ULTRA SONOGRAPHY OF METASTATIC CERVICAL LYMPH NODES IN PATIENTS WITH HEAD AND NECK CANCER: AT KENYATTA NATIONAL HOSPITAL, 2006

DISSERTATION SUBMITTED INPART FULLFILLMENT OF MASTER OF MEDICINE DEGREE IN EAR, NOSE AND THROAT – HEAD AND NECK SURGERY – UNIVERSITY OF NAIROBI

BY

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DECLARATION

This dissertation is my original work and has not to my knowledge been submitted for approval in any other university.

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To my entire family for the invaluable motivation and support.

To my beloved wife;Lydiah for her patience and understanding, my daughter Carolyne and son Peter.

To the last born, MaryAnne for reminding me to do my homework every time I arrive home.

CONTENTS

ABBREVIATIONS

U/S-	ULTRASONOGRAPHY
CDS-	COLOUR DOPPLER SONOGRAPHY
ENT-HN	EAR, NOSE AND THROAT - HEAD AND NECK
KNH	KENYATTA NATIONAL HOSPITAL
CT	COMPUTED TOMOGRAPHY
MRI	MAGNETIC RESONANCE IMAGING
FNAC	FINE NEEDLE ASPIRATE CYTOLOGY
18-FDG	18-FLUORO- 2- DEOXYGLUCOSE
PET-	POSITRON EMMISSION TOMOGRAPHY
IHC –	IMMUNOHISTOCHEMISTRY

ABSTRACT

Main objective: To evaluate the role of High – Resolution U/S in detecting metastatic neck nodes metastases in patients with head and neck cancer.

Study design: Descriptive Cross – Sectional Study

Setting: Kenyatta National Hospital – Nairobi

Methods and materials: Patients with head and neck cancer presenting at Ear, Nose and Throat, Head and Neck Surgery Department – Kenyatta National Hospital, were evaluate for cervical lymphadenopathy by physical, examination, contrast enhanced CT and U/S. The neck findings were correlated with cytopathological findings of lymph node biopsies.

Results: A total of 152 consecutive patients were included in the study 111(73%) patients were males and 41 (27%) were females. The mean age ratio was 54.9 years. General examination and detailed otolaryngological evaluation was done. Neck findings were documented patients were also evaluated using contrast- enhanced CT & U/S 69 patients underwent FNA biopsy of neck nodes. 71 (46.7%) of the patients had palpable clinical lymph nodes, 59 out of 69 patients done FNA were confirmed to have metastatic nodes. CT detected nodes in 54(35.5%) patients; 48 out of the 54 patients were noted to have metastasis after FNA cytology. U/S detected lymph nodes in necks of all patients had nodes which exhibited features of metastasis. 55 (36.2%) patients were correctly diagnosed with nodal metastasis on U/S. Overall agreement between cytopathological findings and P/E, CT, and U/S IN detecting neck nodal metastasis was 85.5%, 81.4%, and 93.6% respectively.

CONCLUSION

U/S proved more accurate in staging cervical lymph node metastases compared with P/E and CT

INTRODUCTION

The condition of the cervical lymph nodes is the single most important prognostic factor, and therefore accurate assessment of nodal status is of critical interest to Head and Neck Surgeons and Radioncologists who manage patients with head and neck cancer. It is widely acknowledged that presence of metastatic node in the neck, regardless of the site of the primary tumor, reduces the 5- year survival rate by 50%. (1-11)

Given the significance of nodal status, accurate staging of cervical Lymph nodes is crucial. Palpation still plays a key role in staging neck nodal diseases but various studies have shown that the method is inadequate and inaccurate in assessing metastatic neck nodes (2, 5,6,12,13,14,15, 16). CT has become the standard imaging modality for staging both primary tumor and the nodal disease of the neck in patients with Head and Neck cancer. However, its reliability as a diagnostic tool for evaluating cervical lymphadenopathy remains controversial. Numerous studies have reported an overall rate of error ranging from 7.5 % to 31 % (6, 13, 15, 16, 17) Due to its inability to outline intranodal – architecture and vascular patterns accurately, its value in staging neck lymph nodes has been queried by several authors. (16, 17, 18) In order to detect lymph nodes on CT, contrast material; has to be administered intravenously, a procedure which is considered a health risk to the patients. Various side effects have been associated with intravenous injection of contrast media ranging from mild allergic reactions to fatal reactions. Over 85% of anaphylactic reactions occur within five minutes after contrast media administration. Some of the life threatening reactions include; severe bronchospasms, convulsions, laryngeal oedema, hypotension and cardiopulmonary failure among others. (19, 20). It is always advisable to obtain informed consent from the patient or guardian and above all have resuscitation facilities readily available before administration of contrast media.

It has been proved that Real – time high – resolution U/S can significantly improve the rate of detection of cervical lymph nodes and therefore can play a significant role in staging metastatic cervical lymph nodes in patients with head and neck cancer (1, 12, 21, 22) U/S is non-invasive, readily available, safe, affordable and acceptable procedure to most patients. It does not require administration of contrast medium; neither does it use ionizing radiation. It is capable of surveying all groups of cervical lymph nodes except median retropharyngeal group of nodes which are difficult to detect with modern conventional diagnostic methods. (23). Nevertheless, U/S is not only able to detect small lymph nodes with diameter of up to 5mm , but can also outline their internal architecture and vascular patterns.

In KNH, U/S has proved to be a very fundamental diagnostic method in evaluation of thyroid masses but its potential in detection of cervical lymphadenopathy in patients with head and neck malignancies has not yet been exploited. Moreover, no conclusive study to determine its value in detecting metastatic cervical lymph nodes has been done in Kenya.

The purpose of the study is to evaluate the value of U/S in metastatic neck node disease and then correlate it with physical examination and contrast enhanced CT of the neck in

terms of relative accuracy and sensitivity in detecting metastatic neck nodes in patients with Head and Neck Cancer. Histopathological results of lymph node biopsies will be used as the gold standard.

CERVICAL LYMPH NODES

EMBRYOLOGY

Lymphatic systems begin to develop towards the end of the 5th week in uterus as lymphatic sacs. Initially, there are six primary sacs [24]; two jugular lymph sacs near the junction of the primitive subclavian veins with anterior cardinal veins which later develop into cervical lymphatic systems; two iliac lymph sacs; one retroperitoneal sac, and one lymph sac dorsal to it, referred to as cistern chyli.Lymphatic vessels develop as outgrowths from the lymph sacs and then grow along the main veins. On the other hand, lymph nodes develop as a result of transformation of lymph sacs along the lymphatic vessels.

Mesenchymal cells surrounding the lymph sacs invade them, forming a network of small lymphatic channels-lymphatic plexus. Mesechymal cells eventually differentiate into sinuses in the nodal hilum and medulla, and also into connective tissue which forms the capsule and the trabecullae that maintain the shape of the lymph nodes.

NORMAL ANATOMY AND PHYSIOLOGY

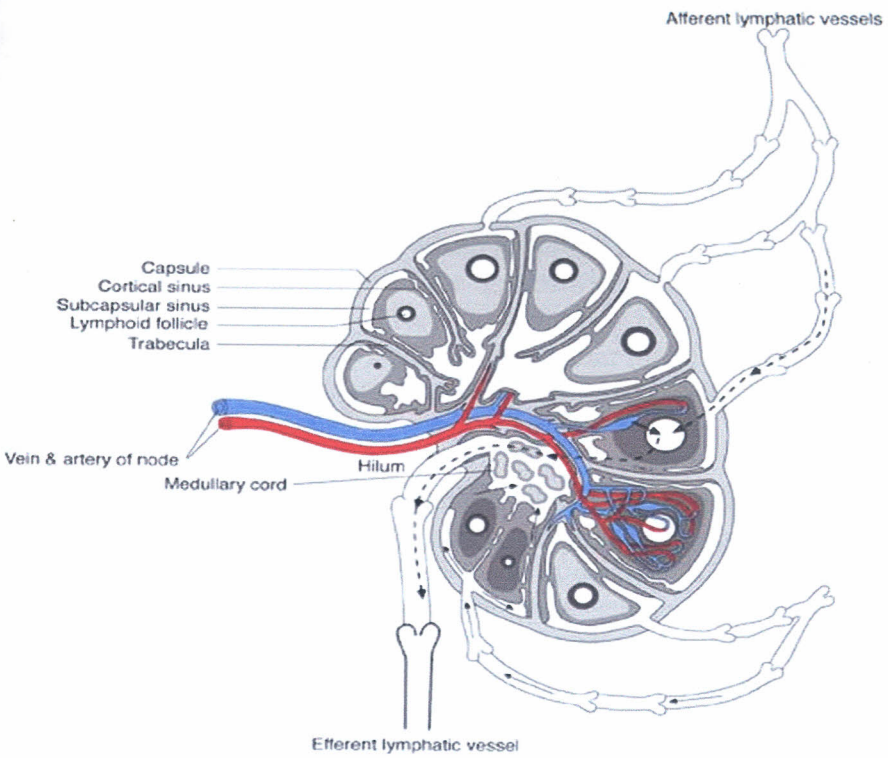
The lymphatic system is composed of the capillaries, vessels and nodes. This network of vessels transports the lymph fluid from body tissues into blood circulatory systems. Lymph is a turbid fluid whose composition is similar to blood except that it does not contain red blood cells and platelets and has high lipid concentration but low protein contents.Capilarries are thin walled vessels formed by continuous endothelial cells and begin as closed saccules. They take up interstitial fluid, proteins, lipids and cells and drain into larger lymphatic vessels which contain numerous valves placed at about 2 to 3 mm intervals along the vessels (2, 25)

The larger vessels are made up of layers of endothelial cells, inner connective tissue layer and circular smooth muscle layer. The vessels are coated by outer connective tissue layer. Circulation of lymph fluid is dependent on; - the actions of the valves which ensure unidirectional flow, contraction of smooth muscle coat of the lymphatic vessels, and the compression by surrounding muscles and pulsation of the arteries in the neighborhood.(2) The lymphatic vessels join up to form larger afferent lymphatic vessels that eventually drain into lymph nodes. Nodes vary in size depending on the site of location in the neck. Nodes located high up in the neck (submandibular and upper jugular groups) tend to be slightly larger than the rest of the cervical nodes. However, the size of normal lymph nodes in the neck ranges from 3mm to 10mm in diameter. (26)

Lymph node has a convex surface and assumes an ovoid shape. It is encapsulated by fibrous connective tissue perforated at various locations by afferent lymphatic vessels draining into it. Nodes are embedded in soft tissues of the neck and are all surrounded by

fat, except the parotid lymph nodes. The substance of the node consists of the cortex and medulla. The cortex forms the outer zone of the node and it is composed of densely packed lymphocytes which form subcapsular sinus, also referred to as marginal sinus, which surrounds the lymph node underneath the capsule. It freely communicates with the inner placed medullarly sinuses.

