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Radio Diagnosis

ROLE OF COMPUTED TOMOGRAPHY IN EVALUATION OF CERVICAL LYMPHNODE METASTSIS IN HEAD AND NECK MALIGNANCIES

Dr Sarang Gosavi Consultant, Shri Siddhivinayak Ganapati Cancer Hospital, Miraj, Maharashtra.

Dr Prashant Naik* Professor And Hod, Smt. Kashibai Navale Medical College And General Hospital, Pune, Maharashtra. *Corresponding Author

ABSTRACT **Introduction:** The most important prognostic factor in head and neck malignancies is the presence or absence of clinically involved cervical lymph nodes. The presence of metastasis in lymph node is said to reduce 5 year survival rate by about 50%. The appropriate diagnosis of the presence of metastatic node is very important for the management of head and neck malignancies. Computed Tomography has the advantage of excellent topographic visualization, devoid of artefacts from superimposition of structures. It helps in accurate assessment of pathology prior to surgical exploration regarding location, extent and complication of the disease. This study is undertaken to develop a systematic method for evaluation of metastasis in cervical lymph nodes and their pathological correlation.

Objective: 1. To assess the Computed Tomography criteria for evaluating cervical lymph nodal metastasis from head and neck malignancies 2. Detection of primary site of malignancy in patients with cervical lymph node metastasis with occult primary malignancy. 3. Comparison between cervical lymph node characterization on Computed Tomography and histopathological examination.

Materials And Methods: Hospital based prospective study. 60 subjects.

Duration Of Study: 12 months Patient selection was done from among those referred to the Department of Radio-diagnosis of for Computed Tomography for evaluation of cervical lymph node metastasis in head and neck malignancies after being clinically diagnosed with symptoms and clinical features suggestive of malignancy in the head and neck or histopathologically proven malignancy during the study period.

Results: The study included 45 males and 16 females. In this study, the most common malignancy was carcinoma of gingivo-buccal sulcus and buccal mucosa followed by carcinoma of tongue and then larynx. The most common lymph node station involved was Ib .In our study, one case presented with metastasis to left level II lymph node in an absence of known primary malignancy of head and neck clinically. On CT scan the primary malignancy was found to be in left tonsillar fossa. Various criteria used to label a lymph node as metastatic on CT scan like size, shape, central nodal necrosis, vascular invasion, heterogenous enhancement were found to be in accordance with the histopathology, taking histopathology as the gold standard

Conclusion: Various criteria's are used to label a lymph node as metastatic on CT scan were found to be in accordance with the histopathology, taking histopathology as the gold standard. So, our study concludes that Computed Tomography definitely has got a pivotal role in the assessment of cervical lymph node metastasis in head and neck malignancies.

KEYWORDS : Lymph nodes, Malignancies, Computed Tomography, Head and Neck

INTRODUCTION

Head and neck imaging has always been a challenge and a difficult task to the radiologist due to the compactly placed vital structures. Before the introduction of cross sectional imaging, radiology played a little role in the evaluation of cervical lymph nodes in head and neck malignancies. Work by P. Som and H. Cutin led to extensive studies on the imaging of the cervical lymph nodes[1].

Various tools for the staging of lymph nodes are palpation, fine needle aspiration cytology (FNAC), ultrasonography (USG), computed tomography (CT), magnetic resonance imaging (MRI) and positron emission tomography (PET) [2,3,4].Each modality offers its own advantage and drawbacks. CT scan and MRI are currently the most widely used techniques and have largely replaced other modalities[5]. Ultrasound is ionizing radiation free, is cheaper and is good at characterizing the lymph nodes, however it is limited to the superficial lymph nodes. MRI requires expensive equipment, is a time consuming process and is thus prone to artefacts secondary to respiration and deglutition.

CT is an imaging technique with high diagnostic value and is widely available. It offers the best risk-benefit ratio for standard care. CT helps in evaluation of both the primary lesion as well the cervical lymph nodes. It has the advantage of excellent topographic visualization and devoid of artefacts from superimposition of structures. It helps in accurate assessment of pathology regarding location, extension and complication of the disease[5].

The other new modalities are nuclear imaging [18-FDG PET], MR spectroscopy (MRS), and Thallium-201 SPECT[6].

