Lymph node status (Core and Non-core)

Reason/Evidentiary Support

Lymph node status may be presented in tabular form for ease of interpretation as follows:

Level and side	Number of nodes examined	Number of nodes positive	ENE minor or major	Number of nodes with ENE
II right	12	3	ENEmi	1
III right	14	2	ENEma	0
etc				

For cases in which an involved lymph node or tumour deposit straddles more than one lymph node level, it is recommended to include it in the level in which the bulk of the deposit is found, with an explanatory comment. In other cases, it may not be possible to precisely divide the neck dissection into individual levels and more than one level may need to be combined. If a neck dissection is received without any level designation, clarification from the surgeon involved is suggested. If this is not obtained, the data may be reported without further qualification, such as “right neck dissection, not further specified”.

“Soft tissue metastasis” refers to a deposit of tumour in connective tissue, without a microscopically identifiable residual lymph node. This may represent venous invasion, lymphatic invasion or, most likely, a totally replaced node or nodes. It does not refer to intralymphatic tumour emboli in adipose tissue surrounding the lymph nodes. In many cases, a soft tissue metastasis is the largest focus of tumour in the specimen. Rarely, very small soft tissue metastases (e.g. < 1 mm in greatest dimension) are identified that appear unlikely to be of nodal origin. Special stains and deeper levels may help to identify a vascular origin for these deposits, and the pathologist may use his/her discretion as to their designation as positive lymph nodes, perhaps with the use of a clarifying comment.

For tumour deposits in which there is residual lymph node tissue with widespread extranodal extension, a combined gross and microscopic estimate of the number of involved lymph nodes is suggested. Correlation with pre-surgical imaging studies may also be of benefit.

The largest metastatic focus may be an intranodal or a soft tissue metastasis. Determination of the size of the largest metastasis may be difficult in cases where multiple tumour deposits are identified in a single lymph node. Options including measuring the greatest dimension of the largest deposit, combining the sizes of the deposits to give an aggregate dimension, and measuring the greatest dimension “end-to-end” from a single slide, including discontinuous tumour deposits. The latter is recommended.

The size of the largest involved lymph node is the basis upon which clinicians determine N category and thereby the stage. Although there is some debate about whether the greatest dimension of the largest tumour deposit or that of the largest involved lymph node is the more relevant measurement, both are considered “core” items in this dataset. This is so as to provide the maximum amount of data that may be relevant for clinical decision-making. The greatest dimension of the largest involved lymph node should be used to determine the pN category. In some cases, the largest node in a specimen may be a reactive node with no tumour. Therefore, the measurement must be of the largest node involved by metastatic tumour.

The prognostic significance of isolated tumour cells (foci <0.2 mm diameter or <200 cells) and micrometastases (foci 2 mm or less in greatest dimension) is currently unknown for head and neck cancers, and their designation is not required as part of the TNM staging. [1-3] Isolated tumour cells are uncommon in metastatic squamous cell carcinoma, but may occur in some less common primary tumours (e.g. Small cell carcinoma of salivary origin). As such, any-sized tumour deposit is considered a positive lymph node for staging purposes.[3,4] Specific identification of tumour deposits as isolated tumour cells or micrometastases and cytokeratin positive non-nucleated cells is not required as part of this dataset, but can be recorded as per local requirements for data collection. Mummified cells and keratin debris may be found and should not be regarded as viable metastatic disease.

Neck dissections may be performed as salvage surgery for a persistent neck mass following adjuvant radiation therapy. In this circumstance, only viable tumour - not necrotic keratinous debris or keratin granulomas - should be considered as a positive lymph node. Extra sampling of residual neck deposits may be required to evaluate these specimens. The prefix “yp” should be added to the TNM category.

