

# “Comparison of resection performed by Peroral and Transoral route on surgical margins in patients with oral squamous cell carcinoma.”

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**Abstract:** *Background: Lip-split incision has been traditionally used to manage the primary oral cavity tumour to ascertain clear surgical margins. Small tumour excision is routinely carried out per orally; however, there is a paucity of data vis-à-vis with the oncological safety of per oral approach in T2/T3 excision of oral squamous cell carcinoma (OSCC). Objective of the study: We compared per oral access over the transoral access in terms of assessing the tumour free surgical margins. Settings & Design: A prospective, interventional, double-blind, randomized control study was conducted among 20 histopathologically proven participants with previously untreated OSCC scheduled for curative intent. Subjects & Method: Participants were randomly allocated to the two intervention used. The primary outcome variables evaluated were the adequacy of the surgical margin. Additionally, the primary tumour resection time between two interventions was assessed. Results: The primary tumour resection time will be significantly extended in Peroral access & no significant difference will be seen pertaining to the adequacy of a safe surgical margin between two intervention. Peroral access will be a choice of surgical approaches that preserve function, minimize complications and maximize cosmetic outcome. Conclusion: Surgical approaches that minimize complications, preserve function with the optimal cosmetic outcome should be utilized whenever feasible. Peroral access may offer significant advantages like avoiding transoral trauma, fastens the healing time & affords better & faster recovery.*

**Keywords:** *Peroral access, Transoral access, Clear margins, Oral squamous cell carcinoma (OSCC), Lip-split incision, Surgical margins.*

## **Introduction:**

Globally, cancer is increasingly being recognized as one of the supreme common reason of bereavement. Oral cancer is a debilitating disease affecting populations of all age groups

residing worldwide. 8<sup>th</sup> utmost common cancer of the world. As per WHO projections, by the end of 2020 the death toll due to cancer may reach up to 10 million cases per year worldwide.

The mainstay of treatment of OSCC involves extensive removal of the primary tumour with safe surgical margins or without post-operative Radiotherapy or Chemotherapy. The oral cavity sometimes make it challenging to equilibrium the need for acceptable margins to preserve function and minimize disfigurement. A surgically positive margin is a predictable deleterious extrapolative factor,<sup>1</sup> it deterrence is frequently an indication for employing “access” procedures. It is imperious to have virtuous access to the tumor to permit for satisfactory three-dimensional excision & allow the lesion with satisfactory margins and reconstruction of the consequential deficiency. The surgical approach are directed to expunge an oral cavity tumor dictated by its mass and location, in count to the surgeon’s inclinations and experience with the surgical procedure.

For advanced OSCC, technique and function are forwent in exchange for enhanced survival. The conventional access method for oral cavity growths has been the lip-split approach with or deprived of a mandibulotomy. Protagonists of the lip-split approach quote superior access and three-dimensional assessment of soft tissue association than with supplementary methods in which the lip is not split.<sup>2</sup> These gains are exclusively true in progressive anterior oral cancers including the mandible. Conventionally, it is believed that surgeon has much better-quality control above the anterior margins in this condition, which translates into wide-ranging tumor margins and enhanced local control.<sup>3</sup> There still look to be a propensity to employ transoral access techniques for medium-sized tumors, despite adequate mouth opening existed for access to the oral cavity tumors.

Splitting the lip via a lateral or mid-line lip-split incision in aggregation with a mandibulotomy to permits the proximal mandible to swing away to increase complete access to the oropharynx & oral cavity tumor. However, up to 35% of morbidity has been reported,<sup>4</sup> with critics that there is a greater rate of the functional discrepancy, postoperative morbidity, and unappealing scarring, even in the finest of hands.<sup>5</sup>

Minimal access techniques are presently being gradually used in the administration of malignant lesions affecting the neck and head, to diminish morbidity without conceding the oncological safety. Peroral access is the technique of choice for managing medium-sized growths restricted to the oral cavity.<sup>6</sup>

Therefore, surgical approaches that minimize complications, preserve function and maximize cosmetic outcome should be fortified in suitable patients whenever feasible. Peroral approach may offer significant advantages because it helps avoid transoral access trauma, it reduces the healing time, and it allows for better and faster recovery. Therefore, we hypothesize that the peroral route would provide a better oncological, functional & aesthetic outcome between the two techniques when used in progressive resections of oral cavity cancer.

### ***Methodology:***

The present prospective, observational, pilot study will be conducted in the department of Oral & Maxillofacial Surgery, Sharad Pawar Dental College and Hospital in coordination with Department of Oral Pathology and Microbiology, Sharad Pawar Dental College & Acharya Vinoba Bhave Rural Hospital, Sawangi (Meghe), Wardha during Oct 2019 to April 2020. The study will be conducted in accordance with the Helsinki declaration and its later amendments or comparable ethical standards and after approval by the institutional ethical guidelines prescribed by Central Ethics Committee on Human Research (C.E.C.H.R) of Datta Meghe Institute of Medical Sciences (**Ref. No. - DMIMS(DU)/IEC/Dec-2019/8609**).

