Standaardrapport
klierexcisie en nekdissectie voor hoofd- en halstumoren

Conclusie

Neoadjuvante therapie: Kies een optie.

Ingezonden lymfeklierstations[1]:

Links:

Rechts:

Centraal compartiment:

Andere:

Lokalisatie primaire tumor: Kies een optie.

Indien gekend, specificeer:

Histologisch tumortype:

Plaveiselcelcarcinoom: Kies een optie.

Nasofaryngeaal carcinoom: Kies een optie.

Speekselkliercarcinoom: Kies een optie.

Indien van toepassing, specificeer type:

Andere: Kies een optie.

Specificeer tumortype:

Differentiatiegraad: Kies een optie.

Indien niet beoordeeld kan worden, specificeer:

[1] Gelieve bij de beschrijving van de ingezonden lymfeklierstations de correcte terminologie te hanteren: level IA (submentaal), IB (submandibulair), II (hoog jugulair), III (midden jugulair), IV (laag jugulair) en V (posterior cervicaal), VI (centraal compartiment: pretracheaal/paratracheaal) en VII (mediastinaal).

Inname perinodaal chirurgisch snedevlak door invasief carcinoom: Kies een optie.

Indien niet ingenomen, specificeer locatie van minimale marge (indien mogelijk):

Indien ingenomen:

Specificeer zijde: Kies een optie.

Specificeer niveau/compartiment:

Indien niet beoordeeld kan worden, specificeer:

Indien andere, specificeer:

** Enkel invullen indien linkszijdige lymfeklieren weggenomen:*

Level IA links (submentale lymfekliergroep): Kies een optie.

Aantal onderzochte lymfeklieren:

Aantal positieve lymfeklieren:

Extranodale uitbreiding: Kies een optie.

Level IB links (submandibulaire lymfekliergroep): Kies een optie.

Aantal onderzochte lymfeklieren:

Aantal positieve lymfeklieren:

Extranodale uitbreiding: Kies een optie.

Level II links (hoog jugulaire lymfekliergroep)[2]: Kies een optie.

Aantal onderzochte lymfeklieren:

Aantal positieve lymfeklieren:

Extranodale uitbreiding: Kies een optie.

Level III links (midden jugulaire lymfekliergroep)[2]: Kies een optie.

Aantal onderzochte lymfeklieren:

Aantal positieve lymfeklieren:

Extranodale uitbreiding: Kies een optie.

[2] Voor lymfeklieren met enkel in level II of level III een metastase van een plaveiselcelcarcinoom bij een onbekende primaire tumor is het absoluut nodig een p16-kleuring te doen, zeker als de tumor niet keratiniserend is. Indien deze lymfekliergroepen beoordeeld worden, dient p16 kleuring uitgevoerd te worden. Gelieve de resultaten van deze kleuring te vermelden onder de variabele “Aanvullende onderzoeken”.

Level IV links (laag jugulaire lymfekliergroep): Kies een optie.

Aantal onderzochte lymfeklieren:

Aantal positieve lymfeklieren:

Extranodale uitbreiding: Kies een optie.

Level V links (posterior cervicale lymfekliergroep): Kies een optie.

Aantal onderzochte lymfeklieren:

Aantal positieve lymfeklieren:

Extranodale uitbreiding: Kies een optie.

Maximale afmeting van grootste lymfekliermetastase (in mm):

Maximale afmeting van grootste aangetaste lymfeklier (in mm):

Metastasen in weke delen: Kies een optie.

Indien metastasen in weke delen, specificeer lokalisatie (level):

Aantasting van niet-lymfatische structuren: Kies een optie.

Aantasting van bloedvat: Kies een optie.

Specificeer naam van bloedvat, indien mogelijk:

Aantasting van zenuw: Kies een optie.

Specificeer naam van zenuw, indien mogelijk:

Aantasting van skeletspier: Kies een optie.

Specificeer naam van skeletspier, indien mogelijk:

Aantasting van andere structuren: Kies een optie.

Specificeer:

** Enkel invullen indien rechtszijdige lymfeklieren weggenomen:*

Level IA rechts (submentale lymfekliergroep): Kies een optie.

Aantal onderzochte lymfeklieren:

Aantal positieve lymfeklieren:

Extranodale uitbreiding: Kies een optie.

Level IB rechts (submandibulaire lymfekliergroep): Kies een optie.

Aantal onderzochte lymfeklieren:

Aantal positieve lymfeklieren:

Extranodale uitbreiding: Kies een optie.

Level II rechts (hoog jugulaire lymfekliergroep)[3]: Kies een optie.

Aantal onderzochte lymfeklieren:

Aantal positieve lymfeklieren:

Extranodale uitbreiding: Kies een optie.

Level III rechts (midden jugulaire lymfekliergroep)[3]: Kies een optie.

Aantal onderzochte lymfeklieren:

Aantal positieve lymfeklieren:

Extranodale uitbreiding: Kies een optie.

Level IV rechts (laag jugulaire lymfekliergroep): Kies een optie.

Aantal onderzochte lymfeklieren:

Aantal positieve lymfeklieren:

Extranodale uitbreiding: Kies een optie.

[3] Voor lymfeklieren met enkel in level II of level III een metastase van een plaveiselcelcarcinoom bij een onbekende primaire tumor is het absoluut nodig een p16-kleuring te doen, zeker als de tumor niet keratiniserend is. Indien deze lymfekliergroepen beoordeeld worden, dient p16 kleuring uitgevoerd te worden. Gelieve de resultaten van deze kleuring te vermelden onder de variabele “Aanvullende onderzoeken”.

Level V rechts (posterior cervicale lymfekliergroep): Kies een optie.

Aantal onderzochte lymfeklieren:

Aantal positieve lymfeklieren:

Extranodale uitbreiding: Kies een optie.

Maximale afmeting van grootste lymfekliermetastase (in mm):

Maximale afmeting van grootste aangetaste lymfeklier (in mm):

Metastasen in weke delen: Kies een optie.

Indien metastasen in weke delen, specificeer lokalisatie (level):

Aantasting van niet-lymfatische structuren: Kies een optie.

Aantasting van bloedvat: Kies een optie.

