

Imaging In Oral Cancers – A Practical Approach

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Abstract: Imaging techniques have become an important element in the field of oral oncology. Continued research has led to technical progress in the existing modalities and addition of newer, exiting and highly accurate techniques. Although this is a boon, it has created differences of opinion regarding the ideal choice of imaging techniques. Inappropriate choice of imaging modality can result in delay in diagnosis and treatment thereby inducing more suffering for the patients. This problem is more so with imaging of oral cancers and responsible decisions of oral clinicians and radiologists is of paramount importance. In developing nations, problem is compounded by various other factors like affordability, availability and awareness. Thus, an imaging protocol needs to be devised that helps a clinician choose the best imaging modality for a particular clinical situation. This review illustrates the imaging protocol in the form of a decision tree, describes the various imaging techniques, their utility in evaluation of oral cancers and practical problems associated with these techniques. [R Jigna NJIRM 2016; 7(1):112-119]

Key Words: Oral Oncology, Imaging modality, Ideal choice, Developing countries, Decision tree.

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Introduction: Oral cavity malignancies have been a significant cause of mortality and morbidity among the human population particularly in developing countries. India has one of the highest incidence of Oral cancer in the world and burden approximates 20-30% of all cancers.^{1,2} Oral cancer ranks number one among men and number three among women in India.³ Treatment related morbidity is particularly high which include problems in speech, swallowing, chewing and cosmetic deformities. After the treatment of a oral cavity cancer the patient can experience a tumor recurrence, rate varying from 18 to 76%^{4,5} and the prognosis continue to be poor with only 50% five year survival rate.

Despite continued research and advances in the field of oral oncology, the survival rates have not improved significantly in decades. This is because of the two main reasons. Firstly, the oral cancer lesions are detected only at an advanced stage when they have invaded the deeper structures and metastasized to another location, most likely the lymph nodes of the neck.⁶ Secondly, there could be an inappropriate assessment of the lesion in terms of depth and extent, bone invasion, status of lymph node involvement and distant metastasis, thereby leading to inappropriate treatment planning and therapy failure.^{7,8} Hence it is important not only to detect the tumors at the earliest but also make an adequate assessment which is critical for appropriate planning of surgical, radiation and chemotherapy treatment.

The three most important tools for detection and appropriate assessment of oral malignancies are the clinical evaluation, assessment with imaging modalities

and histopathological analysis. The clinical evaluation and digital examination needs mastery of skills, and is inferior from the point of view of consistent accuracy and objectivity, more so in inaccessible intra oral sites. Accurate lymph node assessment and appropriate staging are also difficult with clinical examination alone.^{9,10,11} Histopathological examination by biopsy is a useful method to confirm diagnosis and to estimate the malignant potential of tumor. However for accurate grading of malignancy, sampling of tumor tissue from advancing front of cancer would be necessary; this requires access to the site of the tumor, skill of the surgeon, adequate sampling of the tumor tissue and expertise of the pathologist.^{12,13} Hence Assessment with imaging remains the most practical approach for evaluation and adequate assessment of oral malignancies. Advances in the field of imaging have proved to be a boon in this regard. The important applications of imaging in oral cancers include:

Screening for oral cancer: Imaging can be used to determine if a person has any suspicious areas or abnormalities that might be cancerous. Screening for cancer is usually recommended for people who are at increased risk (due to their family history, lifestyle, or age).

Diagnosis/staging: Imaging can give important information regarding location, extent, depth, proximity to anatomical structures and lymph node assessment. Used in this way, imaging can help determine what stage of the cancer and determining the treatment modality.

Guiding cancer treatments: Imaging can be used to make cancer treatments less invasive by narrowly focusing treatments on the tumors thereby minimizing the damage to the adjacent normal tissues. Imaging can also assess if the tumor has been eliminated without any residual tumor tissue remaining.

Determining of a treatment response: Imaging can be used to assess if a tumor is shrinking or if the tumor has changed and is using less of the body's resources than before treatment.

Monitoring for cancer recurrence: Advanced imaging modalities have been useful in accurately differentiate between post chemo-radiation sequelae and tumor recurrences.

