

Appendices

Appendix 1.1.1: TNM Classification for the Primary Tumour

Primary tumor (T)	
TX	Primary tumor cannot be assessed
T0	No evidence of primary tumor
Tis	Carcinoma in situ
Supraglottis	
T1	Tumor limited to one subsite of supraglottis with normal vocal cord mobility
T2	Tumor invades mucosa of more than one adjacent subsite of supraglottis or glottis or region outside the supraglottis (e.g., mucosa of base of tongue, vallecula, medial wall of pyriform sinus) without fixation of the larynx
T3	Tumor limited to larynx with vocal cord fixation and/or invades any of the following: Postcricoid area, preepiglottic space, paraglottic space, and/or inner cortex of thyroid cartilage
T4a	Moderately advanced local disease Tumor invades through the thyroid cartilage and/ or invades tissues beyond the larynx (e.g., trachea, soft tissues of neck including deep extrinsic muscle of the tongue, strap muscles, thyroid, or esophagus)
T4b	Very advanced local disease Tumor invades prevertebral space, encases carotid artery, or invades mediastinal structures
Glottis	
T1	Tumor limited to the vocal cord(s) (may involve anterior or posterior commissure) with normal mobility
T1a	Tumor limited to one vocal cord
T1b	Tumor involves both vocal cords
T2	Tumor extends to supraglottis and/or subglottis, and/or with impaired vocal cord mobility
T3	Tumor limited to the larynx with vocal cord fixation and/or invasion of paraglottic space, and/or inner cortex of the thyroid cartilage
T4a	Moderately advanced local disease Tumor invades through the outer cortex of the thyroid cartilage and/or invades tissues beyond the larynx (e.g., trachea, soft tissues of neck including deep extrinsic muscle of the tongue, strap muscles, thyroid, or esophagus)

T4b	Very advanced local disease Tumor invades prevertebral space, encases carotid artery, or invades mediastinal structures
Subglottis	
T1	Tumor limited to the subglottis
T2	Tumor extends to vocal cord(s) with normal or impaired mobility
T3	Tumor limited to larynx with vocal cord fixation
T4a	Moderately advanced local disease Tumor invades cricoid or thyroid cartilage and/ or invades tissues beyond the larynx (e.g., trachea, soft tissues of neck including deep extrinsic muscles of the tongue, strap muscles, thyroid, or esophagus)
T4b	Very advanced local disease Tumor invades prevertebral space, encases carotid artery, or invades mediastinal structures

Appendix 1.1.2: TNM Classification for the Primary Tumor

Primary tumor (T)	
TX	Primary tumor cannot be assessed
T0	No evidence of primary tumor
Tis	Carcinoma in situ
Lip and oral cavity	
T1	Tumor 2 cm or less in greatest dimension
T2	Tumor more than 2 cm but not more than 4 cm in greatest dimension
T3	Tumor more than 4 cm in greatest dimension
T4a	Moderately advanced local disease* (lip) tumor invades through cortical bone, inferior alveolar nerve, floor of mouth, or skin of face, that is, chin or nose (oral cavity) tumor invades adjacent structure only (e.g., through cortical bone (mandible or maxilla) into deep (extrinsic) muscle of tongue (genioglossus, hyoglossus, palatoglossus, and styloglossus), maxillary sinus, skin of face)
T4b	Very advanced local disease Tumor invades masticator space, pterygoid plates, or skull base and/or encases internal carotid artery