The framework which maintains the shape of the lymph node is composed of trabecullae arising from the inner surface of the capsule and traverses the medulla. These connective tissue strands (trabecullae) also guides the course of blood vessels and nerves within the substance of a lymph node. Medullarly sinuses coalesce into channels which join up to form larger efferent lymphatic vessels that exit the lymph node via the hilum which also forms the entry point of arteries and nerves.



(Adapted from: Michael Ying; Ahuja T.Anil: Ultrasonography of cervical lymph Nodes)

Lymphatic fluid in afferent lymphatic vessels enters into the sub capsular sinuses, pass through the medullarly sinuses, and eventually exit through efferent lymphatic vessels at the hilum in a unidirectional manner. The lymph then flows down the lymphatic vessels to subsequent echelon lymph nodes along a particular lymphatic drainage system to reach the jugular lymph trunks. Right jugular trunk opens into the junction between right internal jugular vein and subclavian vein while left jugular trunk drains into the thoracic duct.

MORPHOLOGICAL FEATURES OF INFLAMMATORY AND METASTATIC NODAL DISEASES

Inflammatory and malignant diseases most often spread from the primary site to the regional lymph nodes by passive transport within the lymphatic vessels. Lymph containing either bacteria or malignant cells reaches the lymph node via afferent lymphatic vessels and therefore, earliest pathological lesions tend to involve the subcapsulsar sinus and nodal cortex. The disease condition may be arrested at this level, or may progress to involve the medulla and hilar regions of the node before being disseminated further down the lymphatic chain.

Inflammatory conditions induce lymphocyte proliferation within the lymphatic follicles leading to sinusoidal enlargement and diffuse widening of the cortex. Thus, reactive nodes tend to have concentric cortical widening while still maintaining the oblong shape. Reactive nodes also tend to have perinodal inflammatory reaction which is associated with diffuse oedema of adjacent of tissues. This is a common feature of tuberculosis lymphadenitis. (1). Progression of the inflammatory disease leads to invasion of the hilum and eventually necrosis of the tissues within the medulla. Furthermore, reactive nodes tend to have increased blood flow and prominent vascualirty due to increase in diameter of blood vessels. Displacement of hilar blood vessels due to intranodal cystic necrosis is a common feature of tuberculosis lymphadenitis (1, 25)

The fate of tumor cells reaching the subcapsular sinus is dependent on the properties of the tumor cells, host local factors and immunological factors and availability of vital nutrients. Tumor cells with high potential of metastasis produce abundant proteolytic enzymes that destroy intranodal connective tissue framework and proliferate by expressing surface markers that facilitate attachment to more host cells. They induce angiogenesis and also recruit more host capillary cells in order to increase their nutrient supply (2, 27). After their deposition in the subcapsular sinus, tumor cells may either, infiltrate the cortex to produce a focal cortical widening and eventually extra capsular extension, or invade the medulla and the hilum. Therefore, metastatic nodal disease induces variable structural changes which include; focal cortical widening thus making the node assume a spherical shape and irregular margins, central necrosis and loss of hilar outline on radiological images. (28)

Metastatic nodes tend to have peripheral vascularity as well as abnormal intranodal vascular patterns. Most metastatic nodes have diverse patterns which include: aberrant course of hilar vessels, displaced vascularity, avascularity and increased peripheral vascularity. Peripheral vascularity has been postulated to be due to angiogenic effects of tumor cells with resultant development of new aberrant capsular feeding vessels (27). Invasion of intranodal vascular, and lymphatic channels eventually lead to dissemination of tumor cells into distant sites and subsequent echelon lymph nodes respectively.

CLASSIFICATION AND STAGING OF CERVICAL LYMPH NODES

There are approximately 150 to 350 lymph nodes that are surrounded by fat and embedded in the soft tissues of the neck between the superficial and preveterbral fascia. Thus, most of them can be identified by physical examination and radiological imaging. In addition, all the groups of cervical lymph nodes are accessible during neck dissection (1, 2, 27). Various classification systems have been described based on retrospective studies of patients undergoing neck dissection. The authors described similar patterns of cancer spread from various primary sites in the head and neck to the cervical nodes. This formed the foundation onto which modifications to radical neck dissection, first described by George Crile, in 1906 (25), has been built. Thus, more conservative surgical approaches are currently being advocated.

The classification with worldwide acceptance ,the American Joint Committee on cancer (AJCC) system, was first described in 1981 by head and neck surgeons at Memorial Sloan Kettering Hospital (2 27). AJCC and the International Union against cancer (UIC) developed a joint tumor staging system in 1988 referred to as Tumor, Node , Metastasis (TNM) system which stages lymph nodes metastases on the basis of physical examination(5)

AJCC (1998) CLASSIFICATION SYTEM
LEVEL

I. This group constitutes submandibular and submental lymph nodes (nodes in the flour of the mouth)

II. Upper internal jugular (Deep Cervical) nodes – located around the upper 1/3 of the internal jugular vein and extend from the skull base to hyoid bone (or level of carotid bifurcation)

III. Middle internal jugular nodes- extending from the level of hyoid bone to cricoid cartilage (or level that omohyoid muscle crosses internal jugular vein)

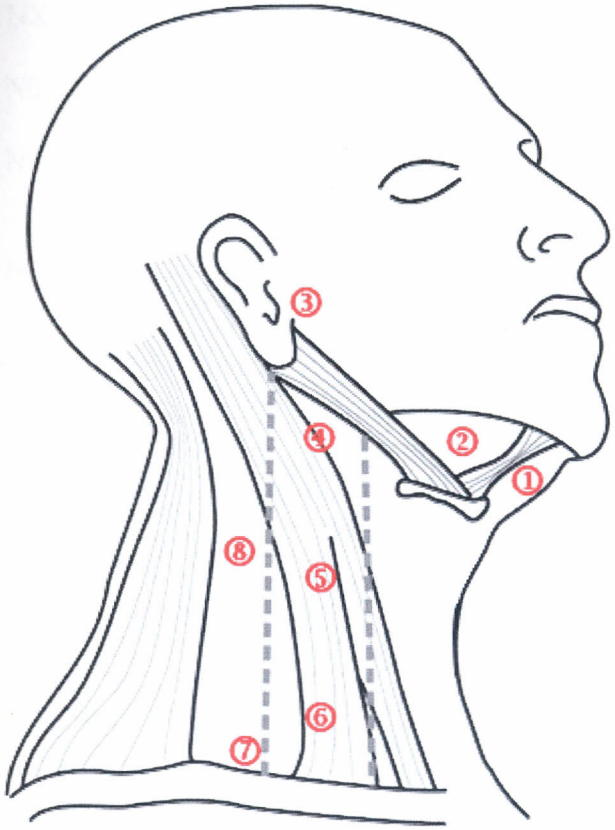
IV. Infraomohyhoid nodes: located along the lower 1/3 of internal jugular vein and extend from cricoid cartilage to the clavicle

V. Posterior triangle nodes: includes spinal accessory nodes, transverse cervical and supraclavicular lymph nodes.

VI. Anterior compartment group of nodes- extending from hyoid bone to suprasternal notch includes: - Para tracheal, pretracheal, precricoid (Delphian) and tracheosophageal groove (Perilaryngeal) lymph nodes

VII. upper anterior Mediastinal lymph nodes

The classification does not include some groups of lymph nodes such as parotid and retro
pharyngeal group of lymph nodes which are often involved by metastases. U/S cannot evaluate accurately lymph nodes located in level VII. However, Hajek et al(1) in 1986, described a nodal classification for ultrasound examination based on eight(8) anatomical regions. They include: - submental nodes, submandibular, parotid nodes, upper, middle and lower cervical nodes, supraclavicular fossa nodes and posterior triangle nodes (29)



① Submental

② Submandibular

③ Parotid

④ upper cervical, above the level of hyoid bone, and along the internal jugular chain

⑤ middle cervical, between the level of hyoid bone and cricoid cartilage, and along the internal jugular chain

⑥ Lower cervical, below the level of cricoid cartilage, and along the internal jugular chain

⑦ supraclavicular fossa

⑧ posterior triangle (also known as accessory chain)

(Adapted from: U/S of cervical lymph Nodes .Article by Michael Ying&Ahuja Anil)

REGIONAL LYMPH NODE CLASSIFICATION

Stage	Description
NX	Regional lymph nodes cannot be assessed
N0	No regional lymph node metastasis
N1	Metastasis in a single ipsilateral Lymph node: 3cm or les in greatest dimension.
N2	Metastasis in a single ipsilateral lymph node, larger than 3 cm but not more than 6 cm in greatest dimension or in multiple ipsilaterral lymph nodes, none more than 6 cm in greatest dimension or in bilateral or contralateral lymph nodes, none larger than 6 cm in greatest dimension.
N2a	Metastasis in a single ipsilateral node, larger than 3cm but not more than 6cm in greatest dimension.
N2b	Metastasis in multiple ipsilateral nodes none larger than 6cmin greatest dimension.
N2c	Metastasis in bilateral or contraletral lymph nodes, none larger than 6 cm in greatest dimension.
N3	Metastasis in a lymph node larger than 6cm in greatest dimension.

TNM nodal staging systems of metastatic cervical lymphadenopathy arising from nasopharyngeal tumors differs from the above described standardized system.

Regional Lymph Nodes Classification for Nasopharyngeal Cancer

Stage	Description
NX	Regional Lymph nodes cannot be assessed.
No	No regional Lymph Node Metastasis
N1	Unilateral metastasis in lymph node(s) 6cm or less in greatest dimension above supraclavicular fossa.
N2	Bilateral Metastasis in lymph node(s), 6cm or less in greatest dimension above the supraclavicular fossa.
N3	Metastasis in lymph node(s) larger than 6cm and/or in the supraclavicular fossa.
N3a	Metastasis in a lymph node greater than 6cm in greatest dimension.
N3b	Metastasis in lymph node(s) of any size in the supraclavicular fossa.

While classification of metastatic neck nodes influences the choice of neck dissection to be employed, nodal staging is crucial in determining the appropriate modality of intervention among, radiotherapy, neck dissection and postoperative radiotherapy.

DIAGNOSIS OF CERVICAL LYMPHADENOPATHY

HISTORICAL PERSPECTIVE

Description of lymphatics was first done in 1622 by Gaspero Aselli (25), when he was carrying out a study based on intestines of a dog. He described vessels with "milky" fluid that drained into a larger central mesenteric node. He named the vessels "serous vessels". In 1653, the relationship between thoracic ducts and major veins was documented by Jean Pecquet, and about a century later, William Hunter and his colleagues, described the anatomy and physiology of the lymphatic. (25) It was until the turn of 19th century that it was discovered that lymph nodes acts as a barrier to cancer spread between primary tumor sites and the rest of the body.