Thus, CT scan is now the most preferred modality for imaging of the lesions of the neck. With the advent of spiral CT, the images maybe acquired only in axial plane and reformatted into any required plane without loss of image quality or further radiation exposure.

MATERIALS AND METHOD

This hospital based prospective study was carried out in the Department of Radio-diagnosis of a medical college and tertiary hospital . Written informed consent was obtained from all patients. The college ethics committee approved the study. Total 60 patients were studied over a duration of 12 months. Patient selection was done from among those referred to the Department of Radio-diagnosis for Computed Tomography evaluation of cervical lymph node metastasis in head and neck malignancies after being clinically diagnosed with symptoms and clinical features suggestive of malignancy in the head and neck or histopathologically proven malignancy during the study period.

Inclusion Criteria:

1. Patients diagnosed as having head and neck malignancy by the clinicians.
2. Patients of known head and neck malignancy presenting with cervical lymphadenopathy.
3. Patients presenting with cervical lymphadenopathy with occult primary malignancy.

Exclusion Criteria:

1.All patients with hypersensitivity to CT contrast agents
2. Pregnant females
3. Patients with dental amalgam or metallic implants in head and neck region causing artifacts leading to compromised scan quality

CT Technique:

All patients were called with minimum 4 hours fasting before the scan. A written consent was obtained from each patient after explaining the examination and possibility of a contrast reaction. Patients were scanned in supine position. Scout films were taken routinely in all patients before starting the scan.

SCANNING PARAMETERS

POSITION – Supine

SCANNING SETTINGS

kVp - 130
mAs – 60

PHASE OF RESPIRATION - Quite breathing

SLICE THICKNESS - 4 mm

PITCH – 2

EXTENT - Skull Base to level of the Clavicles

I.V. CONTRAST - Iohexol 300 or 350 mg/ml

RATE - 2 ml/ sec

SCAN DELAY - 25 sec

TOTAL VOLUME - 80-90 ml

SCOUT VIEW – Yes

DISPLAY FOV - 365sq mm

SCAN FOV - 512sq mm

All patients were monitored for a period of half an hour after the scan, in the department before being sent back.

Statistical Analysis -
Data was analyzed using statistical software. Data depicted in the form of tables and charts wherever required. Statistical tests like chi square test, Fischer's exact probability test ETC have been used. P-values<0.05 is considered to be statistically significant.

Equipment:
CT performed by GE Revolution ACT 16 slice CT

RESULT

Our study included a total of 60 patients of head and neck malignancies referred to the Department of Radio-diagnosis for CT scan of the neck. Written informed consent was taken from every patient before the administration of contrast media. History of any prior allergies, previous contrast reactions and any predisposing factors for impaired renal function were taken. History of any co-morbidities was also asked. This was as per the recommendations of Bettmann Ma[7].

In our study, the contrast media used was Iohexol 300/350mg. The scan parameters are those stated in materials and methods. The scan parameters were modified wherever necessary according to the suggestions by Raman SR et al[8].

In our study, any minor, moderate or major contrast reactions were experienced by none of our patients. Literature states an incidence rate of 0.2 to 0.7%[9] for adverse contrast reactions. Our findings were consistent with those described in literature.

Our study included 45 (75%) males and 15 (25%) females. Maximum patients belonged to age group between 61 to 70 years. The youngest patient was 27 years of age and the eldest being 80 years of age.

The most common primary tumor focus was that of in the oral cavity (gingivo-buccal sulcus + tongue) constituting 58% of the total cases followed by carcinoma of the larynx which constituted 13.3% of the cases. This was in accordance with a study conducted by Kazim Bozdemir et al[10] wherein they found the most common primary tumor focus to be the oral cavity (37.7%) followed by larynx (29.4%). This is also in accordance with the National cancer registry programme by ICMR.

Out of 60 patients, 55 (91.7%) patients have history of addictions. In a study by Moussas GI et al[11], they stated direct relation between addictions and development of head and neck cancers.

Our results were similar to that proposed by P. Som (1) regarding the most common lymph node levels involved in primary tumor of head and neck. The most common level(s) of lymph nodes involved in carcinoma of lip were Ia and Ib, in carcinoma of gingivo-buccal sulcus and buccal mucosa was Ib, in carcinoma of cheek were II,III and IV, in carcinoma of tongue were Ia and Ib, in carcinoma of parotid were Ia and Ib, in carcinoma of pharynx was II, in carcinoma of larynx was III, in carcinoma of thyroid were II, III and IV, in carcinoma of cervical esophagus was Ib and in occult primary was II. Our results were in accordance to the study conducted by Kaur K et al[12].