Appendix 1.1.3: TNM Classification for the Primary Site

Primary tumor (T)	
TX	Primary tumor cannot be assessed
T0	No evidence of primary tumor
Tis	Carcinoma in situ
Nasopharynx	
T1	Tumor confined to the nasopharynx, or tumor extends to oropharynx and/or nasal cavity without parapharyngeal extension*
T2	Tumor with parapharyngeal extension*
T3	Tumor involves bony structures of skull base and/ or paranasal sinuses
T4	Tumor with intracranial extension and/or involvement of cranial nerves, hypopharynx, orbit, or with extension to the infratemporal fossa/masticator space
*Note: Parapharyngeal extension denotes posterolateral infiltration of tumor.	
Oropharynx	
T1	Tumor 2 cm or less in greatest dimension
T2	Tumor more than 2 cm but not more than 4 cm in greatest dimension
T3	Tumor more than 4 cm in greatest dimension or extension to lingual surface of epiglottis
T4a	Moderately advanced local disease Tumor invades the larynx, extrinsic muscle of tongue, medial pterygoid, hard palate, or mandible*
T4b	Very advanced local disease Tumor invades lateral pterygoid muscle, pterygoid plates, lateral nasopharynx, or skull base or encases carotid artery
*Note: Mucosal extension to lingual surface of epiglottis from primary tumors of the base of the tongue and vallecula does not constitute invasion of larynx.	
Hypopharynx	
T1	Tumor limited to one subsite of hypopharynx and/or 2 cm or less in greatest dimension
T2	Tumor invades more than one subsite of hypopharynx or an adjacent site, or measures more than 2 cm but not more than 4 cm in greatest dimension without fixation of hemilarynx
T3	Tumor more than 4 cm in greatest dimension or with fixation of hemilarynx or extension to esophagus
T4a	Moderately advanced local disease Tumor invades thyroid/cricoid cartilage, hyoid bone, thyroid gland, or central compartment soft tissue*
T4b	Very advanced local disease Tumor invades prevertebral fascia, encases carotid artery, or involves mediastinal structures
*Note: Central compartment soft tissue includes prelaryngeal strap muscles and subcutaneous fat.	

Appendix 1.1.4: TNM Classification for the Primary Tumor

Primary tumor (T)	
TX	Primary tumor cannot be assessed
T0	No evidence of primary tumor
Tis	Carcinoma in situ
Maxillary sinus	
T1	Tumor limited to maxillary sinus mucosa with no erosion or destruction of bone
T2	Tumor causing bone erosion or destruction including extension into the hard palate and/or middle nasal meatus, except extension to posterior wall of maxillary sinus and pterygoid plates
T3	Tumor invades any of the following: Bone of the posterior wall of maxillary sinus, subcutaneous tissues, floor or medial wall of orbit, pterygoid fossa, ethmoid sinuses
T4a	Moderately advanced local disease Tumor invades anterior orbital contents, skin of cheek, pterygoid plates, infratemporal fossa, cribriform plate, sphenoid, or frontal sinuses
T4b	Very advanced local disease Tumor invades any of the following: orbital apex, dura, brain, middle cranial fossa, cranial nerves other than maxillary division of trigeminal nerve (V ₂), nasopharynx, or clivus
Nasal cavity and Ethmoid Sinns	
T1	Tumor restricted to any one subsite, with or without bony invasion
T2	Tumor invading two subsites in a single region or extending to involve an adjacent region within the nasoethmoidal complex, with or without bony invasion
T3	Tumor extends to invade the medial wall or floor of the orbit, maxillary sinus, palate, or cribriform plate
T4a	Moderately advanced local disease Tumor invades any of the following: anterior orbital contents, skin of nose or cheek, minimal extension to anterior cranial fossa, pterygoid plates, sphenoid or frontal sinuses
T4b	Very advanced local disease Tumor invades any of the following: orbital apex, dura, brain, middle cranial fossa, cranial nerves other than (V ₂), nasopharynx, or clivus

Appendix 1.2.1: TNM Classification for Regional Nodal Metastases (Nasopharynx)

Regional lymph nodes (N)	
Nasopharynx	
The distribution and the prognostic impact of regional lymph node spread from nasopharynx cancer, particularly of the undifferentiated type, are different from those of other head and neck mucosal cancers and justify the use of a different N classification scheme.	
NX	Regional lymph nodes cannot be assessed
N0	No regional lymph node metastasis
N1	Unilateral metastasis in cervical lymph node(s), 6 cm or less in greatest dimension, above the supraclavicular fossa, and/or unilateral or bilateral, retropharyngeal lymph nodes, 6 cm or less, in greatest dimension*
N2	Bilateral metastasis in cervical lymph node(s), 6 cm or less in greatest dimension, above the supraclavicular fossa*
N3	Metastasis in a lymph node(s)* >6 cm and/or to supraclavicular fossa*
N3a	Greater than 6 cm in dimension
N3b	Extension to the supraclavicular fossa**

*Midline nodes are considered ipsilateral nodes

**Supraclavicular fossa is defined by three points

- [1] The superior margin of the sternal end of the clavicle
- [2] The superior margin of the lateral end of the clavicle
- [3] The point where the neck meets the shoulder

Note that this would include caudal portions of level IV and VB. And all cases with nodes (whole or part) in the fossa are considered N3b

Appendix 1.2.2: TNM Classification for Regional Nodal Metastases (for All H&N Subsites Except for Skin, Thyroid, and Nasopharynx)