Number of imaging modalities are available which are used to evaluate the oral cavity cancers including

Conventional radiography (Panoramic radiography, Intraoral radiography)

Nuclear medicine Scintigraphy

Ultrasonography (US)

Computed Tomography (CT)

Magnetic Resonance Imaging (MRI)

Positron Emission Tomography (PET)

Single Positron Emission Computed Tomography (SPECT)

Positron Emission Tomography/ Computed Tomography (PET/CT)

Screening with conventional Radiography:

Conventional imaging techniques with x-rays are perhaps the most familiar type of imaging. Orthopantomography (OPG) provides a good overall view of the jaws and the dentition.¹⁴ A combination of OPG and intraoral radiography play an important role in the detection of bone invasion especially in determining the supero-inferior extent in carcinoma of the mandibular gingiva. This assessment of the supero-inferior extent is one of the most important factors influencing surgeons in choosing between a rim or segmental resection of the mandible. A study comparing OPG combined with intraoral radiography and CT in detecting the supero-inferior extent of tumor invasion of mandible, concluded that there was no difference in the diagnostic accuracy between the two techniques.¹⁵ Brown et al compared the various imaging modalities like OPG, Scintigraphy, CT and MRI in the management of oral squamous cell carcinomas. OPG showed highest specificity (93%) when compared with other modalities (CT-88%, MRI-86%). However, the sensitivity of OPG was

lower than CT, MRI. Hence, it was suggested that decision to resect the mandible as a part of the management of oral cancer should be taken on the evidence of clinical examination, periosteal stripping and at least two imaging techniques that compliment each other in terms of specificity and sensitivity. A combination of OPG and Scintigraphy has high specificity and sensitivity thereby giving accurate results.¹⁶ These simple techniques also have added advantages like economical, easy availability, familiarity to the clinician, easy and most practical approach in the screening of oral cancers.

However, conventional radiographs cannot show small erosion of the inner cortex and give no information on the medullary bone; It cannot detect the bone changes unless there is 30-50 percent of bone loss.^{17,18} Although an experienced radiologist can get a sense for the approximate three-dimensional location of a tumor from a radiograph, in general, a plain radiograph is two-dimensional and hence important information such as the depth of the carcinoma cannot be assessed. There are also technical limitations for the use of OPGs particularly when there are large or ulcerative tumors.¹⁹

Bone Scintigraphy: Bone imaging with radionuclides is a non-invasive technique for demonstrating the osteoblastic lesion of the skeletal system. It is based on the uptake of a radiotracer that occurs where bone is being formed or repaired. It can be particularly helpful in tumors of head and neck which invade the adjacent bones. A bone loss upto 5 percent can also be detected with accuracy with a bone scan. Such bone invasion occurs more often in tumors of the buccal mucosa and gingiva.²⁰ It is also of particular importance in distant metastasis in the bones. It is economical and has high sensitivity. However, this technique suffers from a lack of specificity. The metabolic changes may occur in several benign dental conditions like healing extraction wounds, dental abscesses, periodontal abscesses, pericoronitis and osteomyelitis and hence produce positive bone scintigrams.²¹

CT Scans: In the neoplasm of head and neck, CT is better able to determine the extent of neoplasm than clinical examination and can reveal lymph nodes that are not clinically apparent. For these reasons CT has become an essential part of the workup of patients who have oral neoplasms. Neoplasms are detected on CT based on their density and morphology. It delineates the bone architecture and hence the extent of bone involvement

by the lesion. Measurement of the volume of oral tumor by three dimensional spiral CT are reliable and are of the greatest benefit to the clinicians in pre and postoperative assessment.²² Perfusion CT is a new imaging technique that has been only recently introduced to the field of head and neck cancer. It assesses tumor vascularity and appears promising in detection of both primary and recurrent cancer.^{23,24} CT-guided biopsy has also gained acceptance because of its safety and high accuracy.²⁵ CT scan is also currently used for radiation therapy planning, with a specific positioning and immobilizing device. It will play an essential role, along with MRI, in the development of conformal radiation therapy.²⁶

However, there are disadvantages with the use of CT. Presence of amalgam fillings and metallic prosthesis in the oral cavity can result in artifacts and obscures the anatomy and pathology in the sections where devices are included. A CT scan is not as useful in cases where soft tissue malignancies are required to be studied. Hence a CT is not recommended in cases of carcinomas of tongue and gingiva, instead MRI is preferred.