Initially, lymphatic mapping was being tried by injecting ink and wax into lymphatic channels. During 18th century, mapping using mercury was invented. However, major breakthrough was realized in 1930s when Thorosplast; a colloid thorium oxide compound that accumulated in cadaveric lymphatic vessels, was reported. Later on, researchers were able to outline lymphatic vessels and lymph nodes using dyes. This eventually led to the birth of lymphangiography in 1952. The method involved cannulation of lymphatic vessels and injection of radiopaque dye which outlined the collecting lymphatic vessels and lymph nodes whose pattern distribution was displayed on x-ray films.

In 1953, Sherman and Ter-pogossian (25) described a modified lymphangiography method; lymphascintigraphy, which utilized radionuclides such as gold -198 , iodine 131, and technetium 99 m incorporated into proteins. The tagged proteins, mainly colloid or albumin, are injected around the primary tumor and then taken up by lymphatic to the regional lymph nodes which are subsequently detected by gamma cameras.

PHYSICAL EXAMINATION

Prior to advent of modern imaging modalities, evaluation of neck nodal metastasis was based on palpation. It still plays a key role in staging neck nodal disease despite its fall abilities. The criteria used for diagnosis of nodal metastasis included; size, firmness and mobility of the lymph nodes (5). Nodes larger than 1.5cm (15mm) in greatest dimension and those fixed to surrounding tissues depicted nodal involvement by tumor.

Palpation is an easy, quick and repeatable procedure but it is prone to several outstanding drawbacks. It is inaccurate in evaluating neck nodes, prone to interobserver variations and cannot access deeply placed lymph nodes especially in subjects with short and fat necks. The incidence of false negative results based on palpation ranges from 16% - 70% while the rate of false – positive ranges from 4% to

42% (5, 13, 14, 36). It is also difficult to differentiate between a single large lymph node from multiple small matted nodes especially if they are deeply placed in the neck (30)

RADIOLOGICAL INVESTIGATIONS

The discovery of the best and most accurate diagnostic method for detecting metastatic neck nodes has eluded researchers for many years Modern sophisticated imaging techniques have improved the accuracy of detecting neck lymph nodes ,though a significant percentage of cervical lymph nodes bearing micro metastasis are still missed. Research on more accurate techniques is still going on.

ULTRASONOGRAPHY

HISTORICAL BACKGROUND

The technology of producing ultrasound was first applied in 1912, during the unsuccessful search for the sunken titanic ship in Northern Atlantic Ocean. Emergence of the submarine menace during the 1914-18 world war led to development of military equipments capable of detecting submerged machines. This was achieved by Langevin and his colleagues, who invented SONAR (SOUND AND NAVIGATION AND RANGING) systems (31, 30). However, breakthrough in development of highly advanced SONAR equipments was realized during the Second World War. Pioneer investigators of diagnostic U/S utilized equipments and technology previously used for industrial and military purposes.

To achieve adequate imaging, the organ or part of the body being scanned had to be immersed in a tank of water. This was first attempted by Dussik brothers in 1937, (31) who tried to visualize the cerebral ventricles by measuring attenuation of U/S beam passed through a human head immersed in water. In the late 1940s, Douglas Howry and John Wild, among other early researchers used the available surplus war materials to develop equipments that employed ultrasonic echoes to detect gallstones and other foreign bodies (31-30).

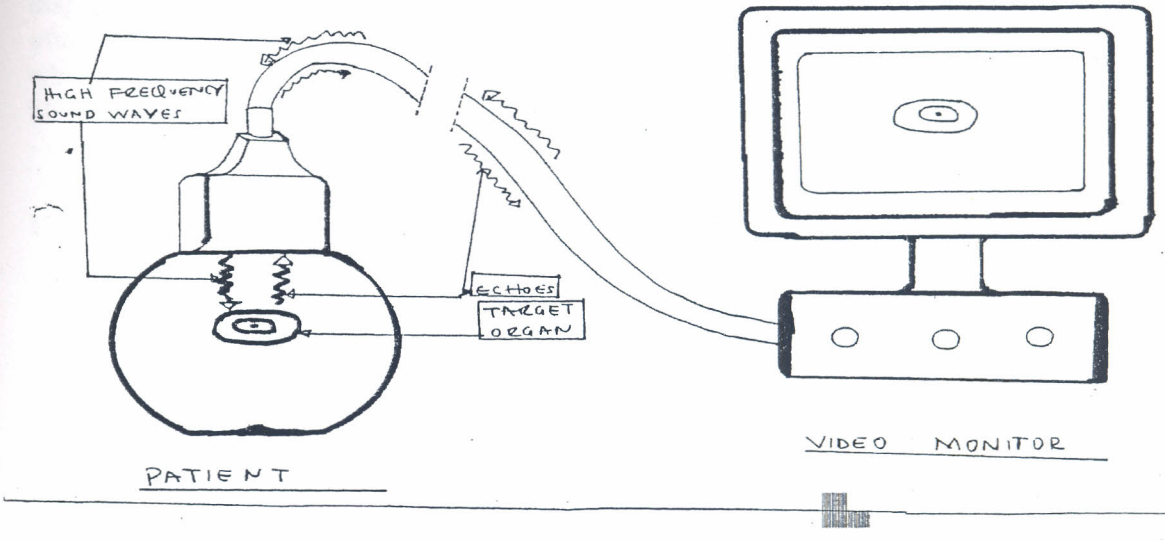
John Wild and Reid (an electronic engineer) developed B.Mode Scanner in the mid 1950s. John Wild is also credited with the demonstration that ultrasound could be utilized to differentiate between normal tissues, benign, and malignant tumors (31) In 1956, a Japanese researcher, Santomur (31), developed Doppler flow scanner in Japan. Real- time scanners were developed in early 1970s, and since then, major advances in developing sosphicated high-resolution U/S scanners have been realized.

BASIC PRINCIPLES OF ULTRASONOGRAPHY

Ultrasound is high frequency sound waves greater than 20,000 cycles per second (Hertz, Hz) that is beyond the human auditory range. The sound waves are generated by vibrations of Piezo-Electric Crystals in the transducer (probe) upon passage of electric current. The vibrations give rise to high frequency sound waves transmitted in

short bursts or pulses at a rate of 1000 per second which eventually penetrate the tissues being examined. However, the sound waves are reflected at interfaces of structures with various acoustic impendance and then picked as echoes in between pulses by the transducer. The returning echoes are converted into an electrical current and then reconstructed into a two dimensional image which is displayed on video monitor. (30, 32, 33)

Diagram:1



The types of transducer best suited for evaluation of the neck region are the linear array phased transducers. They are commonly used to evaluate the neck for nodal and thyroid diseases. Reflected ultrasound information can be displayed in various forms of modes, depending on the type of U/S system in use. Most of the U/S instruments

combine Gray- Scale and Real -Time imaging technologies which involve identification of a target organ by Gray- scale mode and then "freezing" the image on display for proper evaluation. Real- time imaging displays movement of images of the body part being scanned.
Newer generations of U/S systems have in built Doppler Systems which are utilized to demonstrate blood flow within blood vessels. Various types of Doppler Systems have been invented. They include continuous wave, pulsed wave, colour Doppler ad Duplex Doppler Systems. (30, 32) Colour Doppler and Duplex Doppler systems are commonly used to evaluate intranodal vascular patterns (8, 22, 29, 28) Colour Doppler Scanner displays real-time images showing the direction and distribution of blood flowing in vessels as well as images of tissues surrounding these vessels (30) Differing velocities of blood flowing within blood vessels of the organ being displayed are distinguished by different colours assigned by the sonographer. Most often, colour red portrays high velocity vessels (arteries) and blue signifies veins which have low flow velocities. Duplex Doppler Systems determines the velocity of blood flow within a particular blood vessel displayed on a frozen image. (9)

ULTRASONOGRAPHIC CRITERIA FOR NODAL METASTASIS

Modern Real- time Ultrasound Scanners which have High Frequency Linear array transducers have proved very valuable in the assessment of neck nodal status in patients with Head and neck cancer. Combination of Gray-Scale and Colour Doppler Sonography is employed to display both intranodal morphological features and vasculature respectively (2, 7, 21, 35, 29, 28)
Gray – Scale Sonographic criteria used to evaluate neck nodal status includes: - size, shape, hilar echogenicity, nodal margins, and intranodal necrosis (7, 15, 22, 29, 28)

Size

Nodal size alone is not a very reliable criterion of differentiating benign from metastatic Lymph nodes due to overlap of sizes. Small lymph nodes can harbor metastasis deposits and similarly large lymph nodes could be as a result of inflammation (21, 22). Nevertheless, lymph nodes with axial diameter greater than 10mm have a tendency to be metastatic. It has been demonstrated by various researchers that, 80% of lymph nodes with diameter greater than 10mm in patients with Head and Neck Cancer, are malignant (22,34)

Shape

Benign cervical lymph nodes typically assume an oblong or ovoid shape, whereas metastatic nodes tend to be round in shape with Longitudinal /transverse (L/T) axis ratio less or equal to 2. Benign lymph nodes have L/T diameter ratio equal or greater than 2. Shape of the neck nodes is a reliable criterion in differentiating between benign and malignant lymph nodes (1, 7, 21)

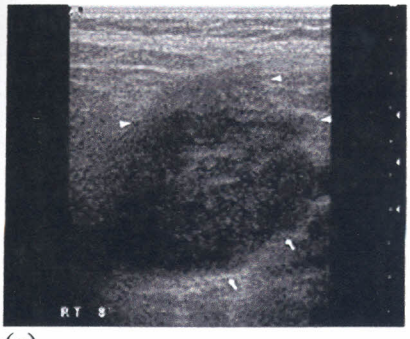
Nodal Margins

Metastatic lymph nodes display sharp margins as opposed to benign nodes which do not show well defined borders on gray- scale U/S. However, reactive nodes exhibit poorly defined margins due to perinodal inflammatory reaction. Similar feature is seen in metastatic lymph nodes with extra capsular tumor spread. Thus, state of nodal margins is not a sensitive criterion for differential diagnosis (1)

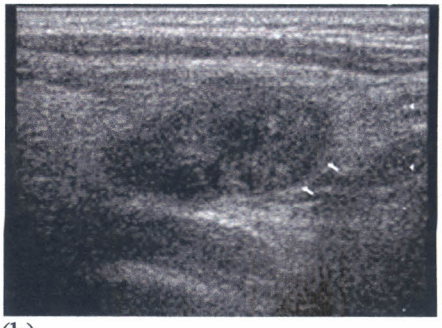
Echogenicity

Metastatic lymph nodes are usually hypoechoic when compared with adjacent soft tissue structures, especially muscles. They appear as well circumcised hypoechoic images. Normal lymph nodes are also hypoechoic but unlike metastatic lymph nodes, they are usually oblong and are not well demarcated. (1, 2, 9)

FIGURE 3 Grey scale ultrasonography scans of lymph nodes



(a)



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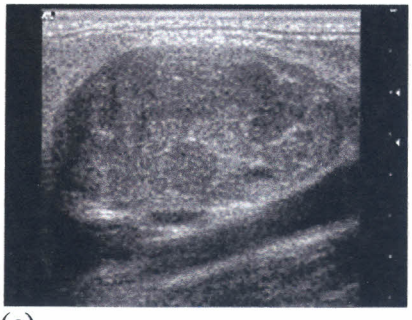

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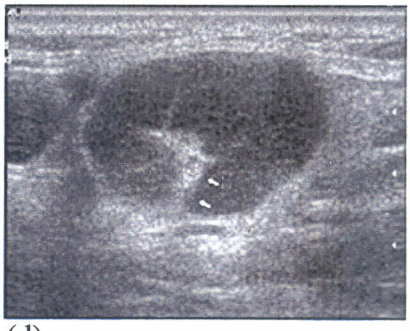


(d)

(a), (c), and (d) shows clear margins while (b) shows diffuse outline, a common feature of benign nodes. (d) Shows hilar echogenicity.

