RADIOLOGICAL AND HISTOPATHOLOGICAL ASSESSMENT OF CERVICAL LYMPH NODES IN PATIENTS WITH ORAL AND OROPHARYNGEAL SQUAMOUS CELL CARCINOMA UNDERGOING NECK DISSECTION AT KENYATTA NATIONAL HOSPITAL

UNIVERSITY OF NAIROBI

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V60/11355/2018

DECLARATION

I do hereby declare that this proposal is my original work and has not been submitted by any other person(s) in any other institution for the award of a degree or otherwise.

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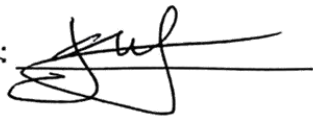V60/11355/2018

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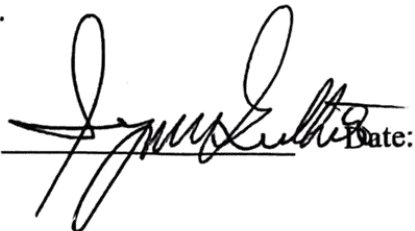
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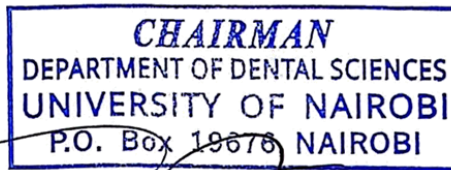
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DEDICATION

I dedicate this work to my late parents, John and Caroline, who taught me the value of education and enabled me to get the best life. I also dedicate this project to my wife Rachael and son Nigel for their love, support and understanding during the long absent hours of my postgraduate training. To my sister Bilha, and my brother Sheldon for their support and encouragement.

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LIST OF ABBREVIATIONS

AJCC   American Joint Committee on Cancer

CT   Computed Tomography

ENE   Extra Nodal Extension

ENT   Ear, Nose and Throat

FNAC   Fine Needle Aspiration Cytology

H&E   Hematoxylin and Eosin

HNSCC   Head and Neck Squamous Cell Carcinoma

HPV   Human Papilloma Virus

KNH   Kenyatta National Hospital

MRI   Magnetic Resonance Imaging

OMFS   Oral and Maxillofacial Surgery

OPSCC   Oropharyngeal squamous cell carcinoma

OSCC   Oral squamous cell carcinoma

PET   Positron Emission Tomography

TNM   Tumor, Nodes, Metastases

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ABSTRACT

STUDY BACKGROUND: Oral and oropharyngeal cancers are in the top 30 most common cancers in the world. Their five-year survival rate is about 86% with early detection and 40% if detected late. This underlies the importance of accurate and timely diagnosis of loco-regional spread to cervical lymph nodes and optimum treatment to increase prognostic outcomes. Unfortunately, cervical lymph node assessment may sometimes be inaccurate, and radiological and histopathologic evaluation may occasionally give conflicting results.

BROAD OBJECTIVE: To investigate the agreement between radiological, and histopathological assessment of cervical lymph nodes in patients with oral (OSCC) and oropharyngeal (OPSCC) squamous cell carcinoma undergoing neck dissection at Kenyatta National Hospital (KNH), irrespective of the stage.

METHODOLOGY: This was a cross-sectional study conducted at KNH. The study population was all patients with a histological diagnosis of OSCC and/or OPSCC scheduled for neck dissection at KNH. Convenience sampling was used to select at least thirty consecutive patients between February and June 2023. Data from reports of the radiological (preoperative) and histopathological (postoperative) assessment of cervical lymph nodes was collected and analyzed. Pattern of agreement, sensitivity and specificity of the various radiological examinations was determined.

RESULTS: Thirty (30) patients (16 males and 14 females) were recruited, with a mean age of 58.1 ± 12.5 years. On radiological assessment, 21 (70%) patients had suspicious nodes, with 18 (85.7%) of them having suspicious nodes in level I and 8 (38.1%) having multi-level suspicious nodes. The most frequent clinical nodal categories were cN2b and cN1 (8; 26.7% and 7; 23.3%) respectively. On histological assessment, 16 (53.3%) patients had metastatic lymph nodes, with level I metastasis in all 16 (100%). The most frequent pathological nodal category was pN3b seen in 6 (20%) patients. There was a fair agreement between patients with clinically suspicious nodes and those with histologically confirmed nodal loco-regional spread ($\kappa = 0.384$, $p < .05$). The level of agreement increased to moderate when the unit of comparison was the cervical nodal level ($\kappa = 0.512$, $p < .05$) and further increased to substantial when the comparison was between clinical (cN) and pathological (pN) nodal categories ($\kappa = 0.629$, $p < .05$). CT scan had a sensitivity (true positive) of 83.3% and a specificity (true negative) of 44.4% while Magnetic Resonance Imaging (MRI) had a sensitivity (true positive) of 100% and a specificity (true negative) of 60%.

CONCLUSION: The most common radiological feature of suspicious lymph nodes identified was an enlarged node of more than 9mm in diameter while the most common histopathological feature of positive lymph nodes was abnormal hilar architecture. There was a substantial agreement between radiological and histopathological assessment of cervical lymph nodes in patients with OSCC/OPSCC. MRI and CT scan had higher sensitivity (true positives) but lower specificity (true negatives).

RECOMMENDATIONS: Magnetic Resonance Imaging (MRI) may be the better imaging for assessing loco-regional spread of OSCC/OPSCC in our setup in comparison to CT scan thus surgeons should request for more MRI. However, there is need to conduct another study with a larger sample size.

CHAPTER ONE: INTRODUCTION

1.1 Background

The incidence of oral and oropharyngeal cancer has been increasing globally with OSCC and OPSCC being the 18th and 26th most common cancer respectively(1). The five-year survival rate is 86.3% when detected while still localized, 69% with regional spread and 40.4% with distant metastasis(2). Treatment especially of advanced disease, is costly and caries a heavy burden to the patient and the society.

OSCC and OPSCC typically spread to the neck lymph nodes and the chest(3). Palpation of the neck is the first pre-operative tool for staging. However, palpation is subjective and yields inaccurate and irreproducible results(4,5). Due to these weaknesses, the American Joint Committee on Cancer (AJCC) recommends that advanced modalities such as radiological imaging should be used for clinical staging. Ultimately, the diagnosis of lymph node metastases is histological (6).

Despite the robustness of imaging to detect metastases, their efficacy is still hotly debated. Studies show that 25% of clinically negative necks show lymph nodes metastases after neck dissection (7). Similarly, while standard CT and MRI have the ability to detect metastatic lymph nodes, their ability to differentiate between benign and malignant small non-enlarged lymph nodes is low (8).

The purpose of this study was to investigate the agreement between radiological and histopathological assessment of cervical lymph nodes in patients with OSCC and OPSCC

undergoing neck dissection at KNH. The data on specificity and sensitivity of the radiological assessments will guide surgeons in deciding which radiological investigations to include in preoperative evaluation of OSCC & OPSCC patients.

1.2 Statement of the problem

Patients with OSCC & OPSCC require radiological examination of their neck and chest to rule out metastasis. If suspicious lymph nodes are detected on imaging and the patient opts for surgery, the nodes are removed surgically together with the primary tumor. Subsequently, diagnosis of tumor involvement is confirmed histologically. On the other hand, stage one disease patients without radiological evidence of loco-regional spread to cervical lymph nodes are not subjected to neck dissection since unnecessary surgical dissection has a relatively high morbidity and adversely affects the patient's quality of life (4)

There are patients who have been subjected to neck dissection on the strength of radiological reports picking out suspicious lymph nodes only for the nodes to turn out negative on histopathology (false positive)(5). On the other hand, there are patients whose necks did not have suspicious lymph nodes radiographically but the surgeon elected to perform neck dissection only for the results to come back positive on histological assessment (false negative)(6). Koech et al found out that only 50% of patients who underwent neck dissection due to OSCC at KNH had lymph nodes positive for tumor(9).

The main debate remains as to the sensitivity, specificity and accuracy of relying on the different radiological assessments to detect loco-regional spread to cervical lymph nodes in patients with

OSCC and OPSCC (10). Sub-Saharan Africa has limited data on these accuracies. Literature review reveals a high concentration of studies in United States, Europe and Asia. Literature analysis also shows variations in the sensitivity, specificity and accuracy across the world (11), (5), (10), (12), (13), (14),(15). The aim of this study was to investigate the agreement between radiological, and histopathological assessment of cervical lymph nodes in patients with OSCC and OPSCC undergoing neck dissection at KNH

1.3 Justification of the study

The status of cervical lymph nodes is one of the most important diagnostic and prognostic indicator in oral and oropharyngeal carcinomas. Accurate assessment of clinically negative and clinically positive cervical lymph nodes has a direct influence on the success of treatment and management. A decision has to be made using information from preoperative assessments to pursue appropriate treatment modalities. In most cases, neck dissection is the standard surgical treatment. However, in cases where there is no regional spread to cervical lymph nodes, neck dissection can be an overtreatment but it cannot be avoided in most cases due to the risk of occult metastasis. Recognizing the delicate balance in neck dissection decision making, this study provides empirical evidence on the sensitivity, specificity and accuracy of radiological and histopathological assessments in order to improve decision making and prognostic outcomes.

1.4 Research objectives

1.4.1 Broad objective

To investigate the agreement between radiological and histopathological assessment of cervical lymph nodes in patients with OSCC and OPSCC undergoing neck dissection at KNH.

1.4.2 Specific objectives

1. To describe radiological features of cervical lymph nodes in patients with OSCC/OPSCC undergoing neck dissection at KNH.

2. To describe histopathological features of cervical lymph nodes in patients with OSCC/OPSCC undergoing neck dissection at KNH.

3. To assess the pattern of agreement between radiological and histological diagnoses of cervical lymph node metastasis in patients with OSCC/OPSCC undergoing neck dissection at KNH.

4. To evaluate the specificity and sensitivity of radiological assessment in diagnosis of cervical lymph nodes metastasis in patients with OSCC/OPSCC undergoing neck dissection at KNH.

1.5 Study variables

Variable	Measurement
Independent variables	
Number of metastatic cervical lymph nodes	-Hindu-Arabic numerals
Size of metastatic cervical lymph nodes	-mm
Architecture of metastatic cervical lymph nodes	-Necrotic/Fatty center/thickened cortex/ Matted
Presence of cancer cells within nodes	-Yes/No
Laterality of metastatic cervical lymph nodes	- Ipsilateral/ Contralateral/ Bilateral
Extra nodal extension	-Yes/No
Dependent variables	
Clinical Staging of metastatic cervical lymph nodes	cN
Pathological Staging of metastatic cervical lymph nodes	pN

Radiological assessment of cervical lymph nodes (Number, size, architecture, level & laterality) forms the basis of clinical nodal categorization (cN). Histopathological assessment of cervical lymph nodes (Number, size, presence of tumor cells, architecture, Extra nodal extension -ENE, level & laterality) forms the basis of pathological staging pN. The clinical nodal categorization is compared to the final pathological nodal categorization which is the gold standard.
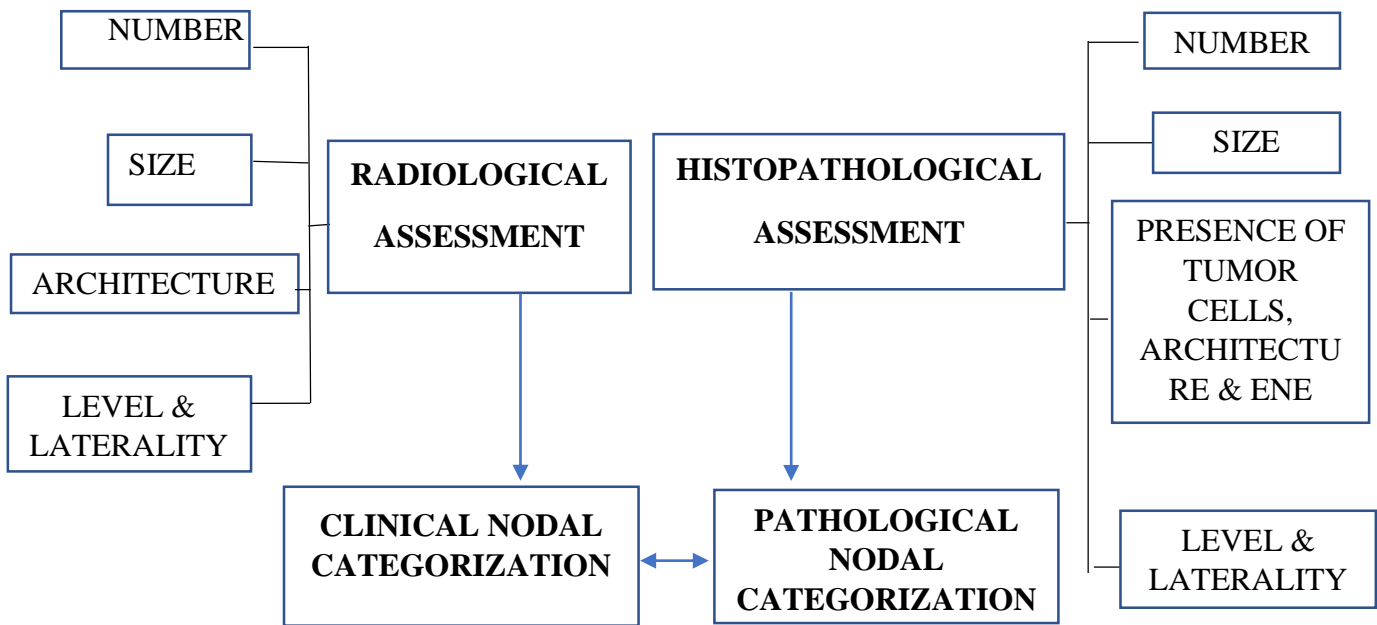
Figure 1. 1 Conceptual framework

CHAPTER TWO: LITERATURE REVIEW

2.1 Anatomy
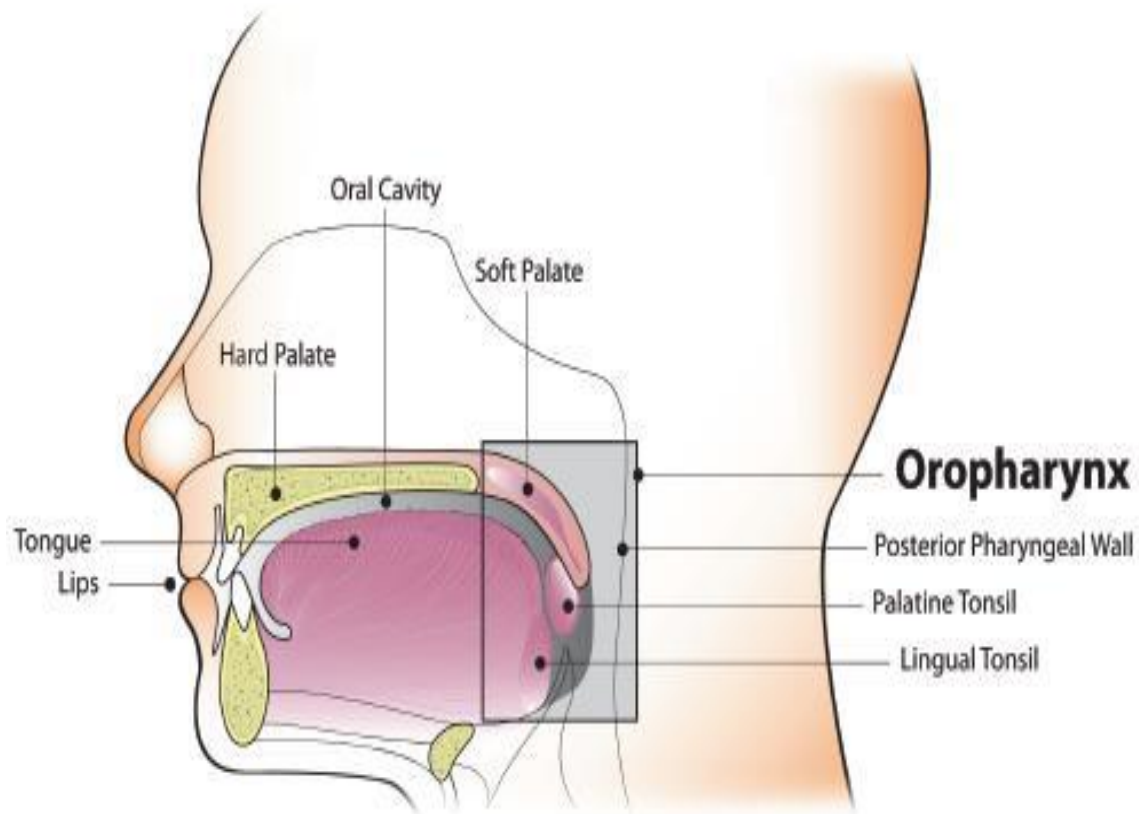
Figure 2. 1 Diagram of the Oral cavity and Oropharynx, adapted from cdc.gov

The oral cavity extends from vermillion of lips to the junction of hard and soft palates. The sub sites under oral cavity include the mucosal lips, anterior tongue, mouth floor, buccal mucosa, lower

and upper alveolar ridges, hard palate and the retro-molar trigone, the latter consisting of mucosa that overlies anterior region of the ascending ramus of the mandible.

The oropharynx begins where the oral cavity ends. It begins at the junction of the hard and soft palates superiorly and circumvallate inferiorly and extends to the posterior soft palate separating the oropharynx from nasopharynx and the hyoid bone inferiorly. The sub-sites in the oropharynx are the base of the tongue inferiorly, tonsillar complex laterally (tonsillar fossa, palatine tonsil and pillars), soft palate superiorly and the posterior pharyngeal wall(16). The anatomy of the oral cavity and oropharynx are illustrated in Figure 2.1 (17).