This study will be conducted on 20 histopathologically proven patients of previously untreated oral squamous cell carcinoma scheduled for surgery with curative intent.

**Sample size determination:**

The sample size was calculated by means of the result of previous studies (**Azhar J. Battoo et al**<sup>6</sup>). The following formula was used to calculate the sample size required for this study at 80% power of study and 95% confidence interval.

Sample size formula for difference between two proportions:

$$n = \frac{(Z\alpha + Z\beta)^2 [P_1(1-P_1) + P_2(1-P_2)]}{(P_1 - P_2)^2}$$

Where,

$Z\alpha$  = level of significance at 5% i.e. 95%

Confidence interval = 1.96

$Z\beta$  = Power of the test = 80% = 0.84

$P_1$  = Proportion of tongue site of tumours = 72% = 0.72

$P_2$  = Proportion of buccal mucosa = 13% = 0.13

$$n = \frac{(1.96 + 0.84)^2 [0.72 \times (1 - 0.72) + (0.13 (1 - 0.13))]}{(0.72 - 0.13)^2}$$

$$= 7.08$$

= 10 Patients needed in each groups.

Therefore, calculated sample size for this study will be 10 patients per group.

**Patients fulfilling the criteria given below will be recruited for the study.**

**Criterion for inclusion:**

1. Patients with Untreated resectable primary oral squamous cell carcinoma
2. Patients with Lesions involving GB complex and buccal mucosa extending up to the retromolar region.
3. Patients with Lesions involving posterolateral surface and base of tongue.

**Criterion for exclusion:**

1. Immuno-compromised patients
2. Patients with OSCC extending beyond the confines of oral cavity (Infra temporal fossa, oropharynx and neck).
3. Patients with OSCC involving the lip and corner of mouth.
4. Patient with a history of previous treatment with surgery/radiotherapy or both.
5. Patients with recurrent and residual diseases.

**Consent:**

- Before starting the study, an informed consent will be acquired from all the patient included in the study.

**Clinical examination:**

- A detailed case history will be recorded.
- Clinical examination of primary tumor will be done and data compiled based on clinical findings. Tumor size will be recorded and each case included in the study will give us a complete TNM Classification and staging, according to the guidelines of AJCC 7<sup>th</sup> edition and Union International Cancer Control (UICC)<sup>7</sup>

**Pre-operative investigations:**

The patients will be subjected to CECT Head in Department of Radio-Diagnosis, AVBRH, Sawangi (Meghe). CECT 16 slices/cut with Axial, Coronal and Sagittal cuts.

Complete Blood investigations will be done. Physician and anesthetist fitness will be obtained for surgery.

**Surgical Protocol:**

- A single senior surgeon having considerable experience in head and neck surgery will operate all the cases.
- After obtaining a pre-anesthetic fitness, patient will be undergo surgical procedure which comprised of :
  - I) Wide Local Excision of Lesion
  - II) Suitable Neck Dissection
  - III) Reconstruction

Patients will be treated according to their staging by the following protocols.

**Type of neck dissection:**

- Patients with clinically negative neck (N0) will be subjected to a Selective Neck Dissection (SND-I-III), as per scientific indications.
- Patients with clinically diagnosed positive lymph node (N+) will be subjected to either Radical Neck Dissection or Modified Radical Neck dissection.

The study design protocol demanded the assessment of the resected mucosal margins of 1-1.5cms approximately in all cases intraoperatively after the resection of the tumor by either Peroral or Transoral route irrespective of size & site of tumor.

**Tumor resection time:**

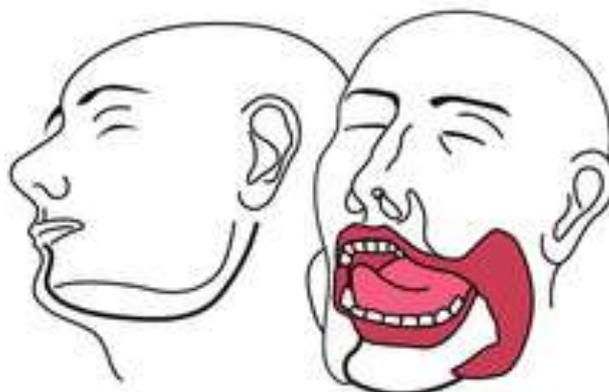
Starting of the incision until the point of delivery of the resected specimen.

