Data Set for the Reporting of Ear and Temporal Bone Tumors

Explanations and Recommendations of the Guidelines From the International Collaboration on Cancer Reporting

Ruta Gupta, MD, MBBS, FRCPA; Ann Sandison, MD; Bruce M. Wenig, MD; Lester D. R. Thompson, MD

• The International Collaboration on Cancer Reporting (ICCR) was established to internationally unify and standardize the pathologic reporting of cancers based on collected evidence, as well as to allow systematic multi-institutional intercountry data collection to guide cancer care in the future. Such collaborative efforts are particularly essential for developing an evidence base for rare neoplasms or those with marked geographic variation in incidence, such as the tumors of the ear and the temporal bone. The ear and the temporal bone, including the external auditory canal and the middle and inner ear, with the closely associated facial nerve, internal carotid artery, and internal jugular vein, is one of the most complex anatomic structures in the head and neck. A wide range of benign and malignant neoplasms arise in this region. The management of these neoplasms involves complex surgery because of the anatomic confines, and as such, both benign and malignant tumors are included in this data set, as the oncologically equivalent management requires a multidisciplinary approach and standardized nomenclature and terminology. Surgical procedures at this site result in multifaceted 3-dimensional specimens that can be difficult to handle at macroscopic exam. A comprehensive macroscopic examination is important for identifying critical prognostic factors and often requires clinical and radiologic correlation. Histologic examination is straightforward for basal cell or squamous cell carcinoma but can be quite challenging for other neoplasms. A summary of the ICCR guidelines for ear tumors is presented, along with discussion of the salient evidence and practical issues.

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The pathology report provides the fundamental information that informs patient care.[1] Thus, it is vital that the pathology report be accurate and include all of the essential prognostic and predictive information.[2] The International Collaboration on Cancer Reporting (ICCR) was established in 2011 through a collaboration between the College of American Pathologists, the Canadian Association of Pathologists-Association Canadienne des Pathologists in association with the Canadian Partnership Against Cancer, the Royal Colleges of Pathologists of Australasia and the United Kingdom, joined in 2013 by the European Society of Pathologists, and followed by the American Society of Clinical Pathology and the Royal College of Physicians of Ireland, Faculty of Pathology, as sustaining members. Specifically, for this data set suite covering all of the head and neck anatomic region, the members of the data set authoring committee were drawn from the additional sponsoring organizations: North American Society of Head and Neck Pathology, the American Academy of Oral and Maxillofacial Pathology, the British Society for Oral and Maxillofacial Pathology, and the International Association of Oral and Maxillofacial Pathologists. The ICCR aims to produce globally standardized, evidence-based reporting data sets for various organ systems by harnessing international experience and expertise.[3] This is particularly useful for rare neoplasms, such as those of the ear and the temporal bone, as well as those tumors with marked geographic variation in incidence, because it brings together complementary resources.

The ear and temporal bone has complex anatomy and several critical structures, including dura and temporal lobe, facial nerve, internal carotid artery, and internal jugular vein, all in very close proximity (Figure 1).[4] Thus, the treatment options for both benign and malignant neoplasms in this area may require functionally destructive and cosmetically disfiguring surgeries equivalent to radical oncologic resections.[5] A comprehensive macroscopic examination is important for identifying critical prognostic factors, such as the

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From the University of Sydney, Royal Prince Alfred Hospital, Camperdown, New South Wales, Australia (Dr Gupta); the Department of Head and Neck and Oral Pathology, Guy's Hospital, London, United Kingdom (Dr Sandison); the Department of Pathology, Moffitt Cancer Center, Tampa, Florida (Dr Wenig); and the Department of Pathology, Southern California Permanente Medical Group, Woodland Hills Medical Center, Woodland Hills (Dr Thompson).

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Corresponding author: Lester D. R. Thompson, MD, Southern California Permanente Medical Group, Woodland Hills Medical Center, Department of Pathology, 5601 De Soto Avenue, Woodland Hills, CA 91365 (email: Lester.D.Thompson@kp.org).

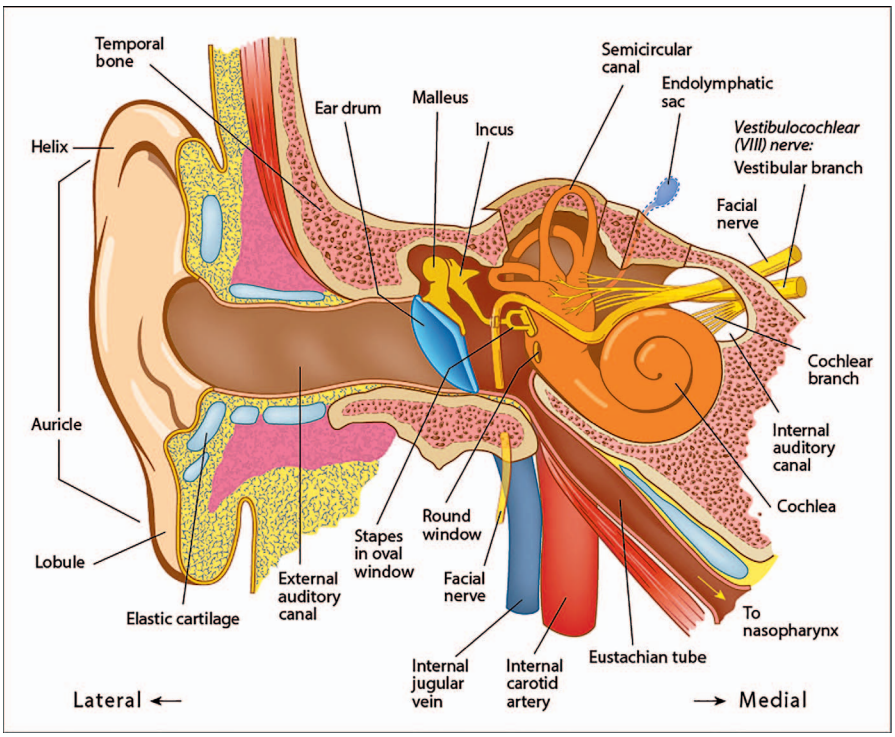

Figure 1. *An illustration of the complex anatomic relationships within the ear and temporal bone. Frequently, disfiguring or destructive surgery is required to remove benign or malignant tumors from these areas. Reproduced with permission from the International Collaboration on Cancer Reporting.*

structures involved, extent of invasion, and proximity to the margins, often requiring clinical and radiologic correlation.[6] The 3-dimensional surgical resection specimens can be difficult to handle at macroscopic exam (Figure 2). Furthermore, specific guidelines for the pathologic examination and reporting of these specimens are largely lacking. Thus, an international collaborative effort as achieved by the ICCR is critical for tumors of the ear and the temporal bone to ensure international uniformity in pathologic examination and facilitate multi-institutional and cross-regional data collection for improved patient management.