Extranodal extension

Extranodal extension (ENE) refers to extension of tumour outside the capsule of a lymph node and into the perinodal soft tissue. It is also known as “extracapsular extension/spread”, but the term “extranodal extension” has been adopted in the 8th edition of the American Joint Committee on Cancer (AJCC) Staging Manual[3] and the Union for International Cancer Control (UICC)[5] and therefore is used here. ENE is a poor prognostic factor in cervical node positive head and neck carcinoma. In HPV-mediated oropharyngeal cancer, the exact clinical significance of ENE has yet to established, and so it is considered a “non-core” item, with reporting up to local discretion.[6-8]

The presence of ENE in other head and neck cancers correlates with the risk of regional recurrence and outcome. It is an important factor for oncologists when considering treatment with postoperative radiotherapy or chemoradiotherapy.[8,9] ENE is subcategorised pathologically as microscopic (ENE_{mi}, less than or equal to 2 mm in extent) and major (ENE_{ma}, more than 2 mm in extent). These subcategories are not required for N categorisation but are recommended for data collection and future analysis.[3] The 5-point grading system for ENE (Lewis et al) is not validated and is not currently recommended.[10]

Interobserver variation in the determination of ENE may be minimised if the following guidance is used.

1) Lymph nodes, especially smaller nodes and those in the parotid area, may not have a complete capsule. The node hilum may merge with adipose tissue, or there may be a rim of lymphoid tissue external to the capsule. Generally speaking, a conservative approach is recommended. For instance, tumour within fat near the hilum of a node should be considered intranodal if benign lymphoid tissue is identified nearby. Tumour within lymphatics near an involved lymph node should not be considered ENE. However, tumour extending beyond a clearly identifiable node capsule is extranodal, even if there is a surrounding lymphoid response. A stromal desmoplastic reaction is not necessarily required.[3]

2) Grossly “matted” lymph nodes. Grossly adherent lymph nodes may represent true macroscopic ENE or several closely-aggregated lymph nodes with thickened nodal capsules without microscopic evidence of ENE. Additional levels and sections are recommended to exclude ENE. The presence of matted nodes, their site, size and an estimated of the number involved, should be included in the gross description and may be mentioned in a comment. At least one study has shown that radiographically matted lymph nodes are a risk factor for distant metastases and decreased survival in oropharyngeal cancer.[11]

3) Lymphatic spread to lymph nodes versus direct extension from the primary tumour. Some tumours may extend directly into lymph nodes without intervening normal tissue. This is not uncommon in parotid tumours as there are multiple lymph nodes within the parotid parenchyma itself, but it also occurs with large oral and oropharyngeal primaries. Direct extension into lymph nodes is staged in the same manner as discontinuous metastases.[3] Determination of ENE should be based on any component of the capsule that is discontinuous with the primary tumour. A comment is recommended for clarity.

4) The lymph node capsule is often markedly thickened and altered by large metastases with obliteration of the subcapsular sinus. ENE is measured as the greatest extent of tumour spread perpendicular to the external aspect of the node capsule. The exact site of the latter is subjective, but may be estimated by examination of the remaining intact capsule and contour of the node (Figures 3 and 4). If the greatest extent of ENE is provided, the measurement can be rounded to the nearest millimetre or tenth of a millimetre, as per local convention (keeping in mind that if ENE is more than 2 mm, the measurement should not be rounded down to 2 mm). More precise measurements are not warranted due to the subjectivity required and lack of known clinical relevance.