CT In Diagnosis Of Occult Primary In Patients Presenting With Cervical Lymph Node Metastasis

Our study includes a case with metastasis in left level II lymph node in an absence of known primary malignancy of head and neck clinically. On CT scan the primary malignancy was found to be in left tonsillar fossa. This is similar to a study conducted by Lee et al[13] who found that palatine tonsils are the most common site in cervical metastasis in unknown primary tumors. Strojan P et al[14] and Issing WJ et al[15] have also documented the occurrence of lymph nodal mass most commonly involving level II lymph nodes in the absence of a known primary malignancy of the head and neck.

The criteria used for detecting metastasis in cervical lymph nodes are as follows:

- Size- The upper limit of normal is 1.5cm for Ib region and 1cm for all other lymph node groups.
- Shape- Spherical shape favours metastasis while “lima bean” shape favours benign nodal hyperplasia.
- Central nodal necrosis
- Vascular compression/invasion.

These criteria's are in accordance to those proposed by Som P.

On surgical removal, the anatomical nodal levels of the nodes were carefully recorded at the time of excision and were matched to those on imaging studies based on location and size.

Size

In our study, 35 (58.3%) patients fulfilled the size criteria to be labelled as metastatic. The sensitivity, specificity and accuracy as per criteria for size are 75, 87.5 and 78.3 % respectively. Using Chi-square test, the 'p' value in our study was <0.001, hence a significant association was found between size of the lymph node and lymph nodal metastasis. Similar results were observed in the study conducted by Pandeshwar et al[16].

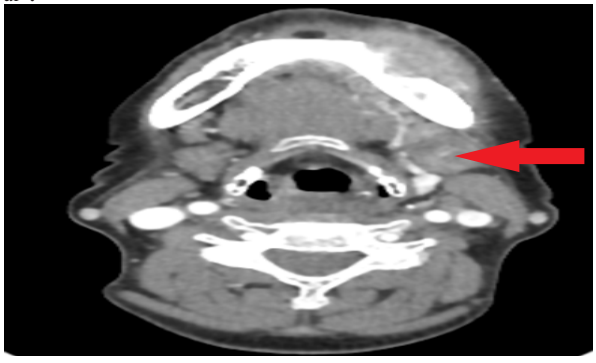

Fig 1-Axial image showing an enlarged left level Ib lymph node (black arrow) in carcinoma of left gingivo-buccal sulcus

Shape

In our study, 31 (51.7%) patients showed spherical shape (longitudinal length to transaxial length <2). The sensitivity, specificity and accuracy are 68.1, 93.8 and 75% respectively. Using Chi-square test, the 'p' value in our study was <0.001, hence a significant association was found between shape of the lymph node and lymph nodal metastasis. Similarly, in a study conducted by Steinkamp et al[17] they found sensitivity, specificity and accuracy of 97, 97 and 97% with the spherical shape.

Central Nodal Necrosis

In our study, 33 (55%) patients showed central necrosis in the lymph nodes. All the nodes that showed central nodal necrosis on CT scan were proved to be metastatic on histopathological correlation. Our results confirm that central nodal necrosis is consistent with lymph node metastasis. This outcome is validated by an earlier study by Morimoto et al. demonstrating the change in density of nodes from homogenous to heterogeneous before advancing to central nodal necrosis.

Thus observation of density of lymph nodes in relation to the primary tumor especially of moderately differentiated and undifferentiated primary tumor sites will aid in diagnosing metastatic nodes[18]. Our findings were also in accordance to the study conducted by Pandeshwar et al[16] where they found that all the lymph nodes that showed central nodal necrosis on CT irrespective of the nodal size

were confirmed to be metastatic on histopathological examination. In our study central nodal necrosis did not show any false positive result which is in accordance to study conducted by Saafan ME et al[19]. Sarvanan et al[20] suggested that the presence of central necrosis was the most specific sign of metastatic lymphadenopathy. They reported 100% specificity for central nodal necrosis criteria. The sensitivity, specificity and accuracy in our study is 75, 100 and 81.7% respectively. Using Chi-square test, the 'p' value in our study was <0.001, hence a significant association was found between central nodal necrosis and lymph nodal metastasis. Our results correlate with a study conducted by Morimoto et al.