The ICCR data set provides guidelines for the reporting of the biopsy and resection specimens of benign and malignant primary tumors of the external auditory canal (EAC), middle ear, and inner ear.[5,9] Cutaneous malignancies of the pinna are excluded, because these are incorporated into the skin and melanoma data sets.[7] The ICCR data sets include core and noncore elements. The core elements are required and considered essential for the clinical management and prognosis or staging of the neoplasms, and usually supported by National Health and Medical Research Council evidence level III-2 (analysis of prognostic factors among persons in a single arm of a randomized control trial) and above.[8] The noncore elements are recommended as good clinical practice but may not be clinically validated or used in management decisions at this time. The ICCR data set includes the minimum reporting requirements for ear and temporal bone tumors while providing the flexibility to include additional elements (noncore) that may be needed at the local level. There is significant variation in the strength of the evidence available for various tumors of the ear and temporal bone, with most data derived from retrospective case series because of the rare nature of the primary neoplasms. A summary of the ICCR guidelines for the reporting of the tumors of the ear and the temporal bone is presented along with a discussion of the salient evidence and practical issues.

DATA SET ELEMENTS

Core (Required) Elements

Operative Procedure.—Surgical resection of the ear and the temporal bone is a significant undertaking, requiring comprehensive preoperative planning, with the resection of functionally critical structures associated with high treatment-related morbidity and mortality.[5,9–12] The resection specimens are often anatomically complex. The anatomic and surgical terminology may also be unfamiliar. Thus, the surgical team should be strongly encouraged to provide orienting marks with sutures and/or diagrams to facilitate optimal orientation and margin assessment. Photographic documentation of the specimen received in the laboratory prior to inking and sectioning is strongly encouraged (Figure 3), because this can be useful for clinicopathologic correlation at the multidisciplinary team meetings. The most commonly seen resection specimens include the following.[6,11]

Sleeve Resection.—This procedure is used for small tumors located along the lateral aspect of the EAC. The specimen usually includes the conchal bowl and the cartilaginous part of the ear canal lateral to the tympanic membrane.

Lateral Temporal Bone Resection.—This procedure is used for more medially located tumors that are confined to the EAC without extension into the middle ear. The lateral temporal bone resection usually includes the cartilaginous and bony parts of the EAC, the tympanic membrane, and the contents of the middle ear.

Subtotal Temporal Bone Resection.—This procedure is used for tumors that extend into the middle ear space and include the entire EAC (Figure 4), the contents of the middle ear, and the cochlear and vestibular structures. The internal carotid artery forms the medial limit of this resection as it passes through the petrous temporal bone.

Radical or Total Temporal Bone Resection.—This radical procedure is indicated for tumors that involve the petrous

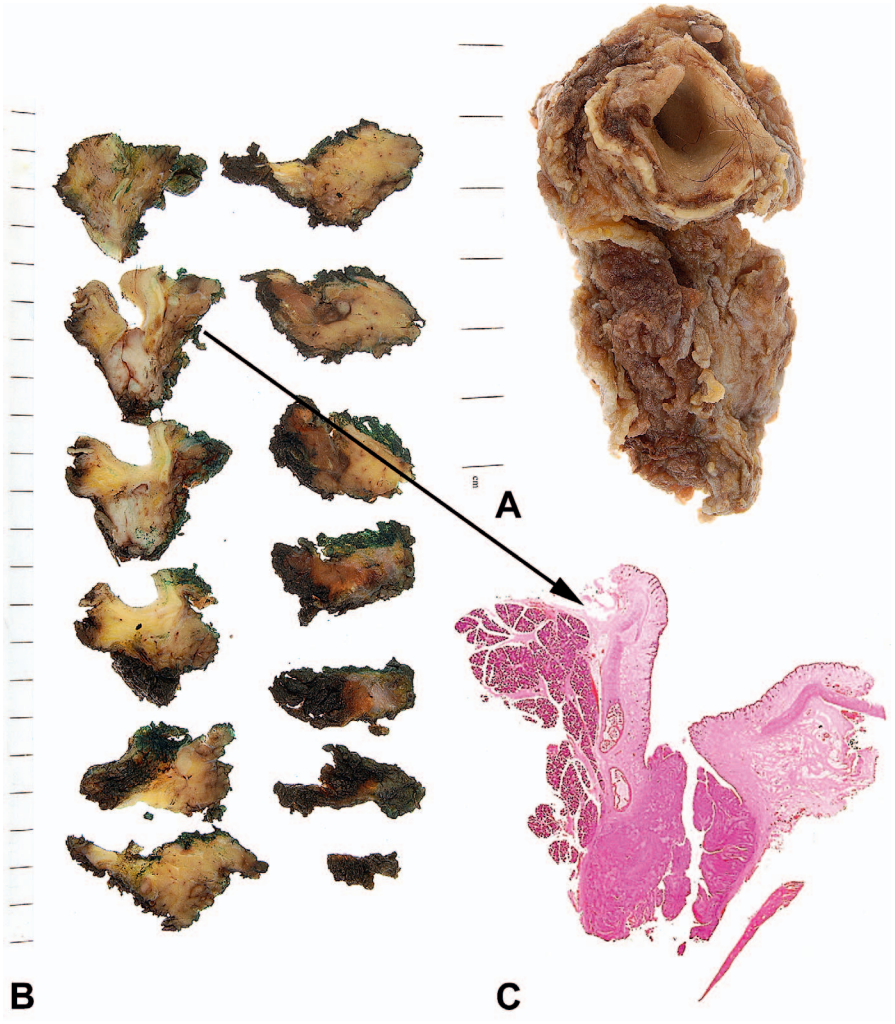

Figure 2. *A complex petrosectomy sample (A) showing orientation and serial sectioning after inking (B). Arrow points to (C) the histologic features of the tumor in relationship to the surrounding structures and margins (hematoxylin-eosin, original magnification ×10).*

apex and extend intracranially or into the infratemporal fossa. This procedure usually includes resection of the petrous part of the temporal bone, with or without the petrous carotid. The stylomastoid complex is also often included in this specimen. Portions of the dura and the facial nerve may also be present.