Specificeer naam van bloedvat, indien mogelijk:

Aantasting van zenuw: Kies een optie.

Specificeer naam van zenuw, indien mogelijk:

Aantasting van skeletspier: Kies een optie.

Specificeer naam van skeletspier, indien mogelijk:

Aantasting van andere structuren: Kies een optie.

Specificeer:

** Enkel invullen indien lymfeklieren in centraal compartiment weggenomen:*

Aantal onderzochte lymfeklieren:

Aantal positieve lymfeklieren:

Extranodale uitbreiding: Kies een optie.

Maximale afmeting van grootste lymfekliermetastase (in mm):

Maximale afmeting van grootste aangetaste lymfeklier (in mm):

Metastasen in weke delen: Kies een optie.

Indien metastasen in weke delen, specificeer lokalisatie (level):

Aantasting van niet-lymfatische structuren: Kies een optie.

Aantasting van bloedvat: Kies een optie.

Specificeer naam van bloedvat, indien mogelijk:

Aantasting van zenuw: Kies een optie.

Specificeer naam van zenuw, indien mogelijk:

Aantasting van skeletspier: Kies een optie.

Specificeer naam van skeletspier, indien mogelijk:

Aantasting van andere structuren: Kies een optie.

Specificeer:

Aanvullende onderzoeken: Kies een optie.

Indien HPV-testen, specificeer methode en resultaten:

Indien EBV-testen, specificeer methode en resultaten:

pTNM classificatie (UICC TNM 8e editie met errata)[4]: pN

Kies de classificatie die van toepassing is:

Primaire carcinomen van de lip en mondholte, grote speekselklieren, neusholte en paranasale sinussen, p16-negatieve orofarynx, hypofarynx, larynx, cutane hoofd- en halscarcinomen (behalve Merkelcelcarcinoom) en onbekende primaire p16- en EBV-negatieve plaveiselcelcarcinomen: Kies een optie.

p16-positief orofarynxcarcinoom: Kies een optie.

Carcinoom van nasofarynx: Kies een optie.

Mucosaal melanoom: Kies een optie.

Voorvoegsels:

r (recidief): Kies een optie.

y (na neoadjuvante therapie): Kies een optie.

[4] De pathologische stadiëring is gebaseerd op de 'TNM Classification of Malignant Tumours' (8e editie, UICC). Een beschrijving van elke pN-categorie is beschikbaar in 'Note 6 – Regional lymph node categorisation' onderaan dit document.

Scope

Lymfeklierresecties en halsdissecties van patiënten met primaire carcinomen en mucosale melanomen van hoofd en de hals. Carcinomen omvatten sinonasale tractus, nasofarynx, mondholte, orofarynx, hypofarynx, larynx en trachea, grote en kleine speekselklieren, oor en slaapbeen. Lymfeklierresecties en halsdissecties voor neuro-endocriene tumoren (graad 1, 2 en 3) en neuro-endocriene carcinomen zijn ook opgenomen in deze dataset, evenals melanomen en cutane carcinomen (behalve Merkelcelcarcinoom).

Opmerkingen:

- Lymfeklierresecties voor lymfomen en sarcomen zijn niet opgenomen in de dataset.
- Deze dataset is niet bedoeld voor een lymfeklier core biopsie of fijne naald aspiraties.
- Voor resecties van recidieven kan de dataset pragmatisch worden gebruikt, hoewel sommige variabelen mogelijk niet toepasbaar of te beoordelen zijn.
- Deze dataset moet worden gebruikt in combinatie met andere ICCR-datasets voor hoofd- en halstumoren. Lymfeklierresecties en halsdissecties kunnen voorafgaan aan, gepaard gaan met of volgen op de biopsie of resectie van een primaire tumor. Gelijktijdig rapporteren van de variabelen van de lymfeklier- en primaire tumordataset verdient de voorkeur, omdat dit clinici de meest uitgebreide informatie biedt voor de categorisatie van het tumorstadium.
- Pathologen moeten rekening houden met de invloed van eerdere ingrepen (bijvoorbeeld een voorafgaande diagnostische lymfeklierexcisiebiopsie bij een patiënt met een halsmassa) op de pN-categorie en verwijzen naar het eerdere chirurgische pathologiemonster, indien beschikbaar. Op dezelfde manier kunnen halsdissecties worden uitgevoerd als 'reddingsoperatie' na bestraling en/of chemotherapie. Deze adjuvante of neoadjuvante ingrepen kunnen van invloed zijn op de pN-categorie door de omvang van de tumor te verkleinen of de tumor misschien helemaal te verwijderen.

Dataset gebaseerd op

Bullock M, Carlson DL, Fonseca I, Katabi N, Taylor SM, Thavaraj S, Williams MD, Helliwell T, Thompson LDR (2024). *Nodal Excisions and Neck Dissection Specimens for Head and Neck Tumours Histopathology Reporting Guide. 2nd edition*. International Collaboration on Cancer Reporting; Sydney, Australia. ISBN: 978-1-922324-49-8.

Bijkomende informatie[5]

Note 1 – Histological tumour type

Primary tumour site is a core item as it is relevant to both treatment and prognosis. Identification of the histological tumour type is crucial for several reasons, including: 1) confirmation that a metastasis is of the same type as the resected primary tumour; 2) facilitating a clinical search in cases of unknown primary tumours; 3) determining the correct T and N categories; and 4) guiding treatment, which varies by tumour type and lymph node status.[18,19]

Histological type is typically determined from the histology at the primary site, but this is not possible for tumours of unknown origin. Tissue from a neck metastasis may be required for ancillary testing (e.g., p16 immunohistochemistry, in situ hybridisation for high risk human papillomavirus (HPV), in situ hybridisation for Epstein Barr virus (EBV) encoded RNA/EBER). For patients with occult primary SSC in level II or III, the cN or pN categories are influenced by EBV and HPV status.[24] EBV-associated and HPV-associated carcinomas are given the N category that applies to nasopharyngeal and HPV-associated oropharyngeal carcinomas, respectively.[18,19]

Verrucous carcinoma and carcinoma cuniculatum are not included in the above list of squamous cell carcinoma (SSC) subtypes, as they are not considered SCC subtypes in the WHO Classification and they have no capacity to metastasise to lymph nodes.