MRI: In head and neck cancers, MRI scan is particularly helpful in soft tissue tumors for its exact extent, localization, tissue differentiation and shows the involvement of the adjacent structures. MRI can assess the presence of marrow edema and hence bone infiltration which cannot be appreciated with CT. The T1 images can delineate the outlines of the lesions and T2 images better assess the composition of lesion whether it is fluid, fat, water or muscle.^{27,28} Fat suppression (FS) MRI improve the detection and delineation of head and neck lesions, because of the abundance of fat and the complex anatomy of the head and neck.²⁹ Contrast-enhanced FS T1-weighted images offer complementary information on the precise characterization of complex tumors such as vascularization, tumor necrosis, perineural tumor spread and meningeal infiltration. FS T2-weighted images offer better contrast between tumors and adjacent muscle, fat and mucosa as compared with contrast-enhanced FS T1-weighted images.^{30,31} Hence by using more than one combination of sequences, important details of the extent and composition of the lesions can be determined.

MRI can better assess the occult metastasis as the lymph nodes give the same signal intensity as the primary tumor.³² In cases of salivary gland tumors, MRI can better assess the fine details of the gland

architecture. It is particularly helpful in detecting deep tissue extension, marrow infiltration/edema, perineural spread and the parotid portion of facial nerve using high-resolution techniques.³³ New MRI techniques are increasingly being researched for use in head and neck malignancies and soon may become part of routine assessment. These include Dynamic contrast-enhanced gradient echo MR imaging, Volumetric interpolated breath-hold examination (VIBE)- sequence MRI, Diffusion weighted imaging MRI sequence and Iron oxide enhanced MRI.³⁴

However there are potential technical limitations such as artifacts due to swallowing, blood circulation and presence of metallic restorations and bridges in the oral cavity. Claustrophobia and the impossibility to remain supine in obstructed airway patients account for a few percentages of technical failure. Another disadvantage of MRI is it good on the bone. That means tumors with more of bone involvement are not delineated well as with the CT. The main hindrance to the use of this modality is the cost factor and availability. This forces the clinician to make an inferior choice which results in errors in accurate assessment thereby compounding the problem.

Ultrasonography: Ultrasound uses sound waves with frequencies above those humans can hear. A transducer sends sound waves traveling into the body which are reflected back from organs and tissues, allowing a picture to be made of the internal organs. In head and neck malignancies it is mainly limited to the tumors in salivary glands and detection of lymph nodes metastasis. For lesions in the parotid, submandibular and sublingual glands, ultrasound is an ideal tool for initial assessment. These are relatively superficial structures accessible by high resolution ultrasound, which provides excellent resolution and tissue characterization without a radiation hazard.³³ The main advantages are low cost and easily accessible technique and can easily guide a fine-needle aspiration.³⁵ However, this technique has several drawbacks: it does not explore the deep structures, it is operator dependent, and it does not provide standardized reference images for the clinicians.

SPECT/CT: SPECT/CT is a imaging technique that combines the functional information from Scintigraphy with the anatomical information from Computed Tomography into one set of images. It measures the concentration of chemicals injected into the body, and

provides images of the chemical function of body parts of interest. In this technique the image obtained by a gamma camera is a 2-D view of 3-D distribution of a radionuclide. SPECT/CT scans, however, are significantly less expensive than PET/CT scans, in part because they are able to use longer-lived more easily-obtained radioisotopes than PET/CT. However, Goerres et al in 2005 concluded that PET/CT is superior to SPECT/CT in assessment of oral carcinomas.³⁶