2.2 Anatomy of the Cervical Lymph nodes
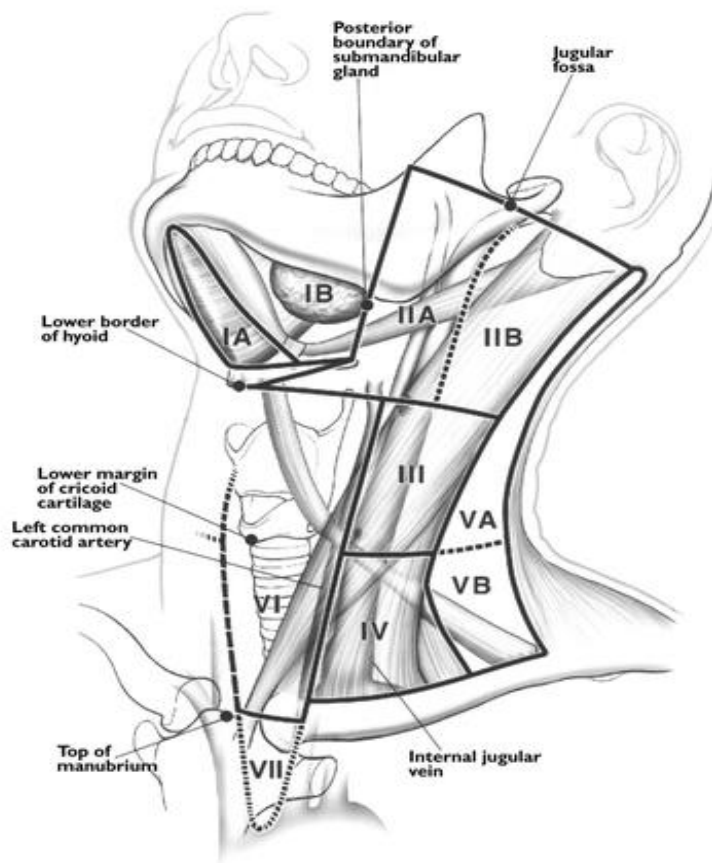
Figure 2. 2 Classification of cervical lymph nodes adapted from AJCC.

Level 1 nodes are sub-mental and sub-mandibular; level 2 nodes are upper internal jugular chain nodes; level 3 nodes are middle internal jugular chain nodes; level 4 nodes are lower internal jugular chain nodes; level 5 nodes are spinal accessory chain nodes and transverse cervical chain nodes; and level 6 nodes are anterior cervical nodes. The classification of cervical lymph nodes as adapted from AJCC is illustrated in Figure 2.2 (18).

2.3 Oral Squamous cell carcinoma (OSCC)

OSCC is the eighteenth most common cancer in the world (1). Africa has limited data due to few cancer registries. OSCC arises from the squamous mucosa lining the oral cavity. The etiology of OSCC is multifactorial. Tobacco use, excessive alcohol consumption and betel nut usage are mostly implicated(19,20).

A study at a Kenyan center established that most patients present with pain and weight loss. Older men (above 50 years) were more affected in comparison to women and majority were farmers. Most patients presented late with advanced disease at stage 4. The most common site involved was the tongue with buccal mucosa following in prevalence. Seventy three percent of the cases were well differentiated on histology (9). Well differentiated OSCC has a better prognosis than poorly and moderately differentiated tumors. Of the patients who underwent neck dissection, 50% had nodal spread to cervical lymph nodes confirmed on histopathology (9).

In patients with metastatic spread of head and neck cancer, 66-80% is to the chest(21,22).

2.4 Oropharyngeal squamous cell carcinoma (OPSCC)

Commonly known as throat cancer, OPSCC affects the base of the tongue, tonsils, soft palate, lateral and posterior pharyngeal walls. Most patients present with a sore throat, odynophagia and dysphagia. More than 90% of OPSCC arise from the squamous epithelial lining the oropharynx (23). OPSCC is divided into two distinct entities; Human Papilloma Virus (HPV) positive OPSCC and HPV negative OPSCC. The latter is associated with tobacco and alcohol use (24).

HPV positive OPSCC is associated with an oral HPV infection and is mostly found in younger population who practice unprotected oral sex, oro-anal sex or with multiple sexual partners (25). It is diagnosed via immunohistochemistry whereby P16, a context-specific biomarker that is overexpressed in HPV infection, is detected (26). Among the many types of HPVs, HPV 16 is the most common type found in OPSCC (27). The prevalence of this high-risk HPV (HPV 16) is however low among patients with Head and Neck Squamous cell carcinoma (HNSCC) at Kenyatta National Hospital (28).

2.5 The Tumor, Nodes and Metastases Staging System

Staging is the core of diagnosis, treatment planning, application of diverse treatment modalities, and follow-up. Staging that is consistent, efficient, accurate and reproducible is associated with proper management of patients with OSCC and OPSCC (10).

The tumor, nodes, metastases (TNM) staging system was developed by the AJCC to guide staging by site. The system is used by clinicians to categorize tumors in the head and neck region and to assess the status of the disease. Staging utilizes all clinical information obtained using physical examination, radiographic imaging, intraoperative and pathologic assessments. This staging system covers the tumor (T) which relates to the characteristics at the primary site, the nodes (N) which is concerned with the degree of involvement of regional lymph nodes, and distant metastases (M) which is the presence or absence of metastasis. Based on the information obtained on tumor, nodes, and metastases, the cancer can be staged as Stage I, II, III, or IV. Each of these stages can have subdivisions denoted as a, b, or c status (29). T4 tumors continue to be subdivided into

moderately advanced (T4a) and very advanced (T4b) categories. Stage IV disease is divided into moderately advanced, local/regional disease (Stage IVA), very advanced local/regional disease (Stage IVB), and distant metastatic disease (Stage IVC) (30). Staging prior to any treatment is denoted as cTNM, after surgical resection pTNM and at recurrence rTNM(30).

2.6 Staging and Treatment of Oral Squamous Cell Carcinoma

The staging of tumors of the oral cavity depends on its spread to the sub sites of the oral cavity (the lips, anterior tongue, mouth floor, buccal mucosa, lower and upper alveolar ridges, hard palate and the retro molar trigone). Level I tumor denotes that it has spread to the lymph nodes of the submandibular region. Level II and III denotes spread to the upper and middle jugular chain lymph nodes (29). The categorization of primary tumor(T) and cervical lymph nodes (cN) in OSCC are summarized in Tables 2.1, 2.2 and Figure 2.3 (30,31)

Table 2. 1 Primary tumor (T) definition for oral squamous cell carcinoma.

TX	Primary tumor cannot be assessed
Tis	Carcinoma *in situ*
T1	Tumor ≤ 2 cm and DOI ≤ 5 mm
T2	Tumor ≤ 2 cm, DOI > 5 mm and ≤ 10 mm or Tumor > 2 cm and ≤ 4 cm and DOI ≤ 10 mm
T3	Tumor > 4 cm or any tumor with DOI > 10 mm
T4a	Moderately advanced local disease
T4a lip	Invades adjacent structures: thru' cortical bone, Inferior alveolar nerve, Floor of mouth, skin of face
T4a oral	Invades adjacent structures: thru' cortical bone of mandible/maxilla, involves antrum, skin

	Note: Superficial erosion alone of bone/tooth socket by gingival primary is not sufficient to classify as T4
T4b	Very advanced local disease: tumor invades masticator space, pterygoid plates, or skull base and/or encases the internal carotid artery
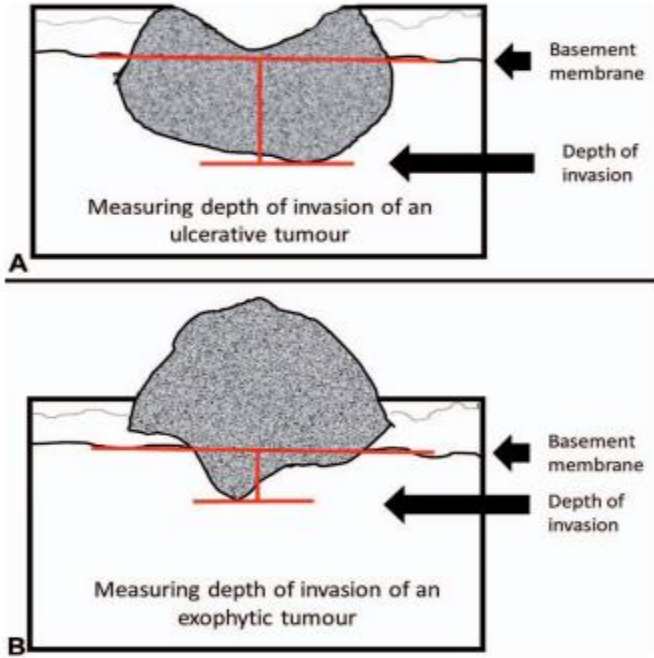
Figure 2. 3 Depth of invasion vs thickness of a tumor

Table 2. 2 Assessment of regional lymph nodes (cN)

NX	Regional lymph nodes cannot be assessed
N0	No regional lymph node metastasis
N1	Metastasis in a single ipsilateral lymph node, ≤ 3 cm without Extra nodal extension ENE-
N2a	Metastasis in a single ipsilateral lymph node > 3 cm and ≤ 6 cm and ENE-
N2b	Metastases in multiple ipsilateral lymph nodes, ≤ 6 cm and ENE-
N2c	Metastases in bilateral or contralateral lymph nodes, ≤ 6 cm and ENE-
N3a	Metastasis in a lymph node > 6 cm and ENE-
N3b	Metastasis in any lymph node(s) with ENE+ clinically

In order to qualify clinical classification of disease as ENE (+), clear evidence of ENE on clinical examination (e.g., invasion of the skin, muscles or tethering to adjacent structures, or cranial nerve, brachial plexus, sympathetic trunk, or phrenic nerve invasion with dysfunction) supported by radiographic evidence is required (30). The staging of OSCC is summarized in Table 2.3(30)

Table 2. 3 Integrated staging of OSCC

Stage 0	Tis, N0, M0		
Stage 1	T1,	N0,	M0
Stage 2	T2,	N0,	M0
Stage 3	T3,	N0,	M0 OR
	T1/T2/T3	N1	M0
Stage 4a (Moderately advanced, local/regional disease)	T4a,	N0/N1/N2,	M0 OR
	T1/T2/T3/T4a,	N2	M0
Stage 4b (Very advanced, local/regional disease)	T4b	N0/N1/N2/N3	M0 OR
	Any T	N3	M0
Stage 4c (Distant metastatic disease)	Any T	Any N	M1

OSCC is treated using ablative surgery plus or minus neck dissection. Surgical treatment is preferred because the accessibility and risk of involvement of bone structures means that when radiotherapy is used, it can lead to osteoradionecrosis of the mandible or maxilla. Studies also show that OSCC are less sensitive to chemotherapy and radiation when compared to oropharyngeal

or laryngeal cancers (32). Adjuvant radiation therapy may be used to treat advanced-stage disease. In cases where there are positive surgical margins, multiple lymph nodes and/extracapsular tumor extension, postoperative chemoradiotherapy can be used to control the disease locally(29).

2.7 Staging and Treatment of Oropharyngeal Carcinoma

The 8th edition of the AJCC published in 2017 differentiates the way Primary tumor and cervical lymph nodes are defined in HPV positive vs HPV negative OPSCC. The categorization of primary tumor (T) and cervical lymph nodes (cN) in OPSCC are summarized in Tables 2.4 and 2.5 (30)

Table 2. 4 Primary tumor (T) definition for OPSCC

TX	Primary tumor cannot be assessed
Tis	Carcinoma *in situ*
T0	Only used in HPV positive OPSCC where no tumor identified, but p16+ cervical node(s) involvement
T1	Tumor 2 cm or less in greatest dimension
T2	Tumor more than 2 cm but not more than 4 cm in greatest dimension
T3	Tumor more than 4 cm in greatest dimension or extends to lingual surface of epiglottis
T4a	Moderately advanced local disease Tumor invades the larynx, deep/extrinsic muscle of the tongue, medial pterygoid, hard palate, or mandible *Note: Mucosal extension to lingual surface of epiglottis from primary tumors of the base of the tongue and vallecula does not constitute invasion of larynx.*
T4b	Very advanced local disease Tumor invades the lateral pterygoid muscle, pterygoid plates, lateral nasopharynx, or skull base, or encases the carotid artery

Table 2. 5 Clinical assessment of regional lymph nodes (cN) in HPV-related (p16-positive) oropharyngeal cancers

NX	Regional lymph nodes cannot be assessed
N0	No regional lymph node metastasis
N1	One or more ipsilateral lymph nodes ≤ 6 cm
N2	Contralateral or bilateral lymph nodes ≤ 6 cm
N3	Lymph node(s) > 6 cm

Clinical assessment of regional lymph nodes (cN) in HPV-negative (p16-negative) OPSCC is similar to OSCC as outlined in Table 2.2. Tumors in the oropharynx can also spread to the retropharyngeal lymph nodes (29).

OPSCC is traditionally treated using radiotherapy as the single modality for T1/2 or N0/1 staging. On the other hand, chemoradiotherapy is the standard for patients with advanced disease, T3/4 or N2b/c/3 staging (29)

2.8 Clinical, Radiological and Histopathological Assessment of Cervical Lymph Nodes in Oral and Oropharyngeal Carcinoma

Clinical assessment of cervical nodes involves physical examination through palpation, imaging techniques (CT, MRI, Positron Emission Tomography (PET) and ultrasound) and nodal biopsies (ultrasound guided Fine Needle Aspirate). There are various studies that have examined these

assessment methods to determine their performance in terms of sensitivity, specificity and accuracy.

The standard for clinical assessment of cervical nodes for metastases is radiological imaging. The main radiological assessments are CT scan and MRI, and are associated with high soft tissue discrimination (13). When lymph nodes are metastatic, they may or may not be clinically palpable. The performance of clinical examination is subjective, and is complicated in cases where a patient has a short neck or has undergone radiotherapy. Examining the accuracy of clinical assessment in generating a definite diagnosis is very important and provides the basis for comparison with the results obtained from histopathological assessment of excised nodes (11).

Radiological assessment of lymph nodes involves an assessment criterion developed from various studies. The main parameters include nodal size, architecture and signs of extra-nodal spread (matted nodes). Nodal architecture assessment includes signs of hilar necrosis, fatty degeneration and increased cortical thickness.(8,33,34)

In a study carried out in three hospitals in Iraq: Al Kindy Teaching Hospital, Ghazi Alhariri hospital, and University of Baghdad Bab Al-Moadham Campus College of Dentistry, researchers sampled 20 patients (11 males, 9 females) with OPSCC that had undergone neck dissection and excision of the primary tumor. Histopathological examination revealed that there were 14 cervical lymph nodes with metastasis, while clinical palpation results indicated 12 true positives, that is cervical lymph nodes with metastasis, while there were 2 false negative, 2 true negatives, and 4 false positives (11). The variance between the 14 positives in histopathological examination and

12 true positives in clinical palpation underlies the value of pre-operative clinical assessment in diagnosis and the decision on carrying a neck dissection.

A study at the Department of Oral and Maxillofacial Surgery at the First Affiliated Hospital of Zhengzhou University in China also sought to establish the accuracy of clinical preoperative assessment comparative to histopathological findings. The study sampled 125 patients (85 males, 40 females) who had undergone neck dissection. Findings revealed that out of all the patients that underwent neck dissection, 37 did not have metastatic lymph nodes according to clinical assessment. However, CT scan detected 44, and ultrasonogram diagnosis detected 38. Both CT scan and ultrasonogram results showed that in 55 of the cases, the lymph nodes in the neck were not metastatic (5).

At the University Health Network in Toronto, the researchers compared preoperative clinical and radiological assessments of the depth (superficial: <5 mm vs deep invaded tumor: ≥5 mm) of metastasis in oral cavity squamous cell carcinoma. The study sampled 53 patients, and demonstrated that positive and statistically significant correlations between clinical and radiographic assessment of depth, which also had a high correlation with histopathological findings in deep invaded tumor cases. In superficial tumor cases, neither clinical or radiographic assessments had a positive or significant correlation with histopathological findings (35), These findings indicate the weaknesses of both clinical and radiological assessments in accurately evaluating the depth of invasion in oral cavity squamous cell carcinomas. However, another researcher investigating the accuracy of MRI in measurement of depth of invasion and bone

involvement in oral cancer and its histopathological correlation, among 70 patients, found a high correlation between radiological and histopathological findings (10). Accurately determining the depth of invasion is critical owing to research studies that have demonstrated a statistically significant correlation between the depth of the tumor and nodal metastasis. Increase in depth is correlated with the increase in cervical nodal metastasis (36).

In Uttar Pradesh, India, a study incorporating 70 diagnosed patients who were scheduled for neck dissection, compared the accuracy of clinical, ultrasonography and postoperative histopathological neck findings. Findings showed that the sensitivity of clinical examination was 80% and ultrasonography was 93.3%, while on specificity clinical assessment was 57% compared to 27.2% for ultrasonography. Histopathological assessment showed that 71% had nodal metastases (6). These results showed that even though ultrasonography had high sensitivity, the low specificity show that clinicians cannot fully rely on it when making decisions on whether to carry out dissection or not, and that it should be used in tandem with clinical examination in preoperative assessments.

In another study in India's P.E.S. Institute of Medical Sciences and Research, the researchers assessed enlarged reactive and positive lymph nodes using clinical, radiological and histopathological techniques, among 24 patients who had undergone neck dissection. Clinical examination showed that there were 31 lymph nodes detected in the 24 patients. The same patients were subjected to contrast-enhanced computed tomography (CECT) which detected 90 enlarged lymph nodes with 21 found to be malignant. However, histopathological analysis isolated 538

lymph nodes with 32 confirmed to be malignant (12). As demonstrated by these findings, both clinical and radiological assessments recorded lower detection rates, with histopathological analysis reporting high detection rate.

Other researchers have compared the accuracy of imaging techniques in detecting cervical lymph node metastasis. A study by Imhof et al reported the accuracy of CT scan to detect cervical metastasis varied depending on the criteria for diagnosis. It was 45% if size of the node was the criteria, 95-100% if central necrosis, 90% if extracapsular spread and less than 40% if based on round shape configuration(37). In general, there are variations in the level of sensitivity and specificity across modalities. A systematic review of 63 studies (with a total sample of 3,029 participants), comparing CT and MRI, showed that CT had a higher sensitivity of 0.77 compared to 0.72 for MRI. However, MRI had a higher specificity at 0.81 compared to 0.72 for CT. Overall, for sensitivity and specificity, MRI demonstrated higher power than CT in the detection of cervical lymph node metastasis (13). To examine the accuracy of conventional imaging modalities (computed tomography, magnetic resonance imaging, ultrasonography) and fine-needle aspiration cytology (FNAC), 62 patients who had undergone primary tumor resection and neck dissection, were sampled for the study and Chi-square tests used to determine sensitivity. Conventional imaging modalities recorded a sensitivity of 82.8% compared to 81.8% for FNAC. The positive predictive value for imaging modalities was 82.8% compared to 100% for FNAC, while the negative predictive values were 73.6% and 66.6% for imaging modalities and FNAC respectively (14). In another study, in terms of sensitivity, specificity and accuracy, contrast-enhanced CT recorded 75%, 98.6% and 91.2% compared to 90.5%, 93.4% and 92.7% for CT Perfusion,

implying the superior power of CT Perfusion in detecting metastatic cervical nodes in OSCC (8). Fluorine-18-fluorodeoxyglucose ([18F] FDG) - positron emission tomography with computed tomography (PET-CT) was also demonstrated to have higher sensitivity when compared to contrast-enhanced CT (15).