These resections may also be accompanied by a parotidectomy and/or a neck dissection, depending upon the extent of the tumor.[13–15] In cases when a neck lymph node dissection is submitted together with a tumor specimen, a separate, linked data set for *Nodal Excisions and Neck Dissection Specimens for Head & Neck Tumours* would be completed.[60]

The data set includes free text to encompass all procedure types if the standard surgeries are not performed (ie, curettage, partial, or extended procedures).

Specimens Submitted.—This section is a corollary of the operative procedure and largely depends on identification of the type of surgical resection performed and documentation of the various structures included. Thus, it forms the cornerstone of further macroscopic examination.

The main specimen would depend upon the type of surgical procedures described above and may be accompanied by the temporomandibular joint, dura, brain tissue, stylomastoid complex, facial nerve, or internal jugular vein, depending upon the extent of the tumor.[16] The regional lymphatic basins of the ear and temporal bone, such as the parotid and ipsilateral neck dissection, may also be included if nodal involvement is suspected clinically or radiologically or if an elective neck dissection is performed for a squamous cell carcinoma.[13–15,17]

Tumor Site.—Documentation of the exact location of the tumor is important because it correlates with the patient outcome.[5,6,9,18,19] The location of the tumor usually guides the surgery, while also influencing local control, and thus, prognosis.[6,19] As an example, patients with well-localized lateral EAC tumors (Figure 4) tend to have a much better outcome with lower functional morbidity compared with those with middle ear involvement. The patient prognosis worsens with the involvement of the facial nerve, the petrous apex, and increasing proximity to the brain.[5,9,17–20]

The tumor site can be readily identified in en bloc, well-oriented specimens.[6] However, this may not be possible in a curettage or an otherwise compromised specimen, which then requires correlation with the imaging findings, operative report, and/or discussion with the treating team.

The ICCR data set does include a "not-specified" option, but as the information in these elements is vital to a comprehensive and clinically relevant pathology report that guides further adjuvant therapy, it should be used in rare instances only after all good-faith efforts to obtain the information have been thoroughly exhausted.

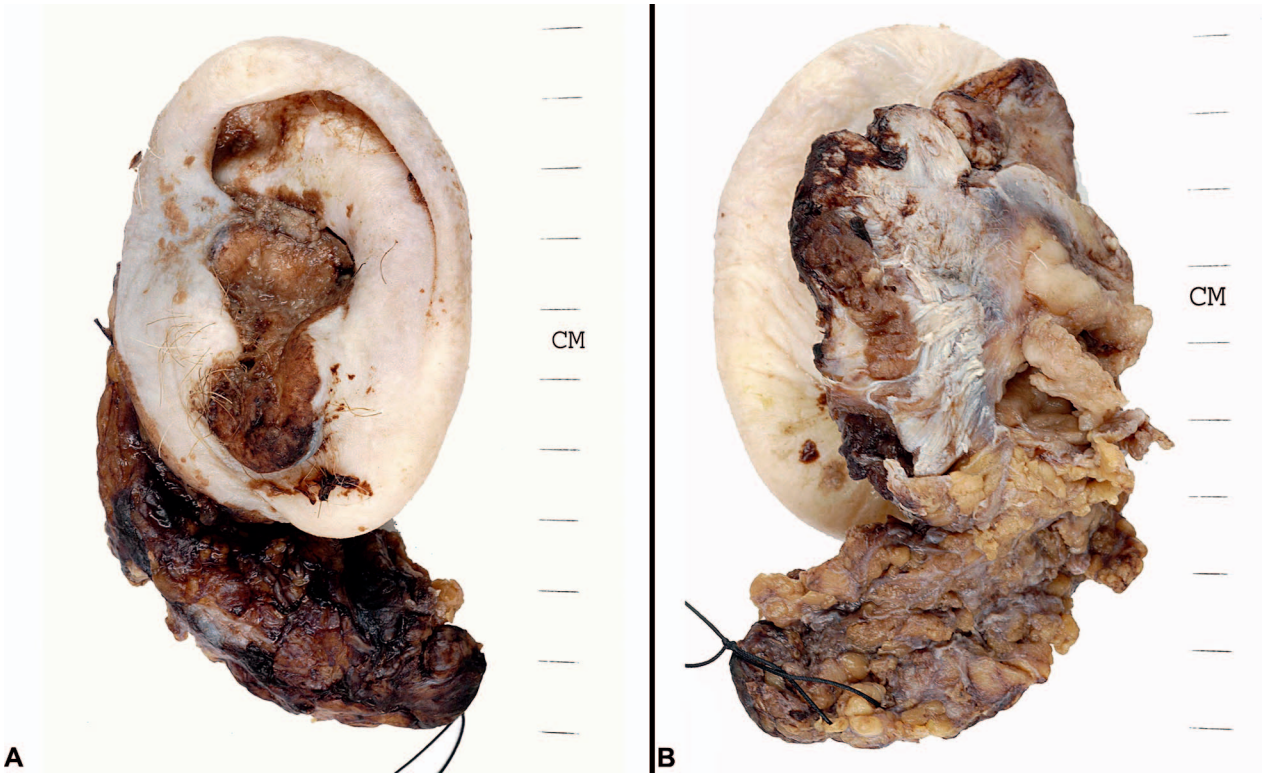

Figure 3. *A well-oriented sample with sutures has been photodocumented to aid in section selection and correlation to margins and key anatomic structures. A, Left ear anterior-lateral. B, Left ear posterior-medial.*

Tumor Dimensions.—Accurate assessment of the tumor size largely depends upon the type of specimen and the extent of the disease. Although identification and macroscopic measurement of the tumor size may be easy in a localized tumor in a well-oriented specimen, it may be impossible in a curettage or debulking specimen. Furthermore, the size of the tumor may be underestimated in the main specimen in cases with an extensive tumor involving separately submitted tissues (such as dura, facial nerve, and stylomastoid complex).[6] In some cases, inclusion of imaging