**Surgical technique:**

**Transoral Route (Lip-Split Technique):**

*Babin and Calcaterra*<sup>2</sup> repopularized the lip-split technique in the late 1970. The neck dissection incision will be on superior extension of incision. Scoring of vermilion border and sagittal division of lip will be done. The vermilion border will be scored and the lip will be divided sagittally. Incision approaches used will be any one of a number of Robson, Roux or Mcgregor .This jagged incision will be carried down circumferentially around mentum or through the mentum, conserving the anatomical subunit. In the midline, neck dissection and the incision, which was carried down below the mantle, will be merged. Raising of bilateral or unilateral cheek flaps will leave the periosteum undamaged. At this point, if general oral cavity entree is required mandibulectomy will be done otherwise the involved mandible and floor of mouth will be resected. Lip components will be reapproximated by doing layer-by-layer closure; for this it is required that, a trifurcation stitch reapproximates the oral vestibule.

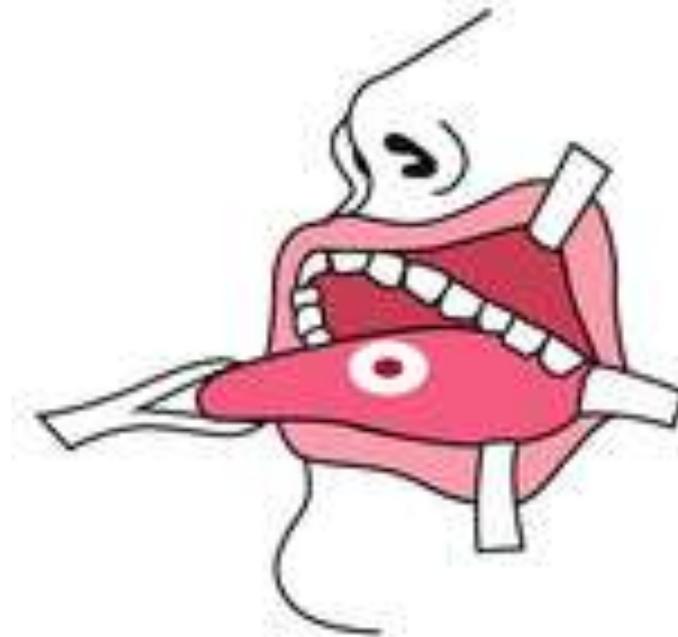
**Figure 1 -Lip-Split Technique.**



***Peroral route technique:***

The subsequent steps are involved in Typical Peroral route procedure are :(1) To simplify the resection, clear surgical field will be obtained by opening the neck and ligating the facial artery or ipsilateral lingual artery. Ligation will depend on site of lesion. End of neck dissection will follow this. (2) Placing cheek retractor and inserting bite block in between the opposite molars will ensure that the mouth opening is used optimally. Before cutting out the lesion, a marking of 1-1.5 cm will be done surrounding the lesion. Resection will be done further keeping in mind the 3-dimensional extent of the lesion. (3) Typical excision includes delivery of per oral resected specimen. If the muscles of floor of mouth are infiltrated by lesion, excision of floor of mouth will be done per orally, and the neck dissection will deliver the specimen. Partial maxillectomy and marginal mandibulectomy will be included in resection if required. (4) Evaluation of resection specimen will be done to make sure surgical resection margins are adequate and for assessment of necessity of further resection.

**Figure 2- Peroral Route Technique.**



***Surgical margin assessment:***

- The lesion will be excised taking 1 – 1.5 cm clinically visible safe surgical margins which will be according to surgeon's perception.
- After excision of the lesion, 4 margins will be excised from edge of the resected specimen.
  - 1) Anterior margin
  - 2) Posterior margin
  - 3) Medial margin
  - 4) Lateral margin
  - 5) Depth
- Excised specimens will be carefully assessed; grossed, labelled and fresh specimen will be delivered to the pathologist intraoperative so that he process it immediately. The pathologists will be blinded for intraoperative evaluation of the resected surgical margins.

- Excised surgical margins submitted for intraoperative evaluation will be examined by intraoperative frozen section biopsy to assess resected surgical mucosal margins.

**Diagnostic criteria:**

A Surgical margin will be:

- Positive-** Normal tissue architecture shows proof of metastatic deposits of dysplastic cells or malignant squamous epithelial cells.
- Negative-** Normal tissue does not show any evidence of the metastatic deposits of malignant squamous epithelial cells.
- Evidence of hyperkeratosis, mild and moderate dysplasia.