2.9 Management of the Neck in Oral and oropharyngeal squamous cell carcinoma

SERIAL FOLLOW UP

Indicated for $T_1N_0M_0$ in highly reliable patients and involves serial neck ultrasounds (38)

SENTINEL LYMPH NODE(S) BIOPSY

Indicated for $T_1N_0M_0$ where a radioactive material (Technetium-99M) is injected into the primary lesion and a detector probe used to isolate specific nodes for excision (38).

RADIOTHERAPY

Radiation (50-56 Gy in 25-30 fractions) is administered to patients as the main modality of treatment if surgery is not feasible or onto the contralateral neck of a patient with OSCC tongue/ floor of the mouth following ipsilateral neck dissection (38)

NECK DISSECTION

Neck dissection can be therapeutic (clinical evidence of metastasis) or elective (no clinical evidence of metastasis)(39,40). It is divided into radical, modified radical and selective. Supra-omohyoid selective neck dissection is indicated for patients with $T_1N_0M_0$ who cannot be

effectively followed up. Neck dissection is indicated for all T_2, T_3, T_4 regardless of N status and any clinically positive node. It is also indicated for negative contralateral neck in patients with OSCC tongue/floor of the mouth that is close to or past the midline (38).

ADJUVANT RADIOTHERAPY

Indicated after neck dissection in patients whose histology report is N_2 or N_3. Patients with N_1 in the background of poor-quality neck dissection (less than 18 nodes isolated ipsilaterally) or whose primary tumor was T_3 or T_4 are recommended to undergo adjuvant radiotherapy too. In addition, if the histology of the primary tumor shows perineural & lympho-vascular spread, then adjuvant radiotherapy is recommended (38)

ADJUVANT CHEMOTHERAPY

Recommended in patients whose histopathology report shows extra nodal extension in any N. It involves injection of high dose ($100mg/m^2$) cisplatin intravenously once every three weeks. In patients who can't tolerate/ are contraindicated to receive this high dose chemotherapy, then a combination of low dose weekly cisplatin with radiotherapy is an option.(38)

2.10 MRI/CT/PET scan Imaging and Imaging centers

2.10.1 Magnetic Resonance Imaging (MRI)

A form of non-ionising radiation based on magnetic resonance of hydrogen ions within various tissues. The patient is placed in a powerful magnetic field that influences the magnetism of the hydrogen ions present in the various tissues of the individual. These are then subjected to a variety

of radio waves, which causes them to alter their magnetism in various time depended patterns, and causing them to emit signals in the process. A radiofrequency receiver connected to a computer detects the signals that are emitted. The end product is useful diagnostic images. Different scanners have different magnetic field strengths measured in Tesla(T) where most of the ones currently in the local market range from 0.3 to 3 Tesla.

MRI utilizes different sequences to optimize on various aspects within a particular tissue/organ being imaged. The most important imaging sequences for head and neck imaging include non-contrast-enhanced T1-weighted images, contrast-enhanced T1-weighted images with fat suppression, and fat-suppressed fluid-sensitive sequences, such as T2-weighted images with fat suppression or short-tau inversion recovery (STIR) images. Images in axial and coronal plane are the most useful. For general purpose, slice thickness should be no more than 5 mm. Some applications, such as evaluation of skull base and perineural spread, may require thinner slice thickness, typically around 3 mm(41).

The excellent soft-tissue contrast and resolution makes MRI an important imaging modality to consider in oncologic imaging. For example, MRI can provide more accurate definition of tumors of the tongue compared to CT scan, and is more sensitive for superficial and mucinous tumors. Although MRI has traditionally relied on the criteria of size and morphology of lymph nodes to distinguish benign and malignant types and thus limiting it accuracy and potentially providing inaccurate staging information, there are other MRI parameters such as T2 signal intensity, dynamic gadolinium enhancement, MR spectroscopy and use of ultra-small superparamagnetic

iron oxide particles and lymphangiographic contrast agents that have greatly improved the accuracy of MRI in distinguishing benign from malignant nodes(42,43).

2.10.2 Computed Tomography (CT)

CT scans range from 3rd generation scans where both gantry and sensors rotate around the patient, to 6th generation machines with dual sources of x-rays and sensors arranged 90 degrees to each other. Fourth generation CT scan machines have a gantry producing a narrow beam of x-rays as it rotates around the body (Tomography). Fixed sensors opposite the gantry pick up varied radiation absorption since tissues vary in density. A computer converts these density values into cross-sectional images from which reconstruction and manipulation is possible into varying slices of coronal, axial, sagittal and 3D reconstruction.

Tumors of the head and neck are identified on CT based upon either anatomic distortion or specific tumor enhancement. In general, tumors enhance more than normal head and neck structures except for mucosa, extraocular muscles, and blood vessels. Compared with MRI, CT provides greater spatial resolution, can be performed with faster acquisition times (thereby virtually eliminating motion artifact), and is better at evaluating bone destruction. Modern multidetector CT technology allows scanning to be performed with slice thickness less than 1 mm. Slice thickness of 3 mm is generally optimal, while slice thickness greater than 5 mm does not offer sufficient spatial resolution. Images should be reconstructed and viewed in both soft tissue and bone windows. Dental amalgam can create severe beam hardening image artifacts that obscure image details in

the scan plane. This problem can be remedied by rescanning the obscured area with angulated gantry.

Evaluation of regional lymph nodes on CT primarily relies upon size criteria as well as the appearance of lymph nodes to differentiate involved from uninvolved lymph nodes. The use of size criteria alone results in frequent false-positive and false-negative assessment of regional nodes. CT is also highly sensitive for detection of extracapsular spread of tumor. Pathologic lymphadenopathy is usually defined radiologically as a node greater than 10 to 11 mm in minimal axial diameter or one that contains central necrosis. The choice of how a lymph node is measured is often controversial and reflects a tradeoff between sensitivity and specificity. In general, size criteria based on measurement of minimal axial diameter are considered the most accurate and effective, and probably the most reproducible. Other features that suggest pathological lymph nodes include rounded shape, loss of normal fatty hilum, increased or heterogeneous contrast enhancement, increased cortical thickness, lymph node clustering and sentinel lymph node location. Although CT is superior to physical examination, the use of size criteria and the presence of central necrosis are limitations that prevent detection of borderline-sized nodes, non-necrotic nodes, or extracapsular spread confined within the radiologically-defined margin of nodes. These cannot be differentiated by CT from reactive or normal nodes. This is an important issue since microscopic or occult nodal adenopathy is not unusual in head and neck cancer.

2.10.3 PET and integrated PET/CT

With PET, injected positron-emitting radionuclides, such as fluorine-18, are taken up by metabolically or functionally active tissues. Images are created by detecting these emissions by an array of detectors and then using reconstruction techniques to create a 3-dimensional image. The most commonly used agent is fluorodeoxyglucose (FDG), which is taken up into cells in different concentrations depending on the relative metabolism of different tissues. It is fairly specific for tumors because metabolic rates are very high in many tumors.

Positron emission tomography has intrinsically lower spatial resolution than other imaging modalities. In addition, it may be difficult to localize the anatomic location of the FDG uptake. These issues are addressed with integrated PET/CT imaging, in which PET and CT are performed sequentially during the same imaging session on a hybrid PET/CT scanner. The images are then coregistered using fusion software, enabling the physiologic data obtained on PET to be localized according to the anatomic CT images.

Historically, CT images obtained from integrated PET/CT scanners had lower spatial resolution compared with dedicated CT scanners. This problem is now being overcome by new generation of PET/CT scanners that offer volumetric CT capability. Positron emission tomography appears to be at least as sensitive and specific as CT and MRI in detecting primary head and neck tumors. A false negative is most likely seen in small lesions and in primary tumors located at pharyngeal lymphoid tissues with high background physiologic activity. Positron emission tomography is

superior to both CT and MRI for detecting regional nodal metastases, as well as distant metastases and second primary tumors. When used for the initial staging of head and neck cancer, integrated PET/CT imaging appears superior to CT, MRI, or PET.

2.10.4 Imaging centers

The imaging centers that most patients who met the inclusion criteria visited to have their radiological examination can be broadly divided into public and private centers. Kenyan public hospitals with MRI and CT scans include county referral hospitals equipped under the Managed Equipment Service (MES), Kenyatta National Hospital, Moi Teaching and Referral Hospital, National Spinal Injury Hospital, Mathari Teaching and Referral Hospital. Private centers around the study area included Vital Ray Health Solutions, German Medical Centre and Plaza Imaging. They use MRI and CT scan machines sourced from different suppliers and of different specifications. Positron emission tomography scans in Kenya are done either at Kenyatta University Teaching and Referral Hospital or Aga Khan University Hospital. The imaging centers are summarized in Table 2.6 and 2.7

Table 2. 6 MRI Imaging centers

MRI CENTRE	MANUFACTURER OF MRI MACHINE	TESLA (T)
Kenyatta National Hospital	Phillips (Ingenia)	3.0
Vital Ray Health Solutions	Toshiba	1.5
Plaza Imaging	General Electric	1.5
German Medical Centre	Siemens	1.5

Table 2. 7 CT Scan imaging centers

CT SCAN CENTRE	MANUFACTURER OF CT SCAN MACHINE	SLICE COUNT
Kenyatta National Hospital	Siemens	128
	Neusoft	64
Vital Ray Health Solutions	Toshiba	16
Plaza Imaging	Siemens	16
German Medical Centre	Siemens	16

CHAPTER THREE: MATERIALS AND METHODS

3.1 Study design

This was a cross-sectional study carried out over a five-month period from February to June 2023. Patients scheduled for neck dissection as part of treatment for OSCC &/OPSCC during this period were recruited for this study. Data was collected from images and reports of the radiological assessment of their cervical lymph nodes. After surgery, the researcher collected data from histology slides and reports of the histopathological assessment of the cervical lymph nodes. The radiological features and the histopathological features were compared. This census design was chosen due to the limited number of patients undergoing similar neck dissection every year (30 patients over a six-month period in the year 2022 at KNH)

3.2 Study area

The study was carried out at Kenyatta National Hospital (KNH). This was at the outpatient clinics (Dental and Ear, Nose and Throat -ENT), radiology and human pathology departments.

Kenyatta National Hospital is the largest national referral and teaching hospital in Kenya. It is located along Hospital Road in Upper hill area of Nairobi, the capital city of Kenya. It serves as a teaching hospital for the University of Nairobi (faculty of health sciences) and Kenya Medical Training College (KMTC). It also has collaborations with other organizations like the Kenya Medical Research Institute (KEMRI), National Radiation Protection Board, African Medical and

Research Foundation (AMREF) and more. Patients seen at this hospital come from the Great Lakes Region, Southern and Central Africa. The hospital has a bed capacity of 2,400 beds and attends an annual number of 949,000 inpatients and 800,000 outpatients annually. It has 50 wards, 24 out-patient clinics, 26 theatres, 82 ICU beds and an Accident & Emergency department. (44). In the year 2021, 45 patients underwent neck dissection for OSCC and OPSCC at KNH.

3.3 Study population

All patients with OSCC/OPSCC proven histologically by incisional biopsy, who had radiological assessment of cervical lymph node metastasis and who were scheduled to undergo neck dissection as part of treatment of the cancer at KNH were recruited. Those with recurrent disease, HIV and those who have had previous management for cancer (surgery, radiotherapy or chemotherapy) were excluded. The patients with OSCC/OPSCC seen at the department of oral & maxillofacial surgery of KNH range from 28-96 years with a mean age of 58 years. Majority are men (61.8%). Most patients are farmers and workers from the informal sector(9).

3.4 Sample size determination

Yamane formula (1967) was used because the population of patients who underwent neck dissection for OSCC/OPSCC in the previous year (2022) over a six-month period was small i.e., N= 30

n= $\frac{N}{1+N(e)^2}$

Where:

n= the sample size

N= the population size

e= the acceptable sampling error

Substituting:

n=$\frac{30}{1+30(0.05)^2}$

n=28

3.5 Sampling procedure

Census of all patients diagnosed with oral and oropharyngeal cancer undergoing neck dissection at KNH over a period of 5 months (February to June 2023). This method was chosen owing to the small number of patients who underwent neck dissection in the past i.e., 30 over a six -month period in 2022.

```
┌─────────────────────────────────────────┐
│ Patients with OSCC/OPSCC scheduled for   │
│ primary tumor excision + Neck dissection │
│ in theatre                               │
└─────────────────────────────────────────┘
                    ↓
          ┌───────────────────┐
          │ Recruitment and   │
          │ consenting        │
          └───────────────────┘
                    ↓
      ┌───────────────────────────────────┐
      │ Collection of data on radiological│
      │ features of cervical lymph nodes  │
      └───────────────────────────────────┘
                    ↓
          ┌───────────────────┐
          │ Patient undergoes │
          │ surgery as        │
          │ scheduled         │
          └───────────────────┘
                    ↓
      ┌───────────────────────────────────┐
      │ Collection of data on             │
      │ histopathological features of     │
      │ cervical lymph nodes              │
      └───────────────────────────────────┘
                    ↓
          ┌───────────────────┐
          │ Data analysis     │
          │                   │
          └───────────────────┘
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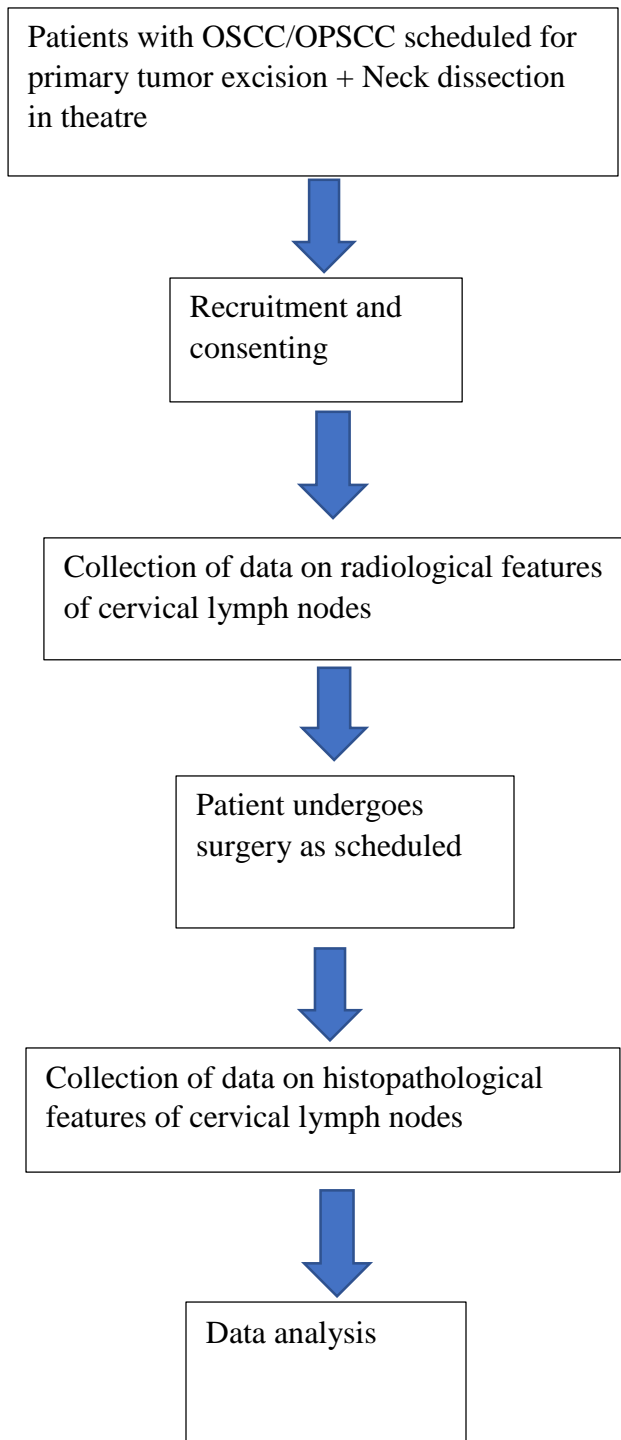
Figure 3. 1 Sampling procedure

3.6 Recruitment and consenting procedures

3.6.1   Inclusion criteria

1.   All incisional biopsy proven patients (in-patients or out-patients) with OSCC and OPSCC

2.   Patients with radiological examination of the neck (CT, MRI) with reports by radiologist

3.   Patients who were scheduled for surgery of the primary tumor and neck dissection

4.   Patients who gave appropriate informed and written consent for neck dissection and histopathological examination.

3.6.2   Exclusion criteria

1. Patients with recurrent disease or who had previously undergone management of the neck (surgery, radiotherapy, chemotherapy)

2. Patients with other potential causes of lymphadenopathy like Human Immunodeficiency Virus, Tuberculosis, Non-Hodgkin Lymphoma

3.7 Data collection procedure

Approval was sought from KNH-UoN Ethics and Research committee and KNH. Biopsy proven patients with OSCC/OPSCC who had radiological assessment of cervical lymph node metastasis and who were to undergo neck dissection as part of treatment of the cancer at KNH were recruited. Consent was taken. Data from images and reports of the radiological assessment of their cervical lymph nodes was collected on data sheets and put on MS Excel sheet. The researcher was present during surgery to ensure meticulous labelling of the lymph node samples. After surgery, data from

histology slides and reports of the histopathological assessment of the cervical lymph nodes was collected on data sheets and put on MS Excel sheet.

3.7.1   Approvals and consenting

Approval was sought from KNH-UoN Ethics and Research committee and KNH. Patients who met the inclusion and exclusion criteria were recruited. Consent was taken.

3.7.2   Radiological examination

As protocol, patients with OSCC or OPSCC were investigated by either CT or MRI. Both the images and the radiologists' reports were the source of data to be collected on radiological assessment. This data was collected on data sheets and transferred onto MS Excel sheet.
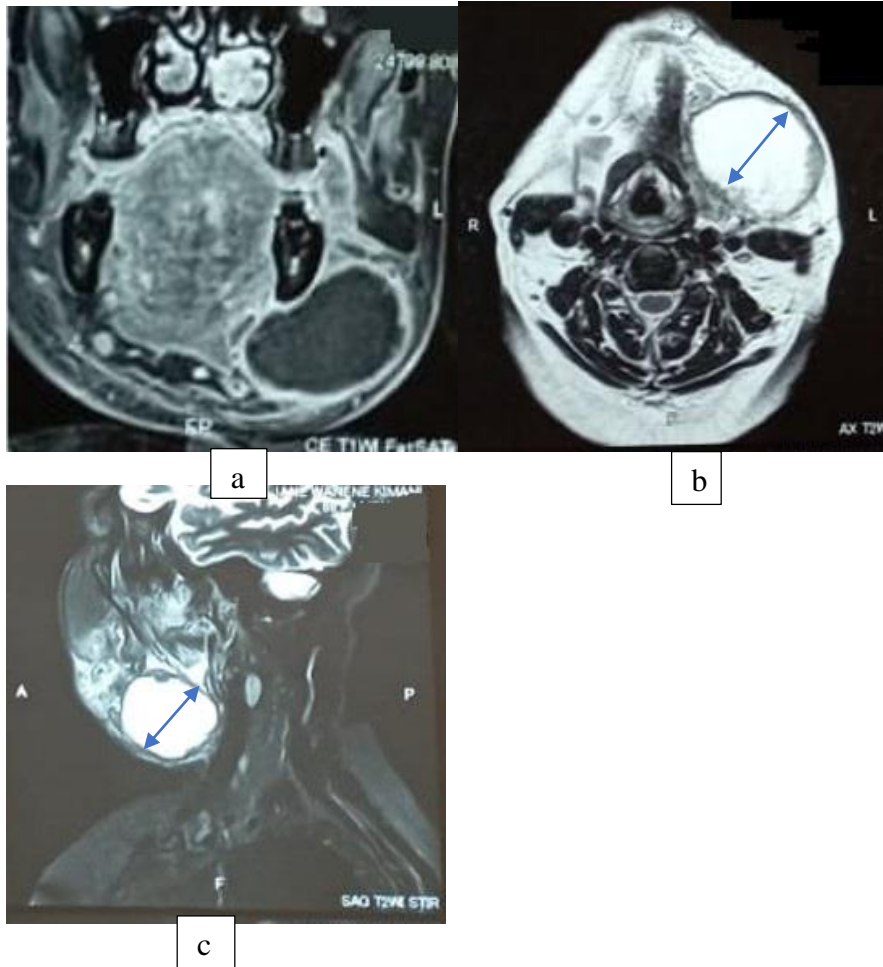
Figure 3. 2 Magnetic Resonance Imaging from the study showing a large necrotic node; a) Coronal Contrast enhanced T1-Weighted with fat saturation, b) Axial T2-Weighted, c) Sagittal T2-Weighted -Short-Tau Inversion Recovery
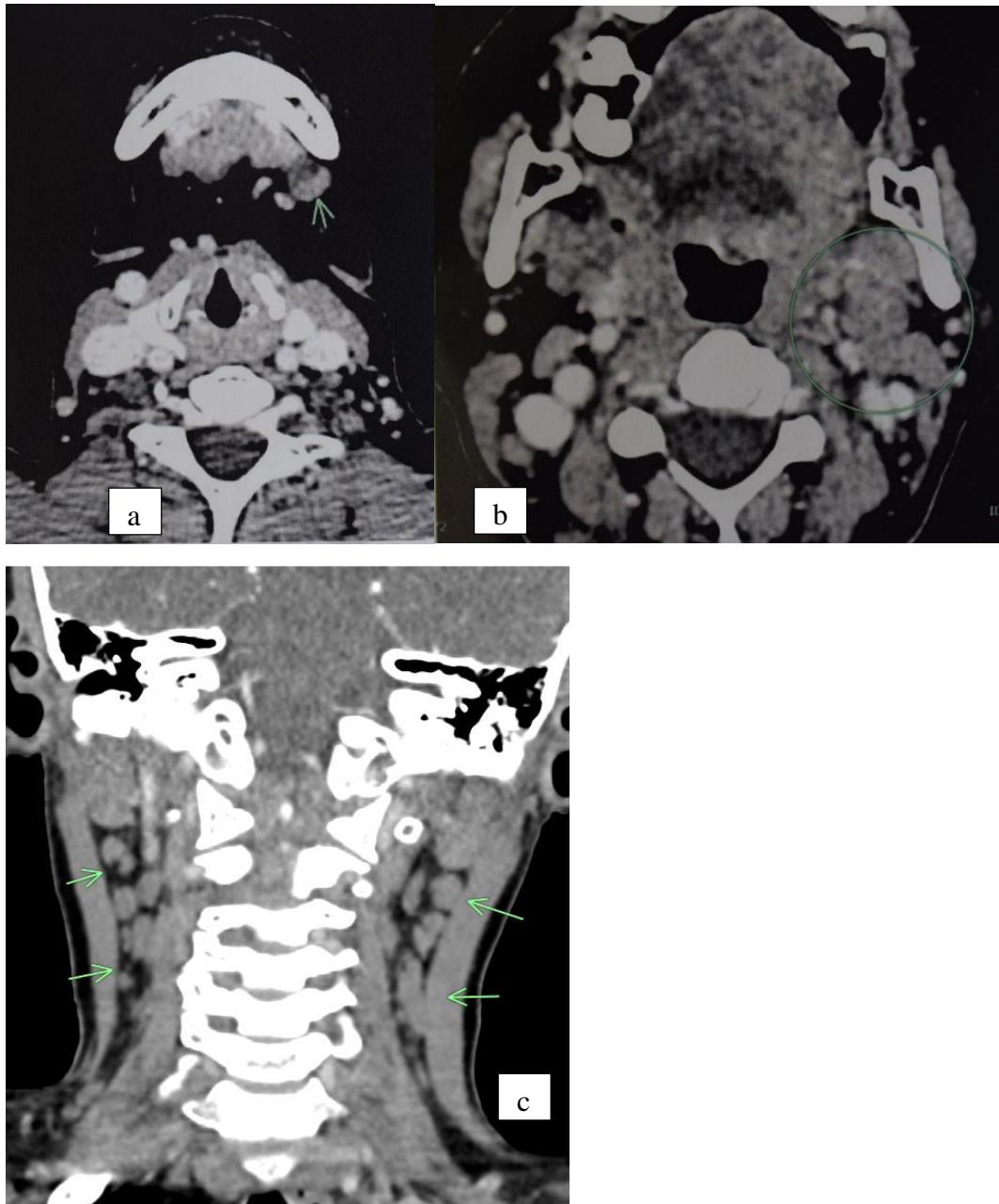
Figure 3. 3 CT scans from the study, soft tissue windows; a)- Axial view showing an enlarged node left level Ib. b) Axial view showing multiple enlarged and matted lymph nodes left level II. c)- Coronal view showing increased number of enlarged nodes level II, III, IV bilaterally

3.7.3   Histopathological examination

During surgery the neck dissection specimen from each cervical level were cautiously labeled and presented in a separate container with formalin preservative then sent to the Clinical Pathologist. The specimens were processed, stained with H&E (Hematoxylin and Eosin) stain and examined under light microscopy. The histology slides and reports by the pathologist were the source of the data on histopathological assessment. This data was collected on data sheets and put on MS Excel sheet.
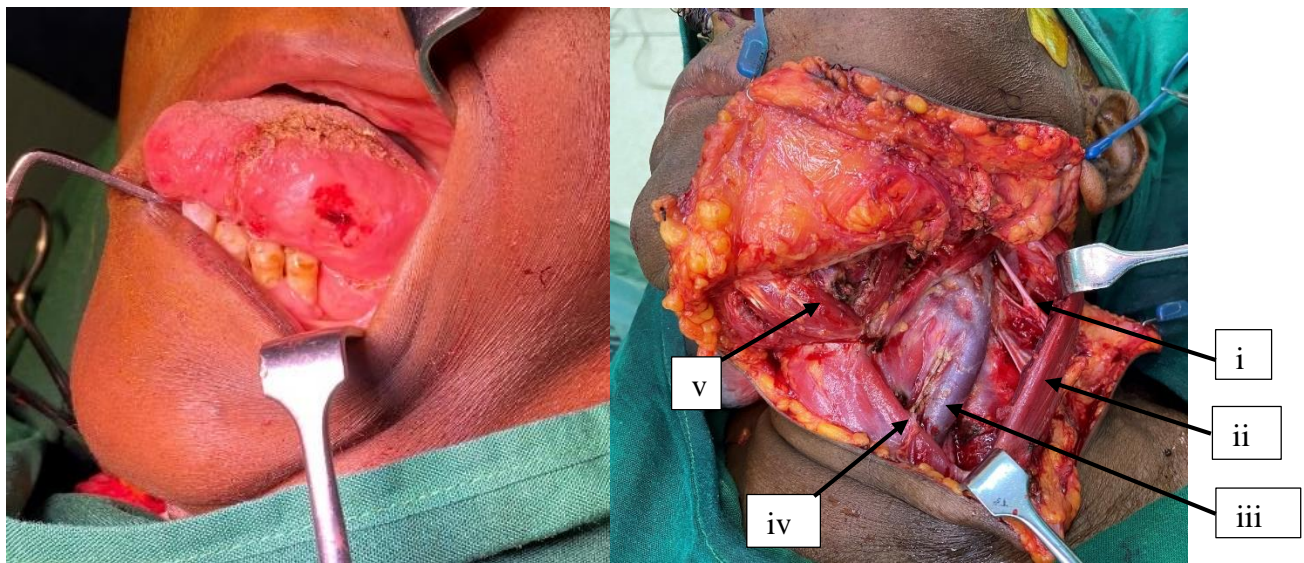
Figure 3. 4 Intraoperative images. a) OSCC left lateral border of the tongue, margins marked with diathermy b) After neck dissection (i-Spinal accessory nerve, ii-Sternocleidomastoid muscle, iii- Internal jugular vein, iv-Omohyoid muscle, v-anterior belly of digastric muscle
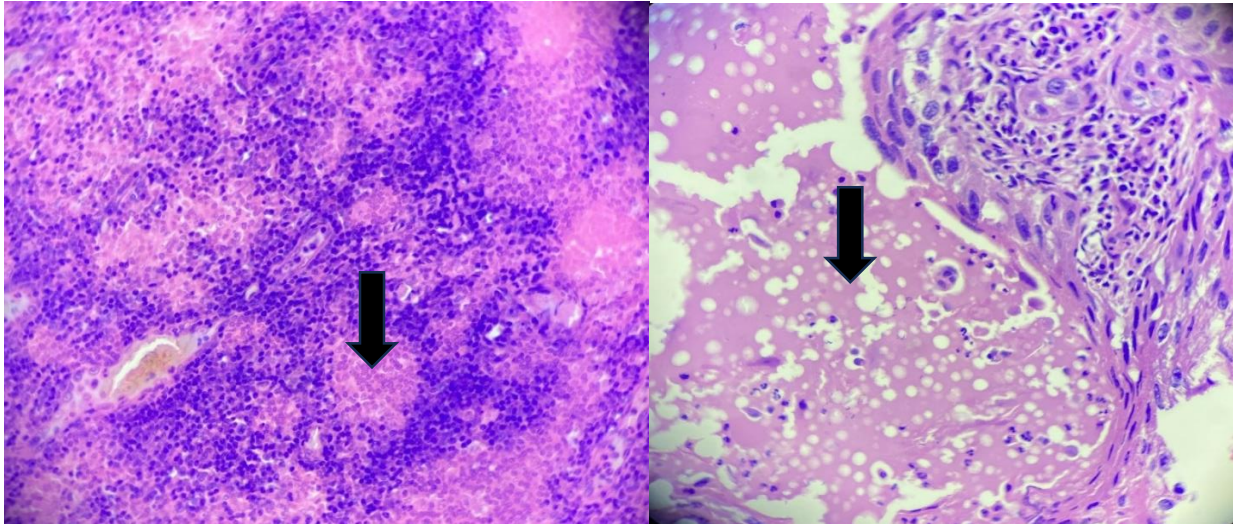
Figure 3. 5 Histopathological assessment-Nodal necrosis (X100 Magnification H&E)
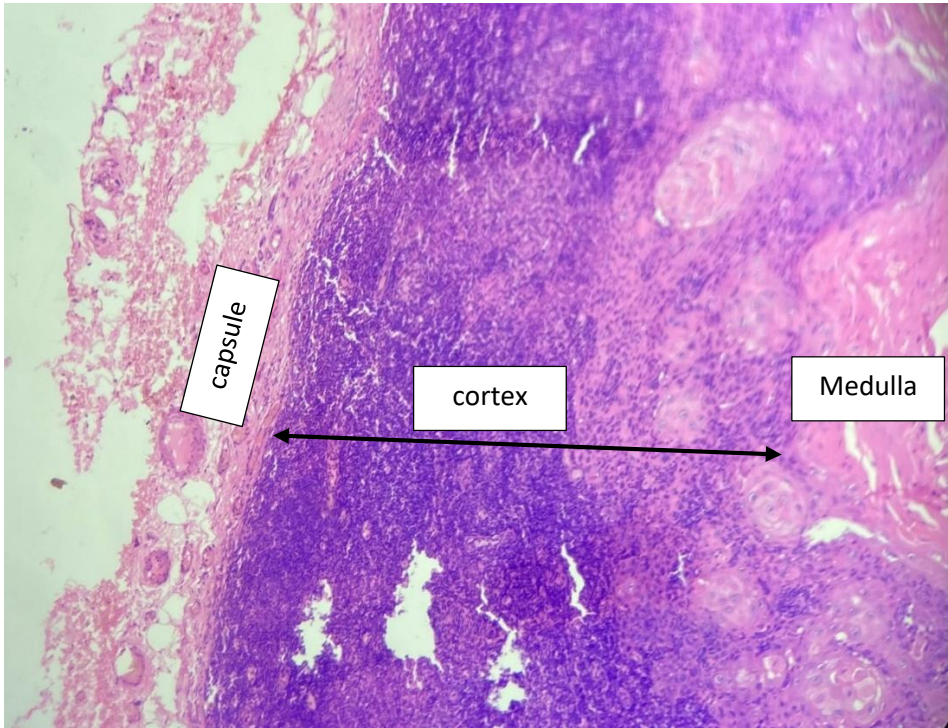
Figure 3. 6 Histopathological assessment- Thickened cortex. X100 Magnification H&E
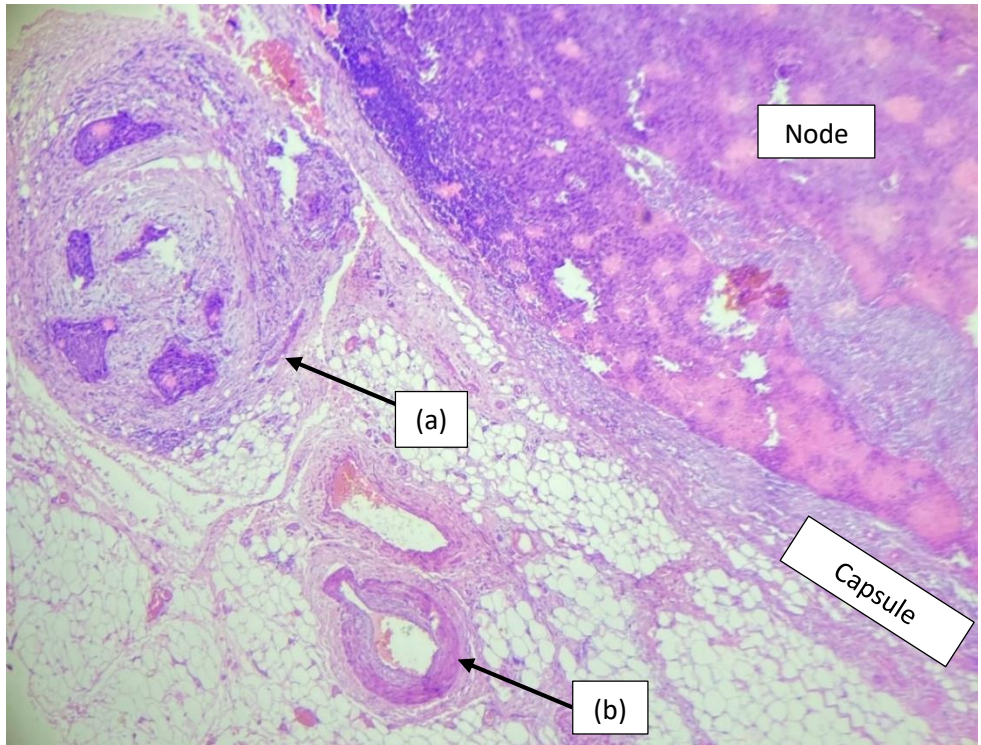
Figure 3. 7 Histopathological assessment- a) Extracapsular and b) Perivascular spread. X100 Magnification H&E
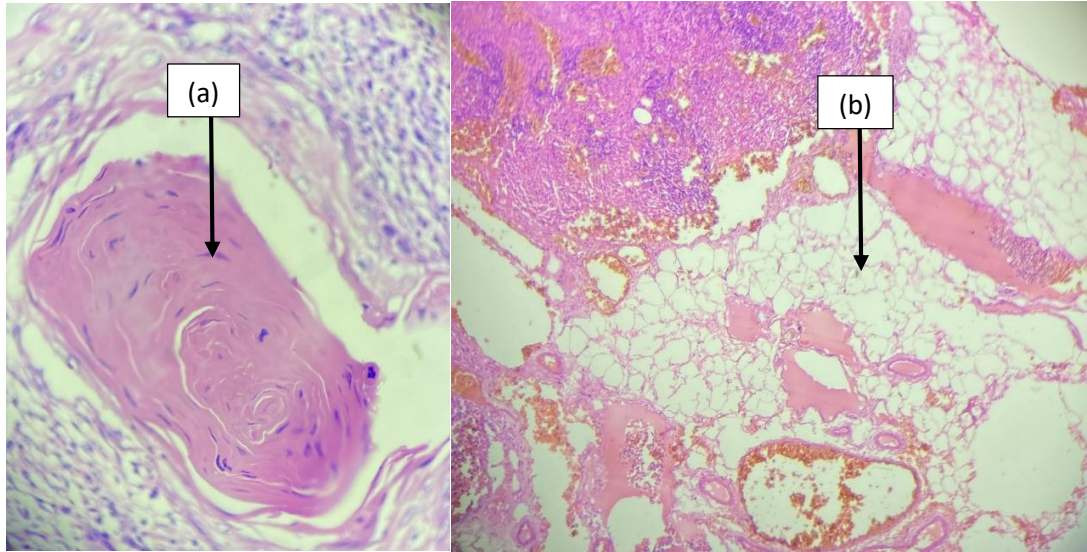
Figure 3. 8 Histopathological assessment- a) Keratin pearl, b) Fatty degeneration. X100 Magnification H&E

3.8 Data management and analysis

Data on clinical, radiological, and histopathological evaluation was analyzed using both descriptive and inferential statistical techniques. Inferential statistics was used to determine the agreement between radiological and histopathological assessments. Analysis was done using SPSS software, Version 25. Univariate analysis was used to calculate frequencies of socio-demographic characteristics, radiographic features & histological findings of cervical lymph nodes.

Bivariate analysis was used to determine the pattern of agreement between the radiological and histological diagnosis of cervical lymph nodes. Pattern of agreement, sensitivity and specificity of the various radiological examinations was calculated. Descriptive statistical techniques were used to summarize data on the sensitivity, specificity and pattern of agreement of radiological, and histopathological evaluation. The data was summarized into frequencies, percentages and means. The level of statistical significance was judged at 95% confidence interval, meaning that the value of $P < 0.05$ indicated that the agreement was statistically significant.

3.9 Ethical considerations

Approvals were obtained from the UoN Ethics Research Committee, Kenyatta National Hospital. Written consent was taken from the patients. Reports of radiological and histopathological assessment were accessed only within KNH and retained within the patients' files. The electronic gadgets with the collected data were password protected. The entire research process complied with strict patient confidentiality and did not collect patient names or any other potential

identifiers. Patients were usually reviewed in the clinics by different consultants and scheduled to be operated on different days of the week. Residents joined the consultants in clinics and theatre as part of training. Therefore, there was no bias on clinical management of the patients by the researcher who was also a resident in training.

3.10   Dissemination of findings

After the approval of the research report, the researcher shared the report with UoN Ethics Research Committee and Kenyatta National Hospital, to be held in the libraries and other repositories. Journal papers, originating from the final report, will be submitted to relevant peer-reviewed journals for publications.

3.11   Study limitations

The researcher relied on radiologists' report on the status of the cervical lymph nodes, this could result in inter-observer variability between radiologists. To minimize this, the radiological images and reports were assessed by one of the supervisors who is a consultant radiologist.

The surgeries were performed by different surgeons thus raising the possibility of different qualities of neck dissection. This was mitigated by having the principal investigator present during all the neck dissections and confirming the neck dissections are done according to ASCO guidelines (38)

The researcher relied on the printed image films from different CT scan and MRI machines supplied by different manufacturers with different specifications. Thus, the quality of radiological examination could differ and ultimately affect the results of the study

The sample population was small. The principal investigator limited this by collecting data from consecutive patients scheduled for neck dissection in both Maxillofacial and ENT departments of KNH.

CHAPTER FOUR: RESULTS

4.1 Socio-demographic Characteristics

A total of 30 patients were included in the study. Of these, 16 (53.3%) and 14 (46.7%) were males and females respectively (M:F=1.14:1). The sample age ranged from 15 – 77 years with a mean age of 58.1 years ($\pm$12.5 SD), a median of 60.5 and a mode of 43 years.

4.2 Distribution of Primary Tumor and Lymph nodes

The patients' tumor characteristics were evaluated based on site of primary lesion, sub sites, histological diagnosis and histological grading. Evaluation of the site of primary lesion showed that 28(93.4%) were in the oral cavity, 1(3.3%) affected both oral cavity and oropharynx while 1(3.3%) was in the oropharynx. Within the sub sites, majority of the patients, 13(28.9%) had tumor in the anterior tongue, followed by 7(15.6%) for both floor of the mouth and buccal mucosa sub sites. The patients' histological diagnosis showed that majority, 29 (96.7%) had OSCC with only 1(3.3%) having OPSCC. The evaluation of histological diagnosis showed that 18(60.0%) were well differentiated, 8(26.7%) were moderately differentiated while 4(13.3%) were poorly differentiated. The site of the primary lesion, sub sites, histological diagnosis and histological grading are summarized in Table 4.1

Table 4. 1 Distribution of primary tumors.

Characteristics		n	%
Site of Primary Lesion	*Oral Cavity*	28	93.4
	Oral Cavity & Oropharynx	1	3.3
	Oropharynx	1	3.3
	Total	30	100.0
Sub sites	*Mucosal lips*	3	6.7
	Anterior tongue	13	28.9
	Floor of the mouth	7	15.6
	Buccal mucosa	7	15.6
	Mandibular alveolar ridge	3	6.7
	Maxillary alveolar ridge	1	2.2
	Hard palate	3	6.7
	Retro molar trigone	2	4.4
	Base of the tongue	2	4.4
	Tonsillar complex	2	4.4
	Soft palate	2	4.4
	Total	45	100.0
Histological Diagnosis	*OSCC*	29	96.7
	OPSC	1	3.3
	Total	30	100.0
Histological Grading	*Well differentiated*	18	60.0
	Moderately differentiated	8	26.7
	Poorly differentiated	4	13.3
	Total	30	100.0

Table 4. 2 Distribution of the number of identified and involved lymph nodes

Case	T Staging	Total number of Lymph Nodes	
		Identified histologically	Involved Histologically
1	T4a	5	3
2	T4a	25	2
3	T3	15	0
4	T2	17	0
5	T3	8	0
6	T1	1	1
7	T4a	2	2
8	T2	10	1
9	T4b	14	2
10	T3	12	0
11	T4a	10	1
12	T4a	4	0
13	T1	5	0
14	T4a	27	3
15	T1	16	0
16	T4a	4	0
17	T4a	7	1
18	T4a	1	1
19	T2	13	0
20	T2	16	0
21	T4a	10	8
22	T4a	14	0
23	T1	4	0
24	T2	12	0
25	T2	16	6
26	T4a	23	0
27	T3	19	5
28	T4a	11	7
29	T4a	14	10
30	T4a	8	6
Total	30	343	59

A paired t-test was conducted to compare the number of lymph nodes dissected out and the number of metastatic lymph nodes confirmed on histology. There was a statistically significant difference in the number of lymph nodes dissected out (M=11.43, SD=6.83) and the number of metastatic lymph nodes (M=1.97, SD=2.81) for the patients; t (29)=7.349, $p < 0.001$. The effect size was large, with a Cohen's d of 1.81 indicating that more than 96% of the number of lymph nodes involved would be below the average number of lymph nodes dissected out. The comparison of the number of lymph nodes identified and involved are summarized in Tables 4.2 and 4.3.

Table 4. 3 Comparison of the number of lymph nodes identified and involved.

Number of Lymph Nodes	n	Mean	SD	95% Confidence Interval of the Difference		t	df	P
				Lower	Upper			
Histologically identified	30	11.43	6.83	6.83	12.10	7.349*	29	<.001
Histologically positive	30	1.97	2.81					

Paired t-test was applied.
*. The mean difference is statistically significant at the level of .05.

The number of histologically identified and histologically positive lymph nodes are summarized in Figure 4.1, according to levels.
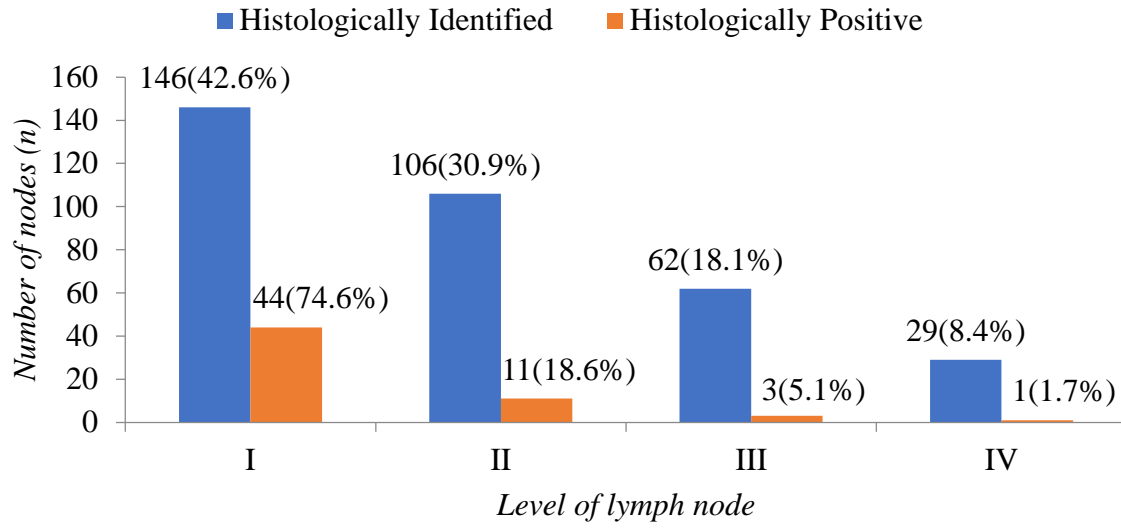
Figure 4. 1 Number of histologically identified and involved lymph nodes by levels.

4.3 Radiological assessment of cervical lymph nodes in OSCC/OPSCC

Evaluation of patient records showed that the patients' imaging modalities were CT scan and MRI in 22(73.3%) and 8(26.7%) patients respectively. Out of the 30 patients, 21(70.0%) had suspicious nodes and 9 (30.0%) patients did not exhibit suspicious nodes. An analysis of the 21 patients with suspicious nodes showed level I was the most suspicious with 18(85.7%) patients followed by level II in 10(47.6%) patients and level III in 2(9.5%) patients. Suspicious nodes were seen in more than one cervical level in 8(38.1%) patients. Characterization of the radiological features of the 38 suspicious nodes showed 28(73.6%) nodes had diameters greater than 9mm, 2(5.3%) nodes had a round shape, 6(15.8%) nodes had abnormal hilum architecture and 2(5.3%) nodes were matted. The lymph node size ranged from 0.0 – 62 mm with a mean size of 12.7 mm ($\pm$13.3 *SD*), a median of 11.5 mm and a mode of 0.0 mm. Some of the patients exhibited more than one evaluation criteria. The radiological nodal categorization had 9(30.0%) patients with cN0 followed by 8(26.7%) and 7(23.3%) patients with cN2b and cN1 respectively. The radiological features of the patients are summarized in Table 4.4 while the distributions of suspicious nodes by levels are summarized in Figure 4.2.