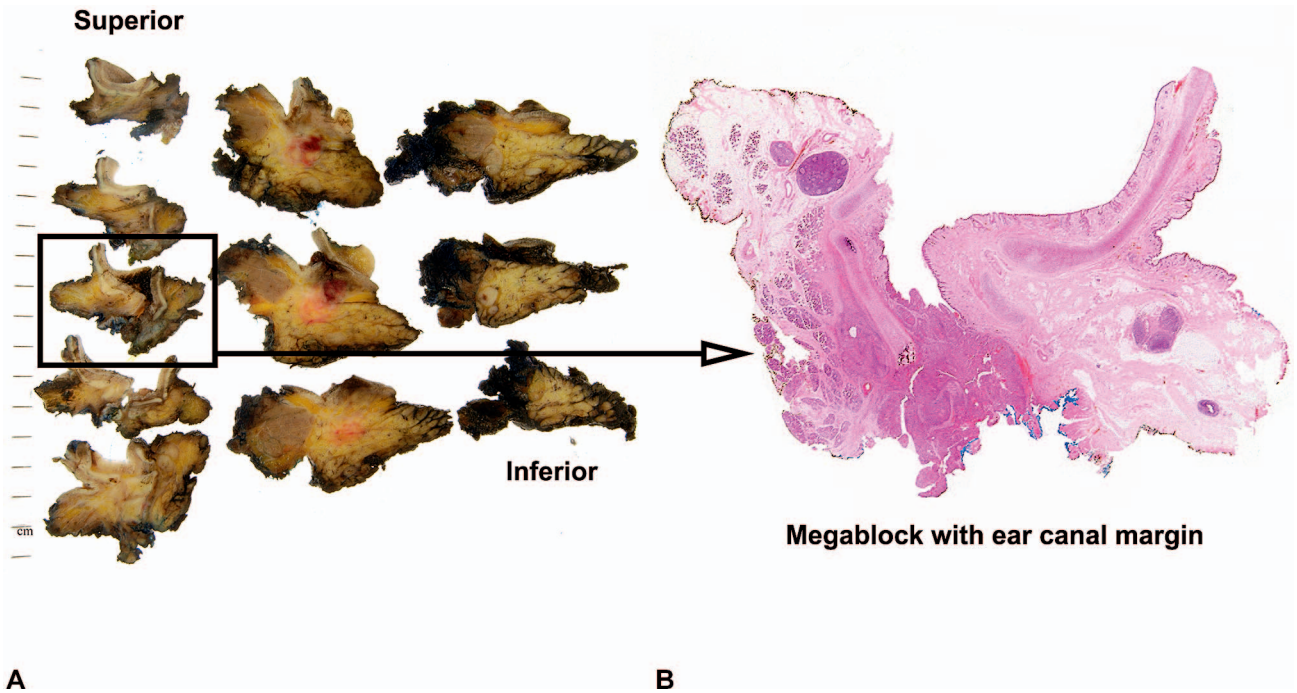

Figure 4. *A, A subtotal temporal bone resection with orientation and margins, serially sectioned. B, The black box section was submitted as a "megablock" (arrow), with identification of tumor on the blue inked canal margin (hematoxylin-eosin, original magnification ×10).*

Table 1. World Health Organization Classification of the Histologic Types of the Tumors of the Ear and the Temporal Bone[a]

Descriptor	ICD-O Codes[b]
Squamous cell carcinoma	8070/3
Ceruminous adenocarcinoma	8420/3
Ceruminous adenoid cystic carcinoma	8200/3
Ceruminous mucoepidermoid carcinoma	8430/3
Ceruminous adenoma	8420/0
Ceruminous pleomorphic adenoma	
Ceruminous syringocystadenoma papilliferum	
Middle ear adenoma (carcinoid)	
Middle ear adenocarcinoma	
Aggressive papillary tumor	8260/1
Endolymphatic sac tumor	8140/3
Vestibular schwannoma	9560/0
Meningioma	9530/0

[a] Reproduced with permission from the World Health Organization (WHO)/International Agency for Research on Cancer.

[b] The morphology codes are from the International Classification of Diseases for Oncology (ICD-O). Behavior is coded /0 for benign tumors; /1 for unspecified, borderline, or uncertain behavior; /2 for carcinoma in situ and grade III intraepithelial neoplasia; and /3 for malignant tumors.

findings may help yield a more accurate size. An attempt should be made to measure the depth of invasion whenever possible, particularly for the various carcinomas, as this has been shown to be an adverse prognostic feature.[21,22]

Histologic Tumor Type.—The histologic classification provides information regarding the behavior of the tumor (ie, benign versus malignant) and also the propensity to develop local, regional, or distant spread. All ear and temporal bone tumors should be classified according to the most recent edition of the World Health Organization (WHO) *Classification of Head and Neck Tumours* (Table 1).[23–29] It is not within the scope of this article to review the histologic features and the differential diagnoses of these lesions, but in general there are limited data because of the rare nature of the tumors. Also, there is limited prognostic experience for most entities.[23,29,30] Among these, squamous cell carcinoma of the EAC is most common and also demonstrates the worst prognosis (Figures 2 through 4).[18,24,30,31] Ceruminous adenoid cystic carcinoma may be indistinguishable from a primary parotid gland tumor, which may require parotidectomy for thorough evaluation.[32,33] However, because of the sometimes extensive surgery required, benign tumors are also included in the classification for the sake of completeness (Figure 5).