The classification system for Neuroendocrine neoplasms (subdivided into tumours and carcinomas) is included, as per the most recent edition of the WHO Classification of Head and Neck Tumours, 5th edition, 2024.[2]

Note 2 – Histological tumour grade

When possible, tumour grade should be determined from the primary tumour, not from a metastasis. Some tumours are high grade or undifferentiated by definition (e.g., non-keratinising nasopharyngeal carcinoma (NPC)), while others do not require grading because behaviour is defined by pathogenesis and is not apparently influenced by morphology (e.g., HPV-associated orpharyngeal carcinoma). For most malignancies, the WHO grading system is most practical and widely utilised. Still, several grading systems are available for many tumours (e.g., mucoepidermoid carcinoma), with differing merits, and as such, recording which system has been applied is more clinically meaningfully (use 'specify' to state the system used).

Note 3 – Margin status

Margin status of the neck dissection is typically only relevant when extranodal extension (ENE) is

[5] Bijkomende informatie ('notes') overgenomen en aangepast vanuit
Bullock M, Carlson DL, Fonseca I, Katabi N, Taylor SM, Thavaraj S, Williams MD, Helliwell T, Thompson LDR (2024). Nodal Excisions and Neck Dissection Specimens for Head and Neck Tumours Histopathology Reporting Guide. 2nd edition. International Collaboration on Cancer Reporting; Sydney, Australia. ISBN: 978-1-922324-49-8.

present, as nodes without ENE are presumed to be removed in toto. Clinical correlation and orientation by the surgeon is required if the neck dissection is received as multiple specimens, so as to avoid a misinterpretation of the location of the true surgical margin.

Margin positivity increases the risk of local recurrence and is an indication for additional radiotherapy to that site.[25-27] The site of margin positivity can be used by the radiation oncologist to direct treatment to the area of greatest risk.

Note 4 – Lymph node status

Lymph node status may be presented in tabular form for ease of interpretation, as illustrated in the reporting guide.

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 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. It does not refer to intralymphatic tumour emboli in adipose tissue surrounding the lymph nodes. Soft tissue metastasis has been found to negatively impact survival in patients who are otherwise node-negative or in those with positive nodes lacking ENE.[28,29] In many cases, a soft tissue metastasis is the largest focus of tumour in the specimen. This is presumed to represent one or more completely replaced lymph nodes and should be recorded as such. Less commonly, small soft tissue metastases (e.g., <1 mm in greatest dimension) are identified that do not appear to be of nodal origin.

Special stains and deeper levels may help to identify a vascular origin for these deposits. The pathologist must use his/her discretion as to their designation as positive lymph nodes, with the use of a clarifying comment.

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

The largest metastatic focus may be an intranodal or a soft tissue metastasis. Often, the maximum dimension of the largest metastatic tumour deposit is determined at gross examination of the specimen. Determination of the greatest dimension of a metastasis may be difficult in cases where multiple

microscopic intranodal deposits are identified. Options including measuring the greatest dimension of the largest microscopic 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 by the authoring committee.

The maximum dimension of the largest involved lymph node may not be the same as the maximum

dimension of the largest metastatic deposit. For instance, this may be due to the presence of an enlarged reactive lymph node in the tumour basin with a microscopic tumour deposit. Both measurements are considered 'core' items in this dataset so as to avoid confusion, to facilitate correlation with imaging studies and to provide the maximum amount of data that may be relevant for clinical decision-making. The greatest dimension of the largest tumour deposit should be used to determine the pN category. In occasional cases, the largest lymph node in the specimen may not even contain tumour. The pathologist may elect to make a comment to this effect. However, it is not considered a necessary reporting element.

The prognostic significance of isolated tumour cells (ITC) (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.[18,19,30,31] ITCs are uncommon in metastatic SCC, 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.[18,19,32] Specific identification of tumour deposits as ITCs or micrometastases is not required as part of this dataset, but can be recorded as per local requirements for data collection, such as in sentinel node dissections. Mummified cells and keratin debris may be found; it should not be regarded as viable metastatic disease and should be considered pN0 for categorisation purposes.

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. The presence and number of necrotic lymph nodes should be added.

Non-lymphatic structures involved is a core item referring to the involvement of **named** tissues (such as the spinal accessory nerve, internal jugular vein or sternocleidomastoid muscle) that are identified either by virtue of the specimen designation or in consultation with the surgeon. Clinical or imaging involvement of some extranodal tissues may imply the need for more aggressive neck dissection, and pathological involvement should be documented in the final report.[33]

Emerging evidence suggests that lymph node ratio (the ratio of positive nodes over total number of nodes resected) may be an independent prognostic indicator of survival in metastatic SSCs of the head and neck.[34-36] As yet, insufficient evidence has been gathered to include this as a reporting guide component.

Extranodal extension

Extranodal extension (ENE) refers to extension of tumour outside the capsule of a lymph node and into the perinodal soft tissue. This is the preferred terminology to 'extracapsular extension/spread'. ENE is an adverse prognostic factor for locoregional relapse and survival in cervical node positive head and neck SSCs.[37] The significance of ENE in HPV-associated oropharyngeal carcinoma has been less certain,[19-21] however some evidence confirms the adverse effect on survival in these carcinomas as well.[38,39]

The presence of ENE is an important factor for oncologists when considering treatment with postoperative radiotherapy and the addition of chemotherapy.[38-41]

Extranodal extension (ENE) is subcategorised pathologically as microscopic (ENE_{mi}, less than or equal

to 2 mm in extent) or major (ENE_{ma}, more than 2 mm in extent). These subcategories are not required for pN categorisation but are core items as they can impact treatment decisions,[37] and are relevant for data collection and future analysis. The more precise measurement of greatest extent of ENE in millimetres is a non-core item, as the reproducibility of this measurement is questionable. Certainly, an attempt to be more precise than tenths of a millimetre is not advised.

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.

