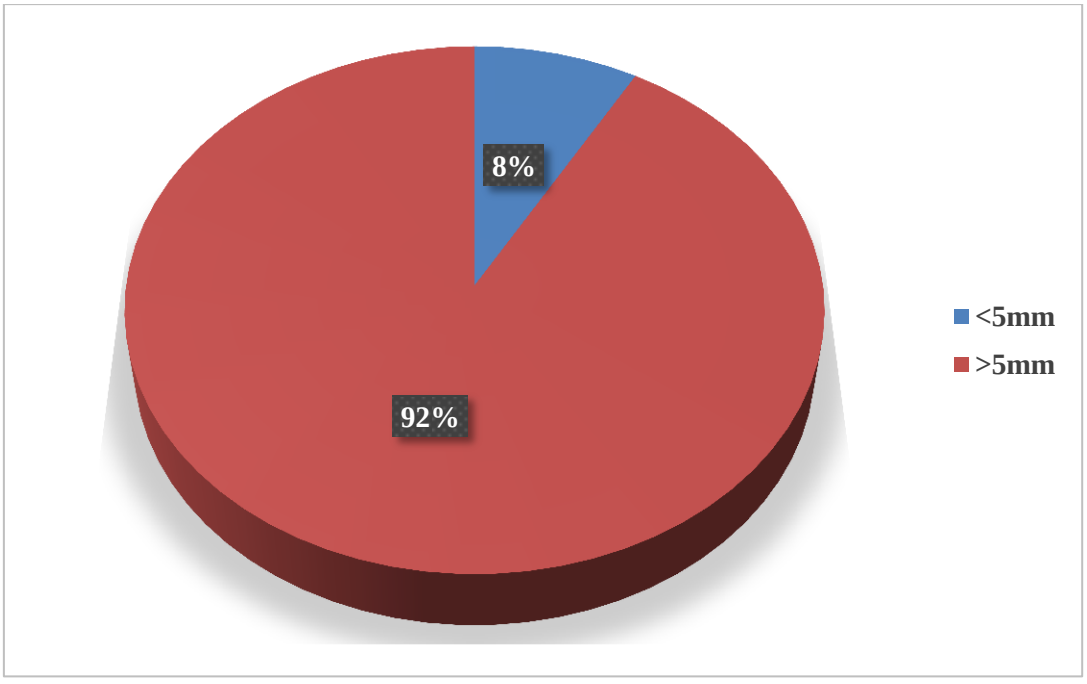

Figure 28:- Distribution of subjects according to depth of invasion

Table 9a:- Distribution of subjects according to margin of resection in histopathology.

MARGIN STATUS (AFF)	FREQUENCY	PERCENT
Adequate	41	66.66
CLOSE	18	31.7
Positive	1	1.66
Total	60	100.0

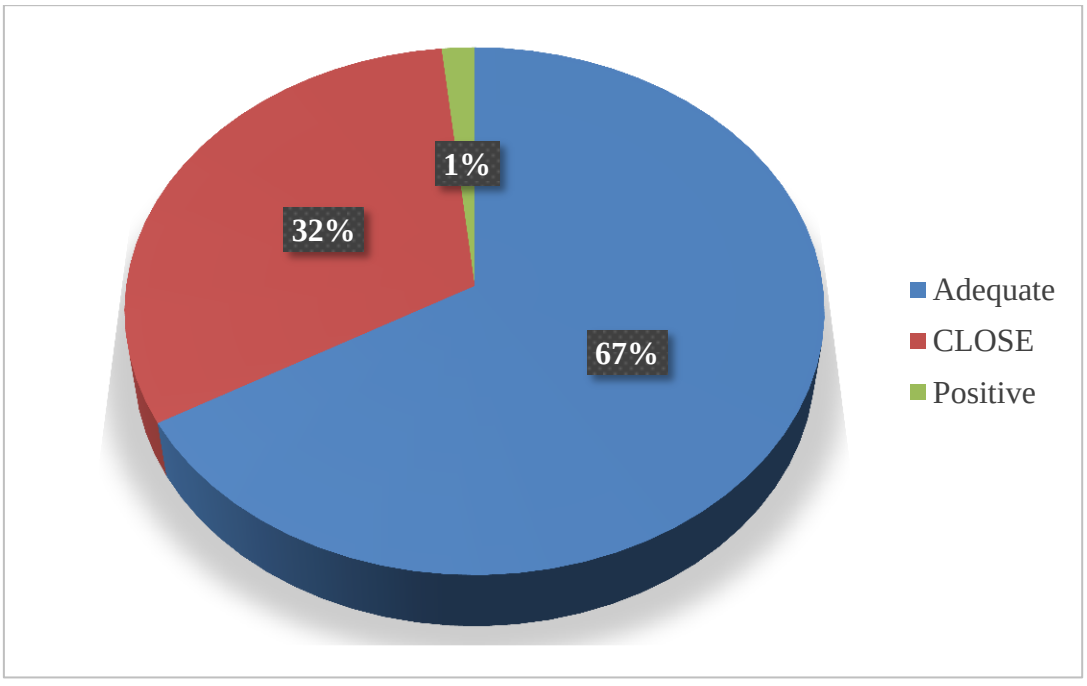

Figure 29:- Distribution of subjects according to margin of resection in histopathology

Table 9b:- Table showing margin of resection intraoperatively and margin of resection before formalin fixation (after complete resection of specimen)

Margin of resection intraoperatively		Margin of resection before formalin fixation (after complete resection of specimen)	
Adequate	Close	Adequate	Close
56	4	54	6

Table 10:- Comparison of margin to tumour before resection and margin of resection in histopathology.

BFF	Histopathology	
Before resection	Adequate	CLOSE
Adequate (56)	41	15
	71.4%	28.6%
Close (4)	0	3
	0%	75%

71.4% subject which had adequate margin before resection was found to have adequate margin in Histopathology. 28.6% subject which had adequate margin before resection was found to have Close margin in Histopathology. Kappa value was 0.198 which means none to slight agreement between before resection and histopathology.

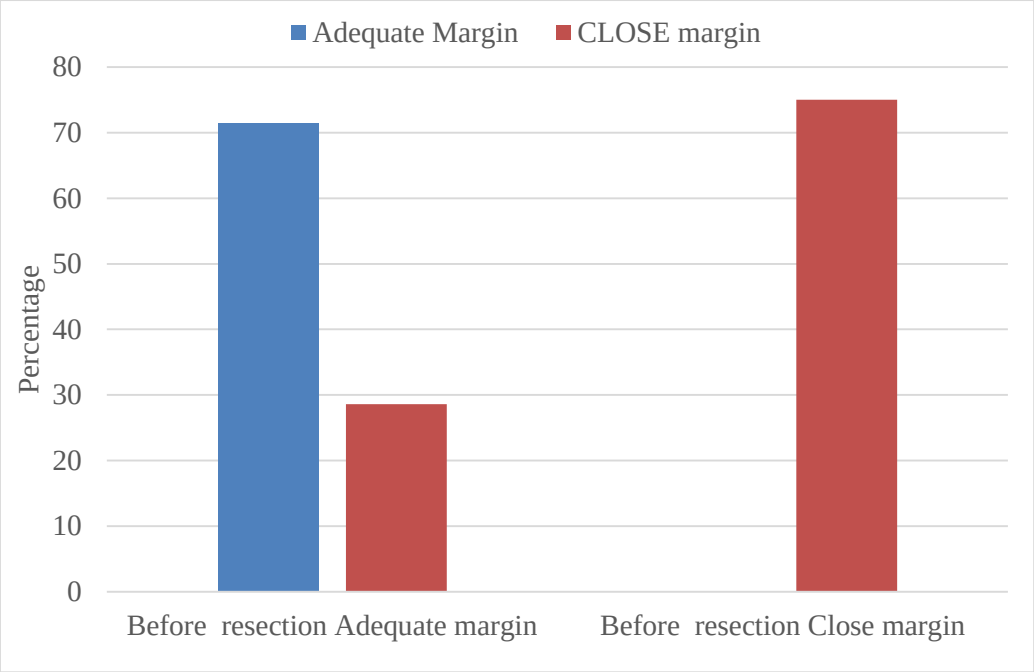

Figure 30:- Graph showing Comparison of margin to tumour before resection and margin of resection in histopathology.

Table 11:- Comparison of margin to tumour after resection before fixation and margin of resection in histopathology.

BFF	Histopathology	
After resection	Adequate	CLOSE
Adequate (54)	39	15
	72.2%	27.8%
Close (6)	1	4
	16.7%	66.7%
Total	40	19
	66.6%	31.7%

72.2% subject which had adequate margin after resection was found to have adequate margin in Histopathology. 27.8% subject which had adequate margin after resection was found to have Close margin in Histopathology. Kappa value was 0.198 which means none to slight agreement between after resection before fixation and histopathology.

Figure 31:- Graph showing Comparison of margin to tumour after resection before fixation and margin of resection in histopathology.

Table 12:- Frequency distribution of position among close margin subjects

CLOSE MARGINS	Frequency	Percent
Anterior	3	16.7
Lateral	2	11.1
Medial	4	22.22
Posterior	8	44.44
Superior	1	5.54

44.4% of close margin had it in posterior followed by medial 22.2%, anterior 16.7%

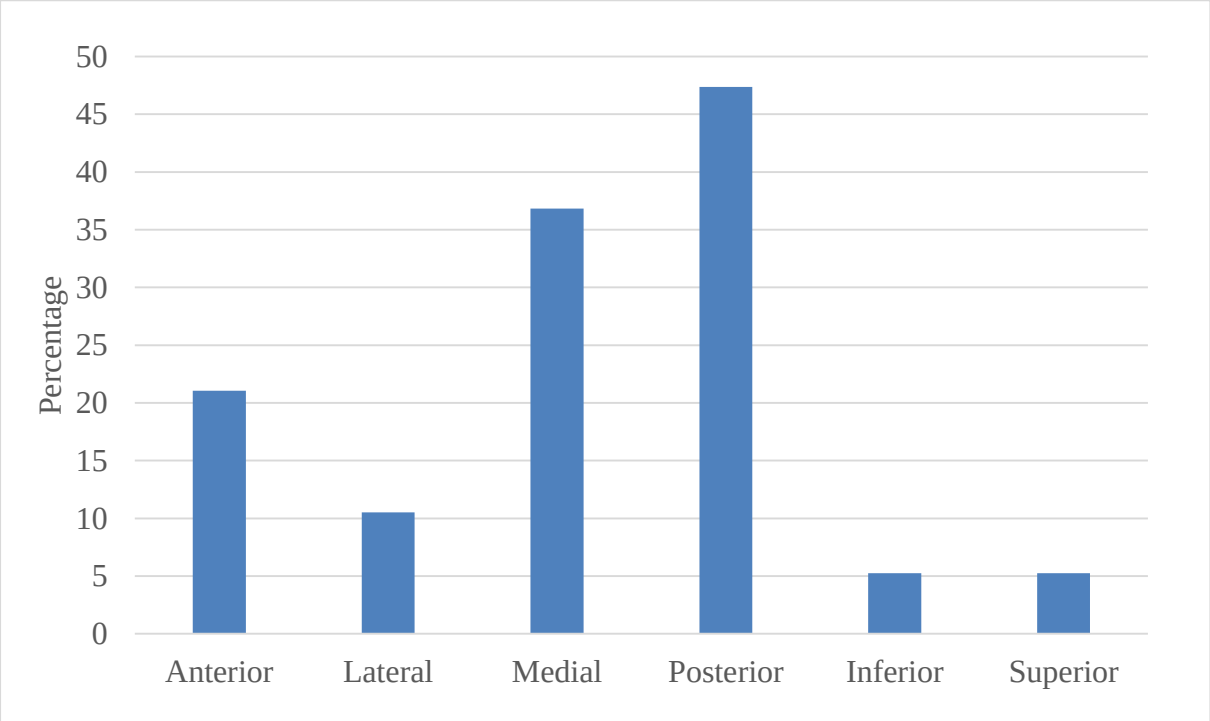

Figure 32:- Graph showing Frequency distribution of position among close margin subjects.

Table 13: Table showing the tumor free distance in patients having close margins.

CLOSE MARGINS	MEASURMENTS							
POSTERIOR (8)	2mm	4mm	3mm	3mm	4mm	3mm	3mm	1mm
ANTERIOR (3)	3mm	2mm	2mm					
MEDIAL (4)	3mm	4mm	3mm	3mm				
LATERAL (2)	2mm							
SUPERIOR (1)	2mm							

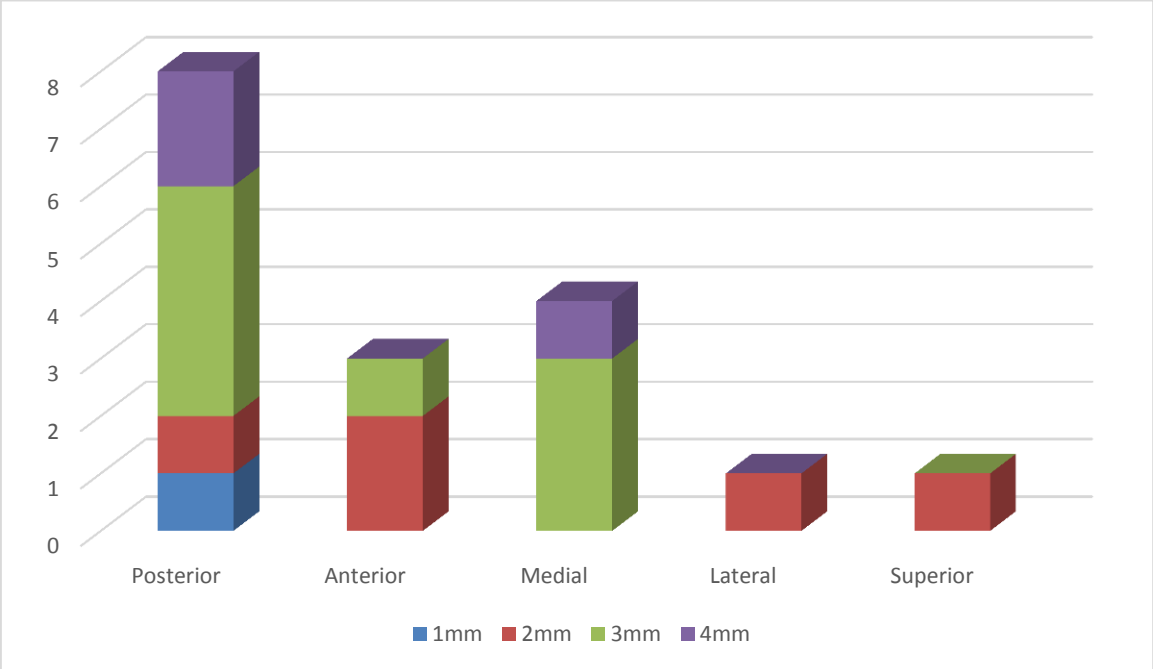

FIG 33:- Graph showing the tumor free distance in patients having close margins

Table 14:- Distribution of subjects according to subjects according to site and margin