Histologic Tumor Grade.—Histologic tumor grade and degree of differentiation inform the behavior, with poorly differentiated/high-grade neoplasms generally associated with a worse outcome and increased risk of regional nodal metastases as opposed to well-differentiated/low-grade tumors.[21] Among the tumors of the ear and temporal bone, a 3-tiered grading system has conventionally been used for squamous cell carcinoma and salivary gland neoplasms (Figure 6).[23] The World Health Organization grading system is applied to meningiomas.[34] At this time, no grading systems are used for the other neoplasms.[23]

Extent of Invasion.—Macroscopic examination of the resection specimen guides tissue selection for histologic examination (Table 2). Macroscopic examination of the tumor extent, photographic documentation, and appropriate annotation of the blocks in a block key, although time and labor intensive, are a critical component of pathologic examination of these specimens. The specimens should be sectioned in a manner that provides the best cross sections of the various anatomic structures and the tumor while also demonstrating the relationship of the tumor to these structures (Figure 4).[6] Detecting and documenting the involvement of these structures, especially temporomandibular joint, stylomastoid complex, parotid gland, etc, are of prognostic significance. Thus, the cylindrical sleeve and lateral temporal bone resections should be cut in the sagittal

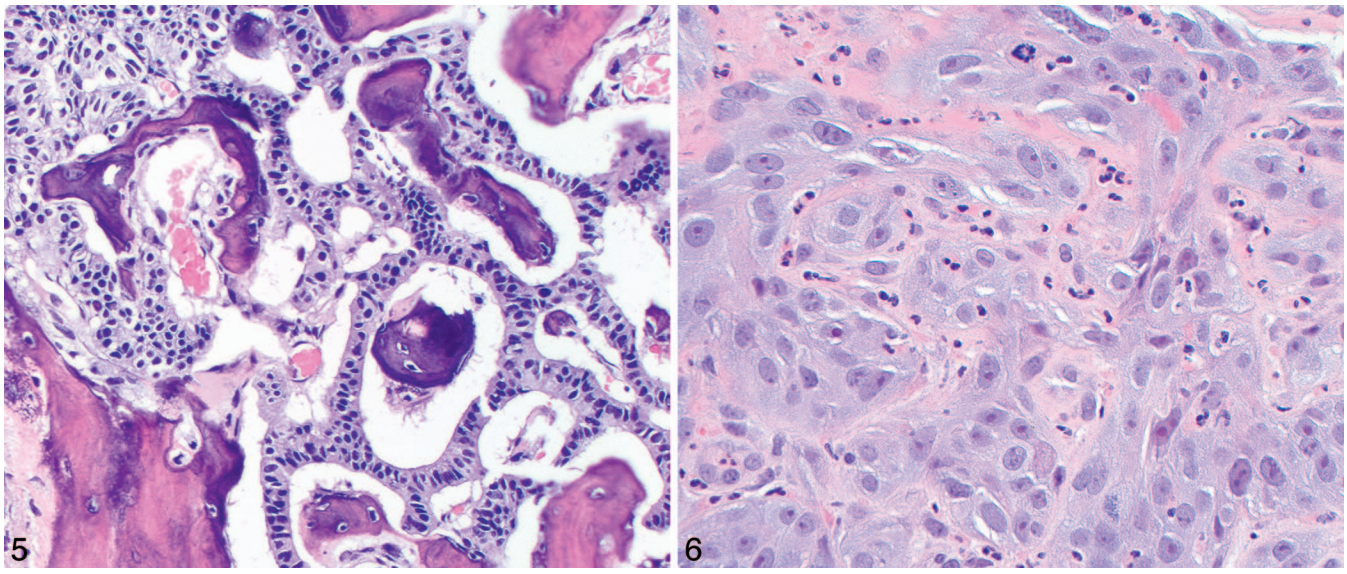

Figure 5. *This benign middle ear adenoma (a neuroendocrine tumor) shows bone invasion of the ossicles, but it is still a benign neoplasm (hematoxylin-eosin, original magnification ×400).*

Figure 6. *An intermediate-grade, moderately differentiated, infiltrative squamous cell carcinoma is noted in this resection sample (hematoxylin-eosin, original magnification ×400).*

Table 2. Pathologic Staging for Tumors of the Ear and Temporal Bone (pT)[a]	
pTx	Assessment not possible on the submitted specimen
pT1	Tumor limited to the EAC without bony erosion or evidence of soft tissue involvement
pT2	Tumor with limited EAC bone erosion (not full thickness) or limited (<0.5 cm) soft tissue involvement
pT3	Tumor eroding the osseous EAC (full thickness) with limited (<0.5 cm) soft tissue involvement, or tumor involving the middle ear and/or mastoid
pT4	Tumor eroding the cochlea, petrous apex, medial wall of the middle ear, carotid canal, jugular foramen, or dura, or with extensive soft tissue involvement (≥0.5 cm), such as involvement of TMJ or styloid process, or evidence of facial paresis

Abbreviations: EAC, external auditory canal; TMJ, temporomandibular joint.

[a] Data derived from Moody et al[40]: Moody SA, Hirsch BE, Myers EN. Squamous cell carcinoma of the external auditory canal: an evaluation of a staging system. *Am J Otol*. 2000;21(4):582–588 and Arriaga et al[46]: Arriaga M, Curtin H, Takahashi H, et al. Staging proposal for external auditory meatus carcinoma based on preoperative clinical examination and computed tomography findings. *Ann Otol Rhinol Laryngol*. 1990;99(9, pt 1):714–721.

plane from anterior to posterior, whereas the more complex subtotal and radical temporal bone resections may require a more comprehensive approach, including sagittal section of the ear canal and axial sections of the pinna and the soft tissues around the temporal bone.[6]

Dimensions of the macroscopically visible tumor should be recorded. The various structures macroscopically involved by the tumor (Table 2), such as skin, aural cartilage, bone (Figure 7), temporomandibular joint, and the parotid gland (Figure 8), and accompanying structures, such as facial nerve, stylomastoid complex, internal jugular vein, dura (Figure 8, B), and brain, should be documented and sampled for histologic examination[31,34] because in many cases the bony and soft tissue structures are histologically indistinguishable.[32,35]

A corollary of the macroscopic examination, the microscopic exam serves to confirm or identify the presence of the tumor in the structures/areas noted during the macroscopic examination. Although structures such as the brain parenchyma and the parotid can be readily recognized histologically, most of the soft tissue, bony, and neural structures in this area do not have distinctive histologic features and are indistinguishable from each other. The tissue response to invasion and destruction, such as ulceration, granulation tissue, desmoplasia, and sclerosis, may further confound the recognition of these structures histologically. However, documentation of the structures involved provides critical prognostic information and guides adjuvant radiotherapy and/or chemotherapy.[12,31,35–37]

Bone/Cartilage Invasion.—Bone/cartilage invasion is ideally assessed both on macroscopic as well as histologic exam (Figures 5 and 7). Correlation with radiologic findings and operative report may be required to determine the clinical and imaging index of suspicion for bone involvement.[38,39]

The extent of bone invasion is essential to stage.[9,17,19,20,35,40] Patients with cartilage/bone involvement will generally require adjuvant therapy and have a poorer prognosis.[5,12,21,35] Thus, it is strongly recommended that histologic sections be taken from the areas of maximum bone involvement (after appropriate decalcification).