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. One study has found that radiographically matted lymph nodes are a risk factor for distant metastases and decreased survival in oropharyngeal cancer.[42]

3. Lymphatic spread to lymph nodes versus direct extension from the primary tumour. Some tumours may extend directly into adjacent lymph nodes without intervening normal tissue. This is common in parotid tumours as there are multiple lymph nodes within the parotid parenchyma itself. This finding is not considered nodal metastatic disease for the purposes of staging, and the concept of 'ENE' will not apply. Rare instances of direct extension into a lymph node from a mucosal site – for example, from a large floor of mouth primary to a level I node – is more controversial and potentially more difficult to evaluate. The general rule of choosing the lower stage in equivocal circumstances should apply, but a clarifying comment and/or discussion with the treating physicians is suggested.

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 1 and 2).

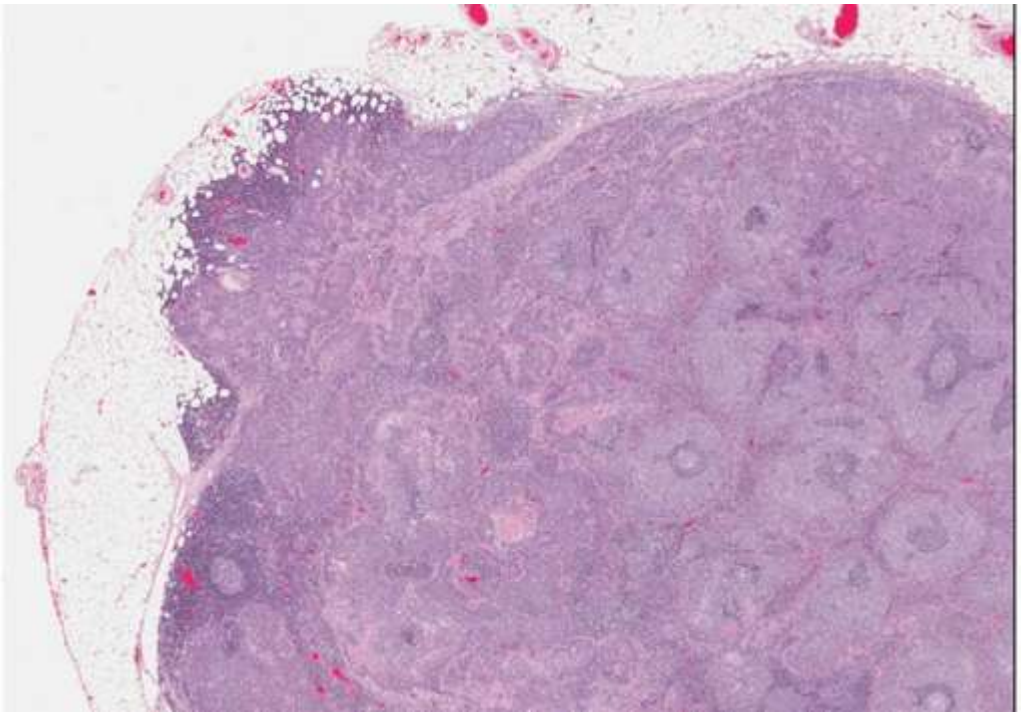

Figure 1: Low power image of a lymph node containing metastatic squamous cell carcinoma, with extranodal extension into perinodal adipose tissue (20x). Permission courtesy of Dr Martin Bullock.

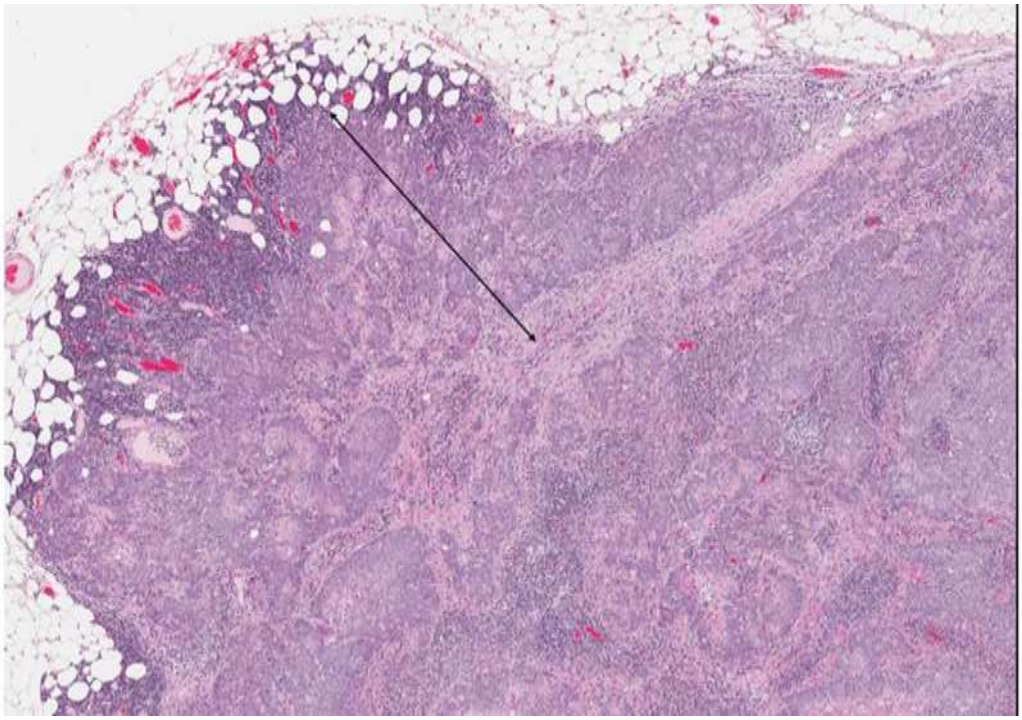

Figure 2: The extent of extranodal extension should be measured from external aspect of the capsule, or estimated site thereof, to the furthest point of tumour extension into the surrounding tissue. Permission courtesy of Dr Martin Bullock.