PET/CT: PET/CT is a physiological imaging for assessment of metabolism within the tissues. It is basically the fusion of the two techniques of PET and CT. CT helps in localization of the tumor and PET helps in characterization.³⁷ Therefore both together as PET/CT gives the anatomical as well as the physiological information regarding a tumor. The main application of PET/CT is in the assessment of patients with cancer using the glucose analogue 2-[18] fluoro- 2-deoxy-D-glucose (FDG). Cancer cells have increased glucose utilization and FDG PET/CT is used to investigate the increased FDG metabolism of malignant cells compared with non-malignant cells. The FDG uptake is evaluated with quantification procedure called as Standard Uptake Value (SUV). FDG PET/CT plays an increasing central role in the detection and management of head and neck cancers because most of the cancers in this region are squamous cell carcinomas. This technique is particularly useful in assessment of occult primary tumors and lymph nodes which are missed in other radiographic techniques. It helps in accurate staging of the carcinomas also assess the post treatment results and responses. The residual tumor and recurrences are also better assessed by this technique. PET/CT better assess the operability upto 95%. This technique is highly sensitive. The specificity is compromised and there are false positive results when there are other infections present. For ex: post chemotherapy, the patients immunity is low and prone for infections. This can result in false uptake of the radiotracer and false positive results.^{38,39} It cannot be used in cases of uncontrolled diabetes where the blood sugar levels are higher than 150mg/dl. The high cost can make it unaffordable to large groups of the population. Cost factor is especially important in developing nations like India where the per capita income of an average individual is about \$ 275 whereas the cost the imaging modalities like PET/CT is over \$500.

Significance of assessing bone invasion: Adequate assessment of tumor is critical for appropriate

treatment planning. Treatment for early stage tumors typically involves radiation and chemotherapy or surgery whereas, advanced stage disease requires a combination therapy of surgery, radiation and/or chemotherapy.⁶ Early bone invasion by a tumor is of paramount importance when treatment is considered, which has a great impact on survival rate. Conservative surgical approach such as marginal resection is carried out in case of superficial bone involvement,^{40,41,42} whereas segmental resection is the treatment of choice in case of bone marrow invasion.⁴³ Inability to detect invasion of the tumor in the bone i.e underassessment may lead to inadequate resection resulting in local recurrences and potential regional or distant metastasis, poor prognosis and reducing the survival rates. On the other hand, overassessment of bone invasion, leads to high rate of futile radical surgical procedures resulting in high morbidity and esthetic and reconstructive difficulties (figure 1). Hence, making an appropriate choice among the various alternatives of imaging modality for adequate assessment of bone invasion by the oral malignancies is of utmost importance and requires the clinicians' discretion and practical approach.

Decision tree in imaging of oral cancers: (figure 2)

The imaging of the oral cancers involves evaluation of primary neoplasm as well as searching the neck metastasis to the lymph nodes. When assessing the primary tumors, an imaging protocol in the form of a 'decision tree' can be followed so that bone invasion can be adequately assessed and prompt treatment can be initiated.

Kalavrezos et al compared the clinical features of oral carcinomas with histologically determined bone infiltration in 60 patients. The study showed that the tumors located at the retromolar area all showed histologic invasion of the tumor in the bone (100%). Tumors of the alveolar process showed bone invasion in 71% cases. In, 52% cases of SCC of the floor of the mouth osseous infiltration was evident. Among the 5 patients with carcinomas of tongue, 2 patients showed bone involvement among 3 patients with carcinoma in buccal mucosa, 1 showed bone invasion. Depending on the data, the tumors of retromolar area and alveolar ridge were considered to be high risk group for bone invasion while tumors of floor of mouth, tongue and the buccal mucosa formed the low risk group for bone invasion.⁷ Thus the site of the tumor plays a role in the choice of the imaging modality.