SUBSITES	Histopathology	
	Adequate	CLOSE
Alveolus	1	3
	25.0%	75.0%
Buccal Mucosa	26	10
	70.3%	27.7%
GBS	7	2
	77.8%	22.2%
Tongue	7	3
	70.0%	30.0%

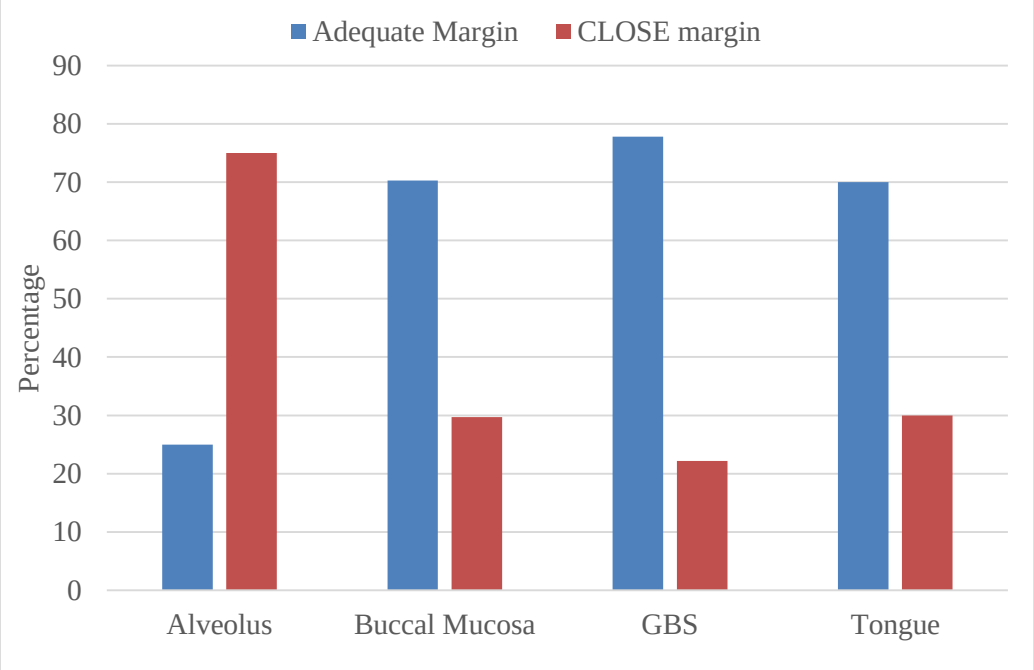

Figure 34:- Graph showing Distribution of subjects according to site and margin.

Table 15:- Distribution of subjects according to recurrence

RECURRENCE	FREQUENCY	PERCENT
Absent	47	78.3
Present	13	21.7
Total	60	100.0

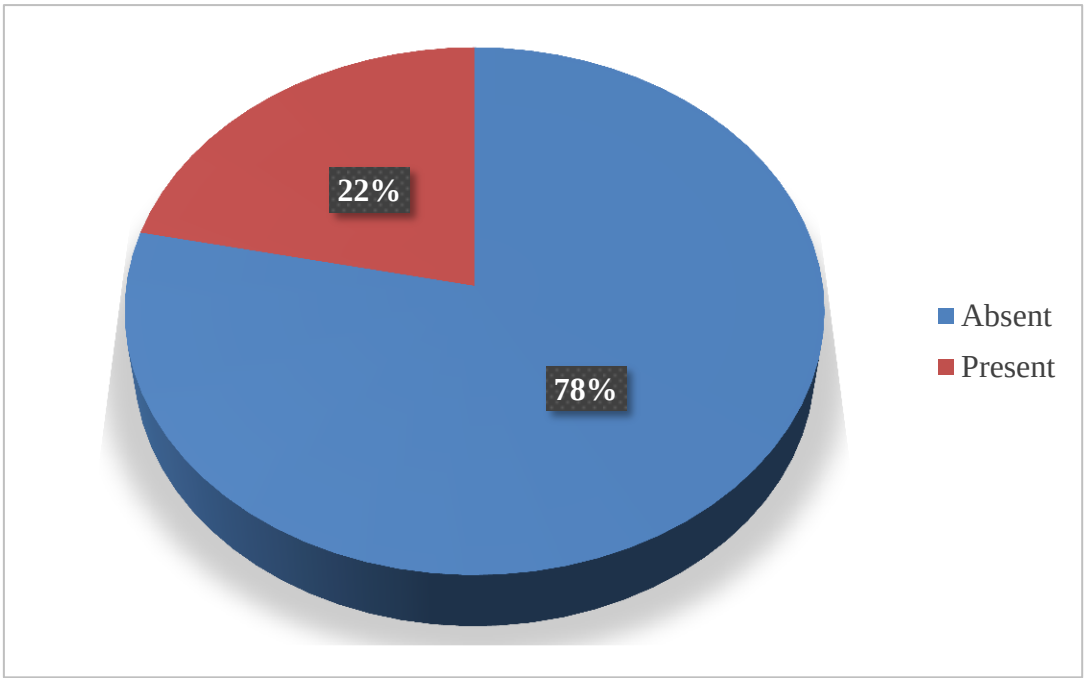

Figure 35:- Distribution of subjects according to recurrence

Table 16:- Distribution of subjects according to follow up status

FOLLOW UP STATUS	FREQUENCY	PERCENT
Disease Free	45	75.0
DIED	12	20.0
Lost to follow up	3	5.0
Total	60	100.0

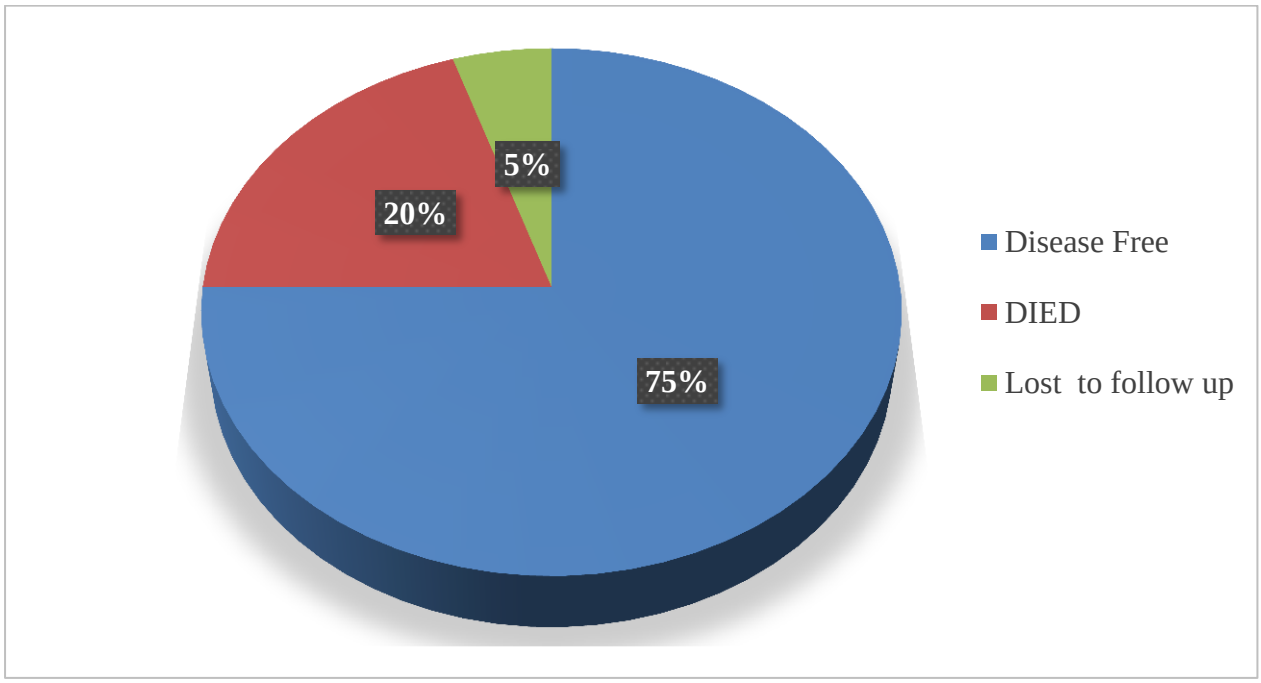

Figure 36:- Distribution of subjects according to follow up status

Table 17:- Distribution of subjects margins of resection and recurrence

MARGIN OF RESECTION	RECURRENCE		Total
	Absent	Present	
Adequate margin	33	7	40
	82.5%	17.5%	100.0%
Close margin	13	6	19
	68.4%	31.6%	100.0%
Total	47	13	60
	78.3%	21.7%	100.0%

Odds ratio was 2.24 (0.633- 7.93)

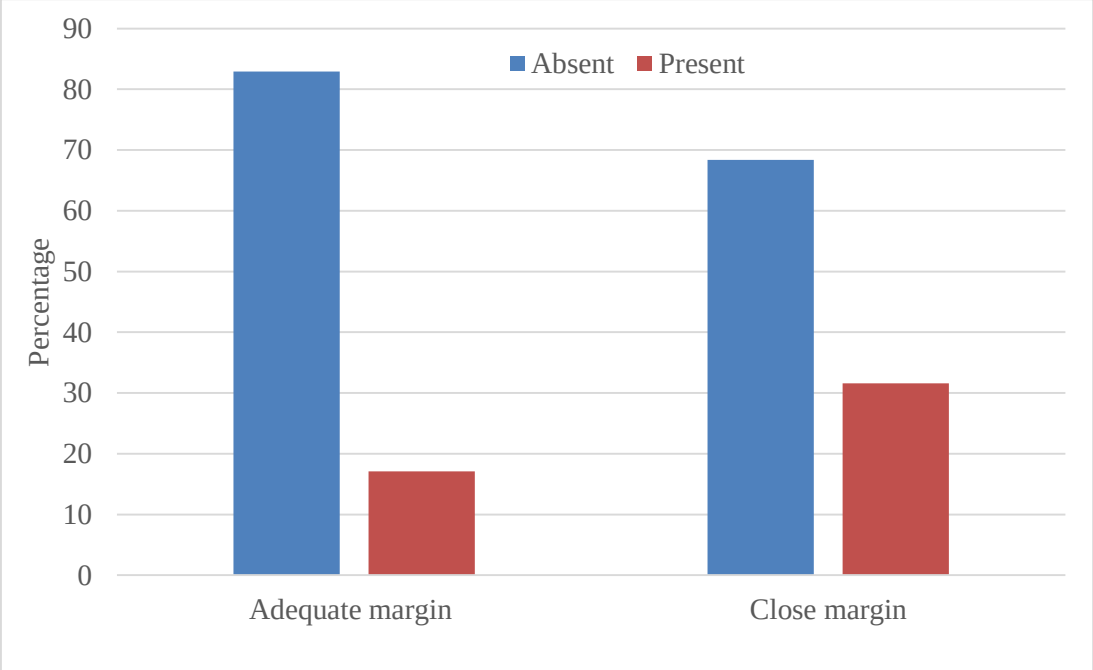

Figure 37:- Graph showing Distribution of subject's margins of resection and recurrence

Table 18:- Distribution of subjects depth of invasion and recurrence

DEPTH OF INVASION	RECURRENCE		Total
	Absent	Present	
≤5mm	12	1	13
	92.3%	7.7%	100.0%
>5mm	35	12	47
	74.5%	25.5%	100.0%
Total	47	13	60
	78.3%	21.7%	100.0%

Odds ratio was 4.114 (0.483- 35.06)

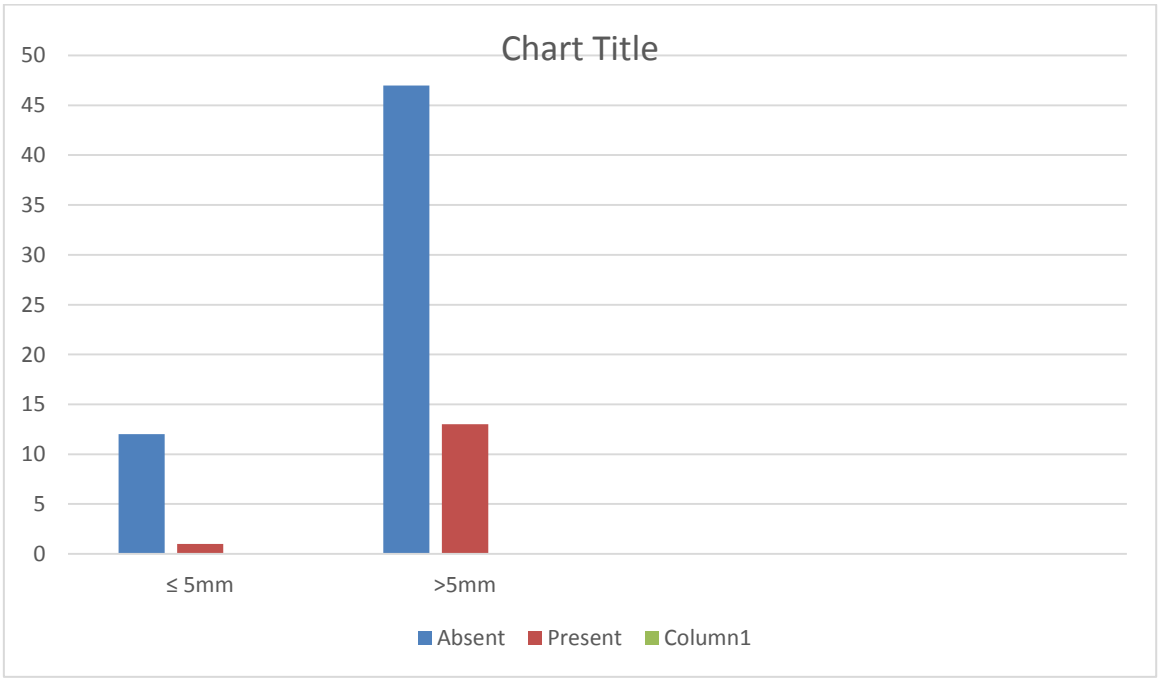

Figure 38:- Graph showing Distribution of subject's depth of invasion and recurrence

Table 19:- Table showing Shrinkage of Margin after formalin fixation(AFF)

SHRINKAGE OF MARGIN AFF	Frequency	Percent
0.1	4	6.66
0.2	10	16.66
0.3	18	30
0.4	10	16.66
0.5	18	30

- Mean shrinkage was 0.34 $\pm$ 0.12 after formalin fixation.

