Editorial Commentary

Cancer staging for rare cancers: should the American Joint Committee on Cancer have a separate staging classification for external auditory canal cancer?

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Cancer staging is an important tool for both clinicians and patients to understand prognosis on a population basis but is fraught with many challenges, particularly when being applied to individual patients. The first edition of the American Joint Committee on Cancer (AJCC) staging manual published in 1977 states that the TNM system is intended to be a "*method of designating the state of a cancer at various points in time and provide a way by which this information can be readily communicated to others, to assist in decisions regarding treatment, and to be a factor in judgment as to prognosis. Ultimately, it provides a mechanism for comparing like or unlike groups of cases, particularly in regard to the results of different therapeutic procedures*" (1). The Eighth edition of the American Joint Committee on Cancer staging manual (AJCC8) has updated more than 12 chapters with new staging systems, five which pertain to head and neck cancer (2). The AJCC readily recognizes the limitation of the TNM system when being applied to individuals and is trying to develop a more personalized approach that not only incorporates the TNM classification, but also considers prognostic factors and risk assessment models (3). Cutaneous squamous cell carcinoma (cSCC) of the head and neck was one chapter updated in AJCC8, and includes cancers of the external auditory canal (EAC). On one level this is a reasonable inclusion considering that most primary EAC cancers are cSCCs and they are rare, accounting for less than 0.2% of head and neck malignancies (4). In countries with high ultraviolet (UV) solar exposure and pale skin, like Australia, most malignancies involving the EAC begin as tumours of the auricle (5). The recent article by Morita *et al.* from Japan, a country with low rates of skin cancer, excludes tumours originating in the auricle. As such, this series is a large single institution cohort of primary EAC cancers, including 60 patients with cSCC treated with curative intent over approximately 16 years (6).

A few different staging systems have been proposed for carcinomas of the EAC and the temporal bone. The University of Pittsburgh (UOP) staging system was developed by Arriaga *et al.* in 1990 (7) and modified by Moody *et al.* in 2000 (4) to account for the unique anatomical constraints of the region, allowing a better understanding of the patterns of spread and resectability. Morita *et al.* (6) highlight the differences between the modified UOP and AJCC8 staging systems for cancers of the EAC, concluding that the UOP staging system had higher prognostic accuracy than AJCC8, and argue that the AJCC staging manual should be updated to account for the anatomical features that differentiate primary cancers of the EAC from that of other head and neck cSCCs. One of the main premises of this article is that staging

systems guide treatment planning, and that both the UOP and AJCC8 staging systems were used to determine treatment and prognosis of patients in their institution. What is remarkable in this publication, is how well AJCC8 performs, given that it has been designed to apply to cSCC across a broad spectrum of anatomical sites, compared to the modified UOP, a dedicated EAC staging system. Both systems provide good survival distributions according to T classification, N classification and stage, and model performance as determined by the C-index was similar for both the modified UOP (0.777, 95% CI: 0.754–0.799) and AJCC8 (0.777, 95% CI: 0.752–0.795). The C-index, developed by Harrell *et al.* (8) is one of several measures of survival model performance. It provides an estimate of the ability of a model to distinguish individuals who experience the outcome from those who remain event free. In this context, the C-index is the chance that an individual who will die from EAC cancer will be assigned a higher stage than a patient who will not succumb to EAC cancer. It is important to note that nearly half of the patients in the series by Morita *et al.* were treated non-surgically, with radiotherapy alone or concurrent chemoradiation (6). Patients were selected for a non-surgical approach if they had advanced co-morbidity or had intracranial extension, or involvement of the pyramidal apex or internal carotid artery. As a result, 23 of the 29 patients treated non-surgically were locally advanced (T3 or T4 category). The inclusion of patients treated non-surgically is a problem because we cannot determine whether the treatment modality (i.e., radiotherapy or chemoradiation), co-morbidity, or extent of disease (i.e., stage) determines the outcome in these patients. Hence a more informative assessment of the staging systems would adjust for effect of co-morbidity and treatment modality.

Several issues arise in this article pertaining to the intention and scope of the AJCC staging manual. Clearly there is a limit as to how many head and neck sites and sub-sites can be classified before complexity overcomes its utility. Similar arguments for separate classifications could be made for cSCC of the nose and eyelids given their unique anatomical constraints, both being much more common than cancer of the EAC. Strictly speaking the T and N classification are not intended to be used for survival prediction in isolation, rather it is the combination of TNM classifications that develops a stage which should predict prognosis. Arguments against this can be made in select circumstances, especially in cSCC of the head and neck (9-11). The Sydney Head and Neck Cancer Institute have argued repeatedly that the cSCC AJCC7 and AJCC8 N classification performs poorly on the basis of distribution (number of cases in each group), monotonicity (stepwise increase in risk), and predictive capacity (survival distribution) (12-17). Morita *et al.* (6) demonstrate similar problems for cancers of EAC, which has a low rate of nodal metastases, with no patients being classified as T2, N2a, N2c, N3a, N3b, or stage 2. Whilst it is difficult in a small cohort of 60 patients, it is important that patients are reasonably well distributed between T and N classifiers, unless there is a particular reason to include a rare classification.

The TNM classifications are intended provide a uniform language that is appropriate for the disease under consideration. Morita *et al.* (6) highlight the problem with T2 tumours, being tumours 2 cm or more in size according to AJCC8. As the length of the EAC is only 2.5–3.0 cm with an average diameter of 0.8 cm, by definition nearly all tumours >2 cm in size are automatically up-staged to T3. They correctly point out that patients with good prognosis (i.e., UOP T2) are rendered advanced (T3 in AJCC8) and all UOP T3 tumours are upstaged to T4 in AJCC8. A different perspective however is to consider the more common scenario of cSCC arising in the auricle extending into the EAC. Using AJCC8, a very large tumour of the periauricular skin with minimal involvement of the EAC would be classified as T3 by AJCC8, but only T1 with UOP. Regardless of its prognostic capacity, the Modified UOP is clearly a more appropriate system for a surgeon contemplating resection of the EAC and temporal bone. What remains surprising, is that its discriminatory and predictive capacity is not far superior to AJCC8. This probably just demonstrates the limitations of staging systems that are based on anatomy, for example in many UV-induced cSCC, it is other prognostic factors, such as perineural invasion and extra-nodal extension that predict curability (18). The molecular pathogenesis of cSCC is relatively unexplored (19,20) and until the tumour biology is better understood a more sophisticated approach to staging cSCC may remain elusive. With such a rare cancer sub-type, it is difficult to make the argument that EAC cancers need their own staging system. Ultimately, we may move to a more biologically-based approach, similar to oropharyngeal cancer, where squamous cell carcinomas of sites such as the EAC, lip and nasal vestibule are assigned different staging systems according to aetiology (UV-

induced or non-UV).

For the present time, the International Consortium on Cancer Reporting (ICCR) has recently developed comprehensive pathology reporting guidelines for specimens of EAC (21). These guidelines should enable uniform multi-institutional data collection and thus assist with development of a staging system for EAC and temporal bone lesions.

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None.

Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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