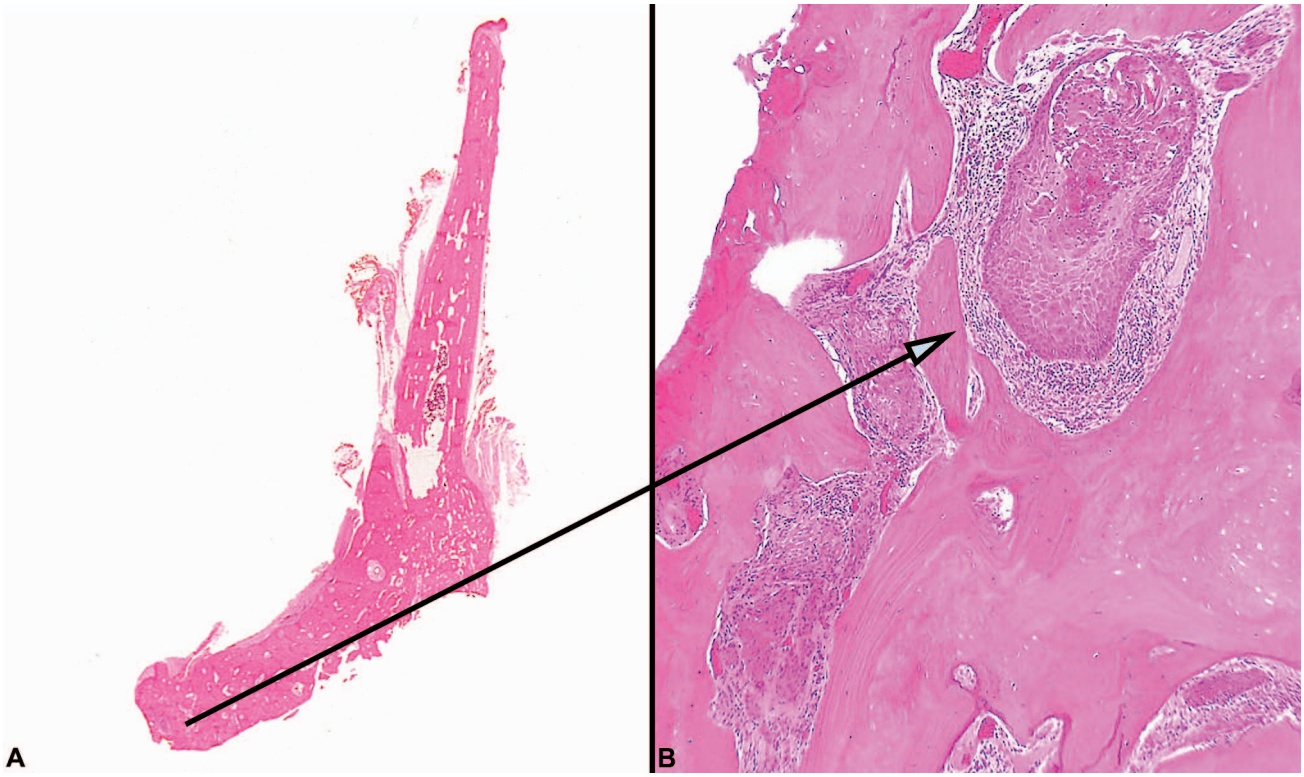

Figure 7. *This bone specimen has been decalcified, and upon histologic exam it demonstrates islands of invasive squamous cell carcinoma (hematoxylin-eosin, original magnifications ×10 [A] and ×200 [B]).*