Note 5 – Ancillary studies

Ancillary testing for head and neck cancers most commonly refers to testing for high risk HPV status in tumours of the oropharynx and EBV status in tumours of the nasopharynx. Ancillary testing should be performed on the primary tumour if possible. Tumours presenting with a lymph node metastasis of squamous cell carcinoma and an unknown primary require testing on the lymph node specimen. When ancillary testing is performed, it is recommended to include the type of testing, the result and interpretive guidelines if applicable.[54]

Ancillary testing for HPV (either using p16 or an HPV-specific method) is a core item for metastases for SCC to level II or III lymph nodes, with an unknown primary. Neck tumours with a lymphoepithelial pattern should be tested for EBV (for example, using in situ hybridisation for EBV-encoded RNA).

Note 6 – Regional lymph node categorisation

Information on lymph node status is crucial for the staging and treatment of head and neck malignancies. The staging described below conforms to the 8th edition of the Union for International Cancer Control (UICC)/American Joint Committee on Cancer (AJCC) Staging Manuals.[18,19]

Regional lymph nodes (pN)

<u>(HPV-INDEPENDENT), HYPOPHARYNX, LARYNX, CUTANEOUS HEAD AND NECK CARCINOMAS (WITH THE EXCEPTION OF MERKEL CELL CARCINOMA) AND UNKNOWN PRIMARY SQUAMOUS CELL CARCINOMAS THAT ARE P16 AND EBV-NEGATIVE</u>

NX Regional lymph nodes cannot be assessed

N0 No regional lymph node metastasis

N1 Metastasis in a single ipsilateral lymph node, 3 cm or less in greatest dimension without ENE

N2 Metastasis described as:

- N2a Metastasis in a single ipsilateral lymph node, 3 cm or less in greatest dimension with ENE or more than 3 cm but not more than 6 cm in greatest dimension without ENE
- N2b Metastasis in multiple ipsilateral nodes, none more than 6 cm in greatest dimension, without ENE
- N2c Metastasis in bilateral or contralateral lymph nodes, none more than 6 cm in greatest dimension, without ENE

N3a Metastasis in a lymph node more than 6 cm in greatest dimension without ENE

N3b Metastasis in a lymph node more than 3 cm in greatest dimension with ENE, or multiple ipsilateral, or any contralateral or bilateral node(s) with ENE

<u>HPV-MEDIATED (p16 POSITIVE) OROPHARYNGEAL (HPV-ASSOCIATED)</u>

NX Regional lymph nodes cannot be assessed

N0 No regional lymph node metastasis

N1 Metastasis in 1 to 4 lymph node(s)

N2 Metastasis in 5 or more lymph node(s)

<u>NASOPHARYNGEAL CARCINOMA</u>

NX Regional lymph nodes cannot be assessed

N0 No regional lymph node metastasis

N1 Unilateral metastasis in cervical lymph node(s), and/or unilateral or bilateral metastasis in retropharyngeal lymph nodes, 6 cm or less in greatest dimension, above the caudal border of cricoid cartilage

N2 Bilateral metastasis in cervical lymph node(s), 6 cm or less in greatest dimension, above the caudal border of cricoid cartilage o N3 Metastasis in cervical lymph node(s) greater than 6 cm in dimension and/or extension below the caudal border of the cricoid cartilage

MUCOSAL MELANOMA

NX Regional lymph nodes cannot be assessed

N0 No regional lymph node metastasis

N1 Regional lymph node metastasis present

Note that (i) Midline nodes are considered ipsilateral nodes and (ii) ENE detected on histopathologic examination is designated as ENE_{mi} (microscopic ENE ≤2 mm) or ENE_{ma} (major ENE >2 mm). Both ENE_{mi} and ENE_{ma} qualify as ENE(+) for definition of pN.

Note that a designation of 'U' or 'L' may be used for any N category to indicate metastasis above the lower border of the cricoid (U) or below the lower border of the cricoid (L). Similarly, clinical and pathological ENE should be recorded as ENE(-) or ENE(+).

Assignment of a pN category is applicable for patients who are treated surgically with a cervical lymph node dissection, rather than single lymph node excisional biopsy, in which case the cN category is used.[18,19]

Nasopharyngeal carcinoma (NPC) commonly presents with bulky nodal neck disease, and a lymph node biopsy may occasionally precede biopsy of the primary site. However, NPC is not a surgically treated disease,[55] and therefore pathologists are rarely called upon to provide a pN category for NPC. A single positive lymph node biopsy would contribute to the cN categorisation.

The reference document TNM Supplement: A commentary on uniform use, 5th Edition (C Wittekind et al. editors) may be of assistance when staging.[56]

Notes on submission of neck dissection specimens

Correct submission of neck dissection specimens is required to obtain the most accurate and clinically useful information. The number of lymph nodes obtained in a neck dissection specimen can be used as a quality metric that is associated with loco-regional recurrence and overall survival in patients with head and neck cancer.[57]

Several points regarding submission of neck dissection specimens are emphasised as follows:

1. Inking of neck dissection specimens. Most neck dissections without lymph node involvement or with limited involvement (in which nodes are freely mobile and not matted or grossly involving non-lymphatic structures), will not need to be inked. However, as margin assessment is recommended,

specimens with large tumour deposits, in which ENE is considered likely, should be inked.

2. Grossly negative lymph nodes should be submitted in toto. Nodes 5 mm or more should be bisected or multisected to give tissue sections of 2-3 mm thickness. Grossly involved lymph node and soft tissue metastases need not be submitted in toto, but one section per centimetre (10 mm) in greatest dimension is a reasonable approach. Sections should focus on potential areas of ENE, involvement of non-lymphatic structures, and the margin.

3. Careful gross examination is required when attempting to estimate the number of lymph nodes involved by a soft tissue mass or matted group of lymph nodes. When submitting lymph nodes that cannot be removed from the surrounding tissue (e.g., parotidectomy specimens), care should be taken not to 'double count' nodes that may be bisected and present in two cassettes. An estimate of the number of nodes in each section, is recommended. In general, the gross estimate of the number of lymph nodes is most accurate, except when tissue originally designated as node is clearly another tissue (e.g., parathyroid gland).

Referenties

1 Merlin T, Weston A and Tooher R (2009). Extending an evidence hierarchy to include topics other than treatment: revising the Australian 'levels of evidence'. *BMC Med Res Methodol* 9:34.