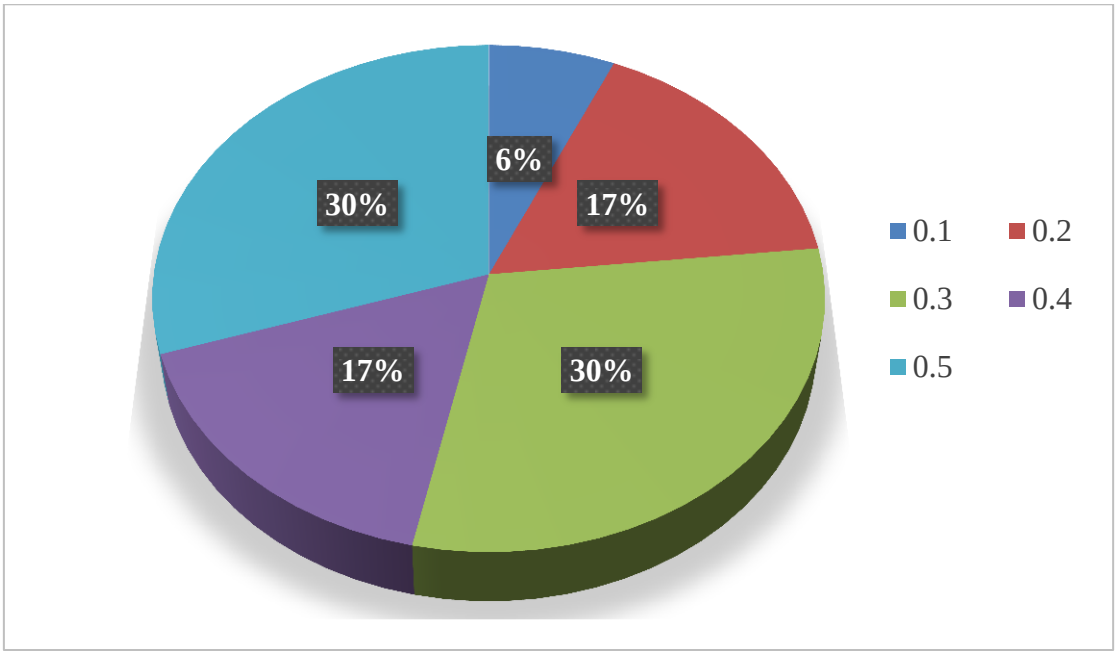

Fig 39:- Figure showing Shrinkage of Margin after formalin fixation

Table 20:- Table showing histopathological evaluation of resection margins

RESECTION MARGINS	SPECIMEN SITE MARGIN	PATIENT SITE MARGIN
Negative	58(96.6%)	60(100%)
Positive	2(3.4%)	0(0%)

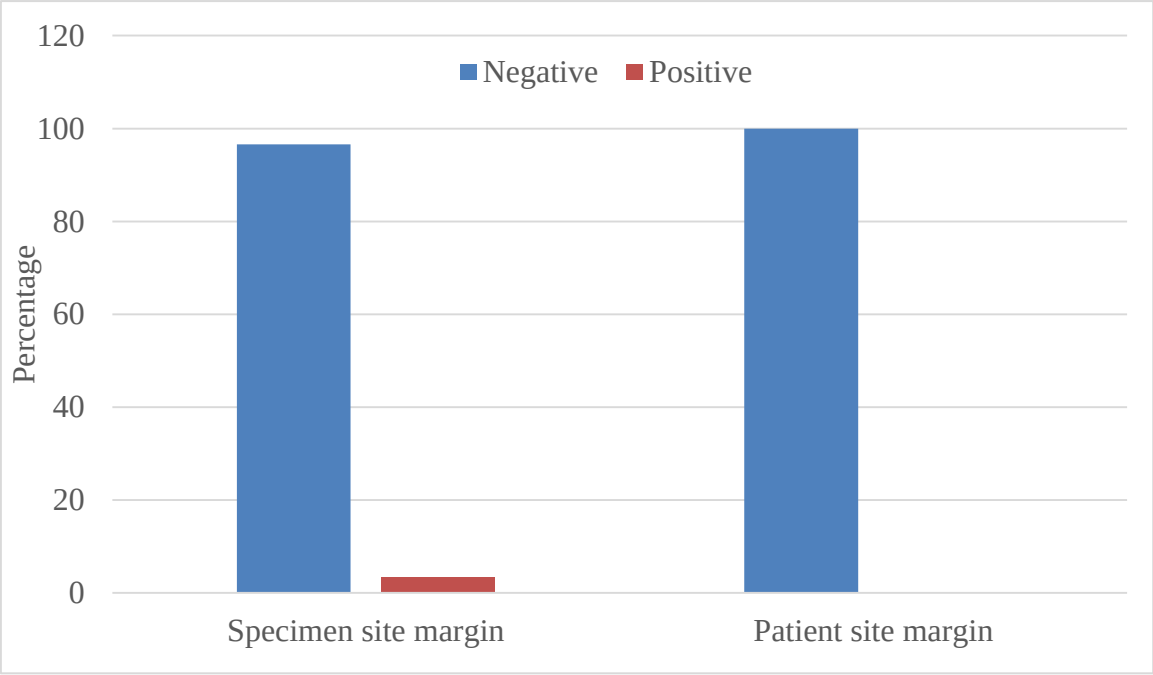

Fig 40:- Graph showing histopathological evaluation of resection margin

Table 21:- Table showing recurrences among patients with close margin at depth.

CLOSE MARGIN AT DEPTH	PERCENTAGE
Recurrence Absent	4(66.7%)
Recurrence Present	2(33.3%)

6 (10%) of the subjects had deep resected margin close margin

4(66.7%) was in tongue and 2(33.3%) was in Buccal mucosa

Among those subjects had deep resected margin close margin 2(33.3%) of the subjects had Recurrence.

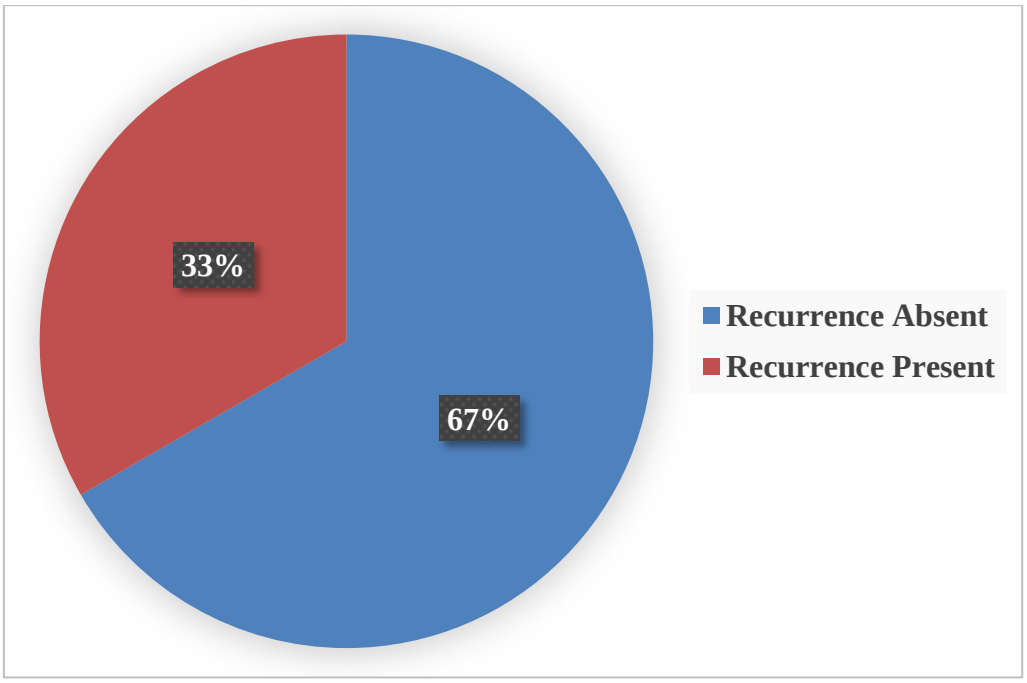

Fig 41:- Figure showing recurrences among patients with close margin at depth

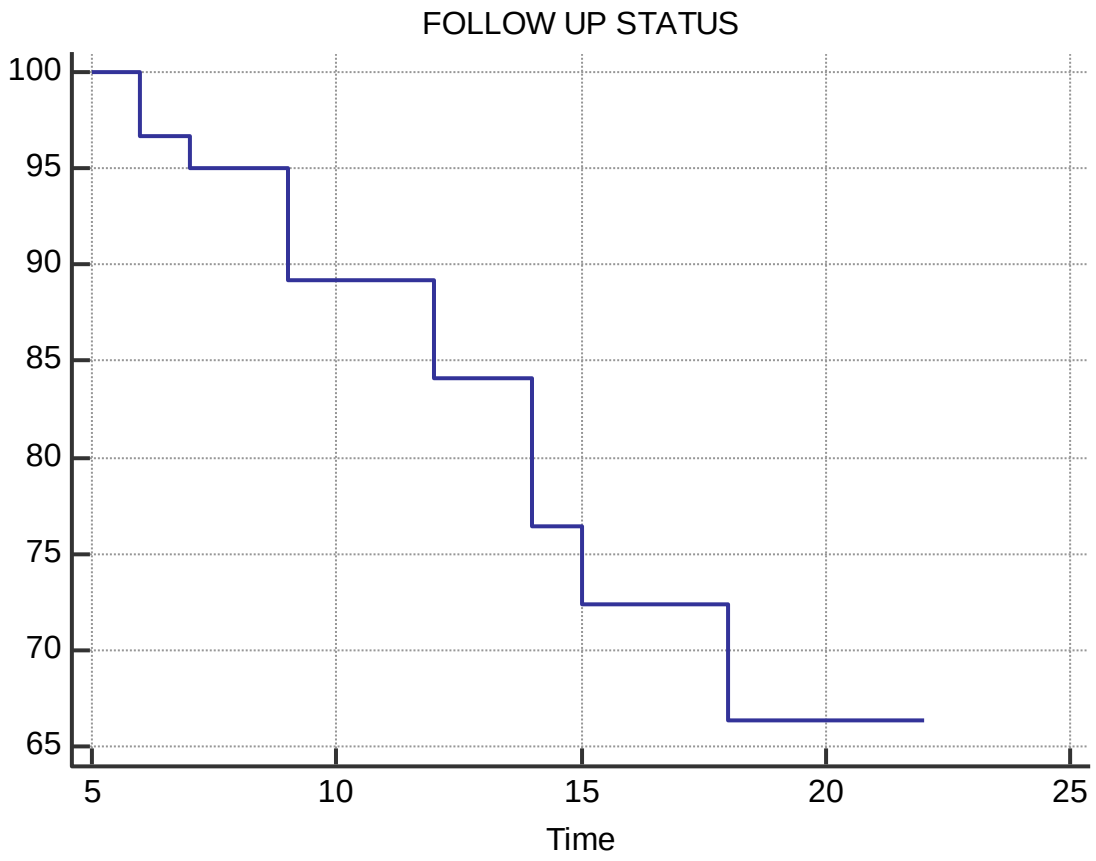

Fig 42:- Kaplan Meier graph showing recurrence

DISCUSSION

DISCUSSION

Oral cancer is the most common cancer in our region. It accounts for majority of head and neck cancers and it contributes 30% of all malignancies in this region. There is high prevalence in the district of Kolar, particularly among the female population due to addiction to tobacco quid. High prevalence of lower gingival buccal sulcus cancers among female population in this region can be attributed to addiction to tobacco quid, which usually causes malignancy in buccal mucosa and lower gingivo-buccal sulcus complex, owing to long duration of contact at this particular site with tobacco quid over long period of time. This addiction is common in females, whereas males are more addicted to smoking in this region. Majority of our study subjects were between the age 40 to 60 years. This is because the female population get addicted to chewable tobacco quid early in life usually in the second or early third decade and over a period of time, they tend to develop cancer which is often ignored or neglected due to lack of awareness, poverty and negligence when it comes to females.

Our study was a prospective analytical study to compare the margins of resection and the distance of the margin from the tumor both on the specimen as well as the patient site in oral cancer surgery.

In sites having the muscular tissue like tongue and buccal mucosa, the muscle tissues contracts much more on exposure to formalin as well as during surgery, due to use of electrocautery where the actin and myosin filament contracts. The mucosal or skin epithelial margin is often visible. However, at a depth, the microscopic spread cannot be evaluated easily and the muscle tends to contract more than the epithelium, thereby giving smaller

resection margins, as surgeons would have tried to keep distance from their specimen at surface (epithelial) level. It is proposed by various authors recently, that the patient site margin (defect) may turn out to be negative, whereas the actual margin which is closest to tumor may be at a depth in the muscle tissue[44]. This can be better assessed by taking a full thickness slice as margin of resection from the specimen wherever the tumor is closest to the resection margin.

In a review article it was observed that for oral cancer, the commonly practiced technique was sampling the tumor bed (Patient directed) and to determine the status of surgical margins. This has been challenged by two recent studies which clearly indicated that specimen based sampling is better. In literature, efficacy of frozen section analysis by patient based sampling to check adequacy of resection may not be effective as the tissue sent for frozen section may not be representative[45]

Majority of our study subjects had tumors involving buccal mucosa 61.7% and oral tongue 16.7% and majority of the patients in our series had locally advanced disease. In our study, 33.3% of patients had metastatic cervical lymph nodes and about 10% of patients had extranodal spread. Majority of the patients (92%) had tumors with depth of invasion $\geq$5mm.

Using the margin size (more than 5 mm) for two anatomical oral cavity subsites, namely, the floor of the mouth and the oral tongue, studies concluded that this prognostic factor did not have a significant impact on survival when adjuvant treatment was given.[3,6]

In our series one patient had positive margin and 18 patients had close margins (31.7%).

Close margins were <5mm after formalin fixation. When margins were checked intra operatively before complete resection, 4 patients who had close margins on measurement intraoperatively, but when margins were checked after resection before formalin fixation 6 patients was found to have close margins. This once again shows that at the depth in the muscle tissue, the margin tends to be close as the muscle contracts and even the electrocautery makes the muscle contract. Therefore the margin of resection would be lesser than what is seen at the surface.