Regional lymph nodes (N)	
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
N2	Metastasis in a single ipsilateral lymph node, more than 3 cm but not more than 6 cm in greatest dimension; or in multiple ipsilateral lymph nodes, none more than 6 cm in greatest dimension; or in bilateral or contralateral lymph nodes, none more than 6 cm in greatest dimension
N2a	Metastasis in single ipsilateral lymph node more than 3 cm but not more than 6 cm in greatest dimension
N2b	Metastasis in multiple ipsilateral lymph nodes, none more than 6 cm in greatest dimension
N2c	Metastasis in bilateral or contralateral lymph nodes, none more than 6 cm in greatest dimension
N3	Metastasis in a lymph node more than 6 cm in greatest dimension

Appendix 2.1: Stage Grouping (the Larynx, All Subsites)

Anatomic Stage/Prognostic Groups

Stage 0	Tis	N0	M0
Stage I	T1	N0	M0
Stage II	T2	N0	M0
Stage III	T3	N0	M0
	T1	N1	M0
	T2	N1	M0
	T3	N1	M0
Stage IVA	T4a	N0	M0
	T4a	N1	M0
	T1	N2	M0
	T2	N2	M0
	T3	N2	M0
	T4a	N2	M0
Stage IVB	T4b	Any N	M0
	Any T	N3	M0
Stage IVC	Any T	Any N	M1

Appendix 2.2: Stage Grouping (Lip and Oral Cavity)

Anatomic Stage/Prognostic Groups

Stage 0	Tis	N0	M0
Stage I	T1	N0	M0
Stage II	T2	N0	M0
Stage III	T3	N0	M0
	T1	N1	M0
	T2	N1	M0
	T3	N1	M0
Stage IVA	T4a	N0	M0
	T4a	N1	M0
	T1	N2	M0
	T2	N2	M0
	T3	N2	M0
	T4a	N2	M0
Stage IVB	Any T	N3	M0
	T4b	Any N	M0
Stage IVC	Any T	Any N	M1

Appendix 2.3: Stage Grouping (Pharynx)

Anatomic Stage/Prognostic Groups

Nasopharynx			
Stage 0	Tis	N0	M0
Stage I	T1	N0	M0
Stage II	T1	N1	M0
	T2	N0	M0
	T2	N1	M0
Stage III	T1	N2	M0
	T2	N2	M0
	T3	N0	M0
	T3	N1	M0
Stage IVA	T3	N2	M0
	T4	N0	M0
	T4	N1	M0
Stage IVB	T4	N2	M0
	Any T	N3	M0
Stage IVC	Any T	Any N	M1
Oropharynx, hypopharynx			
Stage 0	Tis	N0	M0
Stage I	T1	N0	M0
Stage II	T2	N0	M0
Stage III	T3	N0	M0
	T1	N1	M0
	T2	N1	M0
Stage IVA	T3	N1	M0
	T4a	N0	M0
	T4a	N1	M0
	T1	N2	M0
	T2	N2	M0
	T3	N2	M0
Stage IVB	T4a	N2	M0
	T4b	Any N	M0
Stage IVC	Any T	N3	M0
	Any T	Any N	M1

Appendix 2.4: Stage Grouping (Nasal Cavity and Paranasal Sinuses)

Anatomic Stage/Prognostic Groups

Stage 0	Tis	N0	M0
Stage I	T1	N0	M0
Stage II	T2	N0	M0
Stage III	T3	N0	M0
	T1	N1	M0
	T2	N1	M0
	T3	N1	M0
Stage IVA	T4a	N0	M0
	T4a	N1	M0
	T1	N2	M0
	T2	N2	M0
	T3	N2	M0
	T4a	N2	M0
Stage IVB	T4b	Any N	M0
	Any T	N3	M0
Stage IVC	Any T	Any N	M1

Appendix 3: Reconstructive H&N Surgery

Magdalene Foo

H&N reconstructive surgery poses a uniquely difficult challenge as there is a need not only to restore facial aesthetics, but also to restore the complex functions of the upper aerodigestive tract. Resection of H&Nca results in tissue deficits which require tissue repair. Tissue transfer can be divided into non-vascularized, pedicled, and free vascularized flaps.

Non-vascularized Tissue Transfer

Non-vital grafts must gain a blood supply from the recipient bed to maintain viability. This limits the three-dimensional graft size. Non-vascularized skin grafts can be used to cover superficial buccal and floor of mouth defects. Iliac crest free bone graft is most commonly used as an interpositional graft to replace continuity defects in the mandible, which are not more than 6 cm.