NODAL HILUS

Echogenicity of the hilum is attributed to the presence of abundant fluid-filled lymphatic sacs and therefore displaying a characteristic echogenic texture in normal lymph nodes (7)
Pathologic lymph nodes do not usually show echogenicity in the hilus. Metastatic lymph nodes at the early stages of tumor involvement may show echogenicity similar to benign lymph nodes. Thus, nodal hilus cannot be relied upon in determining benign from malignant lymph nodes (29)

INTRANODAL NECROSIS

Intranodal necrosis is a feature of pathologic lymph nodes and can be divided into two categories: coagulation necrosis and cystic necrosis (7) Coagulation necrosis is displayed as an intranodal echogenic focus whereas cystic necrosis simulates echolucent zones within the lymph nodes. Central necrosis is a common phenomenon in lymph nodes infiltrated by non-Hodgkin's lymphomas and squamous cell carcinoma. Tuberculosis lymph nodes, however portrays the intranodal echogenicity due to cystic necrosis.(1)

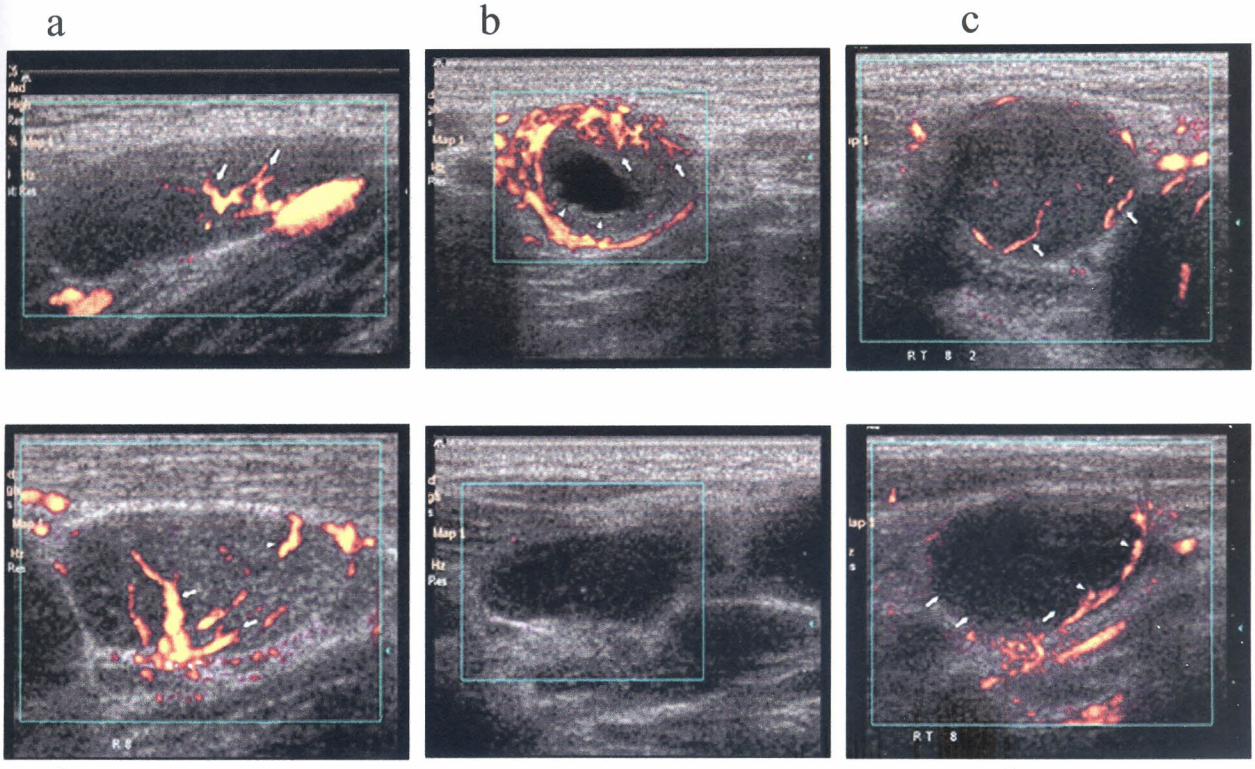
INTRANODAL VASCULATURE

Angioarchitecture of lymph nodes is evaluated with Colour Doppler Sonography (CDS) Vascular patterns of lymph nodes can be classified into three major groups(29) based on location of blood vessels:-

- Hilar Vascular pattern; - CDS displays flow signals branching radially from the nodal hilum.
- Peripheral vascularity; characterized by short vessels which show flow signals mainly in the periphery (cortex) of the lymph node.
- Mixed Vascularity – flow signals demonstrate both hilar and peripheral vascular patterns.

Normal lymph nodes most often display, either hilar vascular pattern or are avascular on CDS. This is due to the fact that they have slow flow rate, small calibre blood vessels, and therefore difficult to detect blood flow using conventional CDS. (1, 8, 22, 28, 29) Pathologic lymph nodes display prominent flow signals due to increased vascularization and blood flow. Reactive nodes show increased hilar flow signals and also have hilar arteries with larger diameters. Malignant lymph nodes show varied vascular patterns. Some malignant nodes display intranodal focal avascular zone, due to central necrosis. Other vascular patterns described in metastatic lymph nodes includes:-displacement of hilar blood vessels and aberrant hilar blood vessels. However, peripheral vascular pattern has been regarded as the most common pattern in malignant nodes (1)

Figure 4: Colour Doppler Sonography Scans showing angioarchitecture of lymph nodes



Lymph nodes showing different vascular patterns. (a)& (d) hilar vascularity ;(b) displaced vascularity with intranodal cystic degeneration; and subcapsular vessels ;(c) aberrant course of intranodal vessels, few subscapular vessels visible: (f) Hilar vessels, subcapsular vessels and displacement of intranodal vessels, (e)
avascular lymph nodes

Numerous previous CDS studies have shown that a Lymph node that is round (L/T<2); has peripheral or focal vascular pattern and shows absence of hilar echogenicity on CDS is most likely metastatic. (1, 8, 22, 28, 29,)

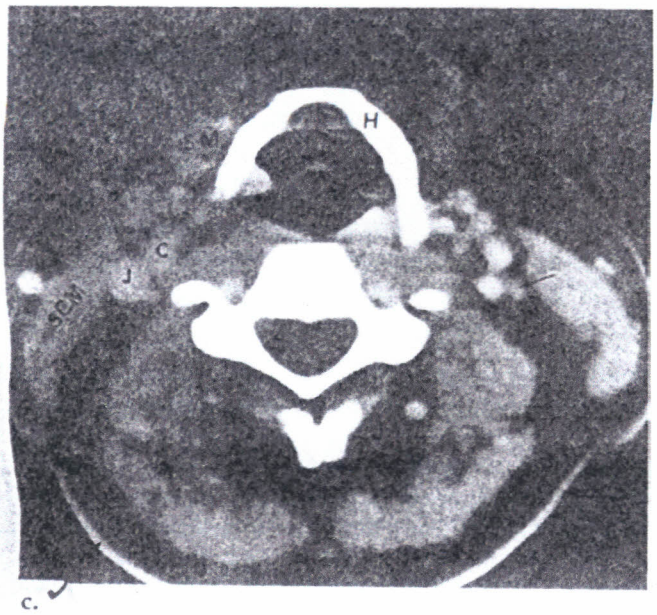
COMPUTED TOMOGRAHY (SCAN)

The invention of computed tomography (CT) in 1972, by Godfrey N. Hounsefield (30), revolutionized the diagnosis of disease in all fields of medicine. The first study of cervical nodal metastasis with CT published in 1981 concluded that CT had a promising role in staging of neck nodal metastasis (26). Since the advent of high-resolution CT- scanners and CT contrast agents, CT has proved to be invaluable diagnostic tool in evaluating patients with head and neck cancer. Numerous studies have indicated that CT compares favourably to palpation in evaluating neck nodes, with overall rate of error ranging from 7.5 % to 18%
(17, 24, 26, 34) However, other reports have suggested that CT has no added advantage over palpation. Furthermore, high rate of error of 31% has been cited in some studies. (13, 16) Size, shape, central necrosis, and grouping of multiple lymph nodes are the commonly used CT diagnostic criteria for assessing neck nodal disease (15, 16, 17, 24, 26, 34)

Central necrosis has been documented by many authors as the most accurate criterion of identifying metastases in lymph nodes on CT. (5, 17, 24, 26, 34) Contrast enhanced- CT features of metastatic lymph node include: central hypo- attenuated zones and irregular – rim – contrast enhancement. However, these features can be simulated by spontaneous lymph node necrosis, abscess formation, cystic degeneration or central adipose metaplasia (fatty degeneration).Minimal axial nodal diameter of 11mm for submandibular and jugular diagnostic nodes, and 10 mm for all other cervical lymph node groups has been proposed as the accurate lymph node size that signifies nodal involvement (2, 5, 27)

Accurate assessment of nodal size is however, influenced by homogenicity, orientation, and the ability to show clear margins of individual nodes. CT is limited in free rotation scan plane selection unlike U/S. Shape of lymph nodes is not a sensitive diagnostic criterion on CT. But it has been shown that, spherical nodes larger than 10mm in diameter are most often metastatic (5, 34)

FIGURE 5



Contrast-enhanced CT scan of the neck at the level of hyoid bone. Normal lymph nodes (Arrows) are seen close to major vessels.