When we compared the margins before complete resection with margins after formalin fixation, 15% of adequate margins at the time of surgery, turned out to be close margin after formalin fixation, and in most of them it was the deep muscular margin. The reason could be shrinkage of margin and shrinkage of the tumor after formalin fixation and also the increased shrinkage at muscular level. Among the 4 patients who had close margin, one turned out to be positive in histopathology. This shows that microscopic tumor spread can be more than the visible margin. In another they found that before formalin fixation, there is a mean decrease in tumour free margin measurement(11.3%)[45.] And unlike our study the decrease is prior to fixation and it is due to intrinsic tissue properties than the effect of fixation.[45]

Compared to the measurement of the margin of resection before delivering the specimen and histopathology (AFF), 29% of adequate margins BFF turned out to be close margins on histopathology. This is due to the shrinkage of margins after formalin fixation. Among the 6 patients found to have close margins after resecting the specimen before formalin fixation, one was falsely found to be close and had adequate margin on histopathology. One patient had positive margin at the depth and 4 had the close margin. Among the visibly close margin, 17% were found to be falsely close as they had adequate margin in histopathology. This was

detected after adding the thickness of the separate resected margin from the tumor site. In another study, the Positive margin phenomenon was explained as microscopic tumour extend beyond clinically palpable and visible tumour. Extensions or Islands of tumour invade out from the main mass of tumour, particularly in muscle tissue as the tumour grows along the muscle fibres in the absence of tumour barrier. In patients who received neoadjuvant chemotherapy, tumour margins during surgery may be diluted margins – appear to be free but may have microscopic disease.[45]

Among the patients having positive or close margins, maximum number (47%) of such margins were found to be the posterior margin showing the difficulty in access and the excessive cautery burns during the posterior part of resection. This was followed by medial margin as it is either close to the midline or close to the floor of mouth. The muscular tissue there be it floor of mouth or tongue tends to contract more. Other studies have shown that close margin is more common in posterior part of the specimen as it is relatively difficult to access and more predisposed to cautery burns[47.]

Among the patients having close margins, a higher percentage of patients were found to have close margins when the primary tumor was in the alveolus(75%) or in the tongue(30%). In lower alveolar tumors, floor of mouth, mucosa and the tongue contract on use of cautery or formalin fixation. In tongue malignancies, musculature contracts much more giving rise to close margins. In tongue, microscopic spread can be far beyond the visible tumor along the muscle fibres. Therefore tongue tumors mandate a wider resection of atleast 1.5cm margin before formalin fixation.

In another study by El- Fol et al in 61 patients,similar to our study the authors observed that tissue shrinkage was maximum for specimens removed from oral tongue (33.3%) and buccal mucosa (47%).[45]

In our study 22% recurred with a minimum follow up period of 6months and average period of follow up of more than one year. Among the patients who had adequate margins, 17.5% recurred. Among those having close margin 31.5% recurred showing the importance of adequacy of margins during resection particularly in muscle tissue. Similar to our study positive or close margins have high rate of local recurrence (35%) than negative specimen margin (29)% as observed by Steven M Sperry[44] .Similar observation was made in other studies in India and US[40].

In our study the lowest value for close margin in the oral cavity was described as less than or equal to 2 mm by two authors: they demonstrated that recurrence-free survival for Squamous Cell Carcinoma was similar for patients with involved margins and with close margins which was significantly worse than that observed in patients with negative margins. They also evaluated the efficacy of postoperative RT for squamous cell carcinomas of the buccal mucosa and concluded that radiotherapy was effective in decreasing locoregional failure in patients with close (less than 2 mm) margins. In fact, close margins not treated with RT showed worse prognosis, when compared with negative margins.[3,4,5]

When we assessed the third dimension, among patients having 5mm or less than 5mm of depth of invasion, only 8% recurred whereas with those having more than 5mm of depth of invasion 25% had local recurrence Similar to our study when depth of invasion is more than 5mm had 24% recurrence, and also unlike to our study most of them was having regional recurrence (cervical node metastasis)[47].

A study by Varvares et al. showed that margins >5mm were associated with better outcomes with recurrence rate of 3.4% whereas margins <5mm or with positive margins resected to negative were 26.4 and 28.6%[48]

Positive or close margin (<5mm) after formalin fixation predispose to early locoregional recurrence. The tissue shrinkage on formalin fixation, contraction of muscle on use of cautery, submucosal spread of tumor along muscle planes have given rise to controversies and discrepancy between operating findings and histopathology reports there by affecting adjuvant treatment and outcomes.[1,40]

In a study done on 268 patients, initial positive margins which were subjected to frozen section and resected again had a relatively poor outcome, However chances of recurrence can be reduced by Adjuvant Radiotherapy. Local recurrence rate for the close margin (less than or equal to 5 mm) was significantly higher compared to those having negative margin.[4]

On assessment of shrinkage of the margins in our series there was the shrinkage of 0.2 to 0.5cm in most of the patients AFF. The average mean shrinkage was 0.4cm in most of the margins with percentage of 25-30%.

Another study in literature showed 30% of shrinkage of soft tissue after formalin fixation which was similar to our study. Different sites have different tendancy to shrink on formalin fixation. Esophageal cancer can have shrinkage of 40% and cutaneous melanoma around 15-25% shrinkage in the margins.[40,49]

In our study, among the separate resected margins which were taken as a full slice both from specimen site and patient site and from the specimen site, 2 patients had positive margins - one of them had positive margin on histopathology. Patient site did not have any positive margin and 2 of our patients had positive margins from specimen site (deep muscular). This shows that at the depth the tissue shrinks and the margin can be positive especially muscular tissue like tongue whereas none of the patient site margin was positive. This is because at the time of surgery surgeon will keep adequate distance from the margin at least at the epithelium where as in the depth the cautery may go close to the tumor or there can be microscopic spread along the muscle fibers and muscle also contract along the surface epithelium. In our study, 3.4% of cases had deep muscular margin positive from specimen site. Another study showed that harvesting margins from the tip of specimen is easier but does not give distance to the margin and can show false positive of tumor involvement of the true surgical margin.[48]

In our study, among the patients who had close margins after resection (deep resected margin) 33% recurred showing the high rate of recurrence, when deep the margins is positive and this mandates a wide margin of resection preferably by taking a separate resected margin from the specimen site and revising the margin on operating table if found to be positive on depth. Similarly in another study the deep margins were positive most of the times and it is always difficult to sample the tissue whereas specimen oriented margin is able to measure the distance from the tumor to margin compared to defect oriented or deep resected margins.[48]

In a retrospective study of 406 patients on correlation between tumour specimen margin and intra operative tumor bed frozen margins, local recurrence or survival was found to be dependent on microscopic assessment of margins from specimen. There was strong correlation between microscopic assessment of margins and outcome with regard to locoregional control. Intraoperative frozen section from tumor bed were not a reliable predictor for adequacy of margins.[44]

Few studies have reported more muscle shrinkage in early cancers compared to locally advanced ones and reported an increased risk of local and nodal recurrence and reduced 5-year survival in patients with positive resection margins and reported a 5-year overall survival rate of 45.5% in patients with positive margins[4]. The drawback of present surgical technique is inability to obtain adequate deep resected margins or tumor bed intra operatively.[4,6,8]

Assessment of specimen based resection margin intraoperatively will help identify close or positive margins. Revision of full thickness resection and not just the epithelium will provide adequate margins in a significant number of patients and ensure disease clearance and better prognosis. According to every oncology group the worst adverse factor for recurrence in head and neck cancers are positive margins and extranodal spread. Therefore intraoperatively if a full slice is taken and the deep margins identified as close or positive margins, and a revision of that margin done at the time of surgery ensures better oncological outcome.

A review article observed that presence of surgical margin devoid of cancer cells has major influence in the outcome of treatment. There is controversy related to tumor free margin distance and assessment of intraoperative margins. Earlier 5mm distance between tumor and surgical margins for laryngeal, pharyngeal and oral cancer became invalid.

Newer technologies of margin assessment such as light spectroscopy and molecular analysis of tissues facilitates the real time assessment for surgical margins but not many studies are available regarding the efficacy.[45]

SUMMARY

SUMMARY

Head and neck malignancy contributes about 30% of all malignancies in our country, 80% of our patients present with locally advanced disease requiring multimodality treatment.

surgery is one of the main modalities of treatment, adequate resection (clearance > 5 mm AFF) of the margin is the primary goal.

The incidence of positive margins following resection in tumours of head and neck is significant, due to its complex anatomy. Surface (epithelial) margin of resection is usually adequate since it is clearly visible to the surgeon. However, the deep margins particularly involving muscles may not be far enough from the tumour due to higher contractility and shrinkage as well as difficult access during surgery. It has been a longtime controversy whether to take tissue from the patient site (defect) or the resected specimen to evaluate the adequacy of clearance when tumor is close to important structures or difficult to access and the surgeon feels the need to evaluate the adequacy of clearance.

Evaluation of a full thickness wedge resection both from the defect (patient site) and the resected specimens wherever the resection is closest to the tumor may contribute in addressing this controversy as to where the cut margins should be from. It will also throw light on the extent of tissue shrinkage on formalin fixation and the discrepancy between epithelial and deeper muscular margins. This was the objective of our study.

Our study is a prospective Analytical study done in 60 patients undergoing surgery for oral malignancy with or without extension to pharynx (head and neck) staged T2 to T4 from December 2019 to July 2021. Exclusion criteria included severe trismus, N3 lymph nodes, surgery for recurrence, history of previous surgery for head and neck tumors and distant metastases.

A full thickness slice of tissue was harvested from the margin closest to the tumor both from specimen as well as patient defect site and was analyzed by histopathology for presence of tumor cells as well as document the actual distance between tumor and margin of resection. The section included muscular or submucosal plane (also in this cut margins) to correlate between epithelial margins and deeper margin. The distance from the visible margin of tumour to the closest margin of resection was measured by a sterile scale and documented both before and after formalin fixation. Detailed histopathological examination was done both on the resected specimen as well as the cut margin from both specimen as well as resected site and the reliability of the cut margin between the specimen and patient site was evaluated.

Our study subjects had tumours involving buccal mucosa 61.7% and tongue 16.7%. In our series one patient had positive margin and 18 patients had close margins (31.7%).

On evaluation of margins intra operatively (visible measurements) before complete resection, 4 patients had close margins but when margins were checked after resection before formalin fixation 6 patients were having close margins and when we compared the margins before complete resection with margins after formalin fixation, 15% of adequate margins at the time of surgery, turned out to be close margins after formalin fixation, and in most of them it was the deep muscular margin. Among the 4 patients who had close margin, one turned out to be positive on histopathology. This shows that microscopic tumor spread can be more than the visible margins and differential shrinkage of tumor and margins occur after formalin fixation. Cautery can further shrink the muscular margin. Microscopic tumor spread can also occur along the muscles in the absence of tumor barriers like periosteum or perichondrium.

Compared to the measurement of the margin of resection before delivering the specimen and histopathology (AFF), 29% of adequate margins BFF turned out to be close margins on

histopathology. This is due to the shrinkage of margins after formalin fixation. Among the 6 patients found to have close margins after resecting the specimen before formalin fixation, one was falsely found to be close and had adequate margin on histopathology. One patient had positive margin at the depth and 4 had the close margin.

Among the patients having positive or close margins, maximum number (47%) of such margins were found to be the posterior margin showing the difficulty in access and the excessive cautery burns during the posterior part of resection

Around 22% patients recurred in our study after average period of follow up of one year. Among patients who had adequate margin on histopathology, 17.5% recurred. Among those having close margin 31.5% recurred showing the importance of adequacy of margins during resection particularly in muscle tissue. On assessment of the third dimension, among patients having 5mm or less than 5mm of depth of invasion, only 8% recurred whereas with those having more than 5mm of depth of invasion 25% had local recurrence.

Among patients who had close margins after resection (deep resected margin) 33% recurred showing the high rate of recurrence.

Positive or close margin (<5mm) after formalin fixation predispose to early locoregional recurrence. The tissue shrinkage on formalin fixation (25-30%) , contraction of muscle on use of cautery, submucosal spread of tumor along muscle planes have given rise to controversies and discrepancy between intra-operative findings and histopathology reports there by affecting adjuvant treatment and outcomes.[1] Normal tissue shrinks more compared to tumor tissue on formalin fixation and muscle shrinks much more (up to 40%).

The patient site margin may turn out to be negative, whereas the actual margin which is closest to tumor may be at a depth in the muscle tissue which is assessed by taking a full thickness slice as margin of resection from the specimen wherever the tumor is closest to the resection margin. This was reflected in our study as the only positive margin from the specimen site.

While using cautery the muscle contracts and margin of resection is superficial and away from actual area of interest, so a full thickness slice from the specimen site could give us correct resection margin, and their distance from the tumour in the closest margin has to be added to the thickness of the resection margin to have the correct value.

The specimen based close or positive margin is more likely to confirm that the margin is positive because on patient defect site surgeon would have gone clear of the tumour. It is uncommon to have a positive margin of resection at the surface.

In our study close margins where more common in tongue (muscular tissue), and lower alveolus (one of the margin being muscle in the floor of mouth).

Larger multi-institutional studies investigating the above mentioned issues would be required to arrive at definite protocols and guidelines and this topic has evoked interest in a few centre of excellence in oncology.

CONCLUSION

CONCLUSION

1. Adequate tumor free margins of resection are mandatory in surgery for head and neck cancers.
2. A margin of at least 1cm from outmost part of the tumor to the line of resection before formalin fixation and at least 5mm after formalin fixation is considered adequate in most regions involving squamous cell carcinoma of head and neck
3. A resection margin of 1mm or less is considered positive and 1 to 5 mm resection margin is considered close.
4. Positive margins carry a high chance of early recurrence in spite of aggressive adjuvant treatment.
5. The resection margins shrink both with electrocautery and formalin fixation normal tissue shrinks more than tumor tissue and muscle shrinks more than epithelium. Therefore deep muscular margin should be included in evaluating adequacy of clearance.
6. On an average tissue shrinks by 25 to 30% on formalin fixation. Muscle shrinks up to 40%.
7. While evaluating adequacy of clearance in the margin closest to tumor, a full thickness slice of tissue from resected specimen is more reliable compared to cut margin from patient site (defect) or random bits of tissue taken for frozen section.
8. Resection of tumor in muscular sites like tongue, buccinator and pharyngeal wall necessitate wide clearance as microscopic spread of tumor can be significantly beyond the visible margin along the muscle fibers as there is no tumor barrier.
9. If there is a close margin during resection, a full thickness slice of revision with adequate width would be better than revision surgery or relying on aggressive adjuvant treatment.
10. Larger multi-institutional studies involving margins of resection will throw light on site wise adequacy of clearance in oncosurgery.