2 WHO Classification of Tumours Editorial Board (2024). *Head and Neck Tumours, WHO Classification of Tumours, 5th Edition, Volume 10.* IARC Press, Lyon.

3 Bal M, Sharma A, Rane SU, Mittal N, Chaukar D, Prabhash K and Patil A (2022). Neuroendocrine Neoplasms of the Larynx: A Clinicopathologic Analysis of 27 Neuroendocrine Tumors and Neuroendocrine Carcinomas. *Head Neck Pathol* 16(2):375-387.

4 Asa SL, Arkun K, Tischler AS, Qamar A, Deng FM, Perez-Ordonez B, Weinreb I, Bishop JA, Wenig BM and Mete O (2021). Middle Ear "Adenoma": a Neuroendocrine Tumor with Predominant L Cell Differentiation. *Endocr Pathol* 32(4):433-441.

5 Rivero A and Liang J (2016). Sinonasal small cell neuroendocrine carcinoma: a systematic review of 80 patients. *Int Forum Allergy Rhinol* 6(7):744-751.

6 Kuan EC, Alonso JE, Tajudeen BA, Arshi A, Mallen-St Clair J and St John MA (2017). Small cell carcinoma of the head and neck: A comparative study by primary site based on population data. *Laryngoscope* 127(8):1785-1790.

7 van der Laan TP, Iepsma R, Witjes MJ, van der Laan BF, Plaat BE and Halmos GB (2016). Meta-analysis of 701 published cases of sinonasal neuroendocrine carcinoma: The importance of differentiation grade in determining treatment strategy. *Oral Oncol* 63:1-9.

8 Uccella S, La Rosa S, Metovic J, Marchiori D, Scoazec JY, Volante M, Mete O and Papotti M (2021). Genomics of High-Grade Neuroendocrine Neoplasms: Well-Differentiated Neuroendocrine Tumor with High-Grade Features (G3 NET) and Neuroendocrine Carcinomas (NEC) of Various Anatomic Sites. *Endocr Pathol* 32(1):192-210.

9 International Collaboration on Cancer Reporting (2024). *Carcinomas of the major salivary glands Histopathology Reporting Guide. 2nd edition*. Available from: https://www.iccr-cancer.org/datasets/published-datasets/head-neck/salivary-glands/ (Accessed 31st July 2024).

10 International Collaboration on Cancer Reporting (2024). *Head & Neck datasets*. Available from: https://www.iccr-cancer.org/datasets/published-datasets/head-neck/ (Accessed 31st July 2024).

11 Ferlito A, Robbins KT, Shah JP, Medina JE, Silver CE, Al-Tamimi S, Fagan JJ, Paleri V, Takes RP, Bradford CR, Devaney KO, Stoeckli SJ, Weber RS, Bradley PJ, Suarez C, Leemans CR, Coskun HH, Pitman KT, Shaha AR, de Bree R, Hartl DM, Haigentz M, Jr., Rodrigo JP, Hamoir M, Khafif A, Langendijk JA, Owen RP, Sanabria A, Strojan P, Vander Poorten V, Werner JA, Bien S, Woolgar JA, Zbaren P, Betka J, Folz BJ, Genden EM, Talmi YP, Strome M, Gonzalez Botas JH, Olofsson J, Kowalski LP, Holmes JD, Hisa Y and Rinaldo A (2011). Proposal for a rational classification of neck dissections. *Head Neck* 33(3):445-450.

12 Robbins KT, Medina JE, Wolfe GT, Levine PA, Sessions RB and Pruet CW (1991). Standardizing neck dissection terminology. Official report of the Academy's Committee for Head and Neck Surgery and Oncology. *Arch Otolaryngol Head Neck Surg* 117(6):601-605.

13 Spiessl B (1992). *TNM Atlas: Illustrated Guide to the TNM/pTNM Classification of Malignant Tumours (UICC International Union Against Cancer)*. Springer, Germany.

14 Gregoire V, Coche E, Cosnard G, Hamoir M and Reychler H (2000). Selection and delineation of lymph node target volumes in head and neck conformal radiotherapy. Proposal for standardizing terminology and procedure based on the surgical experience. *Radiother Oncol* 56(2):135-150.

15 Chiesa-Estomba CM, Urazan JD, Cammaroto G, Mannelli G, Molteni G, Dallari V, Lechien JR, Mayo-Yanez M, González-García J, Sistiaga-Suarez JA, Tucciarone M, Ayad T and Meccariello G (2023). Lymph node metastasis in level IIb in oropharyngeal squamous cell carcinoma: a multicentric, longitudinal, retrospective analysis. *Eur Arch Otorhinolaryngol* 280(2):869-876.

16 Movahed A, Reeves WC, Rose GC, Wheeler WS and Jolly SR (1990). Dobutamine and improvement of regional and global left ventricular function in coronary artery disease. *Am J Cardiol* 66(3):375-377.

17 Contrera KJ, Huang AT, Shenson JA, Tang C, Roberts D, Myers JN, Weber RS, Lai SY, Williams M, El-Hallal M, Jacob D and Zafereo M (2022). Primary and recurrent regional metastases for lateralized oral cavity squamous cell carcinoma. *Surg Oncol* 44:101804.

18 Brierley JD, Gospodarowicz MK and Wittekind C (eds) (2016). *Union for International Cancer Control. TNM Classification of Malignant Tumours, 8th Edition*, Wiley, USA.

19 Amin MB, Edge SB, Greene FL, Byrd DR, Brookland RK, Washington MK, Gershenwald JE, Compton CC, Hess KR, Sullivan DC, Jessup JM, Brierley JD, Gaspar LE, Schilsky RL, Balch CM, Winchester DP, Asare EA, Madera M, Gress DM and Meyer LR (eds) (2017). *AJCC Cancer Staging Manual. 8th ed.*, Springer, New York.

20 Robbins KT, Clayman G, Levine PA, Medina J, Sessions R, Shaha A, Som P and Wolf GT (2002). Neck dissection classification update: revisions proposed by the American Head and Neck Society and the American Academy of Otolaryngology-Head and Neck Surgery. *Arch Otolaryngol Head Neck Surg* 128(7):751-758.