Pedicled Tissue Transfer

In pedicled tissue transfer, the blood supply is via a single dominant vessel or a soft tissue bridge between the donor site and the grafted tissue. Pedicled flaps have a limited arc of rotation and tethering effect in peripheral defects in the H&N.

Pedicled muscle flap e.g. temporalis muscle flap is rotated into the mouth and can reach most operative sites in the mouth, from anterior mandible through floor of mouth up to hard and soft palate. The pedicled pectoralis myocutaneous flap is the 'work horse' of oral cavity reconstruction. It provides skin and muscle or muscle alone, in large volume adequate to fill all oral cavity and most cutaneous defects. It is reliable and carries minimum donor site morbidity. The latissimus dorsi myocutaneous flap though not often used as a pedicled pectoralis myocutaneous flap for H&N surgery provides a large surface area, suitable for covering the side of a face and neck and scalp. It has a long pedicle through the axilla and neck to reach the orofacial cavity.

Myocutaneous composit or pedicled bone in conjunction with muscle flaps, rely on adequate vascular supply through the periosteal perforators of the muscle to the attached bone.

Free Vascularized Tissue Transfer

Microvascular surgery has revolutionized the management of H&Nca. It is a versatile and reliable method of reconstruction with a variety of soft tissue and bone flaps and overcomes the design constraints of distant pedicled flaps. Free flaps are selected to match the properties of the resected tissue and tailored to the surgical defect. The soft tissue flaps most useful for oral maxillofacial reconstruction are the radial forearm, scapular and parascapular, rectus abdominis and latissimus dorsi flaps.

Fasciocutaneous radial forearm flaps, are used in oropharyngeal reconstruction. The main advantage is the relatively hairless thin skin and long vascular pedicle, ideal for replacing mobile mucosal areas such as mouth, tongue, cheek, soft palate, and lateral pharyngeal wall.

Scapular and parascapular flap, used for larger cheek defects or scalp replacement. In midface reconstruction after tumour ablation, the scapula flap is the flap of choice, providing flat cortical bone, together with an independent skin paddle.

Inferior rectus abdominis flap, a myocutaneous flap, useful for obliterating volume defects after resection of the paranasal sinuses or skull base.

Latissimus dorsi flap, large myocutaneous able to cover extensive head and neck defects. Following subtotal or total glossectomies, it is important to combine replacement of mucosal tissue with replacement of tissue volume. Rectus abdominis or latissimus dorsi muscle with overlying skin for the mucosal defect provides plenty of soft tissue. However, this is only tissue bulk but no mobility, and postoperative soft tissue function is poor.

Jejunal flaps are used in oesophageal reconstruction. The benefits are outweighed by intra-abdominal surgery for harvesting, considerably increasing perioperative morbidity and mortality.

Appendix 4: Classification of Neck Dissection

Radical Neck Dissection

Removal of node-containing levels in the neck [levels I–V] and spinal accessory nerve, sternocleidomastoid muscle and the internal jugular vein

Modified Radical Neck Dissection

Removal of node-containing levels in the neck [levels I–V]. The internal jugular vein and/or sternocleidomastoid muscle spared.

Selective neck dissection, as specified by the surgeon

- supraomohyoid neck dissection *dissection of levels I–III, excision of submandibular gland*
- postero-lateral neck dissection *dissection of levels IIA, IIB, III, IV, V*
- lateral neck dissection *dissection of levels II-IV*
- central compartment neck dissection *dissection of level VI, including nodes in the perithyroid, Delphian,¹ trachea-oesophageal and antero-superior mediastinum*
- others, *extended neck dissection, as specified by the surgeon*

Source: Neck Dissection. In Stell and Maran's Head and Neck Surgery. 4th ed. Eds. JC Watkinson, MN Gaze, JA Wilson. Publ Butterworth Heinemann 2000; Upper Aerodigestive Tract (including salivary glands) American College of Pathologists Protocol. January 2005

¹Delphian nodes: midline prelaryngeal nodes, i.e., superficial midline nodes in the neck.

Appendix 5: MR Scanning

The patient should be scanned from the skull base down to the upper border of the manubrium sterni in order to demonstrate the primary tumour, potential sites of local invasion and the regional lymph nodes. A dedicated surface (neck) coil is employed in order to obtain the necessary high resolution. Scans should be obtained in multiple planes and will usually include coronal T1 W and STIR (short TI/Tau inversion recovery) or fat suppressed T2 W, transverse T2 W and post contrast (Gadolinium) transverse and coronal fat saturated T1 W sequences. A transverse T1 W is preferred by some radiologists instead of T2 W. At least one sagittal sequence (especially following contrast) is often useful, particularly for the assessment of lesions involving the tongue base. Some centres are also routinely performing diffusion-weighted imaging.