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ANNEXURE

PROFORMA

Particulars of the patients

Name **Age**
Gender
Occupation
Hospital no
Telephone no
Date of admission
Date of surgery

Chief Complaints	**YES / NO**	**Duration**
• Presence of ulcer/mass in oral cavity		
• Presence of mass/swelling in neck		
• Restricted mouth opening		
• Excessive salivation		
• Difficulty in swallowing		
• Change in voice		
• Loss of appetite		
• Weight loss		
• Generalized weakness		
• Referred ear pain		
• Cough while eating		
• Hemoptysis		
• Loss of teeth		
• Difficulty in protrusion of tongue		
• Neck swelling		

HISTORY OF PRESENT ILLNESS

Onset:
Duration:
Progression:
Aggravating factors:
Relieving factors:

H/O trauma:Y/N
H/O difficulty in swallowing: Y/N
H/O difficulty in breathing: Y/N
H/O change in voice: Y/ N
H/O weight loss: Y/N

Past History **Yes/No**

- Hypertension
- Diabetes Mellitus
- Primary Tuberculosis
- Bronchial asthma
- H/o previous surgery
- Treatment History – Surgery/Radiotherapy/Chemotherapy

PERSONAL HISTORY **Yes/No**

ADDICTIONS:

Smoking

- Filterd Cigarette
- Unfilterd Cigarette
- Bidi
- Hookha
- Pipe

Duration - Packs/Day - Reverse Smoking – Y/N
Stopped since (if stopped)-

Alcohol

Duration- Type- Amount /Day-

Stopped Since (if stopped)-

Tobacco chewing-

- Pan masala
- Gutkha
- Beetle leaves /nuts
- Tobacco Quid

Duration- Frequency- side – Right/Left/Both
Stopped-Y/N If yes Since how many years

ENT EXAMINATION:

ORAL CAVITY :

- Mouth opening- Adequate/Trismus/Grade of Trismus
- Orodental Hygiene- Poor/Satisfactory
  Nicotine stains-Y/N

Site –

- Buccal mucosa
- Retromolar Trigone
- Gingivo-buccal sulcus
- Tongue
- Hard palate
- Floor of mouth

Side - Right/Left
Upper/Lower

PHARYNX:
Size-
Dimension- x cm
Subsites-

Type of Tumor –

- Verrucous
- Ulceroproliferative
- Ulcerative
- Infiltrative

Extent-

- Superior
- Inferior
- Anterior
- Posterior
- Edges

Dimension of tumor	-	x	cm
Tender	–	Y/N	
Skin involvement	–	Y/N	
Bleeds on touch	–	Y/N	

LYMPH NODES:

- Number
- Levels involved
- Size
- Consistency
- Mobile/Fixed
- Skin over the node

NOSE:
EAR:
IDL:

CLINICAL DIAGNOSIS :

STAGING :

INVESTIGATIONS

BIOPSY:

TREATMENT:

TYPE OF TREATMENT:

SURGERY PERFORMED:

NAME OF PROCEDURE

NECK DISSECTION

- SOHND
- MRND
- RND

SITE-

RESECTION YES NO

1. COMPOSITE RESECTION

Hemimandibulectomy

Marginal mandiblectomy

2. WIDE RESECTION

Hemimandiblectomy

Marginal mandiblectomy

RECONSTRUCTION

MARGINS:

	BEFORE FORMALIN FIXATION	AFTER FORMALIN FIXATION
1. DISTANCE		
Closest margin of tumor		
Closest margin of resection		
Tumor size	x cm	x cm

2. CUT MARGINS

SPECIMEN SITE	POSITIVE	NEGATIVE CLOSE
(A) Epithelium		
(B) Subepithelium		
(C) Muscle		

PATIENT SITE	POSITIVE	NEGATIVE CLOSE
(A)Epithelium		

(B)Subepithelium
(C)Muscle

HISTOLOGICAL TYPE:

- Squamous cell carcinoma
- Veruccous
- Papillary
- Acantholytic

HISTOPATHOLOGICAL GRADE:

- Well differentiated
- Moderately differentiated
- Poorly differentiated

ADJUVANT TREATMENT:

RADIOTHERAPY

- Fractions
- Duration

CHEMOTHERAPY

- Number of cycles
- Drug
- Dose
- Duration

RADIO AND CHEMOTHERAPY

DATE OF COMPLETION OF THERAPY

STATUS OF PATIENT:

DATE OF LAST FOLLOW UP:

STATUS OF LAST FOLLOW UP:

1. Disease free:
2. Diseased/Recurrence:
   - Local recurrence Regional recurrence
   - Regional recurrence
   - Locoregional recurrence
   - Distant metastasis
3. Died due to disease:
4. Died due to other causes:
   Lost to follow up:

INFORMED CONSENT FORM

I Mr/Mrs _____ have been explained in my own understandable language, that I will be included in a study which is **"EVALUATION OF SPECIMEN BASED AND PATIENT BASED RESECTION MARGINS IN HEAD AND NECK MALIGNANCIES**".

I have been explained that my clinical findings, investigations, intraoperative findings, post-operative course, will be assessed and documented for study purpose.

I have been explained my participation in this study is entirely voluntary, and I can withdraw from the study any time and this will not affect my relation with my doctor or the treatment for my ailment.

I have been explained about the follow up details and possible benefits and adversities due to interventions, in my own understandable language.

I have understood that all my details found during the study are kept confidential and while publishing or sharing of the findings, my details will be masked.

I have principal investigator mobile number for enquiries.

I in my sound mind give full consent to be added in the part of this study.

Signature/ Thump impression of the patient:
Name:

Signature of the witness:
Name:

Relation to patient:
Date:
Place:

PATIENT INFORMATION SHEET

STUDY SITE: R.L Jalappa Hospital and Research Centre attached to Sri Devaraj Urs Medical college, Tamaka, Kolar.

DETAILS: This is to inform you that we are going to perform a study titled

EVALUATION OF SPECIMEN BASED AND PATIENT BASED RESECTION MARGINS IN HEAD AND NECK MALIGNANCIES

This study help us to evaluate the visible closest margin of resection for microscopic disease from specimen and patient site and also to document the distance from margin of primary tumor to closest margin of resection. Intra operative frozen section analysis will be done which help in proper analysis of disease and avoid future recurrence.

Procedure may be associated with risk and complications such as bleeding, injury to adjacent structure, infections which are extremely rare. Patients in this study will have to undergo routine general investigations on all patients treated for head and neck cancers as a part of initial treatment.

The following information can be discussed with your family members and can decide whether to become part of study. You can ask any question regarding the study .If you agree to participate in the study we will collect information (as per Profoma) from you or a person responsible for you or both. Relevant history will be taken. This information collected will be used only for dissertation and publication.

All information collected from you will be kept confidential and will not be disclosed to any outsider. Your identity will not be revealed.

There is no compulsion to agree to this study. The care you will get will not change if you don't wish to participate you are required to sign/provide thumb impression only if you voluntarily agree to participate in this study.

You will not have any kind of financial benefits for being a part of this study nor will incur any additional expenses for being a part of this study.

You can also withdraw from the study whenever you are not willing to be a part of it for a genuine reason.

For further information contact.
Dr. FESLI LATHEEF (Post graduate)
Mobile no: 9633960833
E-mail id: feslilathif@gmail.com

GUIDE: Dr. S M AZEEM MOHIYUDDIN
Department of ENT and HEAD AND NECK SURGERY
SDUMC, Kolar.