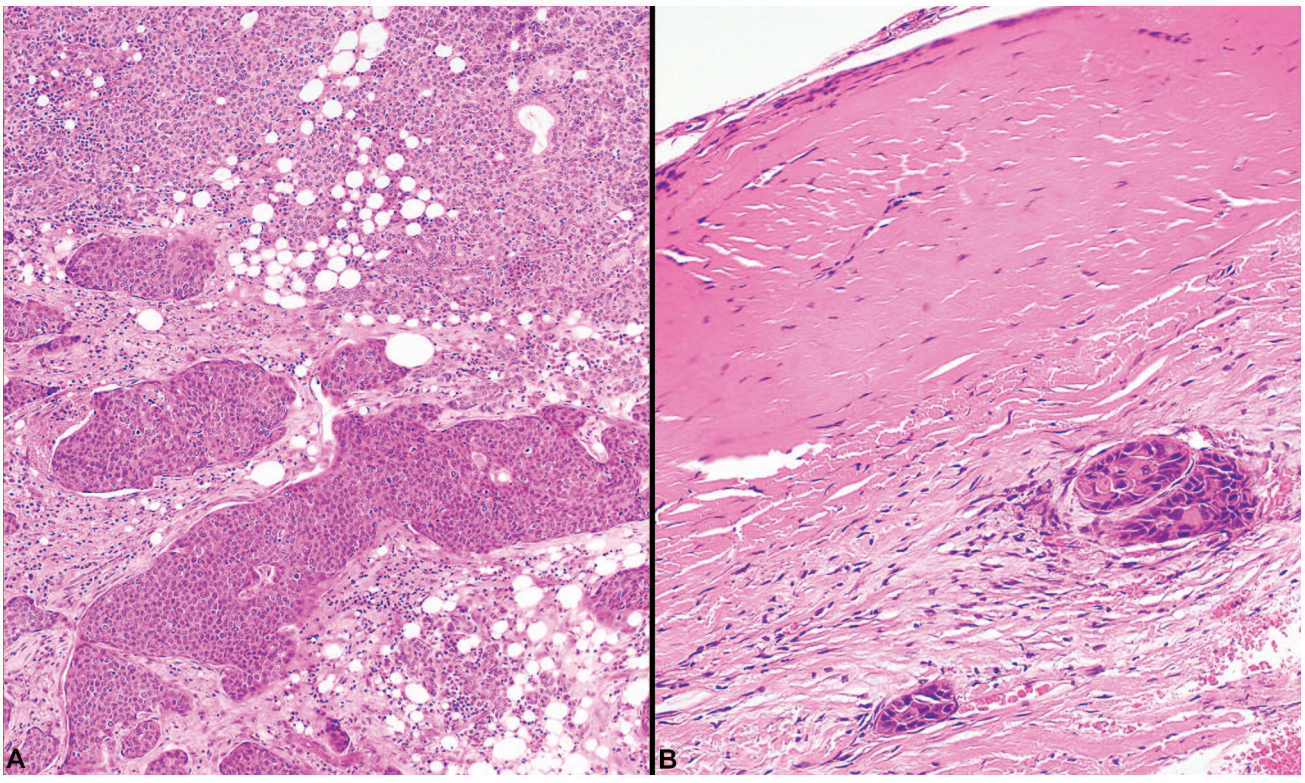

Figure 8. *A, Parotid gland invasion by a squamous cell carcinoma. B, Dural involvement by a squamous cell carcinoma is a significant finding in ear and temporal bone samples (hematoxylin-eosin, original magnifications ×100 [A] and ×400 [B]).*

Perineural Invasion.—Perineural invasion is considered an independent adverse prognostic feature.[22,41,42] Patients with involvement of a large, named nerve (ie, facial) have a poor clinical outcome.[41] Histologic correlation of perineural invasion to a named nerve (facial nerve, glossopharyngeal nerve, tympanic nerve, and great superficial and deep petrosal nerves) requires specific orientation and documentation in the gross specimen and submitted block protocol.

When a small biopsy contains lesional tissue only without nerves, "cannot be assessed" should be selected so as to alert the clinical team that perineural invasion is not reliably excluded and that appropriate radiologic correlation is essential.[38]

Lymphovascular Invasion.—The prognostic significance of lymphovascular involvement has not been separately evaluated for ear and temporal bone tumors. However, it can be inferred from other head and neck tumors that it may be of prognostic significance. Use of standardized information collected in this fashion would facilitate additional research by multiple institutions.

Margin Status.—Margin assessment is the most challenging component of evaluating en bloc resection specimens.[6] Meticulously resected tumors with negative skin, soft tissue, and bone margins carry the best prognosis.[10,19,30,43,44] Assessment of the deep soft tissue and bone margins is often more clinically significant than superficial skin margins (Figure 4).[44] Distance to the margins should be measured in millimeters both macroscopically as well as histologically. Thus, ideally, the margins should be sampled in a radial manner to facilitate measurement. Although the data set requires only the distance to the closest margin and the tissue type at the margin (skin, soft tissue, bone, or parotid), indicating the location (superior/inferior, medial/lateral, anterior/posterior) of the closest margins should be considered a best practice in a well-oriented specimen. Proactive discussion with the surgical team is often essential when involved or close deep soft tissue or bone margins may not have been histologically examined because of intraoperative drilling/burring techniques.[6,11] Additional, critical margins around the styloid process and mastoid may also be resected and sent separately for pathologic evaluation.

Not included in the data set, but suggested, is the pattern of invasion, because patients with squamous cell carcinoma with a dyscohesive, tentacular pattern of infiltration have a higher risk of recurrence compared with those with pushing borders.[22,45]

Pathologic Staging.—Currently, there is no universally accepted staging system for tumors of the ear and the temporal bone. The pathologic T staging recommended (Table 2) is largely determined by modifications of the Pittsburgh staging system,[40,46] based on retrospective clinical and radiologic evidence of patients with squamous cell carcinoma of the EAC and temporal bone, whereas other staging systems are also recognized.[18] Interestingly, none of these systems include nodal metastases, although regional lymph node metastasis is associated with a worse prognosis.[10,20]

Tumors of the inner ear are extremely rare, with some retrospective case series proposing radiologic staging systems for these neoplasms.[47] Curettage or debulking specimens are generally submitted for inner ear tumors. Thus, an accurate clinical staging is probably of greater significance than accurate pathologic staging.

Disease-free and disease-specific survival data are limited; however, it would stand to reason that tumors that extend beyond the temporal bone to involve the dura, present with facial nerve palsy due to nerve involvement, and/or involve

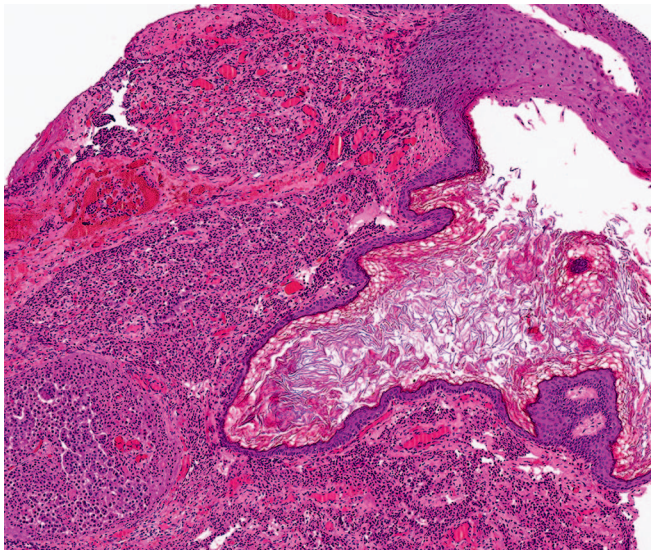

Figure 9. *There is a cholesteatoma intimately associated with a middle ear adenoma (hematoxylin-eosin, original magnification ×200).*

the petrous apex will carry significantly poorer prognosis.[12,23,41,48] Thus, although the Union for International Cancer Control 8th edition staging system for tumors of the ear and the temporal bone is not established, staging may inform standardized therapy rather than use as a prognostic tool.