On CT, presence of groups of three or more lymph nodes, each with maximal diameter of 8mm-15mm (or minimal axial diameter of 8 – 10mm) located along the drainage chain of the primary tumor, is suggestive of nodal involvement (2, 5, 34). Benign nodes appear as elliptical or oblong, homogenous structures that lack peripheral – rim- contrast enhancement on contrast – CT. However, there may be areas of low attention especially in larger nodes due to focal fatty degeneration (26, 34)

Magnetic Resonance Imaging (MRI)

MRI has excellent contrast resolution when compared with CT.It is non- invasive but quite expensive and available in very few centers in the country. MRI diagnostic criteria for cervical lymph nodes metastases is similar to that of CT, that is, central necrosis, nodal groupings and minimum nodal axial diameter of 10mm. Various studies on neck nodal detection with MRI have reported an overall rate of accuracy of 86-87% (2,5, 13, 35)

FINE NEEDLE ASPIRATION (F.N.A) BIOSPY

Fine needle aspiration (biopsy) Cytology (FNAc) was first documented in 1930, by Hayes Martin. (36) It is a very reliable diagnostic tool in the assessment of head and neck masses. The method has a high rate of accuracy especially when used in combination with high – resolution U.S guidance. Sensitivity and specificity ranges of 90-99% and 94-100% respectively, have been documented in literature (35, 37). A study conducted in KNH in 2003, reported an overall FNAc accuracy of 93.6 % in diagnosis of head and neck masses(38). It is a simple, cost-effective, and easily repeatable procedure but its sensitivity is largely dependent on the experience and skill of cytopahologist who perform the procedures and analyze the aspirates. Notable pitfalls of FNAC includes: - insufficient aspirate, bloody aspirate or aspiration of non- representative materials especially when small deeply placed lymph nodes are missed (35)

NEW DIAGOSTIC TECHNIQUES

NUCLEAR IMAGING TECHNIQUES

POSITRON EMMISSION TOMOGRAPHY (P.E.T) SCAN

This new diagnostic method has been reported by authors to be more accurate in evaluating patients with cancers of unknown origin, recurrent head and neck tumors, and those suspected to have occult metastatic neck lymph nodes (17, 18, 36, 39) The method is based on detecting metabolic alterations in neoplastic cells after uptake of radio-labeled glucose. 18-Fluoro- Deoxyglucose (FDG-18) is administered intravenously and then taken up by metabolically hyperactive metastatic cells either in the primary tumor site or metastatic regional lymph nodes.
It is eventually trapped in the intracellular spaces of these cells which appear as "hot" spots on P.E.T camera (17, 18). It has been shown that FDG-PET is superior to CT or MRI in staging neck nodal disease. However, FDG-PET may fail to detect nodes with minute volumes of micro metastasis or metastatic lymph nodes with reduced metabolic activity due to extensive central necrosis. In addition, metabolically active benign nodes may simulate "hot Spots on P.E.T scanner (17, 18)

Sentinel lymph node radiolocalization biopsy (SNRB)

The method of lymphatic mapping was first described by Sherman and Ter-Pogossian in 1953 (25). It involves injection of radio nucleides, Technetium– 99m tagged onto colloids which have a tendency to accumulate in the initial draining nodes without significant absorption into the surrounding tissues. The tagged colloid is injected around the primary tumor and subsequently taken up by the local lymphatic capillaries which join up to drain into the first lymph node through afferent lymphatic vessels. This first lymph node which is identified by radiolocalization using hand held gamma detector placed on the skin, is referred to as: - SENTINEL LYMPH NODE (40). The sentinel nodes are then removed and frozen for histopathological analysis. Accuracy rate of sentinel lymph node radio

localization cited in a recent study ranged between 95 % and 100% (25). Due to variability and complexity of lymphatic drainage systems in the head and neck region (37), there is always the possibility of uptake of radio (labeled) proteins by adjacent lymphatic capillaries that do not necessarily drain the primary tumor site. Moreover, SNRB has the limitation of detecting skip nodal metastases. (22, 25)

Immunohistochemical and molecular analyses

In recent years, intense research has been directed towards identification of oncogene abnormalities which correlate with lymph node metastasis by using tumour makers. Studies carried out using cytokeratin (CK) immunohistochemistry (IHC) on cervical lymph node reported that 5% to 20% of negative neck dissection specimens. After routine histopathological evaluation have nodal metastasis (27, 41). Qualitative CK-real time reverse transcription polymerase chain reaction (PT-PCR) has been recently employed to demonstrate the expression of CK-14RNA in lymph nodes initially reported to be histopathologically negative for malignancy.(41).
Immunohistiochemical studies have demonstrated that expression of Vascular Endothelial Growth Factor [VEGF] which is responsible for tumor angiogenesis is associated with tumor metastasis. It has been postulated that inhibition of VEGF could block tumour angiogenesis and therefore curtail nodal metastasis (42).

Research studies have reported conflicting results on correlation of expression of tumour markers with lymph node metastasis but research is still going on (43). It is hoped that more relevant tumour related factors will be isolated and overcome the limitations of currently used diagnostic modalities which have relied heavily on morphological features in detecting occult nodal metastasis.

LITERATURE REVIEW

Since the successful trials on medical applications of sonography in late 1940s (21, 31,30),U/S has proved valuable in the fields of obstetrics, cardiology and Head and neck surgery. In the recent past, tremendous research effort has been directed towards identification of more accurate techniques of staging neck nodal disease. There are an estimated over 750,000 new cases of head and neck cancers diagnosed worldwide each year(36) and despite advances in diagnostic imaging techniques, mortality rates have not decreased significantly during the past 30 years (44). Previous studies have shown that sonography has a markedly higher sensitivity rate compared to clinical examination in detecting cervical lymphadenopathy (1, 2, 7, 15, 29,36). Most of research work on sonographic assessment of neck lymph nodes has been conducted in North America and East Asian countries, perhaps due to the high incidences of head and neck cancers reported in those countries. Furthermore, no work has been published on African based research studies evaluating the role of ultrasound in neck nodal staging.

Bruneton et al (45) documented sensitivity of sonography of 93% compared with only 78% for palpation in detection of lymph nodes. In another study by Shaik Sajeeda et al (12) nodal staging of 22 out of 25 patients was changed after evaluation with high – resolution ultrasound.
Nobert Gritzman et al (23) found that sonography had a sensitivity of 95% and overall accuracy of 87 % in detection of metastatic neck nodes.

Size

Paul C. Hajeck et al [15] demonstrated that even small nodes with diameters ranging from 5mm to 10mm can be visualized with U/S. They also reported that CT scan, which utilizes nodal size as the main criterion for detecting lymph node involvement by tumour, cannot accurately show nodes in these size ranges. This finding was also confirmed by Ross T. Sutton et al [21] in 1988, after they evaluated 52 patients who had developed neck masses after thyrodectomies. They also noted that there is considerable overlap of size range for benign and malignant nodes and, therefore, concluded that lymph node size alone cannot be relied upon as an indicator of metastasis in neck lymph nodes. Nevertheless, numerous previous studies have shown that metastatic lymph nodes tend to be larger than 10mm in diameter [5, 15, 16, 22] .

Shape

Malignant lymph nodes usually assume a round or spherical shape with a longitudinal versus transverse diameter (L/T) ratio equal or less than -2 [1, 22, 31]. In a study by Shaik Sajaeda et al [12], they reported that L/T ratio is a reliable indicator in differentiating between benign and malignant neck lymph nodes. They found that 80% of clinical lymph nodes with L/T greater than 2 were benign and therefore concluded that lymph nodes with L/T ratio less than 1.4 strongly suggests metastasis. Pierre Vassalo et al [7] found that 80% of malignant nodes evaluated had L/T ratio less or equal to 2 and 85% of benign nodes had L/T ratio equal or greater than -2. They also noted that 90% of malignant nodes showed hilar narrowing accompanied by cortical widening. In their

study, all lymph nodes that had focal cortical widening on U/S were malignant. Similar findings have been reported by many authors in previous studies. [1, 2, 7, 22, 28]

Echogenic Hilus

Echogenic nodal hilum is a common sonographic feature of normal cervical lymph nodes. Absence of nodal hilus has been quoted by various authors as a strong indicator of metastasis [1, 36] Anil Ahuja et al [29] observed that 91.5% of malignant neck lymph nodes did not show echogenic hilus on gray-scale sonography, while study by Pierre Vassalo et al [7] reported that 44% of malignant lymph nodes simulated absence of hilus compared with 8% of benign lymph nodes.

Vascularity

Over 90% of normal cervical lymph nodes larger than 5mm in diameter, show hilar vascularity on colour Doppler sonography, where as malignant ones predominantly show peripheral or mixed vascularity. [1, 29]. Alexander Tschammler et al [28] conducted a survey in an attempt to differentiate benign from malignant lymph nodes using Colour Doppler Sonography (CDS). They were able to classify correctly 88% benign and malignant lymph nodes. They concluded that CDS is a reliable and reproducible diagnostic method that can be utilized to detect benign and malignant lymph nodes by evaluating their intranodal vascular patterns.Similar results were reported by Anne R Buckley, Elaine H. Moss and Andres Blockmann, who reported a CDS sensitivity of 91% in diagnosis of malignant lymph nodes [22]. Anil Ahuja et al [29] observed that, displaced vascularity is a common sonographic feature of tuberculous lymph nodes. They reported that, 91% of nodes that showed intranodal necrosis had displaced hilar vascularity.

Paul C. Hajack et al [15] demonstrated that U/S is highly sensitive in not only evaluating cervical lymphadenopathy, but also demonstration of infiltration of adjacent structures by tumour, specifically, common internal and external carotid arteries and the neck muscles. Combination of gray –scale sonographic lymph node features and CDS vascular patterns were reported by Michael T.C. Ying and Anil T.Ahuja [1] to be highly accurate in differentiating metastatic and benign cervical lymph nodes.

STUDY JUSTIFICATION

Early identification of neck nodal metastases is critical in planning appropriate management of patients with head and neck cancer. Although U/S has proved invaluable in detection and staging of metastatic lymph nodes in studies conducted in various centers outside Africa, no similar studies have been done locally.

Administration of contrast media is necessary to detect neck nodes and account for huge proportion of the cost of imaging.
U/S has been shown to detect neck nodes whose sizes are beyond the range of CT scan and can probably replace contrast media administration and therefore reduce the cost burden to the patient and Government, as well as avoid the risk of adverse effects associated with contrast media administration.
Reduced cost will ensure early diagnosis and management of patients.