MASTER CHART

SERIAL NO	AGE	GENDER	UHID NO	ORAL CAVITY EXAMINATION	BIOPSY	CLINICAL DIAGNOSIS	CLINICAL STAGING	SURGERY	HISTOPATHOLOGY	TUMOR SIZE BFF	TUMOR SIZE AFF	THIRD DIMENSION AFTER FORMALIN FIXATION	MARGIN OF TUMOR RESECTION BF FF	TUMOR RESECTION MARGIN AF FF	DISTANCE OF NEAREST MARGIN TO TUMOR BEFORE RESECETION BFF	DISTANCE OF NEAREST MARGIN TO TUMOR AFTER RESECTION OF MARGIN BFF	DISTANCE OF NEAREST MARGIN AFTER RESECTION OF MARGIN AFF	Distance of shrinkage of closest margin BF and AF FF	MEASUREMENT OF MARGIN FROM THE SPECIMEN SITE	MARGINS OF RESECTION	DISTANCE from deep margin of resection to base of the tumor	CLOSE MARGIN	SUBSITES	CUT MARGIN FROM PATIENT SITE	SIZE OF PATIENT SITE CUT MARGIN	CUT MARGIN FROM SPECIMEN SITE	SIZE OF SPECIMEN SITE CUT MARGIN	D0I	NODAL STATUS	EXTRA NODAL	EXTRA CAPSULAR INVASION	ADJUVANT T	TIME FOR RECURRENCE	FOLLOW UP STATUS		Duration
1	48	F	803043	Ulceroproliferative lesion in right lower GBS 3x4cm	SCC	SCC right GBS	T3N1M0	Composite resection, Right MRND, Bipaddle PMMC Flap Reconstruction	Moderately differentiated squamous cell carcinoma pT2NxMx	3x1.5cm	2.1x 1cm	0.8cm	1.5x1.7x1.2cm(AXPXS)	0.9x1.0x.5 cm (AXPXS)	1cm(superior)	0.8cm	0.5cm	0.3cm (superior margin)	0.3CM	Adequate		None	right GBS	Negative	0.8x0.5cm	Negative	0.7x0.3cm	14mm	free of tumor deposits	NIL	NIL	RT- 30#	No recurrence	DF		1 year 10 months
2	76	F	799562	Ulceroproliferative lesion in right Buccal Mucosa 3x4cm	SCC	SCC right Lower Alveolus	T4aN1M0	composite resection, Right MRND, Bipaddle PMMC Flap Reconstruction	Moderately differentiated squamous cell carcinoma Pt4an0mx, stage 1vA	4x3cm	3.5x2.5cm	1cm	1.5x1x1.2x1.2cm (AXPXSXM)	1x.2x.7x.3cm(AxPxSxM)	1.2cm(Posterior)	0.7cm	0.2cm	0.5cm (posterior)	0.4CM	Close margin	involving bone with destruction	1 0.2 cm(POSTERIOR),0.3cm (medial)	right Lower Alveolus	Negative	2x0.5cm	Negative	0.7x0.4cm	10mm	free of tumor deposits	NIL	NIL	RT- 32#	LOCOREGIONAL SPREAD AND DIED DUE TO DISEASE.	DIED due to disease		1year 6months
3	65	M	806140	Ulceroproliferative lesion in right Buccal Mucosa 3x2cm	SCC	SCC left Buccal Mucosa	T3N1M0	Wide local excision,left MRND, Supraclavicular flap reconstruction	well differentiated squamous cell carcinoma pT2N3Mx	3x2.5cm	3x2cm	1.2cm	1.4x1.2x1.5x1.5cm (AxPxSxI)	0.8x.4x.5x1cm(AXPXSXM)	1.2cm(Posterior)	.8cm	0.4cm	0.4cm (Posterior)	0.5CM	Close margin		2 0.4cm(POSTERIOR)	left Buccal Mucosa	Negative	3x0.5cm	Negative	1.5x0.5cm	5mm	8/16 positive	PRESENT	NIL	RT-35#, 3cycle of adjuvant chemotherapy	REGIONAL	DIED due to disease		6months
4	55	M	809355	Ulceroproliferative lesion in right Buccal Mucosa 3x2cm	SCC	SCC right Buccal Mucosa	T4aN1M0	Bite resection, Right MRND, PMMC Flap reconstruction	Well differentiated squamous cell carcinoma pT2N3Mx stage IV B	3.5X2.5cm	2.2x1.5cm	0.4cm	1.4x1.2x1.5X1.4cm(AXPxSXM)	1X0.5x1x1cm(AXPxSxM)	1.2cm(Posterior)	0.7CM	0.5CM	0.3cm(Posterior)	0.5CM	Adequate	1cm	None	right Buccal Mucosa	Negative	1x0.5cm	Negative	1x0.5cm	6mm	2/13 positive	NIL	PRESENT	RT-33#, 5cycles of adjuvant chemotherapy	Developed 2nd primary and operated	ALIVE		1 year 10 months
5	60	F	806130	Ulceroproliferative lesion in right lower Gingivo-buccal sulcus 2x1.8cm	SCC	SCC right lower GBS	T2N1M0	Composite resection, Right MRND, PMMC Flap Reconstruction	Well differentiated squamous cell carcinoma pT2N1Mx	2x1.8cm	1.5x1cm	1.5cm	1.4x1.4x1.5X.8cm (AXPXSXM)	0.3x1x0.5x0.5cm(AXPXSXM)	1.4cm(Anterior)	0.8CM	0.3CM	0.5cm(Anterior)	0.5CM	Close margin	1cm	3 0.3cm(ANTERIOR)	right lower GBS	Negative	0.5x0.5cm	Negative	0.5x0.5cm	6mm	1/9 positive	NIL	NIL	RT-32#, 3cycles of adjuvant chemotherapy	Nodal recurrence present	ALIVE		1 year 10 months
6	58	F	814889	Verrucous lesion 3x2cm	Verrucous carcinoma left lower GBS	Verrucous carcinoma Left lowerGBS	T4aN1M0	Composite resection, Left MRND,PMMC Reconstruction	Verrucous carcinoma pT1N2bMx	2x2cm	1.5x1.5cm	0.5cm	2x1.5x1.5x1cm (AXPXSXM)	2x0.5x0.5x1cm(AXPXSXI)	1.5cm(posterior)	1cm	0.5cm	0.5cm (Posterior)	0.5CM	Adequate	0.5cm	None	Verrucous carcinoma Left lowerGBS	Negative	2x0.5cm	Negative	1.5x0.5cm	7mm	2/28positive	NIL	NIL	RT-30#	No recurrence	DF		1 year 10 months
7	58	F	815310	Ulceroproliferative lesion in right lower Alveolus 4x3cm	SCC	SCC right upper alveolus	T4aN1M0	Right infrastructure maxillectomy+ left MRND+Reconstruction	Well differentiated squamous cell carcinoma pT4aN2bMx.	4x2.5cm	3x2cm	1cm	1.8x1.4x.8x1.2cm(AXPXMXS)	1.5x1x0.3x0.5cm (AXPXMXL)	1.2cm(superior)	0.8CM	0.5CM	0.3cm (Posterior)	0.1CM	Close margin		4 0.3cm(Medial)	right lower alveolus	Negative	1x1cm	Negative	1x1cm	9mm	2/25positive	NIL	NIL	RT-33#	developed recurrence after 3months of surgery	DIED due to disease		6 months
8	65	F	812570	Ulceroproliferative lesion in left lower Alveolus 3x2cm	Verrucous carcinoma left BM	SCC left Buccal Mucosa	T4aN1M0	Composite resection, Left MRND,PMMC Reconstruction	Verrucous carcinoma t2n1	3x1.5cm	2.2x1cm	0.5cm	2x1.2x2x1.2cm (AXPXSXI)	1.5x0.5x1.8x1cm (AXPXSXI)	1.2cm(Posterior)	0.9cm	0.5CM	0.4cm(Posterior)	0.5CM	Adequate	0.2cm	None	left Buccal Mucosa	Negative	0.5x0.5cm	Negative	0.5x0.5cm	10mm	free of tumor deposits	NIL	NIL	RT-32#	No recurrence	DF		1 year 9 months
9	64	F	819927	Ulceroproliferative lesion in right Buccal Mucosa 5x3cm	SCC	SCC right Buccal Mucosa	T3N1M0	Composite resection, Right MRND, PMMC reconstruction	Squamous cell carcinoma with microinvasion, t2n0	3x3cm	2x2cm	0.1cm	1.5x1.4x1.2cm (AXPXS)	0.5x0.8x0.5cm (AXPXS)	1.2cm(superior)	1cm	0.5cm	0.5cm(Superior)	0.5CM	Adequate		None	right Buccal Mucosa	Negative	0.5x0.5cm	Negative	0.5x0.5cm	<1mm	free of tumor deposits	NIL	NIL	No Adjuvant treatment recieved	No recurrence	DF		1year 9months
10	52	F	824030	Ulceroproliferative lesion in right Buccal Mucosa 3x2cm	SCC	SCC right Buccal Mucosa	T4aN2bM0	Composite resection, Right MRND,Deltopectoral flap reconstruction, SSG	Well differentiated squamous cell carcinoma, t4a	4x3cm	4x3cm	2.5cm	2.5x1.8x2x2.5cm(AXPXSXM)	2.5x1x1.5x2.5cm (AXPXSXI)	1.8cm(posterior)	1.2cm	1cm	0.2cm(Posterior)	0.5CM	Adequate		none	right Buccal Mucosa	Negative	1x0.5cm	Negative	0.5x0.5cm	18mm	1/10positive	NIL	NIL	RT-30#	No recurrence	DF		1year 8months
11	60	F	826656	Ulceroproliferative lesion in left Buccal Mucosa 4x3cm	SCC	SCC left Buccal Mucosa	T4aN2bM0	Composite resection,left MRND,Bipaddle PMMC Reconstruction	Moderately differentiated squamous cell carcinoma, t4a	2x1cm	1.6x1cm	1cm	2x1.2x1.2x2cm(AXPXSXI)	2x0.5x0.8x1.5cm (AXPXSXI)	1.2cm(Posterior)	0.8CM	0.5CM	0.3cm (Posterior)	0.5CM	Adequate		None	left Buccal Mucosa	Negative	1x0.5cm	Negative	1x0.5cm	6mm	free of tumor deposits	NIL	NIL	RT-30#	No recurrence	DF		1year 8months
12	60	F	830630	Infiltrative lesion of 3x2cm in left lower GBS	SCC	SCC left lower GBS involving floor of mouth and left side of tounge	T4aN2aM0	Composite resection,left MRND,PMMC flap reconstruction	Well differentiated squamous cell carcinoma, t4a	3.5x2cm	3.2x2.5cm	2cm	2.5x1.8x1.5cm(AXPXS)	2x1.3x.5cm (AXPXS)	1.5cm(Superior)	1CM	0.5CM	0.5cm(superior)	0.5CM	Adequate	0.3cm	None	left lower GBS involving floor of mouth and left side of tounge	Negative	0.5x0.2cm	Negative	1x0.5cm	6mm	2/21 positive, salivary gland shows infiltration of tumor.	NIL	PRESENT	RT-32#,4cycle of adjuvant chemotherapy	developed locoregional recurrence	DIED due to disease		7months
13	40	M	843193	Infiltrative lesion of 3x2cm in left lateral border of tongue	SCC	SCC left lateral border of tounge	T3N1M0	left hemiglossectomy ,left MRND	Well differentiated squamous cell carcinoma pT3N0Mx	3x2cm	2.4x2cm	1.2cm	2.5x2.5x3cm(AxPxL)	2x2x3cm (AxPxL)	2.5cm(posterior)	2.3cm	2cm	0.2cm (Posterior)	0.8CM	Adequate	0.8cm	None	left lateral border of tounge	Negative	0.8x0.8cm	Negative	0.8x0.8cm	11mm	free of tumor deposits	NIL	NIL	RT-30#	No recurrence	DF		1year 7months
14	62	F	834965	Ulceroproliferative lesion 4x3cm in left buccal mucosa	SCC	SCC left Buccal Mucosa	T4aN0M0	Composite resection, Left MRND,PMMC Reconstruction	Well differentiated squamous cell carcinoma pT3N0M	4x2cm	4x1.8cm	0.5cm	2x1.5x1.5x1.5cm(AXPXSXM)	2x0.7x1x1cm (AXPXSXM)	1.5cm(posterior)	1cm	0.7cm	0.3cm (Posterior)	0.5CM	Adequate	1cm	None	left Buccal Mucosa	Negative	1x0.5cm	Negative	0.5x0.5cm	5mm	free of tumor deposits	NIL	NIL	RT-30#	No recurrence	DF		1year 7months
15	50	F	840817	Ulceroproliferative lesion 5x3cm left buccal mucosa	SCC	SCC left Buccal Mucosa	T4aN2aM0	Composite resection,left MRND,PMMC flap reconstruction	Moderately differentiated squamous cell carcinoma PT3N2bMx	4x3cm	4x3cm	1.5cm	1.5x1.5x2(AXPXS)	.5x.3x1cm (AXPXS)	1.2cm(posterior)	0.8cm	0.3cm	0.5cm(Posterior)	0.5CM	close margin		5 0.3CM(POSTERIOR)	left Buccal Mucosa	Negative	2x0.5cm	Negative	0.5x0.5cm	5mm	6/37 postive, 1 perinodal spill, perineural invasion and moderate degree of lymphoplasmocytic peritumor infiltration.			RT-32#	No recurrence	lost to follow up		1year 4months
16	47	F	842735	Ulceroproliferative lesion 2x3cm left buccal mucosa	SCC	SCC left Buccal Mucosa	T4aN1M0	Bite resection, Left MRND, BipaddlePMMC Flap reconstruction	Well differentiated squamous cell carcinoma ,t4a	3x3cm	2.2x2.6cm	2.6cm	2x1.4x1.4cm(AXPXS)	1.6x1x.5cm(AXPXS)	1.4cm(superior)	.9cm	0.5cm	0.4cm(superior)	0.5CM	Adequate		None	left Buccal Mucosa	Negative	1.5x0.8x0.5cm	Negative	2.5x0.5cm	7mm	free of tumor deposits	NIL	NIL	RT-32#	No recurrence	DF		1year 4months
17	55	F	842009	Ulceroproliferative lesion 3.5x2cm left buccal mucosa	SCC	SCC left Buccal Mucosa	T2N0M0	Wide excision,Marginal mandibulectomy,Left SOHND, Masseter flap reconstruction	Moderately differentiated squamous cell carcinoma PT1N0Mx	2x1cm	10x10mm	2mm	2.6x1.2x1.5X1.6cm(AXPXSXM)	2.0x.5x1.0x1cm (AXPXSXM)	1.2cm(Posterior)	0.8cm	0.5cm	0.3cm(posterior)	0.5CM	Adequate		None	left Buccal Mucosa	Negative	1x0.2cm	Negative	1x0.5cm	2mm	free of tumor deposits	NIL	NIL	RT-32#	No recurrence	DF		1year 4months
18	56	F	843576	Ulceroproliferative lesion 3x1cm left buccal mucosa	SCC	SCC left Buccal Mucosa	T4aN0M0	Composite resection,left MRND,PMMC flap reconstruction	Moderately differentiated squamous cell carcinoma pT3N0Mx	3x1cm	23x5mm	6mm	1.5x2x1.5x1.5cm(AxPxSxM)	1.3x1.5x.5x1cm (AxPxSxM)	1.5cm(Superior)	1cm	o.5cm	0.5cm (Superior)	0.5CM	close margin		6 0.2cm from lateral margin	left Buccal Mucosa	Negative	1x1cm	Negative	2x0.5cm	12mm	free of tumor deposits	NIL	NIL	RT-32#,4 cycle of adjuvant chemotherapy	No recurrence	DF		1year 6months
19	60	F	840692	Ulceroproliferative lesion 4x5cm left buccal mucosa	SCC	SCC left Buccal Mucosa	T4aN1M0	Composite resection,left MRND,Bipaddle PMMC Reconstruction	Poorly differentiated squamous cell carcinoma pT3N0Mx	4x3cm	3.7x2cm	2cm	2.2x1.5x1.5x1.5cm	2x1x.5x1cm(AXPXSXM)	1.5cm(Superior)	1cm	0.5cm	0.5cm (Superior)	0.5CM	Adequate		None	left Buccal Mucosa	Negative	2x1cm	Negative	1x0.5cm	6mm	free of tumor deposits	NIL	NIL	RT-30#	Regional spread recurrence	Died due to disease june18th		1 year 3months
20	60	M	834982	Ulceroproliferative lesion 4x5cm right RMT	SCC	SCC Right RMT involving right GBS	T4aN2bM0	Composite resection,Right MRND, PMMC Reconstruction	Moderately differentiated squamous cell carcinoma PT3N2bMx-Stage IVA	4x5cm	3x1.5cm(RMT), 2x1.5cm(BM)	1,.1cm	1.5x1.2x1.5x.8cm	.7x.5x1x.5cm (AxPxSxM)	1.2cm(Posterior)	0.8cm	0.5cm	0.3cm (Posterior)	0.5CM	Adequate		None	Right RMT involving right GBS	Negative	1x0.5cm	Negative	1.5x0.5cm	10mm	3/26positive	NIL	NIL	RT-32#	No recurrence	DF		1 year 5months
21	57	F	844277	Ulceroproliferative lesion 2x1cm left buccal mucosa	SCC	SCC left Buccal Mucosa	T4aN0Mx	Composite resection,Left MRND, PMMC Reconstruction	Well differentiated squamous cell carcinoma pT1N1Mx	1x1x1cm	1x1cm	0.7cm	1.5x2.4x1.8x1.5cm	1x2x1x1cm (AxPxSxM)	1.8cm(superior)	1.5cm	1cm	0.5cm(superior)	0.5CM	Adequate	1.5cm	None	left Buccal Mucosa	Negative	0.5x0.5cm	Negative	0.5x0.5cm	8mm	3/17 positive	NIL	NIL	RT-32#	Regional spread recurrence	died due to disease sept17th		1year 2months
22	56	F	845466	Ulceroproliferative lesion4x3cm left buccal mucosa	SCC	SCC Left Buccal Mucosa	T4aN1Mo	Composite resection,left MRND,Bipaddle PMMC Reconstruction	Well differentiated Squamous cell carcinoma, t4a	4x3cm	3.5x3cm	1.3cm	2x1.2x1.5x1.5cm	1.5x .3x1x1cm (AXPXSXM)	1.2cm(Posterior)	0.8cm	0.3cm	0.5cm(Posterior)	0.5CM	Close margin	1.3cm	7 0.3CM(POSTERIOR)	Left Buccal Mucosa	Negative	0.5x0.5cm	Negative	0.5x0.5cm	8mm	2/17 positive	NIL	NIL	RT-32#	developed loco regional recurrence within 3months	Died due to disease		1 year 2months
23	58	F	846197	Ulceroproliferative lesion6x4cm left buccal mucosa	SCC	SCC Left Buccal Mucosa	T4aN1Mo	Composite resection,left MRND,Forhead flap Reconstruction	Well differentiated Squamous cell carcinoma PT3N1Mx	5x4cm	5x3.5cm	2cm	1.5x1.5x1.5x1.8cm	0.5x0.5x1x1.2cm(AXPXSXI)	1.5cm(posterior)	1cm	o.5cm	0.5cm(Posterior)	0.5CM	Adequate		None	Left Buccal Mucosa	Negative	2x0.5cm	Negative	1x0.5cm	9mm	1/15 positive	NIL	NIL	RT-32#	No recurrence	DF		1 year 5months
24	55	F	845525	Ulceroproliferative lesion 6x4cm left buccal mucosa	SCC	SCC left Buccal Mucosa	T4aN1M0	Composite resection,left MRND,PMMC flap reconstruction	Well differentiated Squamous cell carcinoma pT1NoMx	3x2cm	2.5x1cm	1cm	2.8x1.5x1.5x1.2cm	2.5x.7x1x.4cm (AxPXSXM)	1.2cm(medial)	0.8cm	0.4cm	0.4cm(Medial)	0.5CM	Close margin		8 0.4cm(medial)	left Buccal Mucosa	Negative	1.5x1cm	Negative	.5x.5cm	10mm	free of tumor deposits	NIL	NIL	RT-33#	No recurrence	DF		1 year 5months
25	80	M	849941	Ulceroproliferative lesion4x3cm left buccal mucosa	SCC	SCC left Buccal Mucosa	T2N0MX	Wide excision Hemimandibulectomy,Left SOHND,PMMC flap reconstruction	Well differentiated Squamous cell carcinoma pT1NoMx	3x3cm	2x2cm	1.1cm	1.6x1.2x1.5x1.5cm	1x.8x1x1cm(AxPxSxM)	1.2cm(Posterior)	1cm	0.8cm	0.2cm(Posterior)	0.5CM	adequate		None	left Buccal Mucosa	Negative	1x1.5cm	Negative	1x0.5cm	2mm	free of tumor deposits	NIL	NIL	RT-32#	No recurrence	died due to other cause		1 year
26	36	F	849293	Ulceroproliferative lesion of 3x3cm left buccal mucosa	SCC	SCC left Buccal Mucosa	T4aN2bM0	Composite resection,Left MRND, PMMC Reconstruction	Well differentiated Squamous cell carcinoma left BM pT2N2bMx3x3cm	3x2.5cm	2.3x2.5cm	1.5cm	1.5x1.2x1.2x1.2cm	0.7x0.4x0.7x1cm (AxPxSxM)	1.3cm(posterior)	0.8cm	0.4cm	0.4cm(Posterior)	0.5CM	Close margin		9 0.4cm(Posterior)	left Buccal Mucosa	Negative	0.5x0.5cm	Negative	0.5x0.5cm	15mm	2/15 positive with perineural and lymphovascular invasion present		NIL	RT-32#	developed regional recurrence within 3months	died due to bone mets 6month back		1year
27	60	F	863937	Ulceroproliferative lesion of 3x2cm right buccal mucosa	SCC	SCC Right Buccal Mucosa	T2N0M0	Wide excision, Right SOHND, Supraclavicular flap reconstruction	Verrucous carcinoma, t2n0	3x2cm	2.5x1.7cm	0.5cm	1.8x1.2x1.4x0.8cm	1.2x.3x0.8x.3cm (AXPXSXI)	1.2cm(Posterior)	0.8cm	0.3cm	0.5cm(Posterior)	0.4CM	Close margin		10 0.3cm(Posterior,Inferior),0.4cm lateral	Right Buccal Mucosa	Negative	0.5x0.5cm	Negative	0.8x0.4cm	5mm	free of tumor deposits	NIL	NIL	RT-33#	Disease free	DF		1year 2months