Table 4. 4 Summary of radiological assessment.

Characteristics		n	%
Imaging Modality	CT Scan	22	73.3
	MRI	8	26.7
	Total	30	100
Patients with Suspicious Nodes	No	9	30.0
	Yes	21	70.0
	Total	30	100
Levels with suspicious nodes of the 21 patients	Level I	18	85.7
	Level II	10	47.6
	Level III	2	9.5
Patients with multiple levels of suspicious nodes	One level	13	61.9
	Two levels	7	33.3
	Three levels	1	4.8
	Total	21	100
Radiological features of suspicious Nodes	Nodes > 9mm in Diameter	28	73.6
	Round Shape Node	2	5.3
	Abnormal Hilum Architecture	6	15.8
	Matted Nodes	2	5.3
	Total	38	100
Radiological Nodal Category	N0	9	30.0
	N1	7	23.3
	N2a	1	3.3
	N2b	8	26.7
	N2c	3	10.0
	N3a	1	3.3
	N3b	1	3.3
	Total	30	100
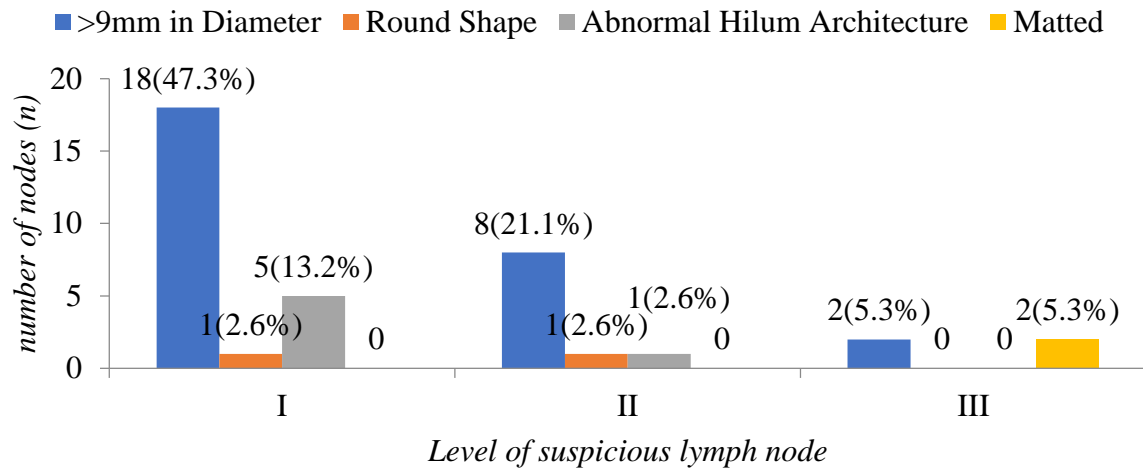
Figure 4. 2 Distribution of radiological features of suspicious nodes by levels.

4.4 Histopathological assessment of cervical lymph nodes in OSCC/OPSCC

Evaluation of the labelled cervical nodal levels that were submitted for histopathology showed that all 30(100%) patients had their level I lymph nodes dissected out. Level II nodes were dissected out in 25(83.3%) patients while 20(66.7%) had their level III nodes dissected. Level IV was the least dissected (11;36.7% patients). A total of 343 lymph nodes were identified, stained using Hematoxylin and Eosin stain then analyzed using light microscopy. Evaluation of the number of nodes dissected out per level showed level I had the most nodes, 146 (42.6%), followed by level II with 106(30.9%), level III with 62(18.1%) nodes Level IV had 29(8.4%) nodes identified.

Out of the 30 patients, 16(53.3%) had tumor spread to the cervical lymph nodes, while 14(46.7%) of the patients did not exhibit any lymph node involvement. Analysis of the 16 patients with metastatic nodes showed 14 (87.5%) had clinically suspicious nodes but 2 (12.5%) had clinically negative nodes prior to surgery. Of the 16 (53.3%) histological positive cases, the most common Tumor (T) categorization was T4a with 11(68.8%) cases followed by T3 with 2(12.5%) cases while T1, T2, and T4b had 1(6.3%) case each. The distribution of Tumor (T) categorization among the histologic positive cases is summarized in Figure 4.3.

Metastatic lymph nodes identified were 59. Most of them were in level I (44;74.6% nodes), followed by level II 11(18.6%), while level III and level IV had 3(5.1%) nodes and 1(1.7%) node, respectively. On characterization of the 59 involved lymph nodes, 30(50.8) nodes had abnormal hilar architecture, 24(40.7%) nodes were greater than 9mm in diameter, 5(16.7%) nodes were

matted. The distribution of the metastatic nodes per criteria and cervical level is summarized in Figure 4.4

The histological nodal categorization had 14(46.7%) patients at pN0 followed by 6(20.0%) patients staged pN3b. pN1, pN2b and pN2c had 3(10.0%) patients each. Only 1(3.3%) patient was staged pN3a. The histological features of the patients are summarized in Table 4.5

Table 4. 5 Summary of histological assessment.

Nodal Characteristics		n	%
Level of Neck Dissection	Level I	30	100
	Level II	25	83.3
	Level III	20	66.7
	Level IV	11	36.7
Nodes identified Histologically per Level	Level I	146	42.6
	Level II	106	30.9
	Level III	62	18.1
	Level IV	29	8.4
	Total	343	100
Patients with metastatic Nodes	Yes	16	53.3
	No	14	46.7
Levels with metastatic nodes of the 16 patients	Level I	16	100.0
	Level II	7	43.8
	Level III	3	18.8
	Level IV	1	6.3
	Level I	44	74.6
	Level II	11	18.6

Number of metastatic Lymph Nodes per level	Level III	3	5.1
	Level IV	1	1.7
	Total	59	100
Histological features of metastatic Nodes	Abnormal Hilum Architecture	30	50.8
	Nodes > 9mm in Diameter	24	40.7
	Matted Nodes	5	8.5
	Total	59	100
Extra nodal Extension among the 16 patients with nodal metastasis	Yes	6	37.5
	No	10	62.5
	Total	16	100
Pathological Nodal categories	N0	14	46.7
	N1	3	10.0
	N2b	3	10.0
	N2c	3	10.0
	N3a	1	3.3
	N3b	6	20.0
	Total	30	100
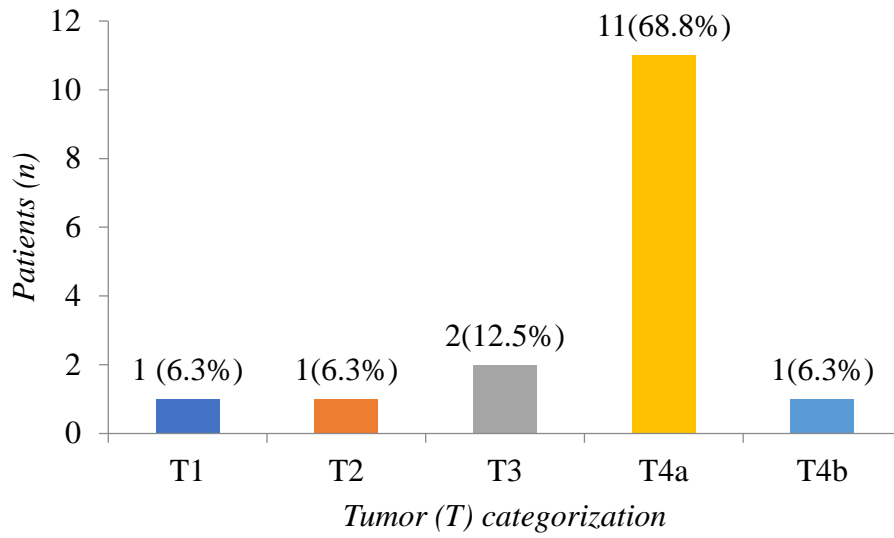
Figure 4. 3 Distribution of Tumor (T) categorization among the histological positive cases.
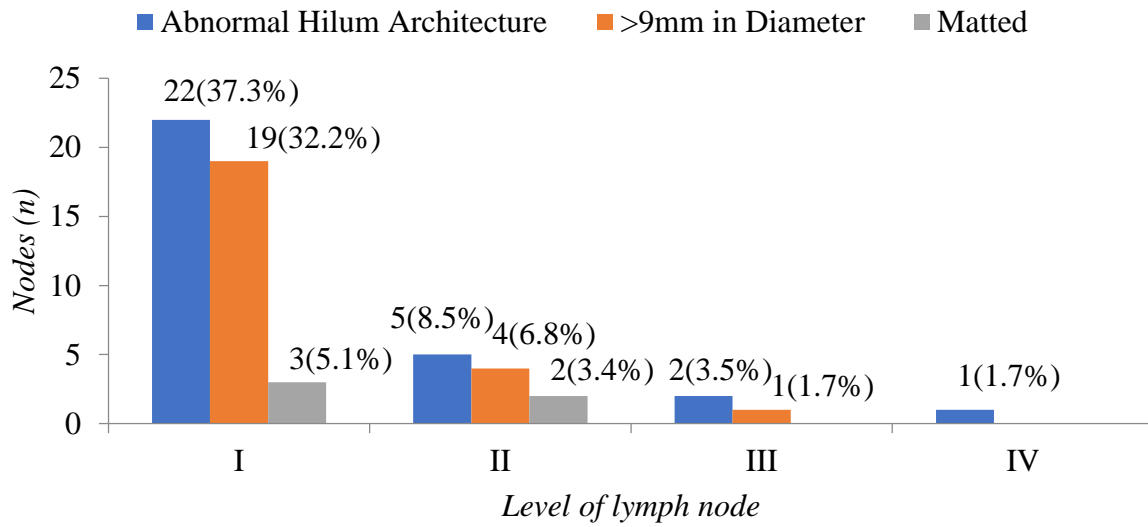
Figure 4. 4 Distribution of metastatic nodes by criteria and cervical levels

4.5 Pattern of Agreement between radiological and histopathological assessment of cervical lymph nodes in OSCC/OPSCC

Due to the small sample size of 30, Cohen's Kappa (κ) test was used to determine the patterns of agreement based on matched (paired) cases for the study. Cohen's kappa was run to determine the pattern of agreement between patients with suspicious nodes and patients with involved lymph nodes. Cohen suggested the Kappa result be interpreted as follows: values ≤ 0 as indicating no agreement and 0.01–0.20 as none to slight, 0.21–0.40 as fair, 0.41– 0.60 as moderate, 0.61–0.80 as substantial, and 0.81–1.00 as almost perfect agreement. There was fair agreement between the two groups of patients, $\kappa = 0.384$, $p < .05$. The pattern of agreement between patients with suspicious nodes and patients with involved lymph nodes is summarized in Table 4.6.

Table 4. 6 Pattern of agreement between patients with clinically suspicious nodes and patients with histological confirmation of involved lymph nodes.

| | | | Patients with suspicious node | | | | |
			No	Yes	Total	Kappa (κ)	p
Patients with involved lymph nodes	No	n	7	7	14	0.384*	.025
		%	23.3	23.3	46.7		
	Yes	n	2	14	16		
		%	6.7	46.7	53.3		
Total		n	9	21	30		
		%	30.0	70.0	100.0		

 Cohen's Kappa (κ) test was applied.
*. Cohen's Kappa (κ) is significant at the level .05.

Cohen's κ was run to determine the pattern of agreement between levels of suspicious nodes and levels of involved lymph nodes. There was a moderate agreement between the two groups of levels of nodes, $\kappa = 0.512, p < .05$. The pattern of agreement between clinically suspicious and histologically confirmed involved lymph nodes is summarized in Table 4.7.

Table 4. 7 Pattern of agreement between cervical levels with suspicious and involved lymph nodes.

Lymph Nodes			Involved			Total	Kappa (κ)	p
			Level I	Level II	Level III			
Suspicious	Level I	n	8	1	1	10	0.512*	<.001
		%	57.1	7.1	7.1	71.4		
	Level II	n	0	1	1	2		
		%	0.0	7.1	7.1	14.3		
	Level III	n	0	2	0	2		
		%	0.0	14.3	0.0	14.3		
	Total	n	8	4	2	14		
		%	57.1	28.6	14.3	100.0		

Cohen's Kappa (κ) test was applied.
*. Cohen's Kappa (κ) is significant at the level .05.

Cohen's κ was run to determine the pattern of agreement between radiological and pathological nodal categories. There was a substantial agreement between the two groups of nodal categories, $\kappa = 0.629, p < .05$. The pattern of agreement between radiological and pathological nodal categories is summarized in Table 4.8

Table 4. 8 Pattern of agreement between radiological and pathological nodal categories.

Nodal categories			Histological							Kappa (κ)	p
			N0	N1	N2b	N2c	N3a	N3b	Total		
Radiological	N0	n	9	0	0	0	0	0	9	0.629*	.009
		%	30.0	0.0	0.0	0.0	0.0	0.0	30.0		
	N1	n	4	3	0	0	0	0	7		
		%	13.3	10.0	0.0	0.0	0.0	0.0	23.3		
	N2a	n	1	0	0	0	0	0	1		
		%	3.3	0.0	0.0	0.0	0.0	0.0	3.3		
	N2b	n	0	0	3	0	0	5	8		
		%	0.0	0.0	10.0	0.0	0.0	16.7	26.8		
	N2c	n	0	0	0	3	0	0	3		
		%	0.0	0.0	0.0	10.0	0.0	0.0	10.0		
	N3a	n	0	0	0	0	1	0	1		
		%	0.0	0.0	0.0	0.0	3.3	0.0	3.3		
	N3b	n	0	0	0	0	0	1	1		
		%	0.0	0.0	0.0	0.0	0.0	3.3	3.3		
	Total	n	14	3	3	3	1	6	30		
		%	46.7	10.0	10.0	10.0	3.3	20.0	100.0		

Cohen's Kappa (κ) test was applied.
*. Cohen's Kappa (κ) is significant at the level .05.

4.5 Sensitivity, Specificity, False Positives and False Negatives of Radiological Investigations

We compared the sensitivity, specificity, false positives and false negatives of the two diagnostic tests (MRI and CT scan) with the histopathological results as the gold standard. Evaluation of the MRI results showed a sensitivity (true positive) rate of 100.0%, a specificity (true negative) rate of 60.0%, a false positive rate of 40.0% and a false negative rate of 0.0%. A McNemar's exact test determined that the difference in the proportions of MRI positive results and histological results was not statistically significant, $p = 0.500$.

Evaluation of the CT Scan results showed a sensitivity (true positive) rate of 83.3%, a specificity (true negative) rate of 44.4%, a false positive rate of 55.6% and false negative rate of 16.7%. A McNemar's exact test determined that the difference in the proportions of CT scan positive results and histological results was not statistically significant, $p = 0.453$.

A comparison between the two imaging modalities showed that there was a difference of 16.7% sensitivity rate between MRI (100.0%) and CT scan (83.3%). A McNemar's exact test determined that the difference in the proportion of positive radiological results and histological results was not statistically significant, $p = 0.180$.

The sensitivity, specificity, false positives and false negatives of the radiological investigations are summarized in Table 4.9

Table 4. 9 Sensitivity, specificity, false positives and false negatives of the radiological investigations.

Diagnostic Tests	Radiological Results		Histological Results			McNemar's test	
			Negative	Positive	Total	n	p
MRI	Negative	n	3	0	3	9	0.500
		%	60.0%	0.0%	33.3%		
	Positive	n	2	4	6		
		%	40.0%	100.0%	66.7%		
	Total	n	5	4	9		
		%	100.0%	100.0%	100.0%		
CT Scan	Negative	n	4	2	6	21	.453
		%	44.4%	16.7%	28.6%		
	Positive	n	5	10	15		
		%	55.6%	83.3%	71.4%		
	Total	n	9	12	21		
		%	100.0%	100.0%	100.0%		

A McNemar's exact test was applied.

CHAPTER FIVE: DISCUSSION, CONCLUSIONS AND RECOMMENDATIONS

5.1 Discussion

The aim of this study was to investigate the agreement between radiological, and histopathological assessment of cervical lymph nodes in patients with OSCC and OPSCC undergoing neck dissection at KNH. Thirty consecutive patients underwent neck dissection of which 343 cervical lymph nodes were identified and analyzed histologically under light microscopy (hematoxylin and eosin staining).

5.1.1 Radiological assessment of cervical lymph nodes in OSCC/OPSCC

This study found that CT scan was the most common radiological modality requested for assessing cervical lymph node metastasis. This was similar to other studies by Horváth et al and Thoenissen et al (14,45). This bias towards CT scan may be partly due to its availability, relative affordability and less taking time compared to MRI.

Approximately 30% of the patients did not have radiological evidence of cervical lymph node metastasis (cN0) but still underwent neck dissection to rule out occult metastasis. Previous studies have shown the prevalence of this prophylactic neck dissection to range from 31% to 60% (5,7,14,46,47). Elective neck dissection is supported by evidence of occult metastasis from previous studies(3,7,32).

Cervical level I had the greatest number of suspicious lymph nodes. This was similar to a prospective study by Narayana et al (12) of 24 patients which found level I (combined Ia and Ib) to be the most prevalent suspicious cervical level. It is well demonstrated that level I has the most

sentinel lymph nodes for primary tumors located in the floor of the mouth(48). Thus, meticulous clinical assessment of level I is very important.

In this study, the most common radiological feature of suspicious lymph nodes identified was an enlarged node of more than 9mm in diameter. Most studies advocate for assessment criteria based on a combination of nodal size, architecture and signs of extra nodal spread like matted nodes(8,33,34). Relying on size criteria for diagnosis of clinical cervical lymph node metastasis reduces the accuracy of CT scan to 45% compared to 95-100% accuracy when based on central necrosis(37). This aspect is important in this study given that calculation of sensitivities and specificities was one of the objectives.

The most frequent clinical nodal categories in this study were cN2b and cN1. This differed from a German retrospective study of 242 patients by Voss et al in 2022 which found cN1 to be the most prevalent clinical nodal category (46). The higher nodal categorization in this current study could be due to the higher number of patients with higher T categorization. It could also be due to factors associated with delays in diagnosis of oral cancer, especially in developing countries(49).

5.1.2 Histopathological assessment of cervical lymph nodes in OSCC/OPSCC

In the current study, level I had the highest number of positive lymph nodes confirmed on histology. Several previous studies found similar results (6,7,47,50). Thoenissen et al(51) found a near equal prevalence between level I and II. On the other hand, Nithya et al(52), when looking specifically at carcinoma of the tongue, found level II to be most commonly involved. Level I and

II are known sentinel lymph nodes of primaries from the oral cavity(48). These levels have to be thoroughly dissected out during neck dissection.

Almost half the patients who underwent neck dissection in the current study did not have cervical lymph node metastasis. Previous studies support this finding (7,9,47,52,53). In contrast, Qiao et al and Mehta et al in retrospective studies found a lower prevalence of 30% and 20% respectively(5,6). As demonstrated by Kligerman et al in a randomized controlled trial of 67 patients with stage 1 and 2 OSCC of the floor of the mouth and tongue, survival rate is better when elective neck dissection is done(40).