Figure 1: Significance of assessment of bone invasion

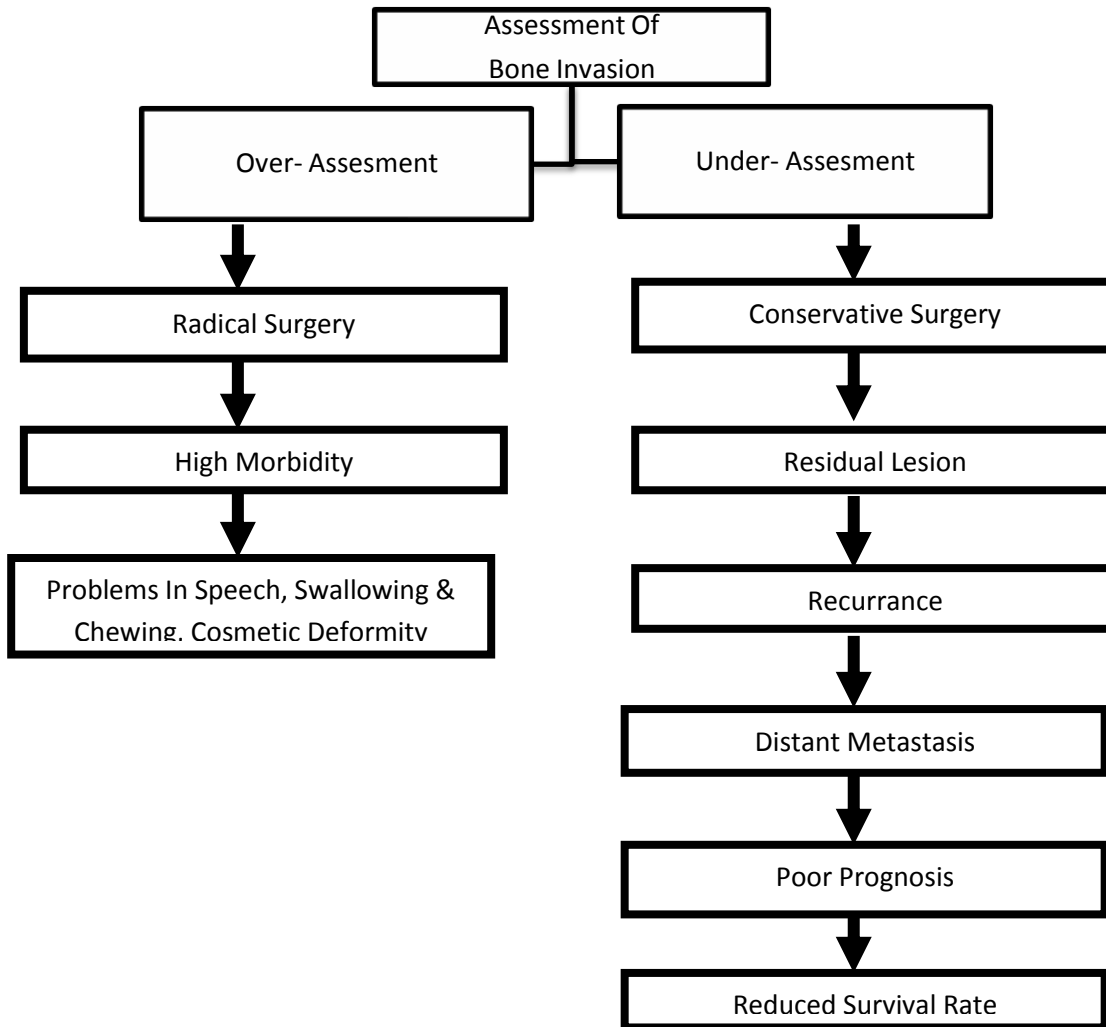
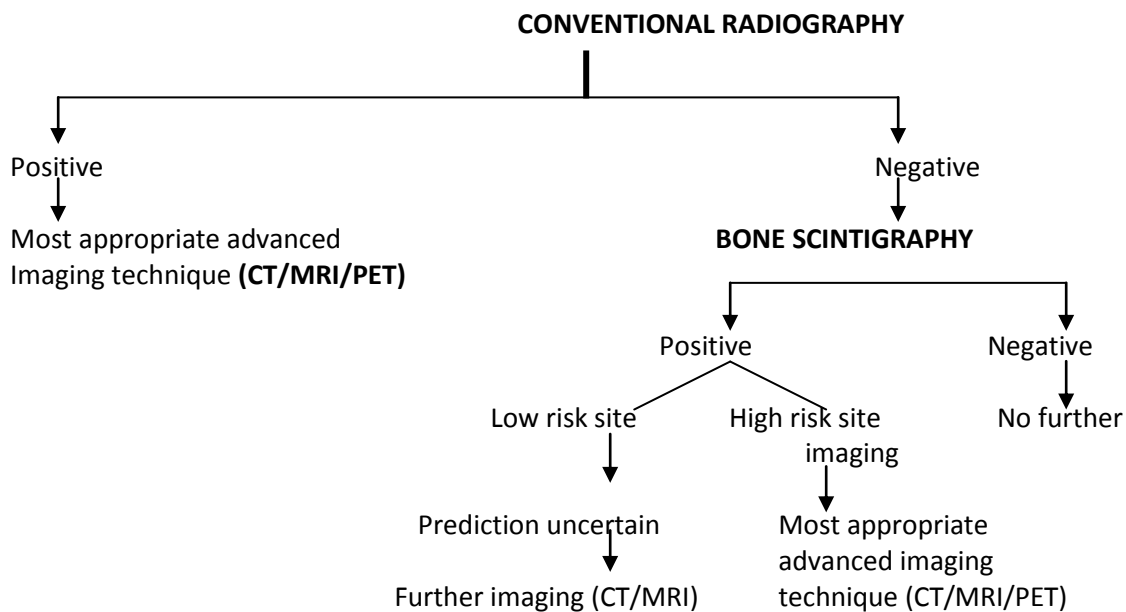