28	50	F	863578	Ulceroinfiltrative lesion of 5x 4cm left buccal mucosa	SCC	SCC left Buccal Mucosa	T4aN1M0	Full thickness wide excision,Partial maxillectomy,MRND,Bipaddle PMMC Reconstruction,Anterior ITF clearance .	Moderately differentiated squamous cell carcinoma T3N0Mx	5x4cm	5x3.5cm	2cm	1.5x1.2x1.2x1.2cm	1x0.3x1x1 (AXPXSXI)	1.2cm(Posterior)	0.7cm	0.3cm	0.4cm(Posterior)	1CM	Close margin		11 0.3CM (POSTERIOR)	left Buccal Mucosa	Negative	1.5x1x0.5cm	Negative	1x1cm	20mm	free of tumor deposits, perineural invasion noted.			RT-33#	Disease free	DF		1year 1month
29	73	F	864846	Verrucous lesion 4X5cm right buccal mucosa	SCC	Verrucous Carcinoma right Buccal Mucosa	T4aN1M0	Full thickness wide excision,hemimandibulectomy,Right MRND,Bipaddle PMMC Reconstruction.	Well differentiated squamous cell carcinoma pT3N0Mx	5x4cm	4.5x 4cm	1.5cm	1.5X1.2X1.2x1cm	1x0.5x0.5x1cm(AXPXSXM)	1cm(Posterior)	0.8cm	0.5cm	o.3cm(posterior)	0.5CM	Adequate		None	right Buccal Mucosa	Negative	0.5x0.5cm	Negative	1x0.5cm	15mm	free of tumor deposits	NIL	NIL	RT-33#	developed locoregional recurrence	DIED due to mof		9months
30	68	F	863293	Ulceroproliferative lesion 7x4 cm right buccal mucosa	SCC	SCC Right Buccal Mucosa	T4aN1M0	Composite resection,Right MRND, Bipaddle PMMC Reconstruction	moderately differentiated squamous cell carcinoma pT3N0Mx	7x4cm	6x3cm	1.5cm	1.5X1.3X1.5X1cm	1x0.5x0.5x0.5cm(AXPXSXM)	1.3cm(posterior)	1CM	0.5CM	0.5cm(Posterior)	0.5CM	Adequate		None	Right Buccal Mucosa	Negative	0.1cm	Negative	0.5cm	15mm	free of tumor deposits, perineural invasion noted.			DENIED RT	No recurrence	DF		1year 1month
31	43	M	870693	Ulceroproliferative lesion 4x3 cm (tongue),3x2cm (left buccal mucosa)	SCC	SCC(synchronous primary) of tongue and left commissure of mouth	T4aN2B (TONGUE),T2 N2BMX(LEFT COMMISSURE)	wide excision,marginal mandibulectomy,extended anterior 2/3rd of hemiglossectomy,Left SOHND, Masseter flap reconstruction of buccalmucosa	well differentiated squamous cell carcinoma,T4a	4x4cm(tongue),3x2 cm (buccal mucosa)	3.3x3.7cm(tongue),2.3x2(buccal mucosa)	1.8cm (tongue),1cm (buccal mucosa)	1.8x0.8x0.8cmx1cm	1.5x0.1x0.3x0.5(AXPXMXL)TONGUE, 2X1XO.5X1CM(AXPXSXI)BM	0.8CM(Posterior)	0.6CM	0.1CM	0.5cm(Posterior)	0.3CM	close margin	0.2cm	12 0.1POSTERIOR,0.3 MEDIAL(TONGUE)	Tongue and left commissure of mouth	Negative	1x0.5cm	Positive	0.3x0.3cm	15mm	2/12positive	NIL	NIL	RT-33#, 4 cycles of adjuvant chemotherapy (CISPLATIN)	No recurrence	DF		1year 1month
32	60	F	869349	Ulceroproliferative lesion 5x3cm left lower GBS	SCC	SCC left lower Gingivo buccal sulcus	T4aN1M0	Composite resection ,left MRND,PMMC Flap reconstruction	well differentiated squamous cell carcinoma, t4a	5x3cm	3.5x2.7cm	2cm	1.8x1x1.4x0.8cm	1.5x.3x1.2x0.3(AXPXSXM)	1cm(Posterior)	0.7cm	0.3cm	0.4cm(Posterior)	0.3CM	Close margin		13 0.3(MEDIAL)	left lower Gingivo buccal sulcus	Negative	2x1cm	Negative	2x0.3cm	8mm	free of tumor deposits	NIL	NIL	DENIED RT	No recurrence	lost to follow up		9months
33	55	F	849789	Ulceroproliferative lesion 5x2cm right lower GBS	SCC	SCC right lower alveolus	T4aN2BM0	Composite resection ,right MRND,PMMC Flap reconstruction	well differentiated squamous cell carcinoma pT4aN0Mx	3x2cm	2.5x1cm	1cm	1.3x1.5x1x1.2cm	1x1.5x0.5x1.2(AXPXMXS)	1cm(medial)	0.7cm	0.5cm	0.2cm(medial)	0.5CM	Adequate		None	right lower alveolus	Negative	1.5x1cm	Negative	2.5x2x0.5cm	7mm	free of tumor deposits	NIL	NIL	RT- 30#	No recurrence	DF		1year 1month
34	53	F	871431	Ulceroproliferative lesion 0f 3x2cm left lower GBS	SCC	SCC left lower gingivo buccal sulcus	T3N0M0	Composite resection,left MRND ,Left Hemimandibulectomy , Bipaddle PMMC flap reconstruction.	Well differentiated squamous cell carcinoma pT4aNoMx	3x1cm	2.5x1cm	2cm	2.5x2.5x2.5cm	2x1.5x1.5cm(AXPXS)	2.5cm(Anterior)	2.3cm	2cm	0.3cm(anterior)	0.5CM	Adequate	bone involved	None	left lower gingivo buccal sulcus	Negative	1x1cm	Negative	2x2cm	10mm	free of tumor deposits	NIL	NIL	DENIED RT	No recurrence	DF		1year1month
35	45	F	875696	Ulcerative lesion of 2x4cm left lower alveolus	SCC	SCC left lower alveolus	T4aN1M0	wide excision ,Hemimandibulectomy ,Left MRND with primary closure/PMMC	Well differentiated squamous cell carcinoma pT4aNoMx	4x2cm	3.5x2cm	1cm	1.5x3x1cmx1.2cm	1.2x3x0.3X1CM(AxPxLxM)	1cm(lateral)	0.7cm	0.3CM	0.4CM(lateral)	0.3CM	Close margin		14 0.3CM(LATERAL)	left lower alveolus	Negative	1x0.5cm	Negative	1x0.3cm	9mm	free of tumor deposits	NIL	NIL	RT-30#	no recurrence	DF		12months
36	58	F	871913	Ulceroproliferative lesion of 5x3cm left buccal mucosa	SCC	SCC left Buccal Mucosa	T4aN2BM0	composite resection, left MRND, Bipaddle PMMC flap Reconstruction	Moderate to poorly differentiated squamous cell carcinoma	6x5cm	5x5.5cm	2cm	1.8x1.4x1.5cm(AXPXS)	1.2x0.5x1cm(AXPXS)	1.4cm(posterior)	0.9cm	0.5cm	0.4cm(Posterior)	0.5CM	Adequate		None	left Buccal Mucosa	Negative	2.5x5cm	Negative	1.5x0.5cm	15mm	3/36 positive	NIL	NIL	RT-30#,5 CYCLES OF ADJUVANT CHEMOTHERAPY	No recurrence	DF		12months
37	45	F	877285	Ulceroproliferative lesion 0f 3x4cm right buccal mucosa	SCC	SCC Right Buccal Mucosa	T3N3AM0	Full thickness wide excision,left MRND,PMMC flap reconstructionfor inner flap and primary closure for outer flap	well differentiated squamous cell carcinoma, t3	3x4cm	2.5x2.5cm, 1x0.5cm	1cm, 0.4cm	2.7x0.8x1cm (AXPXS)LARGE ,	2.5x0.5x1cm (AXPXS)LARGE ,0.8x2.3x2.5cm(AXPXS)SMALL	0.8CM(Posterior)	0.6CM	0.5cm	0.1cm(Posterior)	0.3CM	Adequate	0.4cm(small), 0.5cm(large)	None	Right Buccal Mucosa	Negative	1x1cm	Negative	1x0.3cm	8mm	free of tumor deposits	NIL	NIL	RT-32#	No recurrence	DF		12months
38	40	F	874827	Ulceroproliferative lesion 3x3cm right buccal mucosa involving skin of size 1x1cm	SCC	SCC right Buccal Mucosa	T4aN2BM0	Full thickness wide excision ,Hemimandibulectomy,MRND,Bipaddle PMMC Flap reconstruction	Well differentiated squamous cell carcinoma, t4a	3x2.5cm	2.7x2cm	2.3cm	1.2x1.2x1.3cm(AXPXS)	0.6X0.7x1cm(AxPxS)	1.2CM(Anterior)	1cm	0.6CM	0.4cm(anterior)	0.5CM	Adequate		None	right Buccal Mucosa	Negative	1.5x1cm	Negative	1x0.5cm	25mm	1/18 positive	NIL	NIL	RT-30#	No recurrence	lost to follow up		9months
39	48	M	877280	verrucous growth of 3.5x3 cm over the right dorsum of tongue	Verrucous carcinoma	Verrucous carcinoma of Anterior 2/3rd of tongue	T2N0M0	Adequate glossectomy,SOHND (level I-IV)	Well differentiated squamous cell carcinoma of anterior 2/3rd of tongue- pT3N0Mx -Stage 3	6x5cm	4.3x4.2cm	0.6cm	1X1X0.9X1CM(AXPXMXL)	0.2x0.5x0.3x0.5cm(AXPXMXL)	0.9CM(MEDIAL)	0.6CM	0.3CM	0.3CM(Medial)	0.3CM	close margin		15 0.2cm(ANTERIOR), 0.3(medial)	3.Anterior 2/3rd of tongue	Negative	2x1cm	Negative	1x0.5cm	8mm	free of tumor deposits	NIL	NIL	RT-30#,4 CYCLES OF ADJUVANT CHEMOTHERAPY	No recurrence	DF		12months
40	81	M	880599	Ulceroproliferative lesion of 3x4cm left buccal mucosa	SCC	SCC left Buccal Mucosa	T2N0M0	wide exicision ,SOHND,Buccal pad of fat ,Split skin graft	Well differentiated Squamous cell carcinoma pT2N0Mx	2x2cm	1.4x1.1cm	0.7cm	2x1x1x1cm(AXPXSXI)	2x0.6x0.8x1.2cm(AxPXSXI)	1cm(posterior)	.8cm	0.6cm	0.2cm(Posterior)	0.2CM	Adequate		None	left Buccal Mucosa	Negative	0.5x0.5cm	Negative	1x1cm	7mm	free of tumor deposits	NIL	NIL	RT-30#	no recurrence	DF		12months
41	46	M	880307	Ulcerative lesion of 3x2cm right lateral border of tongue.	SCC	SCC right lateral border of tongue	T4aN0M0	Hemiglossectomy ,Selective neck dissection(I- IV)	Well differentiated Squamous cell carcinoma pT2N0Mx	3x2.2cm	2.5x2cm	1cm	2x1x1.3cm(AXPXM)	1.7x0.6x0.7(AXPXM)	1cm(Posterior)	0.7cm	0.6cm	0.1cm(Posterior)	0.4CM	Adequate		None	right lateral border of tongue	Negative	0.8x0.8cm	Negative	0.8x0.4cm	0.9mm	free of tumor deposits, perineural invasion present.			RT-33#,5 CYCLESOF ADJUVANT CHEMOTHERAPY	No recurrence	DF		12months
42	29	F	882795	Ulceroproliferative lesion of 3x4cm left lateral border of tongue	SCC	SCC left lateral border of tounge	T2N0M0	Hemiglossectomy ,Left MRND	Well differentiated Squamous cell carcinoma pT2N1Mx	3x3.5cm	3x3cm	1.5cm	1.5X1.6x1.5cm (AXPXM)	1x1x1cm(AXPXM)	1.5CM(MEDIAL)	1.3CM	1CM	0.3CM(Medial)	0.2CM	Adequate	0.5CM	None	left lateral border of tounge	Negative	0.5x0.5cm	Negative	0.5x0.2cm	10mm	1/29 positive	NIL	NIL	RT-30#	No recurrence	DF		11months
43	55	F	884820	Ulceroproliferative lesion of 5x4cm left RMT	SCC	SCC left RMT with Leukoplakic patch on right side of tongue	T4aN1M0	Wide excision, Partial glossectomy, Hemimandibulectomy, left MRND,PMMC flap reconstruction,Leukoplakic patch excision on right ,Primary closure ,Tracheostomy	Verrucous carcinoma , t3no	5x4cm	4.5x3.5cm	0.7cm	0.8x1x1(AXPXM)	0.2x0.4x0.5x0.6(AXPXMXS)	1cm(medial)	0.8cm	0.5cm	0.3CM(Medial)	0.5CM	Close margin		16 0.2(ANTERIOR),0.4(POSTERIOR)	left RMT with Leukoplakic patch on right side of tongue	Negative	1x.5cm	Negative	1x0.5cm	7mm	Free of tumor deposits	NIL	NIL	RT-30#	No recurrence	DF		11months
44	49	M	886617	Ulceroproliferative lesion of 8x6cm left buccal mucosa	SCC	SCC left Buccal Mucosa	T4aN3M0	Full thickness excision, Hemimandibulectomy, Left MRND,PMMC and DP flap reconstruction	well differentiated squamous cell carcinoma pT4N2bMx- Stage 1V A	8x5.6cm	7.5x5cm	3cm	2x1.5x2(AXPXM)	1.5x1x1.5(AXPXM)	1.5cm(posterior)	1.3CM	1CM	0.3CM(Posterior)	0.5CM	Adequate		None	left Buccal Mucosa	Negative	1x0.5cm	Negative	1.5x0.5cm	30mm	9/33positive	NIL	NIL	RT-30# ?CT	developed chest wall recurrence and received 2 cycle of palliative CT	died sep23		9months
45	45	F	885365	Ulceroproliferative lesion of 5x3cm left anterior 2/3rd tongue	SCC	SCC left anterior 2/3rd of tongue	T4aNoM0	Subtotal glossectomy, floor of mouth resection,oblique marginal mandibulectomy,left MRND,RIGHT SOHND, Reconstruction with PMMC Flap reconstruction, Tracheostomy	Moderately differentiated Squamous cell carcinoma tongue T3N0Mx	5x3cm	5x2.5cm	1.5cm	1.4X2X1.2(AXPXM)	Positive x1.8x0.5cm(AXPXM)	1.2cm(medial)	.8CM	0.5cm	0.3CM(MEDIAL)	0.5CM	POSITIVE	0.5CM	ANTERIOR Margin - Floor of mouth POSITIVE MARGIN	left anterior 2/3rd of tongue	Negative	1x0.5cm	Negative(medial), positive (FOM)	1x0.5cm	15mm	free of tumor deposits	NIL	NIL	RT- 30#,5 cycles of chemotherapy	No recurrence	DF		11months
46	50	F	880849	Ulceroproliferative lesion 5x4cm left BM	SCC	SCC left buccal mucosa extending upto left RMT		Composite resection ,left MRND,PMMC Flap reconstruction	Well differentiated squamous cell carcinoma pT1N1Mx	5x3cm	4.5x3.5cm	2.6cm	1.5X1.4x1.5X2cm (AXPXSXM)	1x0.5x0.7x1.5(AxPxSXM)	1.4cm(posterior)	.8CM	0.5CM	0.3cm(Posterior)	0.5CM	Adequate	0.5CM	None	left buccal mucosa extending upto left RMT	Negative	1x1cm	Negative	0.5x0.5cm	20mm	1/35 positive	NIL	NIL	RT-25#, 2 cycles of chemotherapy	developed locoregional recurrence	died 2 months back		9months
47	45	F	888703	Ulceroproliferative lesion 2x2cm right buccal mucosa	SCC	SCC Right Buccal Mucosa	T2N2BM0	Wide excision, Right SOHND, PMMC flap reconstruction	Moderately differentiated squamous cell carcinoma pT2N1	4x2cm	3.5x2cm	0.5cm	1.8x2x2cm(PxSxI)	0.8X1x1cm(PXSXI)	1.8cm(posterior)	1CM	0.8CM	O.2CM(Posterior)	1CM	Adequate		None	Right Buccal Mucosa	Negative	1x1cm	Negative	1x1cm	5mm	1/22positive	NIL	NIL	RT-30#	No recurrence	DF		10 months
48	43	F	888263	Ulceroproliferative lesion of 1x1cm right buccal mucosa	SCC	SCC Right BM	T2N0Mo	wide excision +Sohnd+Buccal pad of fat	No tumor cell found	1x1cm	.5x.2cm	0.1cm	2.4X2X2X2.2CM(AXPXSXI)	1.8x1x1.2x1.2(AXPXSXI)	2cm(posterior)	1.5CM	1CM	0.5cm(Posterior)	1.5CM	Adequate		None	Right BM	Negative	0.5x0.5cm	Negative	1.5X1.5cm	3mm	free of tumor deposits	NIL	NIL	No RT/cT	No recurrence	DF		10 months
49	58	F	892145	Ulceroproliferative lesion of 2x2cm Right BM	SCC	SCC Right BM	T2N0M0	Composite resection+ Right MRND+PMMC Reconstruction	Well differentiated Squamous cell carcinoma - T1N0Mx	2x2cm	1.5x1.5cm	1cm	1.5x2x1.5cm(AxPxM)	1x1.7x1.3(AxPxM)	1.5CM(Anterior)	1.2CM	1CM	0.2CM(Anterior)	0.5CM	Adequate		None	Right BM	Negative	1x0.5cm	Negative	1x0.5cm	10mm	free of tumor deposits	NIL	NIL	denied RT	No recurrence	DF		9 months
50	45	F	890479	Ulceroproliferative lesion of 3x3cm right lower gbs	SCC	SCC right lower Gingivo buccal sulcus(verrucous type)	T3N1M0	Composite resection ,Right MRND,PMMC Flap reconstruction	Moderately differentiated squamous cell carcinoma pT2N0Mx	3.5x2cm	3.3x1.3cm	0.5cm	1x2x1.2cm(AXPXM)	0.6x1.9x1cm(AxPxM)	1cm(anterior)	0.8cm	0.6cm	0.2CM(Anterior)	o.4cm	Adequate		None	right lower Gingivo buccal sulcus	Negative	1.5x1.5cm	Negative	1x0.4cm	5mm	free of tumor deposits	NIL	NIL	27/27#	No recrrrence	DF		9 months
51	55	F	892199	Ulceroproliferative lesion 4x3cm Right buccal mucosa	Verrucous carcinoma right buccal mucosa pT2N0Mx	SCC right Buccal Mucosa	T4aN0M0	Right wide excision ,Extended mandibulectomy , right MRND, Reconstruction,forehead flap,PMMC flap reconstruction, Tracheostomy	Verrucous carcinoma right buccal mucosa-pT2N0Mx	4x3cm	4x3cm	0.5cm	1x2x0.8cm(AXPXM)	0.4x1.8x0.3cm(AXPXM)	.8CM(Medial)	0.6CM	0.3CM	0.3CM(Medial)	0.5CM	Close margin		17 O.4(ANTERIOR), 0.3(MEDIAL)	right Buccal Mucosa	Negative	4x0.5cm	Negative	0.5x0.5cm	5mm	free of tumor deposits	NIL	NIL	DENIED RT	No recurrence	DF		9 months
52	45	F	891721	Ulceroproliferative lesion of 4x3cm right BM	SCC	SCC right lower GBs	T4aN1M0	Right composite resection , right MRND,PMMC flap reconstruction	Well differentiated squamous cell carcinoma-pT2N0Mx	3x2cm	3x1cm	1cm	1.4x1.8x1.4X1.5(AXPXMXS)	0.9x1.5x1.5x1cm(AxPxMxS)	1.4cm(Anterior)	1cm	0.9cm	0.1cm(Anterior)	0.5CM	Adequate		None	right lower GBs	Negative	0.5x0.5cm	Negative	1x0.5cm	5mm	free of tumor deposits	NIL	NIL	30/30#	no recurrence	DF		9 months
53	60	F	895201	Ulceroproliferative lesion of 3x2cm left buccal mucosa	SCC	SCC left BM	T4aN1M0	Composite resection+ Left MRND+PMMC Reconstruction	Well differentiated squamous cell carcinoma, t3	3x2cm	2.5x1cm	0.8cm	2X1.2X1.8X2.5(AXPXMXS)	2x0.5x1x 2.5cm(AxPXMXS)	1.2CM	0.8CM	0.5CM	0.3cm(Posterior)	0.5CM	Adequate		None	left BM	Negative	0.5x0.5cm	Negative	1x0.5cm	6mm	Free of tumor deposits	NIL	NIL	32/32#	no recurrence	DF		8months
54	67	M	892608	Ulceroproliferative lesion of 3x3cm left lateral border of tongue	SCC	SCC left lateral border of tongue	Ct3n0m0	left Hemiglossectomy + Left MRND	Well differentiated squamous cell carcinoma of left lateral border of tongue- pT2N0Mx -Stage 2	3x2.5cm	3x2.5cm	2cm	1.5x2.3x2x1.5cm(AxPxMxL)	1.2x2x0.7x1cm(AxPxMxL)	2cm(MEDIAL)	1.2cm	O.7cm	0.5CM(MEDIAL)	0.5CM	Adequate	0.4cm	None	left lateral border of tongue	Negative	1x0.5cm	Negative	0.5x0.5cm	7mm	free of tumor deposits	NIL	NIL	32/32#	No recurrence	DF		8months
55	74	F	898266	Ulceroproliferative lesion on left buccal mucosa of 6x3cm	SCC	SCC left lower gingivobuccal sulcus	T4aN1M0	Bite resection + Left MRND +ITF compartment clearance +Double Flap (PMMC+DP FLAP)	Well differentiated squamous cell carcinoma-pT3N0Mx- Stage III	4x3cm	3.5x3cm	2cm	3.5X1.4X2CM(AXPXS)	4x0.5x1.7(AxPxS)	1.4cm(posterior)	1CM	0.5cm	0.5cm(Posterior)	0.8CM	Adequate		None	left lower gingivobuccal sulcus	Negative	1x0.8cm	Negative	1.2x0.8cm	15mm	free of tumor deposits	NIL	NIL	30/30#	No recurrence	DF		8months