AIM: To assess the value of high-resolution sonography as a primary imaging modality in diagnosis and management of metastatic neck lymph nodes in patients presenting with head and neck cancer at ENT-. Head and Neck Surgery Unit, in Kenyatta National Hospital

Specific objectives

- To document the commonest sonographic features displayed by metastatic cervical nodes on gray scale U/S.
- To evaluate performance of U/S in detecting metastatic neck nodes.
- To compare U/S versus P/E and CT scan in staging neck nodal disease.

METHODOLOGY:

STUDY DESIGN- PROSPECTIVE CROSS-SECTIONAL STUDY

Patients were recruited at the ENT- clinic KNH and dental clinic in Kenyatta.

Imaging was carried out in KNH and U.O.N radiology units and plaza imaging center-general accident house- Nairobi.

STUDY HYPOTHESIS

Null hypothesis: U/S cannot be an alternative to the administration of contrast medium in diagnosis of metastatic neck node disease using CT in patients with head and neck cancer.

Alternative hypothesis: U/S can obviate the utilization of contrast medium in the diagnosis of metastatic neck node disease using CT, in patients with head and neck cancer.

Inclusion criteria

- All patients with head and neck malignancies
- Patients presenting at ENT clinic from other outpatients clinics or wards referred for FNAc or open biopsy of cervical lymph nodes.
- Patients scheduled for definitive management (radiotherapy, chemotherapy or surgery) who require restaging of the primary tumour and neck nodes.Patients suspected to have metastatic cervical lymphadenopathy.

Exclusion Criteria

- Patents who have already received treatment - (radiotherapy to the neck/ Neck dissection) or chemotherapy
- Patients with massive, matted neck nodes />6cm.

MATERIALS AND METHODS.

Study population.

A total of 152 consecutive patients with confirmed or suspected primary head and neck cancer were included in the study carried out over six months period.

Routine general examination and detailed otolaryngologic examination was conducted on each patient. The location of palpable nodes was classified in neck levels I to VI. The number, size and mobility of the nodes was documented.

All patients underwent routine diagnostic procedures, which included panendoscopy, examination under anaesthesia, and biopses taken from suspected primary sites. Examination under local anaesthesia was carried out in those patients with apparent and easily accessible primary cancer localizations and biopsies were also taken.

5mm slice thickness axial transverse CT scan imaging with contrast enhancement performed to all patients. Third and fourth generation CT scanner (Philips, tomoscan CXQ, Netherlands. & Philips Tomoscan Netherlands respectively) were used.

The CT findings were documented indicating the site, size, presence of central necrosis, multiplicity, and presence of ring enhancement of nodes detected

54(35.5%) patients had detectable neck nodes on contrast-enhanced CT and therefore were regarded as having metastatic nodal disease.

Neck evaluation with U/S was performed by two radiologists (A.O; MW), who were blinded of the clinical diagnosis. Examinations were conducted with high-resolution array scale. U/S using 7.5 MHz and 12.5 MHz linear array probes. Colour Doppler sonography scans were performed on all nodes detected.

Lymph node shape was determined by measuring the longitudinal (L) and transverse (T) diameters on the same scan and L/T ratio calculated. Lymph nodes were grouped into two categories based on L/T; L/T≥2 and L/T < 2.

The size of lymph node was documented indicating the largest diameter identified at a given neck level by U/s.

Echogenicity was assessed and nodes were classified into three echogenic features:

Present hilar echogenicity; absent hilar echogenicity and intranodal necrosis.

Vascularity was also evaluated and nodes were separated into four classes: Hilar, peripheral, mixed (peripheral/ hilar), and avascular.

The margin was evaluated and nodes classified into two groups according to the features of their margins, sharp and diffuse.

Criteria for diagnosis of malignancy in the nodes were: mixed or peripheral vascularization, size (diameter >10mm), shape (L/T <2).

71 patients had palpable neck nodes and 69 of them underwent FNA biopsy of the nodes. Nodes, which were palpable and less than 6cm in diameter, were selected for biopsy. The level and neck side where biopsy was taken was indicated in the laboratory request form, which was labeled with a red sticker for easier identification. The specimens were stained and eventually examined. The specimens were analyzed by the same pathologist(M.U.)who was blinded of the clinical diagnosis. Cytological findings were used as gold standard and were compared with the findings of P/E, CT, and U/S.

SAMPLE SIZE

Number of patients to be included in the study will be determined using the Fisher's formula (46)

$$n = \frac{Z^2 1-\alpha p(1-p)}{\delta^2} \qquad n = \frac{1.645^2 \times 0.82 \times 0.17}{(0.05)^2}$$

$$\approx 151$$

n = Sample Size to be determined

z = standard normal deviation corresponding to 90% confidence internal

δ = *Absolute precision (5%)*

α = level *of significance*

P- Specificity of standard test used to evaluate neck lymph node metastasis at the ENT unit. The standard test is contrast enhanced CT which has a specificity of (82%)

ETHICAL CONSIDERATION

- Patients were inducted after voluntarily signing informed consent and for those not eligible to sign (e.g. children) the guardians signed on their behalf.

- Study was carried after approval by the Ethical Committee of Kenyatta National Hospital

- The information obtained from individual patients was treated with confidentiality.

STUDY LIMITATION

- Few neck dissections done, therefore not possible to determine sensitivity/specificity of U/S.
- Timing of contrast administration and scanning affected the detection of neck nodes.
- CT scanning delay – slow machine.
- Prohibition of patients referral to other facilities offering similar services outside KNH.
- Breakdown of CT scan machine. Jan – Feb 2006.
- *High cost of imaging with CT scan.*

RESULTS.

A total of 152 patients were included in the study. The youngest patient inducted was 17 years old and the oldest, 83 years. The mean age ratio was 54.9 years. 111(73%) were males while 41(27%) were females.

The commonest primary site was larynx 55(36.2%) followed by nasopharynx 28(18.4%). Malignant tumors were found in 18(11.8%) in the tongue, in 10 (6.6%) in oropharynx; in 9(5.9%) in the Sinonasal region and in 8(5.3%) in the hypopharynx.

One patient had `carcinoma of the skin overlying the tail of the Rt parotid (**table 1**).

Site of primary tumour- (table 1).

	Frequency	Percent
Thyroid	1	.7
Larynx	55	36.2
External ear	2	1.3
Tonsil	1	.7
neck nodes	1	.7
nasopharynx	28	18.4
hypopharynx	8	5.3
sinonasal	9	5.9
skin rt infraauricular	1	.7
Parotid	4	2.6
cervical oesophagus	6	3.9
Maxilla	3	2.0
mandible (osteogenic ca)	1	.7
Tongue	18	11.8
oropharynx	10	6.6
Nose	1	.7
Palate	3	2.0
Total	152	100.0

The tumor staging after PIE, CT and endoscopic evaluation wasT1 9(5.9%), T2-20(13.2%), T3 39(25.7%) and T4 83(54.5%).

One patient had Hodgkins lymphoma of cervical nodes and therefore not staged using TNM classification.

Primary Tumour staging – T (table 2).

		Frequency	Percent
Valid	1	9	5.9
	2	20	13.2
	3	39	25.7
	4	83	54.5
	Total	151	99.3
Missing	System	1	0.7
Total		152	100.0

86(56.6%) patients were staged as NO nodal stage,; 18(11.8%) as N1, 26(17.1%) as N2, and 21 (13.9%) as N3.

Nodal staging – N- (table 3).

		Frequency	Percent
Valid	0	80	52.3
	1	18	11.8
	2	32	2i.0
	3	21	13.8
	Total	151	99.3
Missing	System	1	0.7
Total		152	100.0

Majority of the patients 110(73.7 had different grades of squamous cell carcinoma as the histological type of the primary tumour. 30(20.0%) had anaplastic carcinoma and 4(2.6%) had adenoid cystic carcinoma.

PRMARY SITE BIOPSY – histology- (table 4)

		Frequency	Percent
Valid	Anaplastic Ca	29	19.1
	follicular cell carcinoma	1	.7
	Squamous cell carcinoma (SCC)	111	73.1
	hodgkin's lymphoma	1	.7
	pleomorphic sarcoma	1	.7
	adenoid cystic Ca	4	2.6
	verucous carcinoma	1	.7
	oesteogenic Ca	1	.7
	Adenocarcinoma	3	2.0
Total		152	100.0

Three (2%) patients had lung metastases.

71(46.7%) patients had palpable cervical lymph nodes and 69 of the 71 patients underwent FNA biopsy of a single node each.

Out of 69 lymph nodes biopsies, 59 were confirmed to be metastatic and 10 were reported as benign. Comparison between P/E and cytological findings showed agreement in 85.5% of cases, or 59 of 69 neck nodes.

A total of 54 (35.5%) patients had detectable nodes on CT.

52(34.2%) patients had nodes that exhibited ring enhancement and 46 of them had nodes that showed features of central necrosis. 48(81.4%) nodes out of the 59 that were confirmed to have metastasis FNA cytology, were correctly diagnosed on CT.

Out of 17 patients staged as not having features of metastasis in the neck nodes identified on CT, 11(18.6%) were confirmed to have metastasis after FNAc .

A total of 152 patients were evaluated using U/S, and the node with largest diameter in each patient documented. 108 (71.2%) were located in level II, 28(18.4%) levelII, 7(4.6%) level I; 5(3.3%) level IV, and 4(2.6%) level IV.(**Table 5**)

US – neck level of nodes identified by U/S (Table 5).

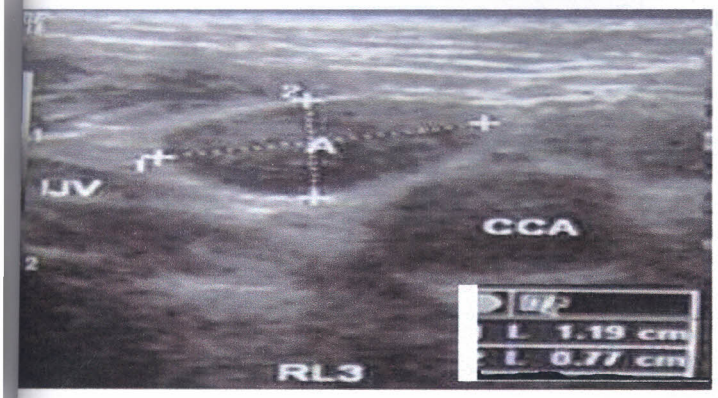
		Frequency	Percent
Valid	I	7	4.6
	II	108	71.1
	III	28	18.4
	IV	4	2.6
	V	5	3.3
	Total	152	100.0

67 (44.1%) out of 152 lymph nodes had L/T < 2, and therefore assumed round shape where as 85 (55.9%) had L/T≥2 and were oval or oblong in shape.