21 Robbins KT, Shaha AR, Medina JE, Califano JA, Wolf GT, Ferlito A, Som PM and Day TA (2008). Consensus statement on the classification and terminology of neck dissection. *Arch Otolaryngol Head Neck Surg* 134(5):536-538.

22 Medina JE (1989). A rational classification of neck dissections. *Otolaryngol Head Neck Surg* 100(3):169-176.

23 Paleri V, Urbano TG, Mehanna H, Repanos C, Lancaster J, Roques T, Patel M and Sen M (2016). Management of neck metastases in head and neck cancer: United Kingdom National Multidisciplinary Guidelines. *J Laryngol Otol* 130(S2):S161-s169.

24 Lewis JS, Jr., Beadle B, Bishop JA, Chernock RD, Colasacco C, Lacchetti C, Moncur JT, Rocco JW, Schwartz MR, Seethala RR, Thomas NE, Westra WH and Faquin WC (2017). Human Papillomavirus Testing in Head and Neck Carcinomas: Guideline From the College of American Pathologists. *Arch Pathol Lab Med* 142(5):559-597.

25 Leemans CR, Tiwari R, van der Waal I, Karim AB, Nauta JJ and Snow GB (1990). The efficacy of comprehensive neck dissection with or without postoperative radiotherapy in nodal metastases of squamous cell carcinoma of the upper respiratory and digestive tracts. *Laryngoscope* 100(11):1194-

1198.

26 Smeele LE, Leemans CR, Langendijk JA, Tiwari R, Slotman BJ, van Der Waal I and Snow GB (2000). Positive surgical margins in neck dissection specimens in patients with head and neck squamous cell carcinoma and the effect of radiotherapy. *Head Neck* 22(6):559-563.

27 Harris JP, Chen MM, Orosco RK, Sirjani D, Divi V and Hara W (2018). Association of Survival With Shorter Time to Radiation Therapy After Surgery for US Patients With Head and Neck Cancer. *JAMA Otolaryngol Head Neck Surg* 144(4):349-359.

28 Jose J, Moor JW, Coatesworth AP, Johnston C and MacLennan K (2004). Soft tissue deposits in neck dissections of patients with head and neck squamous cell carcinoma: prospective analysis of prevalence, survival, and its implications. *Arch Otolaryngol Head Neck Surg* 130(2):157-160.

29 Kaul P, Malhotra M, Arora V, Agarwal N, Singh MP and Garg PK (2023). Prognostic significance of soft tissue deposits in head and neck squamous cell carcinoma: a systematic review and meta-analysis. *Int J Oral Maxillofac Surg* 52(9):917-922.

30 Ferlito A, Shaha AR and Rinaldo A (2001). Evolution in the philosophy of neck dissection. *Acta Otolaryngol* 121(8):963-966.

31 Devaney KO, Rinaldo A and Ferlito A (2007). Micrometastases in cervical lymph nodes from patients with squamous carcinoma of the head and neck: should they be actively sought? Maybe. *Am J Otolaryngol* 28(4):271-274.

32 Alkureishi LW, Burak Z, Alvarez JA, Ballinger J, Bilde A, Britten AJ, Calabrese L, Chiesa C, Chiti A, de Bree R, Gray HW, Hunter K, Kovacs AF, Lassmann M, Leemans CR, Mamelle G, McGurk M, Mortensen J, Poli T, Shoaib T, Sloan P, Sorensen JA, Stoeckli SJ, Thomsen JB, Trifiro G, Werner J and Ross GL (2009). Joint practice guidelines for radionuclide lymphoscintigraphy for sentinel node localization in oral/oropharyngeal squamous cell carcinoma. *Ann Surg Oncol* 16(11):3190-3210.

33 Harish K (2005). Neck dissections: radical to conservative. *World J Surg Oncol* 3(1):21.

34 Tsai MH, Chuang HC, Chien CY, Huang TL, Lu H, Su YY, Yang CH, Lai CC, Tsai WL, Lin YT and Fang FM (2023). Lymph node ratio as a survival predictor for head and neck squamous cell carcinoma with multiple adverse pathological features. *Head Neck* 45(8):2017-2027.

35 Wang K, Tian W, Xu X, Peng X, Tang H, Zhao Y, Wang X and Li G (2022). Positive lymph node ratio predicts adverse prognosis for patients with lymph nodes metastatic hypopharyngeal squamous cell carcinoma after primary surgery. *Transl Cancer Res* 11(3):463-474.

36 Gartagani Z, Doumas S, Kyriakopoulou A, Economopoulou P, Psaltopoulou T, Kotsantis I, Sergentanis TN and Psyrri A (2022). Lymph Node Ratio as a Prognostic Factor in Neck Dissection in Oral Cancer Patients: A Systematic Review and Meta-Analysis. *Cancers (Basel)* 14(18):4456.

37 Huang SH, Chernock R, O'Sullivan B and Fakhry C (2021). Assessment Criteria and Clinical Implications of Extranodal Extension in Head and Neck Cancer. *Am Soc Clin Oncol Educ Book* 41:265-278.

38 Benchetrit L, Torabi SJ, Givi B, Haughey B and Judson BL (2021). Prognostic Significance of Extranodal Extension in HPV-Mediated Oropharyngeal Carcinoma: A Systematic Review and Meta-analysis.

Otolaryngol Head Neck Surg 164(4):720-732.

39 An Y, Park HS, Kelly JR, Stahl JM, Yarbrough WG, Burtness BA, Contessa JN, Decker RH, Koshy M and Husain ZA (2017). The prognostic value of extranodal extension in human papillomavirus-associated oropharyngeal squamous cell carcinoma. *Cancer* 123(14):2762-2772.

40 Cooper JS, Pajak TF, Forastiere AA, Jacobs J, Campbell BH, Saxman SB, Kish JA, Kim HE, Cmelak AJ, Rotman M, Machtay M, Ensley JF, Chao KS, Schultz CJ, Lee N and Fu KK (2004). Postoperative concurrent radiotherapy and chemotherapy for high-risk squamous-cell carcinoma of the head and neck. *N Engl J Med* 350(19):1937-1944.