In this study, the most common histopathological feature of positive lymph nodes was abnormal hilum architecture. Pandeshwar et al found most metastatic cervical lymph nodes to have central necrosis. Presence of tumor distorts the architecture of the lymph node by causing necrosis, deposition of keratin pearls, among others. Most of these architectural changes can be seen on radiological examination and inform their assessment and subsequent clinical staging(47).

A third of all the positive nodes in this study had extra nodal extension. The prevalence of extra nodal extension in other studies ranges from 24% to 45% (46,50,53). Extra nodal extension lowers the prognosis in OSCC(54). It is recommended that adjuvant chemotherapy be administered after neck dissection in patients with extra capsular spread(38).

The most prevalent pathological nodal category in this study was pN3b. This was similar to studies by Rabie et al and Voss et al (46,53). This however contrasted to the study by Thoenissen et al(51) who found N1 and N2b to be most prevalent. N3b was introduced as part of TNM staging in the

AJCC 8th edition of 2018 and may not be captured in research done prior to 2018. (30). N3b denotes extra nodal extension and has poor prognosis(54). AJCC recommends adjuvant chemotherapy for N3b(30).

5.1.3 Pattern of agreement between radiological and histological assessment of cervical lymph nodes in OSCC/OPSCC

In this study, there was a fair agreement between patients with clinically suspicious nodes and the patients with histologically confirmed nodal metastasis. This low pattern of agreement could be due to the overreliance on size criteria in identifying suspicious nodes on radiology. The level of agreement increased to moderate when the unit of comparison was the cervical nodal level. The agreement increased to substantial when the comparison was between clinical (cN) and pathological (pN) nodal categories.

This suggests that ultimately, the clinical (radiological) nodal assessment in TNM staging, which considers a combination of size, numbers, laterality and extra nodal extension, is an effective tool in predicting lymph node metastasis

5.1.4 Sensitivity and specificity of radiological investigations in diagnosis of cervical lymph node metastasis

In this study, CT had a sensitivity (true positive) of 83.3%. This was within the range of 52% to 83% found in other similar studies. However, the 44.4% specificity of CT scan in this study was lower than the range of 68%-98% from other studies(8,13,33,34,45). A common factor in the studies by Suryavanshi et al(8), Sumi et al(33) and Saafan et al(34) was their use of three or more

criteria in assessing cervical lymph node metastasis (Central necrosis with peripheral enhancement, conglomeration of three or more lymph nodes and short axial diameter size criteria) The lower ability to exclude metastasis (specificity) in this study could be due to the overreliance on the size criteria. This could in turn contribute to overtreatment of the neck.

The sensitivity (true positive) of MRI in this study was higher at 100%. The range observed in other studies was between 66%-81%. On the other hand, the specificity of MRI in this study was 60%. This was lower than other studies which ranged from 68% to 80% (13,45). The wide variation in sensitivity and specificity of MRI in this study could be due to the smaller number of patients who had MRI as their radiological investigation before surgery.

In this study, the false positive rates were 55.6% and 40% for CT and MRI respectively (cumulatively 50% false positive for radiological assessment). This implies approximately half of the patients without metastatic nodal disease were found to have been falsely categorized as positive on radiological assessment. Other studies have shown false positive rates of 2%-32% from radiological assessment. The relatively higher false positive rate in this study correlates to the lower specificity of CT and MRI found. On the other hand, the false negative rates in this study were 16.7% for CT and none for MRI. This is similar to previous studies which found a false negative rate of 17%-48%(8,13,33,34,45).

Our study has a few limitations. First, the sample size was relatively small. However, this was similar to other cross sectional studies where data was collected before and after surgery (8,12). Secondly, there was possibility of bias in the reporting of the radiological images. This was

mitigated by having an independent radiologist re-assess the radiological images for inter observer variability. Thirdly, the surgeries were performed by different surgeons thus raising the possibility of different qualities of neck dissection. This was mitigated by having the principal investigator present during all the neck dissections and confirming the neck dissections are done according to ASCO guidelines (38)

5.2 Conclusion

The most common radiological feature of suspicious lymph nodes identified was an enlarged node of more than 9mm in diameter while the most common histopathological feature of positive lymph nodes was abnormal hilar architecture. There was a substantial agreement between radiological and histopathological assessment of cervical lymph nodes in patients with OSCC/OPSCC. MRI and CT scan had higher sensitivity (true positives) but lower specificity (true negatives).

5.3 Recommendations

Magnetic Resonance Imaging (MRI) may be the better imaging for assessing loco-regional spread of OSCC/OPSCC in our setup in comparison to CT scan thus surgeons should request for more MRI. However, there is need to conduct another study with a larger sample size.

REFERENCES

1. Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, et al. Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. CA Cancer J Clin. 2021 May;71(3):209–49.

2. SEER [Internet]. [cited 2022 Sep 20]. Cancer of the Oral Cavity and Pharynx - Cancer Stat Facts. Available from: https://seer.cancer.gov/statfacts/html/oralcav.html

3. Norling R, Buron BMD, Therkildsen MH, Henriksen BM, von Buchwald C, Nielsen MB. Staging of Cervical Lymph Nodes in Oral Squamous Cell Carcinoma: Adding Ultrasound in Clinically Lymph Node Negative Patients May Improve Diagnostic Work-Up. PLoS ONE. 2014 Mar 20;9(3):e90360.

4. Tomita H, Yamashiro T, Heianna J, Nakasone T, Kobayashi T, Mishiro S, et al. Deep Learning for the Preoperative Diagnosis of Metastatic Cervical Lymph Nodes on Contrast-Enhanced Computed ToMography in Patients with Oral Squamous Cell Carcinoma. Cancers. 2021 Feb 3;13(4):600.

5. Qiao Y, Wang Y, Kang P, Li R, Liu Y, He W. The assessment of the accuracy of clinical preoperative lymph node. Medicine (Baltimore). 2019 Jan;98(4):e13778.

6. Mehta N, Sharma R, Madhok R, Agrawal T, Sharma V. A Clinical, Radiological, and Histopathological Correlation of Neck Nodes in Patients Undergoing Neck Dissection. Int J Appl Basic Med Res. 2018 Mar;8(1):9–13.

7. Hoda N, BC R, Ghosh S, KS S, B VD, Nathani J. Cervical lymph node metastasis in squamous cell carcinoma of the buccal mucosa: a retrospective study on pattern of involvement and clinical analysis. Med Oral Patol Oral Cir Bucal. 2021 Jan;26(1):e84–9.

8. Suryavanshi S, Kumar J, Manchanda A, Singh I, Khurana N. Comparison of CECT and CT perfusion in differentiating benign from malignant neck nodes in oral cavity cancers. Eur J Radiol Open. 2021;8:100339.

9. Koech KJ, Bulimo W, Karanja S, Wanzala P. Sociodemographic, clinical and pathological features of oral squamous cell carcinoma in a Kenyan Centre. East Afr Med J. 2021;98(11):4316–24.

10.   Sharma, Himanshu, Maheshwari, Ghanshyam, Mannan, Naima. Accuracy of MRI in measurement of depth of invasion in oral cancer and its histopathological correlation. Int J Med Sci Diagnosis Res IJMSDR. 2019;3:30–4.

11.   Mahdi AN, Issa SA, Abdulrazaq SS. Efficacy of Clinical Palpation to Detect Cervical Lymph Node Metastasis of Oropharyngeal Cancer. Indian J Forensic Med Toxicol. 2021 Sep 5;15(4):259–64.

12.   Narayana ML, Kumarguru BN, A HA, Gaur U, Lakshmi P, Sravani AL. Correlation of clinical, radiological and histopathological cervical lymph node involvement in oral cancer. Int J Otorhinolaryngol Head Neck Surg. 2020 Jan 24;6(2):311–5.

13.   Sun J, Li B, Li CJ, Li Y, Su F, Gao QH, et al. Computed tomography versus magnetic resonance imaging for diagnosing cervical lymph node metastasis of head and neck cancer: a systematic review and meta-analysis. OncoTargets Ther. 2015;8:1291–313.

14.   Horváth A, Prekopp P, Polony G, Székely E, Tamás L, Dános K. Accuracy of the preoperative diagnostic workup in patients with head and neck cancers undergoing neck dissection in terms of nodal metastases. Eur Arch Oto-Rhino-Laryngol Off J Eur Fed Oto-Rhino-Laryngol Soc EUFOS Affil Ger Soc Oto-Rhino-Laryngol - Head Neck Surg. 2021 Jun;278(6):2041–6.

15.   Dejaco D, Uprimny C, Widmann G, Riedl D, Moser P, Arnold C, et al. Response evaluation of cervical lymph nodes after chemoradiation in patients with head and neck cancer - does additional [18F]FDG-PET-CT help? Cancer Imaging Off Publ Int Cancer Imaging Soc. 2020 Sep 29;20(1):69.

16.   Osborne RF, Brown JJ. Carcinoma of the oral pharynx: an analysis of subsite treatment heterogeneity. Surg Oncol Clin N Am. 2004 Jan;13(1):71–80.

17.   HPV and Oropharyngeal Cancer | CDC [Internet]. 2021 [cited 2022 Sep 21]. Available from: https://www.cdc.gov/cancer/hpv/basic_info/hpv_oropharyngeal.htm

18.   Som PM, Curtin HD, Mancuso AA. An imaging-based classification for the cervical nodes designed as an adjunct to recent clinically based nodal classifications. Arch Otolaryngol Head Neck Surg. 1999 Apr;125(4):388–96.

19.   La Vecchia C, Tavani A, Franceschi S, Levi F, Corrao G, Negri E. Epidemiology and prevention of oral cancer. Oral Oncol. 1997 Sep;33(5):302–12.

20.   IARC Working Group on the Evaluation of Carcinogenic Risks to Humans. Betel-quid and areca-nut chewing and some areca-nut derived nitrosamines. IARC Monogr Eval Carcinog Risks Hum. 2004;85:1–334.

21.   Ferlito A, Shaha AR, Silver CE, Rinaldo A, Mondin V. Incidence and sites of distant metastases from head and neck cancer. ORL J Oto-Rhino-Laryngol Its Relat Spec. 2001 Aug;63(4):202–7.

22.   Hasegawa T, Tanakura M, Takeda D, Sakakibara A, Akashi M, Minamikawa T, et al. Risk factors associated with distant metastasis in patients with oral squamous cell carcinoma. Otolaryngol--Head Neck Surg Off J Am Acad Otolaryngol-Head Neck Surg. 2015 Jun;152(6):1053–60.

23.   Shibahara T. [Oral cancer -diagnosis and therapy-.]. Clin Calcium. 2017;27(10):1427–33.

24.   Barón AE, Franceschi S, Barra S, Talamini R, La Vecchia C. A comparison of the joint effects of alcohol and smoking on the risk of cancer across sites in the upper aerodigestive tract. Cancer Epidemiol Biomark Prev Publ Am Assoc Cancer Res Cosponsored Am Soc Prev Oncol. 1993 Dec;2(6):519–23.

25.   Shah A, Malik A, Garg A, Mair M, Nair S, Chaturvedi P. Oral sex and human papilloma virus-related head and neck squamous cell cancer: a review of the literature. Postgrad Med J. 2017 Nov;93(1105):704–9.

26.   El-Naggar AK, Westra WH. p16 expression as a surrogate marker for HPV-related oropharyngeal carcinoma: a guide for interpretative relevance and consistency. Head Neck. 2012 Apr;34(4):459–61.

27.   Isayeva T, Li Y, Maswahu D, Brandwein-Gensler M. Human papillomavirus in non-oropharyngeal head and neck cancers: a systematic literature review. Head Neck Pathol. 2012 Jul;6 Suppl 1:S104-120.

28.   Aswani J, Anzala O, Mwang'ombe N. High Risk Human Papillomavirus in Head and Neck Squamous Cell Carcinoma Patients at Kenyatta National Hospital, Kenya. Afr J Health Sci. 2019;32(2):1–14.

29.   Richard V. Smith, MD MGM MD. Quick reference guide to TNM Staging of Head and Neck Cancer and Neck Dissection Classification. 4th ed. American Academy of Otolaryngology-Head and Neck Surgery; 2018. 7,11,12,17,28-25.

30.   Amin MB, Greene FL, Edge SB, Compton CC, Gershenwald JE, Brookland RK, et al. The Eighth Edition AJCC Cancer Staging Manual: Continuing to build a bridge from a population-based to a more "personalized" approach to cancer staging. CA Cancer J Clin. 2017 Mar;67(2):93–9.

31.   Müller S, Boy SC, Day TA, Magliocca KR, Richardson MS, Sloan P, et al. Data Set for the Reporting of Oral Cavity Carcinomas: Explanations and Recommendations of the Guidelines From the International Collaboration of Cancer Reporting. Arch Pathol Lab Med. 2019 Apr;143(4):439–46.

32. Driessen DAJJ, Dijkema T, Weijs WLJ, Takes RP, Pegge SAH, Zámecnik P, et al. Novel Diagnostic Approaches for Assessment of the Clinically Negative Neck in Head and Neck Cancer Patients. Front Oncol. 2020;10:637513.

33. Sumi M, Ohki M, Nakamura T. Comparison of Sonography and CT for Differentiating Benign from Malignant Cervical Lymph Nodes in Patients with Squamous Cell Carcinoma of the Head and Neck. AJR Am J Roentgenol. 2001 Apr;176(4):1019–24.

34. Saafan ME. Assessment of Cervical Lymph Nodes in Squamous Cell Carcinoma of the Head and Neck. Surg Curr Res [Internet]. 2013 [cited 2023 Jun 21];03(04). Available from: https://www.omicsonline.org/assessment-of-cervical-lymph-nodes-in-squamous-cell-carcinoma-of-the-head-and-neck-2161-1076.1000145.php?aid=18377

35. Alsaffar HA, Goldstein DP, King EV, de Almeida JR, Brown DH, Gilbert RW, et al. Correlation between clinical and MRI assessment of depth of invasion in oral tongue squamous cell carcinoma. J Otolaryngol - Head Neck Surg J Oto-Rhino-Laryngol Chir Cervico-Faciale. 2016 Nov 22;45(1):61.

36. Rupa P, Shah A. Clinicopathological Correlation between Depth of Tumor and Neck Node Metastasis in Oral (Tongue and Buccal Mucosa) Carcinoma. Int J Head Neck Surg. 2021;12(1):6–10.

37. Imhof H, Czerny C, Dirisamer A. Head and neck imaging with MDCT. Eur J Radiol. 2003 Mar;45 Suppl 1:S23-31.

38. Koyfman SA, Ismaila N, Crook D, D'Cruz A, Rodriguez CP, Sher DJ, et al. Management of the Neck in Squamous Cell Carcinoma of the Oral Cavity and Oropharynx: ASCO Clinical Practice Guideline. J Clin Oncol Off J Am Soc Clin Oncol. 2019 Jul 10;37(20):1753–74.