SERIAL NO	AGE	GENDER	UHID NO	ORAL CAVITY EXAMINATION	BIOPSY	CLINICAL DIAGNOSIS	CLINICAL STAGING	SURGERY	HISTOPATHOLOGY	TUMOR SIZE BFF	TUMOR SIZE AFF	THIRD DIMENSION AFTER FORMALIN FIXATION	MARGIN OF TUMOR RESECTION BF FF	TUMOR RESECTION MARGIN AF FF	DISTANCE OF NEAREST MARGIN TO TUMOR BEFORE RESECTION BFF	DISTANCE OF NEAREST MARGIN TO TUMOR AFTER RESECTION OF MARGIN BFF	DISTANCE OF NEAREST MARGIN AFTER RESECTION OF MARGIN AFF	Distance of shrink age of closest margin BF and AF FF	MEASUREMENT OF MARGIN FROM THE SPECIMEN SITE	MARGINS OF RESECTION	DISTANCE from deep margin of resection to base of the tumor	CLOSE MARGIN	SUBSITES	CUT MARGIN FROM PATIENT SITE	SIZE OF PATIENT SITE CUT MARGIN	CUT MARGIN FROM SPECIMEN SITE	SIZE OF SPECIMEN SITE CUT MARGIN	DH	NODAL STATUS	EXTRA NODAL	EXTRA CAPSULAR INVASION	ADJUVANT T	TIME FOR RECURRENCE	FOLLOW UP STATUS		Duration
56	58	M	900205	Ulceroproliferative growth of 4x3cm right buccal mucosa	SCC	SCC right buccal mucosa	T2N0M0	Right wide excision ,SOHND,Supraclavicular flap reconstruction.	well differentiated squamous cell carcinoma-pT2N0Mx -StageIIc	3x2cm	2.2x2cm	1.2cm	2X1.5X1.8X1.2CM(AXPXSXM)	1.5x1x1.5x0.5cm(AXPXSxI)	1.2CM	0.8cm	0.5CM	0.3CM(INFERIOR/MEDIAL)	0.5CM	Adequate	0.2cm	None	right buccal mucosa	Negative	1x1cm	Negative	1x0.5cm	8mm	free of tumor deposits	NIL	NIL	32/32#	No recurrence	DF		8months
57	45	M	901647	Ulceroproliferative lesion of 2x2cm Right BM	SCC	SCC right BM	T4aN1M0	Composite resection+Right MRND+Bipaddle ppmc flap reconstruction	Well differentiated squamous cell carcinoma-pT3N0MX- Stage III	2x2cm	2x1.8cm	2cm	2.2X1.5x2.2X1cm(AXPXMXS)	1.7x1x2x0.2cm(AXPXMXS)	1CM	0.7CM	0.2CM	0.5cm(Superior)	0.5CM	Close margin		18 0.2cm(SUPERIOR)	right BM	Negative	1x1.5cm	Negative	0.5x0.5cm	20mm	free of tumor deposits	NIL	NIL	32/32#	no recurrence	DF		7months
58	58	F	889849	Ulceroproliferative lesion of 4x3cm right lateral border of tongue	SCC	SCC right lateral border of tongue	T3N0Mx	Subtotal glossectomy, floor of mouth resection,oblique marginal mandibulectomy,rightMRND,left SOHND, Reconstruction with PMMC Flap reconstruction, Tracheostomy	Well differentiated squamous cell carcinoma-pT3N0MX- Stage III	4x3cm	3.5x2.3cm	1.8cm	2X2X1.8CM(AXPXM)	2x2x1.2cm (AxPxM)	1.8CM	1.3CM	1.2CM	0.1CM(MEDIAL)	0.5CM	Adequate		None	right lateral border of tongue	Negative	1x0.5cm	Negative	1x0.5cm	12mm	free of tumor deposits	NIL	NIL	30/30#	No recurrence	DF		7months
59	48	F	903390	Ulceroproliferative lesion of 5x4cm left BM	SCC	SCC left BM	T4aN0M0	Composite resection,left MRND,Bipaddle PMMC Reconstruction	Well differentiated squamous cell carcinoma-pT3N0MX- Stage III	5x4cm	4x4.5cm	3cm	2X2X2CM(AXPXM)	1x1x2x1cm(AxPxMxS)	1.6CM	1.2CM	1CM	0.2cm(Posterior)	0.5CM	Adequate		None	left BM	Negative	1.5x.5cm	Negative	1x0.5cm	15mm	free of tumor deposits	NIL	NIL	32/32#	no recurrence	DF		7months
60	60	F	910536	Ulceroproliferative lesion of 4x3cm right BM	SCC	SCC left BM	T4aN0M0	Composite resection,Right MRND,Bipaddle PMMC Reconstruction	Well differentiated squamous cell carcinoma - PT4aN0MX- Stage IVA	3.5x3cm	3.2x3cm	2cm	1.5X1.2X1.5cm(AXPXS)	1.1x0.7x1.2(AXPXS)	1.2CM	.9CM	0.7CM	0.2cm(Posterior)	0.5CM	Adequate		None	left BM	Negative	1.5X5cm	Negative	1x0.5cm	18mm	free of tumor deposits	NIL	NIL	32/32#	no recurrence	DF		6months