Figure 2 : Decision Tree For Imaging Of Oral Cancers



Nakayama et al assessed the diagnostic accuracy of panoramic radiography, panoramic radiography combined with intraoral radiography and CT in detecting the bone invasion by gingival carcinoma. They concluded that Panoramic radiography and Intraoral radiographs should be adopted as the initial imaging modality to determine the extent of superior inferior invasion of the bone in cases of carcinoma.¹⁵ A positive finding of bone invasion justifies the need for further sophisticated imaging techniques such as the CT, MRI or PET/CT depending on the clinical situation. However, a negative finding on OPG+IR does not rule out the possibility of bone invasion by the tumor. Hence further investigations may be required depending on the clinicians' discretion.

A nuclear imaging Scintigraphy is highly sensitive technique to assess the bone involvement and occult metastasis in the skeleton.^{44,45} Bone involvement can be predicted with 98% sensitivity in this technique. However, since the technique suffers from lack of specificity chance for false positives is high and hence careful assessment of results is necessary. In such cases the site of tumor helps in assessment. If the tumor is located in high risk areas, the bone involvement by the tumor is almost always present. In tumors localized in low risk areas, the prediction is uncertain and hence further diagnostic tests are recommended. For patients with negative bone scanning, the risk of osseous infiltration is low.

Choice among further sophisticated imaging modalities depend on number of factors like availability, affordability and clinical situation. If clinical findings are suggestive of bone involvement, the preferred imaging method is CT as it assesses bone architecture better. If the clinical findings are suggestive more of soft tissue involvement and nodal metastasis, MRI is the preferred imaging modality.

In addition to these, several new techniques that aid in diagnosis and staging of oral carcinomas like SPECT and PET/CT are also available. PET/CT is superior and is of particular value in investigation of occult primary tumors, staging primary disease, detection of residual and recurrent lesions.³⁸ Though these techniques have proved their utility in oral cancer assessment, its use is limited because of high cost and limited availability.

Nodal metastasis can be accurately assessed with Ultrasonography, CT, MRI or newer technologies like PET^{46,47,48}

In cases of salivary gland tumors ultrasonography is inexpensive and invaluable tool particularly in subperforally placed tumors within parotid, submandibular glands. When deeper portion of the gland is involved, an MRI or CT is mandatory to evaluate the complete tumor extent, local invasion and perineural spread. For all tumors detected in the sublingual gland and minor salivary gland, an MRI should be performed as the risk of malignancy is high.³⁴ The role of nuclear medicine and PET scan, in imaging of parotid masses has not yet been established.⁴⁹

Conclusion: Imaging in oral cancer is a crucial investigations and an appropriate decision of the clinician is critical in terms of mortality and morbidity. With multiple choices available, it can be difficult to make the apposite judgment. In such situations, following a simple imaging protocol can fetch better results. In developing country like India, additional factors like cost and availability of imaging modalities have a bearing on the decisions taken by the clinicians. Following the imaging protocol will lessen the burden on both the patient and health care system as unnecessary procedures can be circumvented.

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