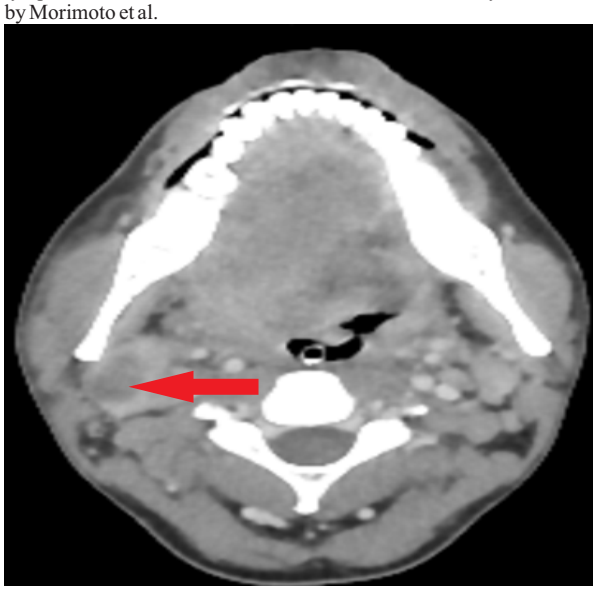

Fig 2- Axial Image Showing An Enlarged Right Level Ii Lymph Node With Central Necrosis(black Arrow) In Carcinoma Of Right Half Of Anterior 2/3rd Of Tongue

Vascular Invasion/ Compression

In our study, 13 (21.7%) patients showed vascular invasion/ compression by the lymph nodes. All the nodes that showed vascular invasion/compression on CT scan were proved to be metastatic on histopathological correlation. Vascular invasion/ compression was considered when any of the following criteria were fulfilled. The criteria were compression and deformation of CCA or ICA, obliteration of IJV on segmental axial CT, displacement of CCA or ICA, tumor encasement of greater than 180 degrees of circumference of the carotid vessels, the segmental deletion of fat or fascial planes between tumor and CCA or ICA and ill defined CCA or ICA wall. The results were in accordance to study conducted by Yu Q et al[21]. The sensitivity, specificity and accuracy in our study is 29.6, 100 and 48.3% respectively. Using Chi-square test, the 'p' value in our study was 0.03, hence a significant association was found between vascular invasion and lymph nodal metastasis. Our findings were consistent with the study conducted by Adem M et al[22].

Fig 3-Axial Image Showing Enlarged Level IV lymph Node Encasing The Left Common Carotid Artery(black Arrows) In Carcinoma Of Pharynx

CALCIFICATION

In our study, none of the patients showed presence of calcification in the lymph nodes. This is in accordance to a study conducted by Eisenkraft et al[23] where they found calcification in lymph nodes in less than 0.5% of primary head and neck malignancies.

Sensitivity, Specificity, Positive Predictive Value (PPV), Negative Predictive Value (NPV) and Accuracy of CT scan for diagnosis of cervical lymph node metastasis in head and neck malignancies.

Our study has sensitivity, specificity, negative predictive value, positive predictive value and accuracy of 75%, 87.5%, 94.3%, 56%, and 78.3% respectively.

In a study by Kazim et al, sensitivity, specificity, positive predictive value, negative predictive value and accuracy rate was 70, 91, 79, 86 and 84 % respectively[10].

Saafan ME et al reported reported sensitivity, specificity, positive predictive value, negative predictive value and accuracy rate of CT as 82.9, 89.7, 95, 68.4 and 84.8 % respectively[19].

In a separate study by Thakur JS et al sensitivity, specificity, positive predictive value, negative predictive value and accuracy was reported as 80, 90, 92.3, 75 and 85% respectively[24].

Kallali BN et al reported sensitivity, specificity, positive predictive value, negative predictive value and accuracy rate of CT as 89.4, 100, 83.3,25 and 85.7 % respectively[25].

Righi et al. reported sensitivity, specificity, positive predictive value, negative predictive value and accuracy rate of CT as 60, 100, 100, 85 and 87 % respectively[26].