Appendix 6: MRI, CT, and USS Diagnosis of Nodal Involvement

MRI/CT

Size of Node

The simplest criterion for tumor involvement is increased maximum transverse diameter of a node. However, normal nodes vary in size, 2–19 mm, and metastatic nodes may measure significantly less than 10 mm. Therefore, the higher the upper limit of normal diameter the greater the specificity but the lower the sensitivity. Widely accepted normal upper limits are 11 mm in the jugulodigastric, 8 mm in the retropharyngeal, and 10 mm in all other regions.

Number of Nodes

A cluster of three or more nodes in the tumour drainage pathway increases the index of suspicion and allows the normal maximum to fall to 9 mm in the jugulodigastric and 8 mm elsewhere.

Shape of Node

A change in shape of the lymph node from elliptical to round is also suggestive of tumour infiltration.

Appearance of Node

The presence of necrosis in lymph nodes of any size is highly suggestive of squamous cell carcinoma metastases. On CT (Fig. 3) this is seen as irregular, low-density, unenhancing areas and on MRI (Fig. 3) as irregular high-signal areas on STIR and T2 W sequence and low-signal, unenhancing areas on the T1 W sequence. On both modalities extranodal tumour extension may be seen as nodes with

ill-defined margins, irregular peripheral enhancement, engorged surrounding lymphatics and (on MRI) a halo of ill-defined high signal on the STIR sequence [1].

Ultrasound

This identifies lymph nodes down to 3 mm diameter and is sensitive for the early detection of loss of normal architecture, tumor-induced necrosis and extralymphatic spread. Tumour disruption of normal nodal vascularity is detectable at an early stage with Doppler ultrasound. It is useful to guide fine-needle aspiration of suspicious nodes and relatively cheap and easy to follow up equivocal nodes.

Combining grey scale appearances with colour Doppler criteria² ultrasound demonstrates a sensitivity of 87% (compared to 81% for MRI and CT, rising to 86% for MRI with the addition of diffusion-weighted imaging) and a specificity of 86% (compared to 63% for MRI and 76% for CT) [2]. The addition of ultrasound-guided fine needle aspiration biopsy achieves a specificity of 98% [3]. Currently therefore ultrasound is the most reliable widely available technique for assessing cervical lymphadenopathy and may become more accurate in combination with emerging techniques such as elastography (using ultrasound to assess the elasticity of tissues) [4].

References

1. Mack MG, Rieger M, Baghi M, et al. Cervical lymph nodes. *EJR*. 2008;66:493–500.
2. Wu LM, Xu JR, Liu MJ, et al. Value of magnetic resonance imaging for nodal staging in patients with head and neck squamous cell carcinoma: a meta-analysis. *Acad Radiol*. 2012;19(3):331–40.
3. Bondt RBJ, Nelemans PJ, Hofman PAM, et al. Detection of lymph node metastases in head and neck cancer: a meta-analysis comparing US, USgFNAC, CT and MR imaging. *EJR*. 2007;64:266–72.
4. Som PM, Brandwein-Gensler MS. Lymph nodes of the neck. In: Som PM, Curtin HD, editors. *Head and neck imaging*. 5th ed., vol. 2. St Louis: Mosby; 2011, P. 2287–383.

²Presence of peripheral or chaotic intranodal vascularity).

Appendix 7: Applying Clinical Guidelines: A Synthesis of Evidence and Practice in Guideline Adoption

Peter Ross

Guidelines including those from NICE help shape the evidence base for decision making by providing clinicians with a set of scientifically developed statements with regard to which diagnostic test to use and when. However, although guidelines are regarded as an important part of the quality assurance process, research shows that adherence to their recommendations is sometimes variable among physicians. For example, one study in the Netherlands showed that GP compliance with national guidelines for drug prescription was only followed in 61% of cases [1].

In general, there is little understanding of the reasons for the variation in rates of guideline adoption among physicians. A systematic review of the literature identified seven disparate categories of barriers that affected physician guideline adoption including a lack of awareness, a lack of agreement, as well as other external barriers [2]. However, while such reviews are helpful in identifying the factors that influence guideline adoption, they do not expand on the how and why of non-adherence to guideline recommendations. Further, the general innovation literature tells us that guideline adoption is unlikely to be a binary decision. Instead, guideline adoption is likely to follow a complex and iterative trajectory of diffusion and contingent engagement so that “cookbook” approaches to their implementation are unlikely to work [3, 4].