39. Kowalski LP, Sanabria A. Elective neck dissection in oral carcinoma: a critical review of the evidence. Acta Otorhinolaryngol Ital Organo Uff Della Soc Ital Otorinolaringol E Chir Cerv-facc. 2007 Jun;27(3):113–7.

40. Kligerman J, Lima RA, Soares JR, Prado L, Dias FL, Freitas EQ, et al. Supraomohyoid neck dissection in the treatment of T1/T2 squamous cell carcinoma of oral cavity. Am J Surg. 1994 Nov;168(5):391–4.

41. Thust SC, Yousry T. Imaging of skull base tumours. Rep Pract Oncol Radiother J Gt Cancer Cent Poznan Pol Soc Radiat Oncol. 2016;21(4):304–18.

42. Weissleder R, Elizondo G, Wittenberg J, Lee AS, Josephson L, Brady TJ. Ultrasmall superparamagnetic iron oxide: an intravenous contrast agent for assessing lymph nodes with

MR imaging. Radiology [Internet]. 1990 May 1 [cited 2023 Jun 29]; Available from: https://pubs.rsna.org/doi/10.1148/radiology.175.2.2326475

43.   Barentsz JO, Tekkis PP. Use of USPIOs for Clinical Lymph Node Imaging. In: Bulte JWM, Modo MMJ, editors. Nanoparticles in Biomedical Imaging: Emerging Technologies and Applications [Internet]. New York, NY: Springer; 2008 [cited 2023 Jun 29]. p. 25–40. (Fundamental Biomedical Technologies). Available from: https://doi.org/10.1007/978-0-387-72027-2_3

44.   Who We Are – Kenyatta National Hospital [Internet]. [cited 2023 Jan 30]. Available from: https://knh.or.ke/index.php/goals/

45.   Thoenissen P, Heselich A, Burck I, Sader R, Vogl T, Ghanaati S. The role of magnetic resonance imaging and computed tomography in oral squamous cell carcinoma patients' preoperative staging. Front Oncol. 2023;13:972042.

46.   Voss JO, Freund L, Neumann F, Mrosk F, Rubarth K, Kreutzer K, et al. Prognostic value of lymph node involvement in oral squamous cell carcinoma. Clin Oral Investig. 2022 Nov;26(11):6711–20.

47.   Pandeshwar P, Jayanthi K, Raghuram P. Pre-operative contrast enhanced computer tomographic evaluation of cervical nodal metastatic disease in oral squamous cell carcinoma. Indian J Cancer. 2013;50(4):310–5.

48.   Shoaib T, Soutar DS, MacDonald DG, Camilleri IG, Dunaway DJ, Gray HW, et al. The accuracy of head and neck carcinoma sentinel lymph node biopsy in the clinically N0 neck. Cancer. 2001 Jun 1;91(11):2077–83.

49.   Lima AM, Meira IA, Soares MS, Bonan PR, Mélo CB, Piagge CS. Delay in diagnosis of oral cancer: a systematic review. Med Oral Patol Oral Cirugia Bucal. 2021 Nov 1;26(6):e815–24.

50.   Andersen PE, Warren F, Spiro J, Burningham A, Wong R, Wax MK, et al. Results of selective neck dissection in management of the node-positive neck. Arch Otolaryngol Head Neck Surg. 2002 Oct;128(10):1180–4.

51.   Thoenissen P, Heselich A, Deeg S, Al-Maawi S, Tanneberger A, Sader R, et al. Extent of Neck Dissection and Cervical Lymph Node Involvement in Oral Squamous Cell Carcinoma. Front Oncol. 2022;12:812864.

52.   Nithya CS, Pandey M, Naik BR, Ahamed IM. Patterns of cervical metastasis from carcinoma of the oral tongue. World J Surg Oncol. 2003 Jul 3;1(1):10.

53.   Rabie E, Schouwstra C. The Correlation between Clinical and Pathological Lymph Node Status in Oral Squamous Cell Carcinoma. J Oral Cancer Res. 2021 Jun 14;4(1):49–56.

54.   Noda Y, Ishida M, Ueno Y, Fujisawa T, Iwai H, Tsuta K. Novel pathological predictive factors for extranodal extension in oral squamous cell carcinoma: a retrospective cohort study based on tumor budding, desmoplastic reaction, tumor-infiltrating lymphocytes, and depth of invasion. BMC Cancer. 2022 Apr 13;22(1):402.

APPENDIX 1: DATA COLLECTION FORM

Serial Number: ……………………………

Age …………

Gender ……………

1. Site of primary lesion: A) **Oral Cavity** ☐   B) **Oropharynx** ☐
2. Subsites: ☐ Mucosal lips   ☐ Base of the tongue

                    ☐ Anterior tongue   ☐ Tonsillar complex

                    ☐ Floor of the mouth   ☐ Soft palate

                    ☐ Buccal mucosa   ☐ Posterior pharyngeal wall

                    ☐ Mandibular alveolar ridge

                    ☐ Maxillary alveolar ridge

                    ☐ hard palate

                    ☐ Retromolar trigone

3. Histological diagnosis of primary lesion……………………………………………
4. Grade: ☐ Well differentiated   ☐ Moderately differentiated   ☐ Poorly differentiated
5. Primary tumor (T) definition:
   (a) Oral:

   ☐ T1   ☐ T2   ☐ T3   ☐ T4a   ☐ T4b

   (b) HPV negative Oropharyngeal SCC:

   ☐ T1   ☐ T2   ☐ T3   ☐ T4a   ☐ T4b
   (c) HPV positive Oropharyngeal SCC:

   ☐ T0   ☐ T1   ☐ T2   ☐ T3   ☐ T4

6. Neck imaging modality:

   ☐ MRI   ☐ CT

7. Assessment of regional lymph nodes on imaging (cN):
   (a) Oral SCC

☐ cN0   ☐ cN1   ☐ cN2a   ☐ cN2b   ☐ cN2c   ☐ cN3a   ☐cN3b

    (b) HPV negative Oropharyngeal SCC

☐ cN0   ☐ cN1   ☐ cN2a   ☐ cN2b   ☐ cN2c   ☐ cN3a   ☐cN3b

    (c) HPV positive Oropharyngeal SCC

    ☐ cN0   ☐ cN1   ☐ cN2   ☐ cN3

    (d) Extra Nodal extension on radiographs:

      ☐ YES   ☐ NO

    (a) If YES, which level(s)?
      ☐ Ia   ☐ Ib   ☐ II   ☐ III   ☐ IV   ☐ V
        ☐ VI

8. Positive nodes on imaging before neck dissection:

    ☐ Ia   ☐ Ib   ☐ II   ☐ III   ☐ IV   ☐ V
☐ VI

9. Type of neck dissection:
☐ Radical   ☐ Modified radical   ☐ Selective
10. Level of neck dissection:

    ☐ Ia   ☐ Ib   ☐ II   ☐ III   ☐ IV   ☐ V   ☐ VI

11. Pathological stage of cervical nodes:
    (b) Oral SCC

  ☐ pN0   ☐ pN1   ☐ pN2a   ☐ pN2b   ☐ pN2c   ☐ pN3

    (c) HPV negative Oropharyngeal SCC

☐ pN0   ☐ pN1   ☐ pN2a   ☐ pN2b   ☐ pN2c   ☐ pN3

    (d) HPV positive Oropharyngeal SCC

☐ pN0   ☐ pN1   ☐ pN2

    (e) Extra nodal extension on histopathology
      ☐ YES   ☐ NO
    (f) If YES, which level(s)?
      ☐ Ia   ☐ Ib   ☐ II   ☐ III   ☐ IV   ☐ V
        ☐ VI

12. Positive nodes on histology after neck dissection:

☐ Ia   ☐ Ib   ☐ II   ☐ III   ☐ IV   ☐ V
☐ VI

13. Metastasis to the lungs

☐ YES   ☐ NO

	Radiographic	Histopathology
Assessment of regional lymph nodes (cN vs pN)	e.g., cN2a	e.g., pN3
Positive lymph nodes (Levels)	e.g., Levels I, II and III	e.g., None
Nodes with Extra Nodal Extension	e.g., None	e.g., Level III

APPENDIX 2: CONSENT FORMS

APPENDIX 2A: ADULT PARTICIPANT INFORMATION AND CONSENT FORM (ENGLISH)

UNIVERSITY OF NAIROBI (UoN)

FACULTY OF HEALTH SCIENCES

P O BOX 19676 Code 00202

Telegrams: varsity

(254-020) 2726300 Ext 44355

KNH-UoN ERC

Email: uonknh-erc@uonbi.ac.ke

Website: http://wwww.erc.uonbi.ac.ke

Facebook: https://www.facebook.com/uonknh.erc

Twitter: @UONKNH_ERC https//twitter.com/UONKNH_ ERC

PARTICIPANT INFORMATION AND CONSENT FORM

ADULT CONSENT FOR ENROLLMENT IN THE STUDY

(To be administered in English or any other appropriate language e.g., Kiswahili translation)

Title of Study: **RADIOLOGICAL AND HISTOPATHOLOGICAL ASSESSMENT OF CERVICAL LYMPH NODES IN PATIENTS WITH ORAL AND OROPHARYNGEAL SQUAMOUS CELL CARCINOMA UNDERGOING NECK DISSECTION AT KNH**

Principal Investigator\and institutional affiliation: **DR. ROLLINS OMURUONI MAKOKHA, UNIVERSITY OF NAIROBI. (UON)**

Co-Investigators and institutional affiliation:

Dr. Olabu Beda   Radiologist & Lecturer Human Anatomy (UON)

Dr. Butt Fawzia   Oral and Maxillofacial Surgeon & Lecturer Human Anatomy (UON)

Prof. Guthua Symon   Chief Consultant in Oral and Maxillofacial Surgery (UON)

Dr. Dimba Elizabeth   Senior Lecturer Oral Pathology & Oral Medicine (UON)

Introduction:

I would like to tell you about a study being conducted by the above listed researchers. The purpose of this consent form is to give you the information you will need to help you decide whether or not to be a participant in the study. Feel free to ask any questions about the purpose of the research, what happens if you participate in the study, the possible risks and benefits, your rights as a volunteer, and anything else about the research or this form that is not clear. When we have answered all your questions to your satisfaction, you may decide to be in the study or not. This process is called 'informed consent'. Once you understand and agree to be in the study, I will request you to sign your name on this form. You should understand the general principles which apply to all participants in medical research: i) Your decision to participate is entirely voluntary ii) You may withdraw from the study at any time without necessarily giving a reason for your withdrawal iii) Refusal to participate in the research will not affect the services you are entitled to in this health facility or other facilities. We will give you a copy of this form for your records.

May I continue? YES / NO

This study has approval by The Kenyatta National Hospital-University of Nairobi Ethics and Research Committee Protocol No. **P771/10/2022**

WHAT IS THIS STUDY ABOUT?

The researchers listed above are interviewing individuals who are attending Kenyatta National Hospital and who have Oral and/or Oropharyngeal squamous cell carcinoma (cancer of the mouth and/or throat). The purpose of the research is to investigate the agreement between radiological and histopathological assessment of cervical lymph nodes in patients with oral and oropharyngeal carcinoma undergoing neck dissection at KNH. Participants in this research study will be assessed for primary tumors and examination of the cervical lymph nodes will mainly rely on radiological findings. The WHO and American Joint Committee on Cancer criteria for tumor, nodes, metastases (TNM) staging system will be used to stage the disease.

There will be approximately 30 participants in this study. We are asking for your consent to consider participating in this study.

WHAT WILL HAPPEN IF YOU DECIDE TO BE IN THIS RESEARCH STUDY?

If you agree to participate in this study, the following things will happen:

You will be interviewed by a trained interviewer in a private area where you feel comfortable answering questions and the interview will last approximately 5 minutes. You will also undergo medical examination of the oral cavity (mouth) and/or the oropharynx (throat), cervical lymph nodes (neck) and chest for metastatic disease.

After the interview and medical examinations have finished, we will ask for a telephone number where we can contact you if necessary. If you agree to provide your contact information, it will be used only by people working for this study and will never be shared with others. The reasons why we may need to contact you include booking an appointment for treatment or to clarify any information received during the interview and medical examination process.

ARE THERE ANY RISKS, HARMS DISCOMFORTS ASSOCIATED WITH THIS STUDY?

Medical research has the potential to introduce psychological, social, emotional and physical risks. Effort should always be put in place to minimize the risks. One potential risk of being in the study is loss of privacy. We will keep everything you tell us as confidential as possible. We will use a code number to identify you in a password-protected computer database and will keep all of our paper records in a locked file cabinet. However, no system of protecting your confidentiality can be absolutely secure, so it is still possible that someone could find out you were in this study and could find out information about you.

Also, answering questions in the interview may be uncomfortable for you. If there are any questions you do not want to answer, you can skip them. You have the right to refuse the interview or any questions asked during the interview.

It may be embarrassing for you to have your medical examination; we will do everything we can to ensure that this is done in private. Furthermore, all study staff and interviewers are professionals with special training in these examinations/interviews.

You may feel some discomfort during the clinical examination. In case of an injury, illness or complications related to this study, contact the study staff right away at the number provided at the end of this document. The study staff will treat you for minor conditions or refer you when necessary.

ARE THERE ANY BENEFITS BEING IN THIS STUDY?

You may benefit by receiving free dental/clinical examination and advice on how to get medical treatment. You will also be advised on where to seek treatment. We will refer you to a specialist clinic for care and support where necessary. Also, the information you provide will help us better understand the pattern of agreement between radiological, and histopathological assessment of cervical lymph nodes in patients with oral and oropharyngeal carcinoma. This

information is a contribution to science and will enable us to better assess the neck in patients with the above cancer and treat them accordingly.

WILL BEING IN THIS STUDY COST YOU ANYTHING?

No, the study will not cost you any money.

WILL YOU GET REFUND FOR ANY MONEY SPENT AS PART OF THIS STUDY?

You will not spend any money or be required to purchase anything for the purpose of the study.

WHAT IF YOU HAVE QUESTIONS IN FUTURE?

If you have further questions or concerns about participating in this study, please call or send a text message to the study staff at the number provided at the bottom of this page.

For more information about your rights as a research participant you may contact the Secretary/Chairperson, Kenyatta National Hospital-University of Nairobi Ethics and Research Committee Telephone No. 2726300 Ext. 44102 email uonknh_erc@uonbi.ac.ke. The study staff will pay you back for your charges to these numbers if the call is for study-related communication.

WHAT ARE YOUR OTHER CHOICES?

Your decision to participate in research is voluntary. You are free to decline participation in the study and you can withdraw from the study at any time without injustice or loss of any benefits.

CONSENT FORM (STATEMENT OF CONSENT)

Participant's statement