In separate study conducted by Hohlweg-Marjert et al. sensitivity, specificity, positive predictive value and negative predictive value was reported as 60, 90, 74 and 92 % respectively[27].

In separate study conducted by Yoon et al. sensitivity, specificity, positive predictive value and negative predictive value was reported as 77, 99, 96 and 95 % respectively[28].

Akoglu et al. reported sensitivity of 77%, specificity of 85%, positive predictive value of 91% and negative predictive value of 96% for CT scan [29].

Karaman et al. stated sensitivity, specificity, positive predictive value and negative predictive value of CT as 81, 90, 82 and 90 % respectively[30].

In another study conducted by Kansara A et al. sensitivity, specificity, positive predictive value, negative predictive value and accuracy was reported as 50, 90, 83, 64 and 70 % respectively[31].

In a separate study done by Geetha et al. sensitivity, specificity, positive predictive value, negative predictive value and accuracy was reported as 50, 100, 100, 57 and 70 % respectively[32].

In a different study conducted by Haberal I et al. sensitivity, specificity, negative predictive value, positive predictive value and accuracy was reported as 81%, 96%, 85%, 90%, and 87% respectively[33].

In a meta-anaylsis carried out by de Bondt et al, they reported sensitivity varying from 55 to 95% and a specificity of 39 to 96% for assessing neck node metastasis using CT scan[34].

However, in a study conducted conducted by Hasan Mirmohammad Sadeghi et al sensitivity, specificity, negative predictive value, positive predictive value and accuracy was reported as 69.23%, 27%, 25%, 71.42% and 38% respectively[35].

Overall, in the literature review sensitivity of CT has been indicated as 59 to 97% and that of specificity as 81 to 94 %. The accuracy ranges from 68 to 92.30%.

In our study, sensitivity, specificity and accuracy of CT scan in detection of cervical lymph node metastasis in head and neck malignancies is in accordance with the literature.

Using Chi square test, the 'p' value is <0.001. CT showed statistically

significant agreement with histopathology for the detection of malignancy in cervical lymphadenopathy. Our results are similar to those observed by Pandeshwar et al[16]and Saafan ME et al[19].

DISCUSSION

A number of CT criteria have been proposed to assess the presence of cervical nodal metastasis and to distinguish such nodes from reactive nodes. More recently, there have been a variety of studies utilizing MR imaging and helical CT.

1. Size And Shape Criteria

Lymph node size greater than 1 cm except for jugulo-diagastric and submandibular region (size criteria greater than 1.5cm), is considered metastatic. Retropharyngeal nodes should not exceed 8 mm in maximum diameter or 5 mm in short axis diameter[36]. The ratio of the maximum longitudinal nodal length to the maximum axial nodal length (L/T) should be greater than 2 for normal hyperplastic nodes, while a value of less than 2 strongly suggests that the node contains metastatic carcinoma[37]. RECIST (Response Evaluation Criteria In Solid Tumors) 1.1 measures lymph nodes in the short axis on axial images. Nodes ≥ 15 mm are pathologically enlarged and measurable, and lymph nodes measuring 10–15 mm in short axis are reportable as pathologic nontarget sites[38]. Curtin et al. evaluated the sensitivity and specificity of different size criteria for metastatic disease and found that a 1-cm size cutoff in the largest axial diameter achieved 88% sensitivity and 39% specificity, whereas a 1.5-cm cutoff resulted in 56% sensitivity and 84% specificity[39]. All of these imaging criteria describe homogeneous, sharply outlined lymph nodes[1].

An oblong or lima-bean shape is thought to be representative of a normal lymph node, whereas a spherical shape is more likely to be associated with metastasis. Numerous studies now strongly support the criteria of a long-to-short axis ratio less than 2 as representing a node that contains metastatic carcinoma[40]. Shape is a crucial aspect to include in the evaluation of a suspicious node because hyperplastic nodes will often meet size criteria but possess a long-to-short axis ratio of more than 2. The use of shape criteria may be of particular importance in nodes that are not enlarged, and it is important to recognize that spherical nodes are not necessarily hyperplastic. Although shape criteria were designed to be asserted in the context of enlarged nodes, as many as 82%-86% of metastatic lymph nodes may be round but less than 10 mm[41,42].