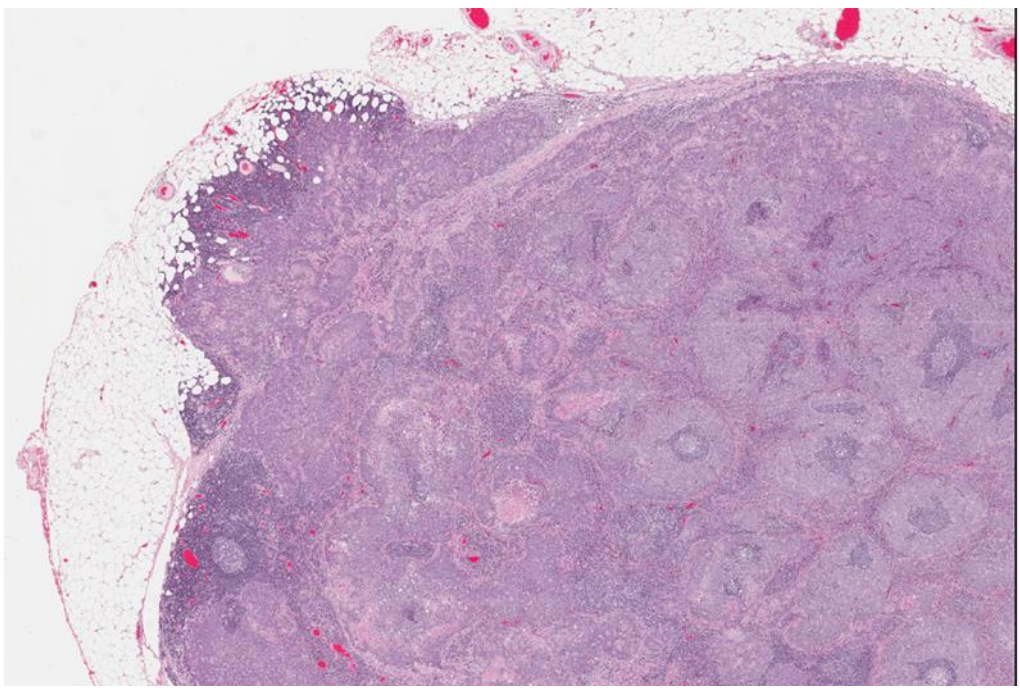

Figure 3. Low power image of a lymph node containing metastatic squamous cell carcinoma, with extranodal extension into perinodal adipose tissue (20x). *Copyright Dr Martin Bullock. Reproduced with permission.*

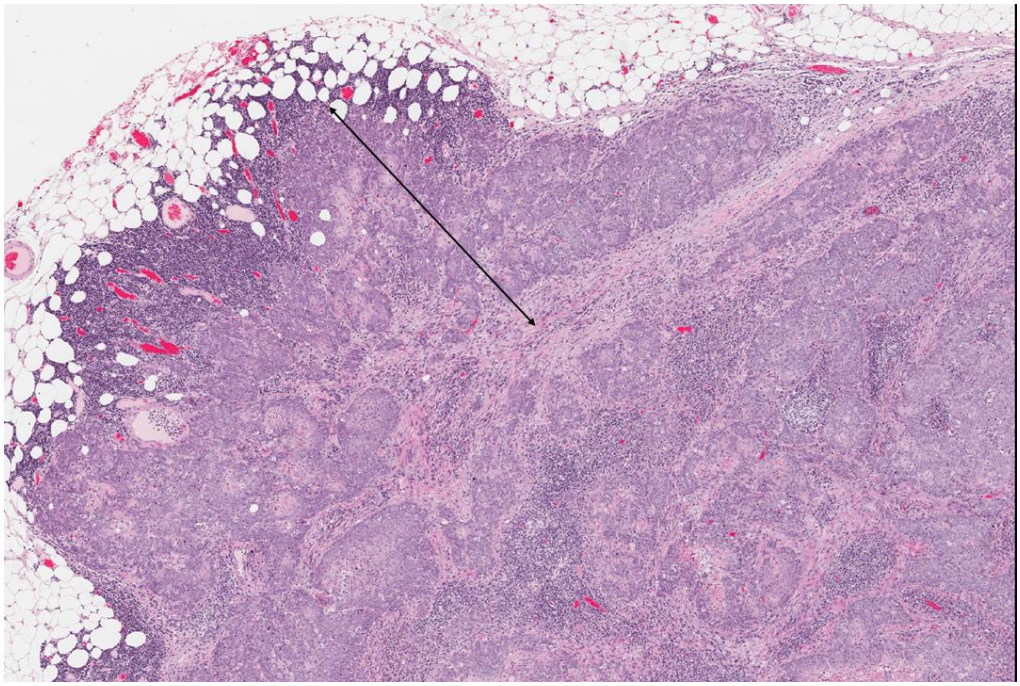

Figure 4. The extent of extranodal extension should be measured from external aspect of the capsule, or estimated site thereof, to the furthest point of tumour extension into the surrounding tissue. *Copyright Dr Martin Bullock. Reproduced with permission.*

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