**Cytological criteria of malignancy:**

- Primary criteria to observe in frozen section will be
  - (1) Tumor diathesis.
  - (2) Nuclear cytoplasmic ratio.
- If both features mentioned above are observed, the pathologist should check the following criteria mentioned below.<sup>8</sup>

**Table 1: Cytological criteria of malignancy**

<i>Category 1</i>	<i>Category 2</i>
Variation in cell shape	Naked nuclei
Variation in cell size	Irregular chromatin clumping
Nuclear pleomorphism	Binucleation/multinucleation
Increased number and size of nucleoli	Abnormal mitotic figures

**Reporting of the results to surgical team:**

The results of frozen section will be immediately informed to the surgical team, so that they will be able to make decisions intraoperative. Whenever it is possible, re-excision will be done for all the patients with positive margins. All the excised specimens were returned to the surgical team in their proper-labeled bottles.

**Post operative evaluation:**

- Postoperative Outcomes will be recorded and compared between peroral and transoral route will be Facial scar, Lip competency, Facial disfigurement and Injury to corner of mouth.
- The patients will be evaluated for four parameters: Facial scar, Lip competency, Facial disfigurement & Injury to corner of mouth.

**Evaluation criteria:**

- Facial scar-** Mild/Moderate/Severe.<sup>9</sup>

**Table 2: Facial scar.**

Clinical assessment	Score
No facial scar	0
Mild	1
Moderate	2
Severe.	3

- **Lip competency-** (lower score indicates better function, Range 1–3)<sup>5</sup>

**Table 3: Lip competency.**

Clinical assessment	Score
At rest	1
On effort	2
Incompetent	3

- **Facial disfigurement-** Mild/Moderate/Severe.<sup>10</sup>

Table 4: Facial disfigurement.

Clinical assessment	Score
No facial disfigurement	0
Mild	1
Moderate	2
Severe.	3

Patients themselves on above criteria will assess facial scar, Disfigurement. At the same time, the examiner evaluated the patient for the same criteria.

- **Injury to corner of mouth-** Yes/No

After all Intraoperative and postoperative evaluation as mentioned above the data will be transcribed into an Excel worksheet (Microsoft Corp, Redmond, Wash) for study.

***Expected Outcome:***

Surgical approaches that conserve function, diminish complications and maximize cosmetic result should be encouraged in suitable patients when possible. If superiority of Peroral route over Trans oral route is established, it will provide a new insight in choosing the best approach with minimal complications for extirpation of primary OSCC.

***Discussion:***

The OSCC is one of the promptly mounting oral cancers in the prose of oncology. More than 90% of oral cancers are preventable and almost all oral cancers are curable with minimal morbidity and mortality if detected early. Unfortunately, in India majority of the patients present in an advanced stage where treatment, if at all offered is associated with major morbidity. Hence, primary or secondary prevention of oral cancer is of utmost importance. Many studies on oral squamous cell carcinoma have been reported from this region<sup>11,12,13</sup>. Lohe et al reported on evaluation of correlation of serum lipid profile in patients with oral cancer and precancer<sup>14</sup>. Studies on different biochemical factors associated with oral cancer were reported by Mallick et al<sup>15</sup>, Chole et al<sup>16</sup> and Korde et al<sup>17</sup>. Agrawal et al reported about Touch Imprint Cytology as an alternative to frozen section in intraoperative assessment of cervical metastasis in oral squamous cell carcinoma<sup>18</sup>. Mokbel Khalefa et al reported on Ten years incidence of intracranial complications of chronic suppurative otitis media<sup>19</sup>. The development of Peroral techniques for minimal-invasive surgery in narrow spaces has challenged this concept of 5-mm free margins due to anatomical limitations, without decrease in disease control reported. Peroral surgery may offer significant advantages because it helps avoid Transoral access trauma, it reduces the healing time, and it allows for better and faster functional recovery. While all of these advantages are certainly of benefit to the patient,

Peroral approaches can result in intraoperative situations whereby visibility of critical structures and tissue handling is hampered as a consequence of the confined workspace and thus can impact on the adequacy of the surgical resection. It is, therefore, of critical importance to analyze the surgical margin status after this type of intervention.

Though access techniques have a certain protagonist to play in managing of oral cavity tumors, they are related with morbidities in term of utility, healing and cosmetic. Therefore, we presume that both methods meet the exceptional access to the oral cavity for the extirpation of cancer. Although one would deliberate that, the prevention of a facial scar would be a convincing reason for performing out a Peroral route in aggregation with a Transoral route technique.

### **Conclusion:**

The choice of approach have to be used prudently depending upon the site and size of the lesion, presence or absence of trismus and surgeons experience. The choice of approach should not compromise the oncological outcomes; however, a surgical approach that ascertains tumour free surgical margins with minimal complications should be used. With the inclination more towards the minimal access procedures, the Peroral route may be the choice of access if the inherent drawbacks of Transoral route are overcome by it.

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