2. Central Necrosis

On CT, a necrotic node has a central region of fluid attenuation that represents all of these components. On contrast-enhanced CT, such nodes have a central region of low attenuation (10 to 25 HU) and a variably thick and variably enhancing nodal rim. Central nodal necrosis occurs when neoplastic infiltration of the medullary portion of lymph nodes outstrips the blood supply[43,44,45]**.** Nodal necrosis in the presence of a head and neck cancer primary tumor is the most valuable sign of metastatic involvement, with specificity between 95% and 100%[46]**.**

3. Extranodal Tumor Extension

Once tumor penetrates the nodal capsule, it extends into the adjacent soft tissues. This tumor growth has been variously referred to as extranodal, extracapsular or transcapsular tumor spread, and it is associated with a decrease in survival. The presence of such macroscopic extranodal tumor extension is identified on contrast enhanced CT as an enhancing, often thickened nodal rim, usually with infiltration of the adjacent fat planes. As the node enlarges, the incidence of extracapsular tumor spread rises, so that it is reported to be present in 53% of lymph nodes in size range of 2 to 3 cm and in 74% of lymph nodes larger than 3 cm. Overall, such tumor spread occurs in 60% of nodes less than 3 cm in diameter[47]. It is essential to check if the extracapsular nodal tumor has invaded adjacent structures such as the internal carotid artery, common carotid artery, retropharyngeal soft tissues or bone.

4. Vascular Invasion

The extension of nodal tumor to the adjacent internal carotid artery is a grave prognostic finding. The degree of arterial wall invasion can be variable, but from an oncologic consideration, tumor invasion of the arterial adventitia is as important as greater degrees of arterial invasion into the muscularis and intima that may be seen on imaging as narrowing of the arterial lumen[1]. If the artery is entirely surrounded by tumor, however there are some reports that suggest no adventitial involvement at surgery. Conversely, if just a tip of tumor touches the artery, it is unlikely that the arterial wall has been invaded, yet at surgery such cases may have adventitial tumor spread. In general, the greater the tumor extension around the artery, the more likely it is that the artery is involved. Thus, arterial wall invasion is likely when more than 270° of the arterial circumference is surrounded by tumor[48]**.** The invasion of vital structures or extra nodal spread occurs once the capsular barrier is breached causing obscuration of the margins of the lymph node. Prognostically and therapeutically this is relevant as resection then becomes uncertain. In this respect, invasion of common or internal carotid is probably most important, specifically, when tumor appears to encase or surround the carotid artery; surgery is not a choice[49,50].

The metastatic lymph nodes can compress and involve the adjacent internal jugular vein.

5. Nodal Enhancement

Although not typical, metastatic lymph nodes show mild to moderate heterogeneous enhancement on post contrast images.

6. Calcifications

Calcifications in the metastatic lymph nodes are mostly dystrophic calcifications. It is generally thought that dystrophic calcification occurs when there is not enough blood supply to ischemic or necrotic tissues at the centre of a tumor that has grown beyond a certain extent. This tumor growth in turn causes impaired cellular respiration, reduced production of carbon dioxide, and an increase in the alkalinity of the extracellular fluid, resulting in the creation of a microenvironment in which calcium is easily deposited[51]**.** Calcified lymph nodes are most commonly found with thyroid carcinoma due to the presence of psammomatous calcifications with papillary and medullary carcinoma. The calcifications in papillary carcinoma may have a speckled appearance. Calcifications may also be seen in metastatic mucinous adenocarcinomatous nodes, primarily from breast, lung, and colon primary tumors[1]. Eisenkraft examined 2,300 CT scans of the neck and reported that the incidence of cervical node calcification was 1% (26/2,300), and that 12 cases of them had malignant tumors including 1 case of tongue squamous cell carcinoma[23].

Limitations

There were few limitations to our study as well. Firstly, extracapsular nodal spread was not included in the CT criteria for diagnosis of lymph node metastasis in our study. It being an important criteria further studies in future are required. Secondly, only one case of occult primary was found in the given study period. For better knowledge of role of CT scan in indentifying occult primary in patients presenting with cervical lymph node metastasis, a larger sample size is required.

CONCLUSION

To conclude, various criteria used to label a lymph node as metastatic on CT scan were found to be in accordance with the histopathology, taking histopathology as the gold standard. So, our study concludes that Computed Tomography definitely has got a pivotal role in the assessment of cervical lymph node metastasis in head and neck malignancies.

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