So should we be worried about a lack of convergence in guideline adherence? The answer probably depends on the reason for the divergence of practice. If for example the lack of adherence is due to a lack of awareness or familiarity with the guideline, then intervention strategies to improve adoption rates would surely be beneficial. If, on the other hand, the barrier to adoption, as one qualitative study found, stems from a lack of agreement due to a perceived lack of applicability, then interventions to promote guideline adherence may be counter-productive [5].

National guidelines can only be fully embraced if they are aligned with the values and conditions pertaining to patients and clinicians at a local level. To understand how and why physicians adopt clinical guidelines further qualitative research is needed as factors beyond robustness of evidence will inevitably influence the individual adoption decision. These may include among other things; clinical experience, the power of local opinion leaders and champions, as well as the state of healthcare budgets [6].

In practice rationality is likely to be ‘bounded’ by resource constraints so that the decision to adopt a guideline will be the result of a process of ‘satisficing’ whereby the best possible decision in the circumstance is made [7–8]. As a result, we should not perhaps be surprised if the same guidelines are interpreted and implemented in different ways in different contexts. After all, in a post-positivist world achieving a consensus is always going to be a contentious process and guideline development and implementation is no exception. Guidelines should not be viewed as tramlines because in the final analysis their diffusion will always depend on the integration of best clinical evidence, local clinical expertise and patient centred consultation [9].

Gone are the days of a ‘one best way’ approach to healthcare provision. Patient advocates increasingly expect to be a part of the decision process and want guidelines that will help them to choose the intervention that best fits their needs and values.

References

1. Grol R, Dalhuijsen J, Thomas S, Veld C, Rutten G, Mookink H. Attributes of clinical guidelines in general practice: observational study. *BMJ*. 1998;317:858–61.
2. Cabana M, Rand C, Powe N, Wu A, Wilson M, Abboud P, Rubin H. Why don't physicians follow clinical practice guidelines? A framework for improvement. *JAMA*. 1999;282:15.
3. Van de Ven A. Central problems in the management of innovations. *Manage Sci*. 32(5).
4. Sackett D, Rosenburg W, Gray J, Haynes R, Richardson W. Evidence based medicine: what it is and what it isn't. *BMJ*. 1996;312:71–2.
5. Lugtenberg M, Zegars-van Schaick J, Westert G, Burgers J. Why don't physicians adhere to guideline recommendations in practice? An analysis of barriers among Dutch general practitioners. *Implementation Science* 2009, 4:54.
6. Wong W, Ross P, Corcoran M. Evidence-based guideline recommendations on the use of positron emission tomography imaging in head and neck cancer from Ontario and guidelines in general- some observations. *Clin Oncol*. 2013;25:242–5.
7. Simon HA. *Administrative behavior*. New York: McMillan; 1947.
8. Simon HA. *The new science of management decisions*. New York: Harper and Row; 1960.
9. McCartney M, Treadwell J, Maskrey N, Lehmen R. *BMJ*. 2016;353(8059): 337–8.

Appendix 8: Haemato-lymphoid Tumours

Katherine Sisson, Tom Roque

Extranodal lymphoma accounts for 25–50% of lymphoma within the H&N. Nodal lymphoma is often an extension of systemic disease. Within the paranasal sinuses and Waldeyers ring (tonsils, base of tongue and oropharynx) the most frequent lymphoma is diffuse large B-cell lymphoma. Within the nasal cavity, primary lymphoma is the second most common malignant neoplasm after SqCC and the most frequently encountered is the extranodal NK/T-cell lymphoma. This tumour has a strong association with EBV. Within the paediatric population, Burkitt's lymphoma is the most common lymphoid neoplasm.

Extranodal MALT (mucosa associated lymphoid tissue) marginal zone B-cell lymphoma is not uncommonly encountered in the salivary glands, thyroid and ocular adnexal structures. There is a strong association with the autoimmune disorders Sjogren's disease and Hashimoto's thyroiditis.

The main aim of diagnostic imaging, including FDG PET/CT in people presenting with lymphoma in the H&N, is to establish the extent of disease. The role of FDG PET/CT is considered in the monogram which discusses lymphoma.