Importantly, only skin squamous cell carcinoma of the EAC is covered by the American Joint Commission (AJCC) on Cancer 8th-edition staging manual.[49]

The lymph nodes within the parotid gland as well as those surrounding the parotid gland and neck nodes form the regional nodal drainage basin of the tumors of the EAC and the temporal bone.[11,15,50] When lymph nodes are included in any specimens from the head and neck, the ICCR has developed a linked but separate *Nodal Excisions and Neck Dissection Specimens for Head & Neck Tumours Histopathology Reporting Guide*,[60] which would be completed in conjunction with the *Ear and Temporal Bone Tumours Histopathology Reporting Guide*.[59] However, it is critical to distinguish *direct extension* into an intraparotid node from *metastases* to a lymph node with extranodal extension. The former should be accounted for in the pT stage and the latter in the pN stage. Correlation with macroscopic examination is helpful in this context. Documentation of the extranodal extension is important because it is associated with poor prognosis.[49,51] The most common metastases to the intraparotid lymph nodes are from cutaneous primary tumors (squamous cell carcinoma or melanoma) that rarely arise as primary salivary gland neoplasms.

The ICCR recommends that the suffixes m (multiple tumors), r (recurrent tumors), and y (posttherapy tumors) as suggested by AJCC be used while staging tumors of the EAC and temporal bone. The suffixes indicate an aggressive biology and contribute to the prognostic information.[50]

Noncore (Recommended) Elements

Tumor Focality.—Identification of multifocal or bilateral tumors is important in the context of certain syndrome or inherited neoplasms. Separate data sets should be used for reporting each additional neoplasm. Paraganglioma,[52,53] schwannoma,[54] meningioma,[54] and endolymphatic sac

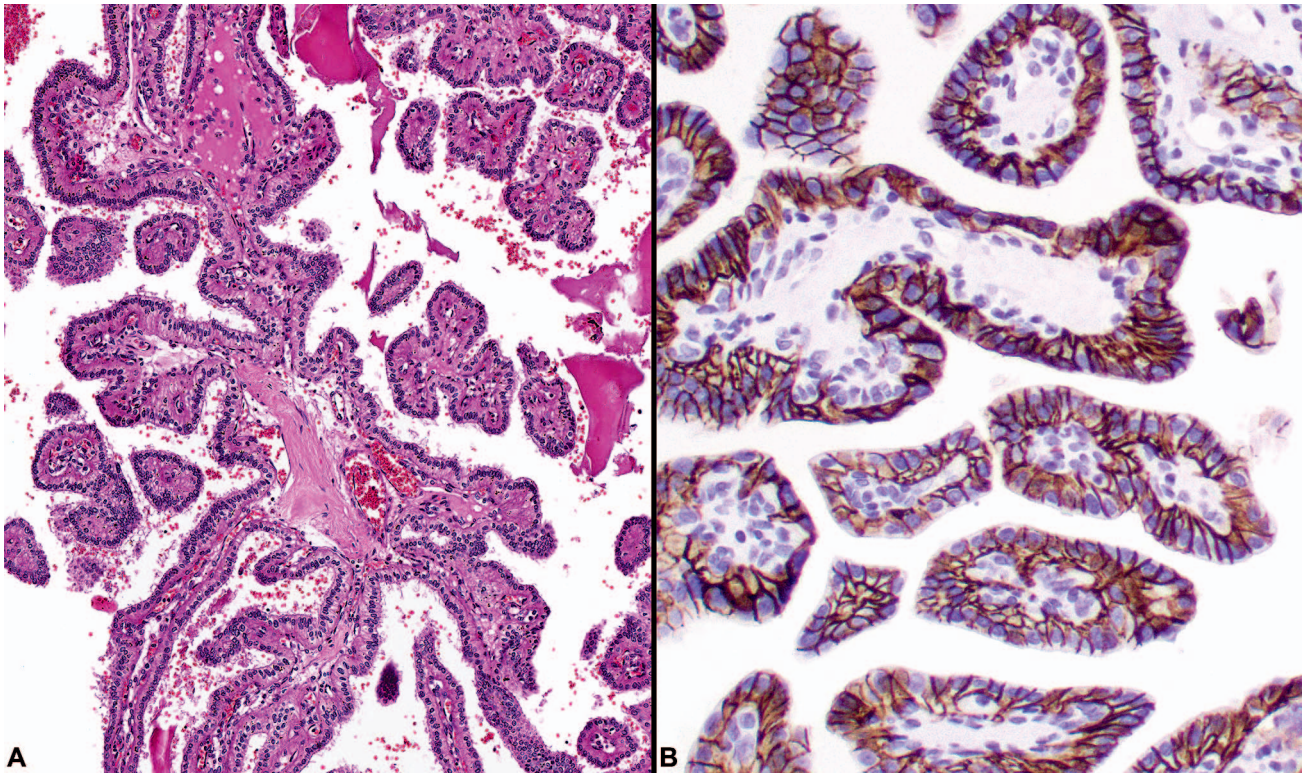

Figure 10. *A, An endolymphatic sac tumor shows fragments of bone and a delicate papillary architecture. B, CAIX yields a very strong membrane reactivity in this endolymphatic sac tumor, a characteristic finding for this neoplasm not seen in other ear and temporal bone primary tumors (hematoxylin-eosin, original magnification ×200 [A]; original magnification ×400 [B]).*

tumor[55] may be multifocal/bilateral, raising the possibility of familial or syndromic association, and requiring appropriate clinical investigation or confirmation.

Coexistent Pathology.—The ability to identify coexistent pathology depends largely on the type of specimen. Management and prognosis may also be complicated by the coexistent pathology. Presence of acute or chronic osteomyelitis presents challenges for adjuvant radiotherapy and chemotherapy.[56] Otitis media has been associated with poor survival.[10] Previous radiation (most often for nasopharyngeal carcinoma[57] or for recurrent cutaneous squamous cell carcinoma[50]) may alter histologic interpretation. Cholesteatoma is a common concurrent finding (Figure 9).

Ancillary Testing.—Immunohistochemistry may be used to confirm a diagnosis (Figure 10), whereas additional testing may serve prognostic or therapeutic goals (eg, SDHB, PD-L1).[29,53,58]

CONCLUSIONS

The ear and the temporal bone is a complex anatomic site that is affected by a wide variety of relatively uncommon benign and malignant neoplasms. There are limited guidelines regarding the prognostic factors and patient outcomes of the tumors affecting this region. The employment of an internationally standardized reporting data set should not only facilitate the examination of these specimens, but also data collection for future research and international benchmarking.

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