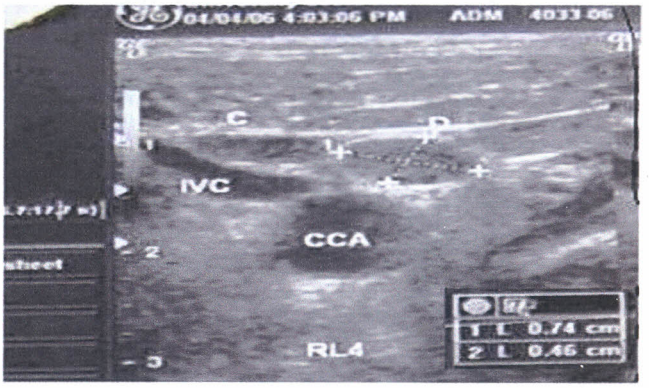
Hilar echogenicity was displayed by 119 (78.3%) lymph nodes whereas 21 (13.8%) nodes were hypoechoic and 12 (7.9%) nodes exhibited intranodal necrosis.

Majority of the lymph nodes 131 (86.2%) had sharp margin compared with 21 (13.8%) that displayed diffuse margin. A total 67(44.1%)nodes exhibited hilar vascularity, 60(39.5%) displayed mixed vascular pattern, 24(15.8%) displayed peripheral pattern, and only one was avascular.

Figure 1: Gray –scale sonography of neck nodes . (a) Normal lymph node (with a large longitudinal diameter) adjacent major neck vessels;(b,d,f)-multiple nodes; (e) round shaped (L/T <2) node



(a)



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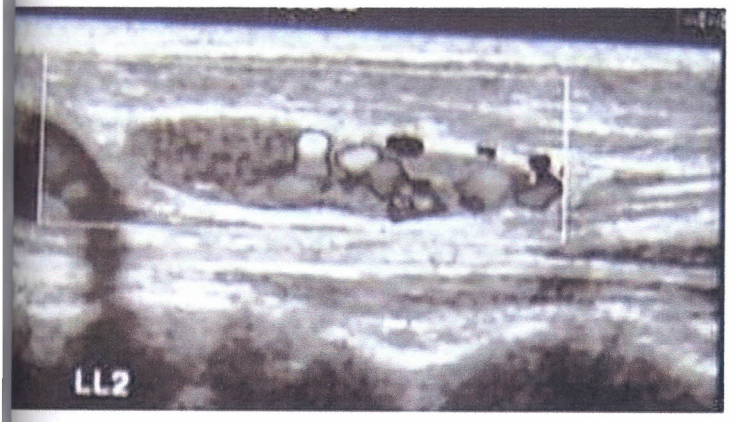
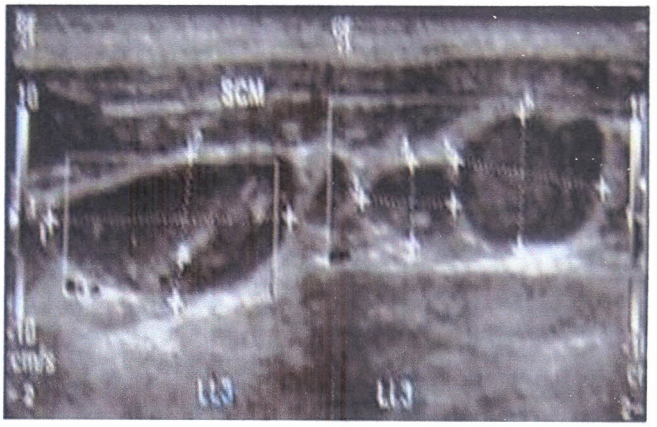
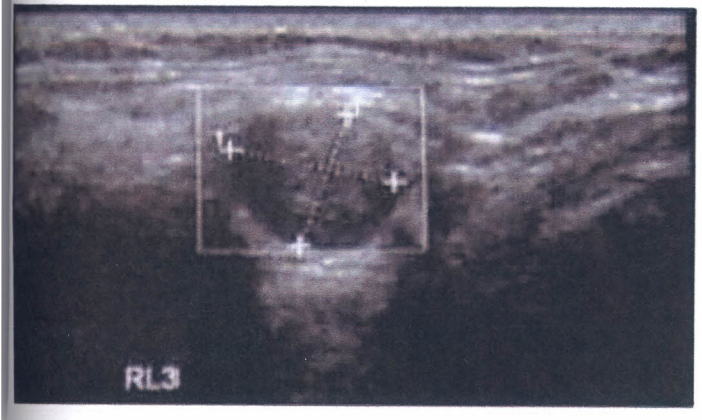
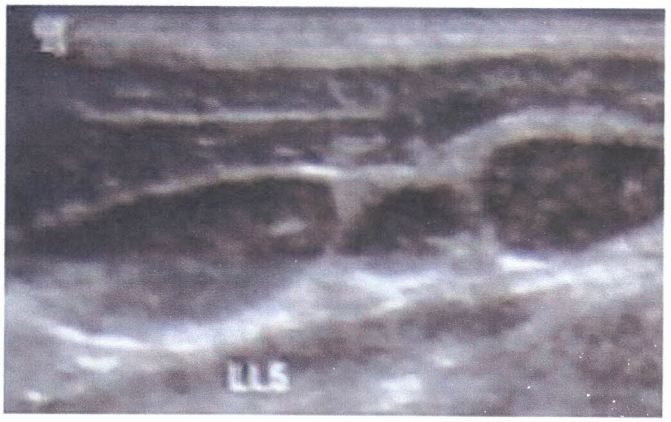


(c)



(d)





57(37.5%) patients had nodes that met the diagnostic criteria for nodal metastasis by U/S .They displayed either peripheral, or mixed vascularity, had L/T<2, displayed sharp margins and were echogenic. 55(36.2%)patients had nodes that were confirmed to have metastases U/S failed to detected nodal disease in 2(1.3%)patients but was in agreement with the cytological results in 8(5.3%) patients whose nodes were benign. In this study U/S correctly identified 93.2% nodes that had metastases.(table 6)

TABLE 6

U/S METASTATIC NECK NODE * FNAC Cross tabulation

			FNA cytology		Total
			positive	negativ	
Ultrasound METASTASIS IN NODES	POSITIVE	Count	55	2	57
		% within FNAC histology	93.2%	20.0%	82.6%
	NEGATIVE	Count	4	8	12
		% within FNAC histology	18.6%	80.0%	17.4%
Total		Count	59	10	69
		% within FNAC histology	100.0%	100.0%	100.0 %

FIGURE 2

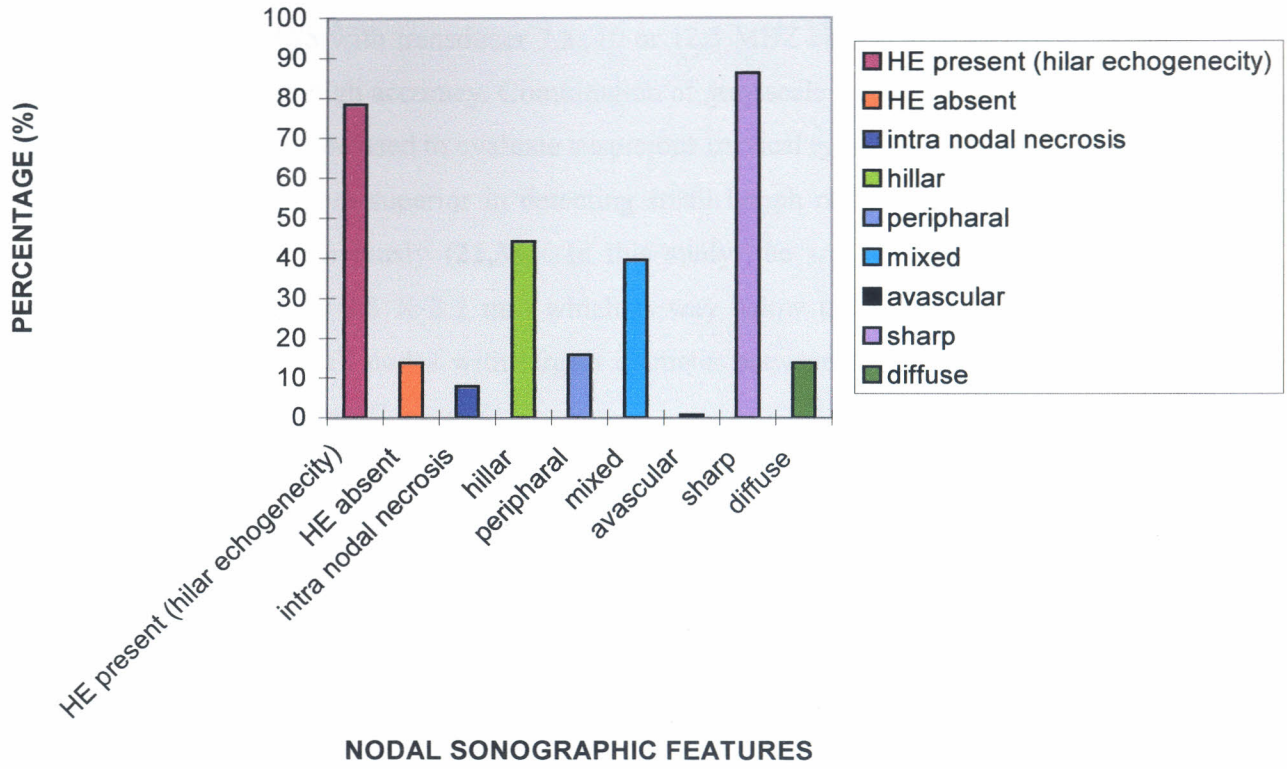
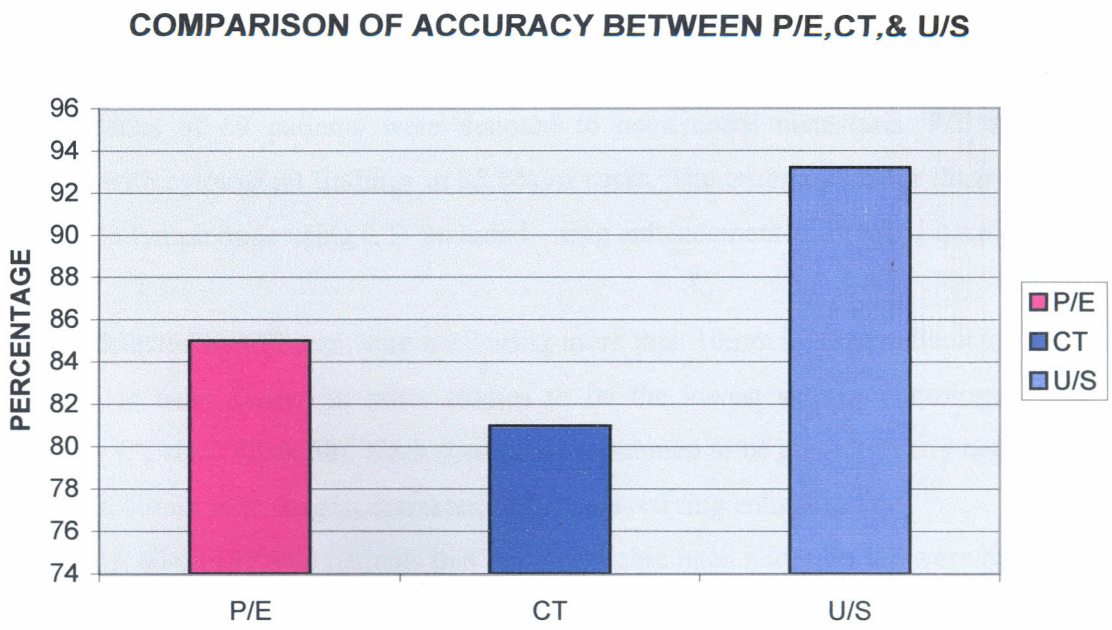


FIGURE 3



DISCUSSION.