I have read this consent form or had the information read to me. I have had the chance to discuss this research study with a study counselor. I have had my questions answered in a language that I understand. The risks and benefits have been explained to me. I understand that my participation in this study is voluntary and that I may choose to withdraw any time. I freely agree to participate in this research study.

I understand that all efforts will be made to keep information regarding my personal identity confidential.

By signing this consent form, I have not given up any of the legal rights that I have as a participant in a research study.

I agree to participate in this research study: Yes/No

I agree to provide contact information for follow-up: Yes/No

Participant printed name:……………………………………………………….

Participant signature / Thumb stamp:……………………………………………..

Date:…………………………………………………………………………………..

Researcher's statement

I, the undersigned, have fully explained the relevant details of this research study to the participant named above and believe that the participant has understood and has willingly and freely given his/her consent.

Researcher's Name:………………………………………………………………….

Date:………………………..   Signature:……………………………………………..

Principle Investigator:

DR. ROLLINS OMURUONI MAKOKHA,

School of Dental Sciences, University of Nairobi,

Tel: 0711 126 573

Email: rollaya.roma@gmail.com

Lead Supervisor:

Dr. Beda Olabu BSC ANATOMY(UON), MBCHB(UON), MSC ANATOMY(UON), M.MED RADIOLOGY(UON)

Lecturer,

Department of Human Anatomy, University of Nairobi.

Email: beda.olabu@uonbi.ac.ke

Chairperson,

KNH-UoN Ethics Review Committee

Tel: (2544-020) 2726300-9

Email: uonknh_erc@onbi.ac.ke

APPENDIX 2B: FOMU YA RIDHAA YA MTU MZIMA YA USAJILI WA UTAFITI

Mada ya utafiti: TATHMINI YA RADIOLOJIA NA HISTOPATHOLOJIA YA LIMFU NODI ZA SHINGO KWA WAGONJWA WENYE SARATANI YA MDOMO NA KOO WANAOFANYIWA UPASUAJI WA SHINGO KATIKA HOSPITALI YA KITAIFA YA KENYATTA.

Mkuu wa uchunguzi na uhusiano wa taasisi: Daktari ROLLINS OMURUONI MAKOKHA, Chuo Kikuu cha Nairobi.

Wachunguzi wenza na uhusiano wa taasisi:

Dr. Olabu Beda   Radiologist & Lecturer Human Anatomy (UON)

Dr. Butt Fawzia   Oral and Maxillofacial Surgeon & Lecturer Human Anatomy (UON)

Prof. Guthua Symon   Chief Consultant in Oral and Maxillofacial Surgery (UON)

Dr. Dimba Elizabeth   Senior Lecturer Oral Pathology & Oral Medicine (UON)

Utangulizi:

Ningependa kukueleza kuhusu utafiti unaofanywa na watafiti ambao wametajwa hapo juu. Lengo la fomu hii ya ridhaa ni kukuwezesha kufanya uamuzi kuwa iwapo utashiriki katika utafiti au la. Tafadhali uliza swali lolote kuhusiana na lengo la utafiti, nini itafanyika wakati unaposhirika kwenye utafiti, hatari na manufaa ya utafiti, haki yako kama mtu aliyejitolea kwa hiari na jambo linguine lolote kuhusiana na utafiti au fomu hii ambalo halijaeleweka. Baada ya kuyajibu maswali yote yalivyo, waweza kuamua kushiriki kwenye utafiti au kutoshiriki. Mchakato huu unafahamika kama 'ridhaa inayofahamika'. Pindi tu utakapoelewa na kukubali kuwa kwenye utafiti, tafadhali nakili jina lako na kutia sahihi kwenye fomu hii. Inafaa uelewe sheria za kawaida ambazo hutumiwa na washiriki wote katika utafiti wa kimatibabu: i) Uamuzi wako wa kushiriki ni wa hiari kabisa ii) Waweza kujiondoa kwenye utafiti wakati wowote bila kupatiana sababu iii) Kukataa kushiriki hakutaadhiri wajibu unaopaswa kutekeleza katika kituo hiki cha afya ama vitu vinginevyo. Tunakupa nakala ya fomu hii kwa ajili ya rekodi zako.

Naweza kuendelea? Ndio/La?

Utafiti huu umeidhinishwa na hospitali ya Kitaifa ya Kenyatta-Kamati ya maadili na utafiti,Chuo Kikuu cha Nairobi.

Nambari ya Itifaki……………..

Utafiti huu unahusu nini?

Watafiti walioorodheshwa hapo juu wanawahoji watu ambao wana ugonjwa wa saratani ya mdomo na koo na ambao wameratibiwa kufanyiwa upasuaji wa shingo katika hopitali kuu ya Kenyatta na ile ya chuo kikuu cha Nairobi. Madhumuni ya utafiti ni kuchunguza uhusiano kati ya tathmini ya radiolojia, na ile ya histopatholojia ya nodi za limfu za shingo kwa wagonjwa walio na saratani ya mdomo na koo. Washiriki katika utafiti huu watakuhoji kisha watachunguzwa ndani ya mdomo na koo palipo na uvimbe au vidonda vya saratani.

Kutakuwa na takriban washiriki thelathini katika utafiti huu. Tunaomba idhini yako ya kuzingatia kushiriki katika utafiti huu.

NI NINI KITAKACHOFANYIKA IWAPO UTAAMUA KUWEKO KWENYE UTAFITI?

Iwapo utakubali kushiriki kwenye utafiti, mambo yafuatayo yatafanyika:

Utahojiwa katika eneo la faragha ambapo unahisi vizuri kujibu maswali na mahojiano yatachukua takriban dakika tano. Pia utafanyiwa uchunguzi wa kimatibabu kwa ajili ya kidonda au uvimbe wa saratani ya mdomo na koo. Mtafiti atachunguza shingo na kifua chako kisha ataangalia eksirei zako. Baada ya upasuaji, ataangalia ripoti ya histopatholojia kutoka kwenye maabara.

Baada ya mahojiano na uchunguzi wa kimatibabu kukamilika, tutaomba nambari ya simu ambapo tunaweza kuwasiliana nawe ikibidi. Ukikubali kutoa maelezo yako ya mawasiliano, yatatumiwa na watu wanaofanya kazi katika utafiti huu pekee na kamwe hayatashirikiwa na wengine. Sababu ambazo tunaweza kuhitaji kuwasiliana nawe ni pamoja na kuweka miadi ya

matibabu au kufafanua habari yoyote iliyopokelewa wakati wa mahojiano na mchakato wa uchunguzi wa matibabu.

JE, KUNA HATARI ZOZOTE AU MADHARA YANAYOHUSISHWA NA UTAFITI HUU?

Utafiti wa kimatibabu una uwezo wa kusababisha hatari za kisaikolojia, katika mahusiano, hisia na kimwili. Yafaa tujaribu iwezavyo kupunguza hatari hizo. Hatari moja ambayo inaweza kutokea ni ukosefu wa siri. Yote utakayotuambia yatabaki kuwa siri. Tutatumia kodi Fulani kukutambua katika tarakilishi iliyo na neon la siri. Data na nakala zetu zote tutazifungia kwa kabati. Hata hivyo, hakuna chombo cha kuhifadhi siri yako ambacho ni salama kabisa na huenda mtu akafumbua kwamba ulishiriki katika utafiti na apate habari kukuhusu.

Aidha, kujibu maswali kwenye mahijiano huenda kukawa kugumu kwako. Iwapo kuna maswali hutaki kujibu waweza kuyaacha. Una haki ya kukataa mahojiano au swali lolote litakaloulizwa kwenye mahojiano.

Inawezekana liwe ni jambo lla aibu kwako kufanyiwa uchunguzi. Tutahakikisha ya kwamba yoye hayo yatafanyiwa mahali pa siri. Hali kadhalika watakaofanya mahojiano ni watu wenye weledi na ujuzi. Huenda usihisi vizuri wakati wa kukaguliwa. Ikitokea ya kwamba umejeruhiwa, umekuwa mgonjwa au shida nyingine inayohusiana na utafiti huu imetokea, piga simu kwa nambari ambazo ziko mwishoni mwa nakala hii. Wahudumu watakutibu au wakutume kwingineko iwapo itahitajika kufanya hivyo.

KUNA MANUFAA YOYOTE KATIKA UTAFITI HUU?

Utafaidika kwa kupata uchunguzi wa ugonjwa bila malipo. Tutakutuma kliniki spesheli iwapo tutahitajika kufanya hivyo. Habari utakayotupa itasaidia kuelewa vyema uhusiano wa tathmini ya radiolojia na histopatholojia ya limfu nodi za shingo kwa wagonjwa walio na saratani ya mdomo na koo. Habari hiyo itachangia ufahamu katika sayansi na nia ya kupata na

kudhibitisha ugonjwa kwa njia ya haraka. Ugonjwa ukishadhibitishwa na daktari wataweza kuwachunguza zaidi na kuwatibu wagonjwa.

JE, UWEPO KATIKA UTAFITI HUU KUTAKUGHARIMU CHOCHOTE?

Haihusiki

UTARUDISHIWA PESA ZOZOTE UTAKAZOTUMA KATIKA UTAFITI?

Hautatumia pesa zozote lakini iwepo utatumia pesa zozote utarudishiwa

IWAPO UKUMBANE NA MASWALI SIKU ZA USONI

Iwapo utakuwa na maswali zaidi kuhusu utafiti huu tafadhali piga au utume arafa kwa nambari iliyoko mwishoni mwa nakala hii ili kuwasiliana na wahudumu wetu.

Kwa habari zaidi kuhusu haki yako kama mshiriki wa utafiti waweza kuzungumza na Katibu/Mwenyekiti, Hospitali ya Kitaifa ya Kenyatta-kamati ya maadili na utafiti Chuo Kikuu cha Nairobi, Nambari ya simu 2726300 Ext. 44102 Barua pepe:uonknh_erc@uonbi.ac.ke.

Wahudumu watakulipa hela zako ukishatumia nambari hizo iwapo mawasiliano yatahusu utafiti.

CHAGUO LAKO LINGINE NI LIPI?

Uamuzi wako wa kushiriki katika utafiti huu ni wa hiari. Una ruhusa ya kukataakushiriki katika utafiti na waweza kujiondoa katika utafiti bila hasara yoyote na bila kukiukiwa kwa haki yako.

FOMU YA RIDHAA

Kauli ya Mshiriki

Nimesoma fomu hii ya ridhaa ama nimesomewa ujumbe. Nilipata fursa ya kujadiliana na mtafiti kuhusu utafiti huu. Maswali yangu yamejibiwa kwa lugha ambayo naielewa na

nimeelezwa manufaa na hatari ziliwepo. Naelewa kuwa ushiriki wangu kwa utafiti huu ni wa hiari na naweza kujiondoa wakati wowote. Nimekubali kwa hiari kushiriki katika utafiti huu.

Naelewa juhudi zitafanywa ili kuuhifadhi habari yangu kwa kibinafsi.

Kwa kutia sahihi fomu hii ya ridhaa, sijawacha haki zangu za sharia kama mshiriki katika utafiti.

Nimekubali kushiriki katika utafiti huu: Ndio………... La………….

Nimekubali kupeana nambari za simu ili nifuatiliwe: Ndio…………La………...

Jina la mshiriki lililochapishwa: ………………………………………………..

Sahihi ya mshiriki/alama ya kidole ……………………   Tarehe………………..

Kauli ya mtafiti ………………………………………………………………..

Mimi, ambaye nimeitisha sahihi, nimetoa maeleza kamili kuhusiana na utafiti huu kwa mshiriki ametajwa hapo juu ya kwamba mshiriki ameelewa na akatoa ridhaa yake kwa hiari.

Jina la Mtafiti: Dr. ROLLINS OMURUONI MAKOKHA   Tarehe: ………………..

Sahihi: ………………………………………..

Kazi yake katika utafiti: Mkuu wa uchunguzi

Kwa habari zaidi zungumza na:

Mkuu wa Uchunguzi:

Daktari ROLLINS OMURUONI MAKOKHA,

Shule ya Kisayansi ya Meno, Chuo Kikuu cha Nairobi,

Nambari ya Simu: 0711 126 573

Barua pepe: rollaya.roma@gmail.com

Msimamizi Mkuu:

Daktari Beda Olabu BSC ANATOMY(UON), MBCHB(UON), MSC ANATOMY(UON), M.MED RADIOLOGY(UON)

Mhadhiri,

Idara ya Anatomia ya Binadamu, Chuo Kikuu cha Nairobi.

Barua pepe: beda.olabu@uonbi.ac.ke

Katibu/Mwenyekiti

Hospitali ya Kimataifa ya Kenyataa-Kamati ya maadili na utafiti Chuo Kikuu Cha Nairobi,

Nambari ya Simu. (254-020) 2726300-3

Barua pepe: uonknh_erc@uonb

APPENDIX 3: ETHICS RESEARCH COMMITTEE APROVAL

UNIVERSITY OF NAIROBI
FACULTY OF HEALTH SCIENCES
P O BOX 19676 Code 00202
Telegrams: varsity
Tel:(254-020) 2726300 Ext 44355

KNH-UON ERC
Email: uonknh_erc@uonbi.ac.ke
Website: http://www.erc.uonbi.ac.ke
Facebook: https://www.facebook.com/uonknh.erc
Twitter: @UONKNH_ERC https://twitter.com/UONKNH_ERC

KENYATTA NATIONAL HOSPITAL
P O BOX 20723 Code 00202
Tel: 726300-9
Fax: 725272
Telegrams: MEDSUP, Nairobi

Ref: KNH-ERC/A/84

24th February, 2023

Dr. Rollins Omuruoni Makokha
Reg. No. V60/11355/2018
Dept. of Dental Sciences
Faculty of Health Sciences
University of Nairobi

Dear Dr.Makokha,,

RESEARCH PROPOSAL: RADIOLOGICAL AND HISTOPATHOLOGICAL ASSESSMENT OF CERVICAL LYMPH NODES IN PATIENTS WITH ORAL AND OROPHARYNGEAL SQUAMOUS CELL CARCINOMA UNDERGOING NECK DISSECTION AT KNH AND UON-DH   (P771/10/2022)

This is to inform you that KNH-UoN ERC has reviewed and approved your above research proposal. Your application approval number is **P771/10/2022.** The approval period is 24th February 2023 – 23rd February 2024.

This approval is subject to compliance with the following requirements;

  i. Only approved documents including (informed consents, study instruments, MTA) will be used.

  ii. All changes including (amendments, deviations, and violations) are submitted for review and approval by KNH-UoN ERC.

  iii. Death and life threatening problems and serious adverse events or unexpected adverse events whether related or unrelated to the study must be reported to KNH-UoN ERC 72 hours of notification.

  iv. Any changes, anticipated or otherwise that may increase the risks or affected safety or welfare of study participants and others or affect the integrity of the research must be reported to KNH-UoN ERC within 72 hours.

  v. Clearance for export of biological specimens must be obtained from relevant institutions.

  vi. Submission of a request for renewal of approval at least 60 days prior to expiry of the approval period. Attach a comprehensive progress report to support the renewal.

  vii. Submission of an executive summary report within 90 days upon completion of the study to KNH-UoN ERC.

Protect to discover

APPENDIX 4: LETTERS OF INSTITUTIONAL PERMISION
APPENDIX 4A: KNH

KNH/R&P/FORM/01

KENYATTA NATIONAL HOSPITAL
P.O. Box 20723-00202 Nairobi'

Tel.: 2726300/2726450/2726565
Research & Programs: Ext. 44705
Fax: 2725272
Email: knhresearch@gmail.com

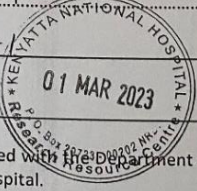## Study Registration Certificate

1. Name of the Principal Investigator/Researcher
   ROLLINS OMURUONI MAKOKHA

2. Email address: rollaya.roma@gmail.com   Tel No. 0711126573

3. Contact person (if different from PI)

4. Email address: ....   Tel No. ....

5. Study Title
   RADIOLOGICAL AND HISTOPATHOLOGICAL ASSESSMENT OF CERVICAL LYMPH NODE IN PATIENTS WITH ORAL AND OROPHARYNGEAL SQUAMOUS CELL CARCINOMA UNDERGOING NECK DISSECTION AT KNH AND UON-DH

6. Department where the study will be conducted ...... DENTAL
   (Please attach copy of Abstract)

7. Endorsed by Research Cordinator of Department where study will be conducted.

   Name: Dr Kinyua Kittela   Signature ....   Date 1/3/23

8. Endorsed by KNH Head of Department where study will be conducted.

   Name: Dr. A. Kenyanya   Signature ....   Date 1/3/23

9. KNH UoN Ethics Research Committee approved study number P771/10/2022
   (Please attach copy of ERC approval)

10. I ROLLINS OMURUONI MAKOKHA .... commit to submit a report of my study findings to the Department where the study will be conducted and to the Department of Medical Research.

    Signature............ Makokha ....   Date 01/03/2023

11. Study Registration number (Dept/Number/Year)___ Dental ____ 122 /2023
    (To be completed by Medical Research Department)

12. Research and Program Stamp _____
    [stamp: KENYATTA NATIONAL HOSPITAL 01 MAR 2023]

All studies conducted at Kenyatta National Hospital **must** be registered with the Department of Medical Research and investigators **must commit** to share results with the hospital.