41 Bernier J, Domenge C, Ozsahin M, Matuszewska K, Lefebvre JL, Greiner RH, Giralt J, Maingon P, Rolland F, Bolla M, Cognetti F, Bourhis J, Kirkpatrick A and van Glabbeke M (2004). Postoperative irradiation with or without concomitant chemotherapy for locally advanced head and neck cancer. *N Engl J Med* 350(19):1945-1952.

42 Spector ME, Chinn SB, Bellile E, Gallagher KK, Ibrahim M, Vainshtein J, Chanowski EJ, Walline HM, Moyer JS, Prince ME, Wolf GT, Bradford CR, McHugh JB, Carey T, Worden FP, Eisbruch A and Chepeha DB (2016). Matted nodes as a predictor of distant metastasis in advanced-stage III/IV oropharyngeal squamous cell carcinoma. *Head Neck* 38(2):184-190.

43 Vaish R, Mittal N, Mahajan A, Rane SU, Agrawal A and D'Cruz AK (2022). Sentinel node biopsy in node negative early oral cancers: Solution to the conundrum! *Oral Oncol* 134:106070.

44 Keam B, Machiels JP, Kim HR, Licitra L, Golusinski W, Gregoire V, Lee YG, Belka C, Guo Y, Rajappa SJ, Tahara M, Azrif M, Ang MK, Yang MH, Wang CH, Ng QS, Wan Zamaniah WI, Kiyota N, Babu S, Yang K, Curigliano G, Peters S, Kim TW, Yoshino T and Pentheroudakis G (2021). Pan-Asian adaptation of the EHNS-ESMO-ESTRO Clinical Practice Guidelines for the diagnosis, treatment and follow-up of patients with squamous cell carcinoma of the head and neck. *ESMO Open* 6(6):100309.

45 Machiels JP, René Leemans C, Golusinski W, Grau C, Licitra L and Gregoire V (2020). Squamous cell carcinoma of the oral cavity, larynx, oropharynx and hypopharynx: EHNS-ESMO-ESTRO Clinical Practice Guidelines for diagnosis, treatment and follow-up. *Ann Oncol* 31(11):1462-1475.

46 National Institute for Health and Care Excellence (2018). *Cancer of the upper aerodigestive tract: assessment and management in people aged 16 and over*. Available from: https://www.ncbi.nlm.nih.gov/books/NBK553116/ (Accessed 18th July 2024).

47 Lai SY and Ferris RL (2020). Evolving Evidence in Support of Sentinel Lymph Node Biopsy for Early-Stage Oral Cavity Cancer. *J Clin Oncol* 38(34):3983-3986.

48 National Comprehensive Cancer Network (2024). *Head and Neck Cancers: NCCN Guidelines Version 4.2024*. Available from: https://www.nccn.org/guidelines/guidelines-detail?category=1&id=1437 (Accessed 18th July 2024).

49 Liu M, Wang SJ, Yang X and Peng H (2017). Diagnostic Efficacy of Sentinel Lymph Node Biopsy in Early Oral Squamous Cell Carcinoma: A Meta-Analysis of 66 Studies. *PLoS One* 12(1):e0170322.

50 King C, Elsherif N, Kirwan R, Schilling C, Hall G, Morgan P, Collins L, Sandison A, Odell E and Thavaraj S (2021). Serial step sections at narrow intervals with immunohistochemistry are required for accurate histological assessment of sentinel lymph node biopsy in oral squamous cell carcinoma. *Head Neck*

43(10):2985-2993.

51 Broglie MA, Haerle SK, Huber GF, Haile SR and Stoeckli SJ (2013). Occult metastases detected by sentinel node biopsy in patients with early oral and oropharyngeal squamous cell carcinomas: impact on survival. *Head Neck* 35(5):660-666.

52 Schilling C, Stoeckli SJ, Haerle SK, Broglie MA, Huber GF, Sorensen JA, Bakholdt V, Krogdahl A, von Buchwald C, Bilde A, Sebbesen LR, Odell E, Gurney B, O'Doherty M, de Bree R, Bloemena E, Flach GB, Villarreal PM, Fresno Forcelledo MF, Junquera Gutiérrez LM, Amézaga JA, Barbier L, Santamaría-Zuazua J, Moreira A, Jacome M, Vigili MG, Rahimi S, Tartaglione G, Lawson G, Nollevaux MC, Grandi C, Donner D, Bragantini E, Dequanter D, Lothaire P, Poli T, Silini EM, Sesenna E, Dolivet G, Mastronicola R, Leroux A, Sassoon I, Sloan P and McGurk M (2015). Sentinel European Node Trial (SENT): 3-year results of sentinel node biopsy in oral cancer. *Eur J Cancer* 51(18):2777-2784.

53 Den Toom IJ, Bloemena E, van Weert S, Karagozoglu KH, Hoekstra OS and de Bree R (2017). Additional non-sentinel lymph node metastases in early oral cancer patients with positive sentinel lymph nodes. *Eur Arch Otorhinolaryngol* 274(2):961-968.

54 Singhi AD and Westra WH (2010). Comparison of human papillomavirus in situ hybridization and p16 immunohistochemistry in the detection of human papillomavirus-associated head and neck cancer based on a prospective clinical experience. *Cancer* 116(9):2166-2173.

55 Yoshizaki T, Ito M, Murono S, Wakisaka N, Kondo S and Endo K (2012). Current understanding and management of nasopharyngeal carcinoma. *Auris Nasus Larynx* 39(2):137-144.

56 Wittekind C, Brierley JD, van Eycken AL and van Eycken E (eds) (2019). *TNM Supplement: A Commentary on Uniform Use, 5th Edition*, Wiley, USA.

57 Divi V, Harris J, Harari PM, Cooper JS, McHugh J, Bell D, Sturgis EM, Cmelak AJ, Suntharalingam M, Raben D, Kim H, Spencer SA, Laramore GE, Trotti A, Foote RL, Schultz C, Thorstad WL, Zhang QE, Le QT and Holsinger FC (2016). Establishing quality indicators for neck dissection: Correlating the number of lymph nodes with oncologic outcomes (NRG Oncology RTOG 9501 and RTOG 0234). *Cancer* 122(22):3464-3471.