Modern high resolution U/S with transducer 7.5, 10 or 12.5 MHZ can be used to detect pathologic neck nodes with high accuracy. Combination of gray scale and colour Doppler sonography should routinely be used to evaluate suspicious cervical lymph nodes.

U/S has proved to be far more superior in detecting small lymph nodes up to 5mm in diameter in studies done previously **(21,38)** In this study, the smallest lymph node identified had dimensions of 3.8 X 2.2 mm which is way below the size quoted in literature of 5mm. Many small nodes with largest diameter between 3 and 8 mm were outlined by U/S mainly in level III up to V.

P/E often misses metastatic lymph nodes less than 12mm in diameter.

Nodes measuring more than 15mm are easily palpable but those measuring 12 to 14 mm in largest diameter are usually missed unless they are superficially placed especially in patients who have thin necks or those malnourished It is not easy to determine whether a node palpated is solitary or a confluence of multiple small nodes.

U/S was able to detect multiple lymph nodes in all patients included in the study compared to PIE and CT, which detected nodes in 71(46.7%) and 54(35.5%)patients respectively.

69 out of 71patients that had palpable nodes underwent FNA biopsy of a single node each. In this study, it was not possible to determine sensitivity, and specificity of P/E since all necks of 69 patients were denoted to have nodal metastasis. P/E showed agreement with cytological findings in 85.5% of cases. The criteria used for diagnosis of metastasis in lymph node using CT- included – ring enhancement and central necrosis.

All nodes detected by CT scan were measuring more than 10mm in largest diameter.

This has also been quoted in other studies to be the lowest size of pathologic node detected by CT scan. **(2, 5, 30**). Neck disease was assumed to be present in any neck node greater than 10mm in its largest diameter, and displayed ring enhancement.

In this study, all 54 (35.5%) patients that had detectable neck nodes on CT were regarded as having metastatic neck disease. 48 (81.4%) patients had CT results in agreement with cytological results in detecting nodal metastases. A clinical CT, Pathologic correlative study conducted by Pierre Moreau et al (1990) reported CT accuracy of 81%.

In this study, malignant nodes exhibited round shape (L/TL2) whereas benign nodes showed oblong/ oval shape (L/T≥2) on U/S. However, most of the small nodes with diameters less than 10 mm assumed round shape (L/T≥2) but were not included in the analysis. This is due to the fact that P/E or CT scan could not detect them and therefore not accessible for biopsy. Other studies have reported that round shape (L/T<2) is a sensitive U/S criterion in diagnosing metastatic nodes (**Ref- 1, 7,21).**

Study by Pierre Vassallo et al (1992)evaluating the role of high resolution U/S in differentiating benign from malignant superficial lymphadenopathy in 204 patients noted L/T<2 in 85% of metastatic nodes and L/T>2 in 86% of benign nodes.

Intranodal vascular pattern is evaluated using colour Doppler sonography and peripheral vascular pattern has been reported in many studies as the most common pattern displayed by malignant nodes (ref 21,38) .In this study 24 nodes (15.89%) exhibited peripheral vascularity whereas 60(39.5%) displayed mixed vascularity.

94.7% of the nodes that displayed peripheral vascularity were metastatic and 86.8% of the nodes with mixed vascular pattern showed evidence of metastatic disease after FNA biopsy. It can be deduced from this study that peripheral and mixed vascular patterns are strong criteria in diagnosing nodal metastasis.

Out of the total number of nodes (12) that displayed intranodal necrosis, 91.7%(11) were positive after FNA biopsy. Intranodal necrosis has been regarded as a feature of pathologic lymph nodes especially squamous cell carcinoma and non- Hodgkin's lymphoma **(1)**.

Out of 69 lymph nodes that were histologically evaluated using FNA cytology, 57 (82.6%) had sharp margin. 49(86.0%) of the total nodes with sharp margin (57) were having metastatic disease. However a total of 12 nodes out of the 69 analyzed by FNA cytology displayed diffuse margin. 10 (83.3%) of the nodes with diffuse margins had metastatic disease.

Therefore, in this study, nodal margin was not a sensitive criterion. This however concurs with other studies (1) done previously and it has been noted that benign reactive nodes do display poorly defined margins.

CONCLUSION.

In this U/S has proved to be highly sensitive in detecting small nodes hitherto not detectable by methods routinely used in nodal staging in ENT-KNH unit, namely PIE and CT scan.

U/S upstaged 7 patients (4.6%) staged as NO by CT.

It can be concluded from this observation that U/S can replace contrast medium administration during CT in staging neck nodal disease.

This can have a huge impact on cost reduction to those patients undergoing CT scan.

However, it is important to point out that a more comprehensive prospective study involving pre-operative patients scheduled for neck dissections should be carried out to confirm this important finding.

RECOMMENDATIONS.

1) Prospective study should be carried to evaluate the sensitivity and specificity of U/S in detecting metastatic neck node disease using preoperative patients scheduled for neck dissections.
2) U/S should be included as part of the routine preoperative work up of patients undergoing neck dissections or can be used to complement CT. during head , base of skull and neck imaging .
3) Modern imaging hardware –U/S, CT scan should be installed in KNH- radiology department.

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APPENDIX 1

PRO FORMA

STUDY NO:_____

A. QUESTIONAIRE

Sociodemographic Information

1. Patients Name_____ I.D No _____
2. Age _____
3. Sex Male _____ Female_____

B. PHYSICAL EXAMINATION

01. Diagnosis _____ Site of Primary Tumour _____

LYMPH NODE GROUPS PALPATED:

LEVEL	NODES	SIZE (mm)	MOBILITY	SIDE
I	1	_____	_____	_____
	2	_____	_____	_____
	3	_____	_____	_____
	4	_____	_____	_____
II	1	_____	_____	_____
	2	_____	_____	_____
	3	_____	_____	_____
	4	_____	_____	_____
III	1	_____	_____	_____
	2	_____	_____	_____
	3	_____	_____	_____
	4	_____	_____	_____
IV	1	_____	_____	_____
	2	_____	_____	_____
	3	_____	_____	_____
	4	_____	_____	_____

V	1	_____	_____	_____
	2	_____	_____	_____
	3	_____	_____	_____
	4	_____	_____	_____
VI	1	_____	_____	_____
	2	_____	_____	_____
	3	_____	_____	_____
	4	_____	_____	_____

CODE:

MOBILITY

F – FIXED

M – MOBILITY

C. INVESTIGATIONS

1. Biopsy HISTIOLOGY

I primary site – (i) Punch biopsy

_____

(ii) Endoscopic guided biopsy

_____

(iii) Incision Biopsy

_____

(iv) Excision Biopsy

_____

II Neck Nodes – (i) FNAC (site_____)

_____

(ii)Excision biopsy

_____

2. Radiological evaluation

Chest X -Ray (Report) - _____

3. Other tests (specify) _____

D. CONTRAST – ENHANCED CT SCAN OF THE NECK

DATE_____

NAME _____ I.D NO_____

DATE WHEN PERFORMED_____

HOSPITAL / INSTITUTION WHERE IMAGING WAS DONE_____

TYPE OF SOFT WARE USED_____

TUMOUR STAGING T_____ N_____ M _____

LYMPH NODES GROUPS IDENTIFIED

Level side of neck	nodes	size(mm)	central necrosis	Multiplicity	Ring Enhancement
I	____	____	____	____	____
II	____	____	____	____	____
III	____	____	____	____	____
IV	____	____	____	____	____
V	____	____	____	____	____
VI	____	____	____	____	____
OTHERS	____	____	____	____	____

CODES;

(A) CENTRAL NECROSIS

PRESENT

_√_

ABSENT

_X_

(B)MULTIPLICITY

SINGLE NODE – S

MATTED NODES – M

(C)RING ENHANCEMENT

PRESENT - _√_

ABSENT - _X_

DATE_____

E. ULTRA SONOGRAPHY OF THE NECK NODES

NAME _____ I.D NO_____

HOSPITAL / INSTITUTION _____

TYPE OF SOFTWARE USED _____

TRANSDUCER USED _____HZ_____

LYMPH NODE GROUPS IDENTIFIED SONOGRAPHICALLY

Codes of Neck	Nodes	Size(mm)L/T	Echogenicity	Vascular pattern	Margin	Side
____	1	____	____	____	____	____
____	2	____	____	____	____	____
____	3	____	____	____	____	____
____	1	____	____	____	____	____
____	2	____	____	____	____	____

1	___	___	___	___
___				
2	___	___	___	___
___				
3	___	___	___	___
___				
1	___	___	___	___
___				
2	___	___	___	___
___				
3	___	___	___	___
___				

CODES

A ECHOGENICITY

	Present (√) Absent (X)
Hilar Echogenicity	_____
Intra nodal necrosis	_____

(B) VASCULAR PATTERN

HILAR	01
PERIPHERAL	02
MIXED (PERIPHERAL/ HILAR)	03
AVASCULAR	04

C MARGIN

SHARP	01
DIFFUSE	02

D. NODES

CODE	GROUP
00	Submental
01	Submandibular
02	Upper jugular (Level II)
03	Mid-jugular (Level III)
04	Lower-jugular (Level IV)
05	Posterior triangle (Level V)
06	Retroauricular
07	Parotid (preauricular)
08	Pretracheal
09	Paratracheal
10	Retropharyngeal