Addendum

Since the preparation of the text there is published the eighth AJCC classification, and with substantial changes made with regard to the TNM staging of head and neck cancer compared with the seventh edition. One of the most significant updates is a separate classification for HPV associated oropharyngeal cancer [OPC], distinguishing it from the staging of HPV negative OPC. This is in recognition of the differences in pattern of disease, treatment approaches and clinical outcomes between people with HPV positive and HPV negative OPC. With regard the T classification, for HPV positive OPC, in contrast to HPV negative OPC, there is no Tx [primary cannot be assessed] and no Tis [carcinoma in situ] classification, justified on grounds of the non-aggressive nature of p-16 positive OPC and the lack of distinct basement membrane in the epithelium of Waldeyer's ring. There is also no stage T4b, because there is no difference in curves between T4a and T4b HPV associated OPC. The N stage is also different for HPV positive cancers, specifically for HPV associated OPC: N1 one or more ipsilateral nodes none larger than 6 cm, N2 contralateral or bilateral nodes none larger than 6 cm, N3 node or nodes larger than 6 cm. T and N classification of HPV negative OPC remains unchanged in the eighth edition.

There are also important changes with regard the classification of nasopharyngeal cancer [NPC], sufficiently so as to justify a separate chapter for NPC. In addition to refinements in T classification there are key alterations in the N staging of the nasopharynx. Specifically, the supraclavicular fossa is no longer included as a relevant landmark. Instead it is replaced by the caudal border of the cricoid cartilage. For example in the eighth edition, N2 is classified as bilateral metastasis in cervical node [s] 6 cm or smaller in greatest dimension, above the caudal border of cricoid cartilage compared with previously N2 classified as bilateral metastasis in cervical node [s] and unilateral or bilateral metastases 6 cm or less in greatest dimension, above the supraclavicular fossa; N3 in the eighth edition classified as unilateral or bilateral metastasis in cervical node [s] larger than 6 cm in greatest dimension, and or extension below the caudal border of cricoid cartilage compared with N3 previously, which was defined as metastasis in a lymph node[s] >6 cm and/or to supraclavicular fossa. Also in the new classification there is no longer N3a and N3b categories and no distinction is made for nodes greater than 6 cm in dimensions [N3a] and extension into the supraclavicular fossa [N2b]. In addition, for NPC, in common with all sites, extra-nodal extension has been added to the N classification,

other than viral related cancer and mucosal melanoma. This feature now forms an important aspect of staging non HPV positive non Epstein Barr virus positive head and neck cancers.

Other modifications in the eighth edition include: the reorganizing of skin cancer [other than melanoma and Merkel cell carcinoma] from a general chapter for the whole body to a specific chapter for head and neck cutaneous skin cancers, division of pharyngeal cancer into three separate chapters; change to the T categories in nasopharynx, oral cavity and skin.

Bibliography

Lydiatt WM, Patel SG, O'Sullivan B, Branwein MS, Ridge JA, Migliacci JC, Loomis AM, Shah JP. Head and Neck cancers—major changes in the AJCC 8th edition cancer staging manual. *Cancer*. 2017;67:122–37.

Glossary and Abbreviations

ChemoRT	Chemoradiotherapy
CT	Computed tomography
ENT	Ear nose and throat
EUA	Examination under anaesthesia
FDG	2-Deoxy-2-[fluorine-18]fluoro-D-glucose
H&N	Head and neck
H&Nca	Head and neck cancer
H&N SqCC	Head and neck squamous cell cancer
HPV	Human papillo-virus
IMRT	Intensity modulated radiotherapy
MRI	Magnetic resonance imaging
ND	Neck dissection
PET	Positron emission tomography
QALY	Quality adjusted life years
RT	Radiotherapy
SqCC	Squamous cell carcinoma
SUV	Standardised uptake value
SUVmax	Standardised uptake value (maximum)
USS	Ultrasound scanning

Index

A

Acinic cell carcinoma, 9
Adenocarcinomas, 8
Adenoid cystic cancer, 52
Adenoid cystic carcinoma, 9
Adjuvant radiotherapy, 12

B

Biopsies, 3
Broders classification, 8

C

Causative factor, 1
11C–choline PET/CT, 53
Cervical lymphadenopathy, 18
Cetuximab, 14
Chemotherapy, 14
Clinical outcomes, 4, 5
Computed tomography (CT)
 advantages, 23–24
 bone invasion, 23
 centrally necrotic squamous, 18, 20
 false positive and false negative rates, 18
 limitations, 24
 normal variants and artefacts, 22
 ORN, 34
 post-surgery acute changes, 21
 right tongue base tumour, 18, 19
 scar tissue the appearance, 21
 for smallest tumours, 19
Cross sectional imaging, 3

D

Dental amalgam, 22, 48
Diagnosis, 3

E

Epidemiology, 2
Epstein Barr Virus (EBV), 8

F

FDG PET/CT
 adenoid cystic cancer, 52
 advanced neck disease, 45
 branchial cyst, 48
 brown adipose tissue FDG uptake, 47
 11C–choline PET/CT, 53
 clinical dilemma, 48
 false negative findings, 38–41
 laryngeal necrosis/chondronecrosis, 34, 36
 metastases detection, 44
 mucoepidermoid cancer, 51
 neck disease, 45
 NICE guidelines, 45
 nodal disease, 48–50
 for non-SqCC, 50–51
 pathological lesions, 29
 physiological FDG uptake
 bilateral, 30
 in neck muscles, 30, 31
 radiation changes, 32–35
 surgical changes, 31–33
 unilateral, 30
 in vocal cord palsy, 30
 post-treatment assessment, 46, 47
 primary diagnosis, 44
 radiotherapy target volume delineation, 47
 response assessment, 46
 skeletal muscle FDG uptake, 48
 small non FDG avid lung metastasis, 45
 soft tissue necrosis, 35, 37
 squamous cell cancer, 48, 49
 surgical flap inflammation, 38

- FDG PET/CT (*cont.*)
 T4 nasopharyngeal and hypopharyngeal cancer, 45
 thyroid FDG uptake, 48
 vertebral osteomyelitis/spondylodiscitis, 35–37
 Waldeyer's ring lymphoid tissue FDG uptake, 48
- Fine needle aspiration, 3
- Free-flap reconstruction, 12
- H**
- Hypoxia detection, 52
- Human papillo-virus (HPV), 1, 2
- Hypopharyngeal cancers, 3
- Hypoxia detection, 52
- I**
- Intensity modulated radiotherapy (IMRT), 13
- L**
- Laryngeal necrosis/chondronecrosis, 34, 36
- Larynx cancers, 3
- Light microscopy, 7
- M**
- M classification, 4
- Magnetic resonance imaging (MRI)
 advantages, 22–23
 diffusion weighted MRI, 22
 disadvantages, 25
 false positive and false negative rates, 18
 limitations, 24
 normal variants and artefacts, 22
 post-contrast enhancement, 21
 post-surgery acute changes, 21
 T2 W MRI, 18
 tongue base carcinoma, 18, 20
- Management, 11
 chemotherapy, 14
 effects of age and comorbidity, 14
 locoregional recurrence, 14
 microscopic excision, 12
 multidisciplinary team, 12
 neck dissection, 12
 palliative surgery, 15
 primary surgery, 12
 radiotherapy (*see* Radiotherapy)
- Metastatic disease, 10
- Mucoepidermoid carcinoma, 9, 51
- Multi-modality treatment, 29
- N**
- N classification, 4
- Naso-endoscopy, 3
- Nasopharyngeal cancers, 2
- Neck dissection (ND), 12
- O**
- Oral cavity cancers, 2
- Organ preservation techniques, 14
- Oropharyngeal cancers, 1, 2, 5
- Osteoradionecrosis (ORN), 25, 34, 36
- P**
- Palliative surgery, 15
- Paranasal sinus and nasal cancers, 3
- Parotid cancers, 3
- Pectoralis myocutaneous flap, 31
- Pleomorphic adenomas, 9
- Proton beam therapy, 13
- R**
- Radiotherapy
 acute effects, 32
 adjuvant radiotherapy, 12
 FDG PET/CT, 47
 FDG uptake, 32, 33
 IMRT, 13
 planning, 21, 22
 proton beam therapy, 13
 stage I/II cancers, 11
 stage III/IV non-metastatic cancers, 11
 theoretical advantage, 11
- Radiotracers, 51–53
- Reconstructive surgery, 19
- Radiotracers, 53
- S**
- Salivary gland tumours, 8, 9
- Small round blue cell tumours, 9
- Soft tissue necrosis, 35, 37
- Soft tissue tumours, 9, 10
- Squamous cell carcinoma (SqCC), 2, 4, 7, 8, 25
- Squamous dysplasia, 8
- Squamous metaplasia, 7

T

T classification, 4

Thymidine 3-Deoxy-3-¹⁸F-Fluorothymidine
(FLT), 51

Tissue necrosis, 34

TNM staging system, 18

Tumour Nodal Metastases (TNM)
system, 4

U

Ultrasound (US)

advantages, 24

fine needle aspiration, 18

limitations, 24

V

Vertebral osteomyelitis/spondylodiscitis, 35–37