



# The updated AJCC/TNM staging system (8<sup>th</sup> edition) for oral tongue cancer

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Comment on: Almangush A, Mäkitie AA, Mäkinen LK, *et al.* Small oral tongue cancers ( $\leq 4$  cm in diameter) with clinically negative neck: from the 7<sup>th</sup> to the 8<sup>th</sup> edition of the American Joint Committee on Cancer. *Virchows Arch* 2018;473:481-7.

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An increasing amount of literature shows solid evidence that the depth of invasion (DOI) of oral cavity squamous cell carcinoma is an independent predictor for occult metastasis, recurrence, and survival (1-3). Furthermore, the DOI of the primary tumor has been a major criterion when deciding to perform elective neck dissection on oral cavity squamous cell carcinoma patients since as early as the mid-1990s (4). A cut-off value of 4 mm has conventionally been used when determining the need for elective neck dissection, based on a study by Kligerman *et al.* (4). Thereafter, several reports have proposed a range of cut-off points for improving survival, detection of occult nodal metastases, and decreasing risk of locoregional recurrence (5,6).

In the current 8<sup>th</sup> edition of the American Joint Committee on Cancer (AJCC) TNM classification system, the DOI of the primary tumor has been integrated into the T category for oral cavity squamous cell carcinoma and has shown to be a major element in reframing the staging system (7). Accordingly, primary tumors previously classified as T1 are now upstaged to T2 if there is presence of invasion of more than 5 mm beyond the basement membrane, and primary tumors that had been defined as T2 are upstaged to T3 if the DOI is more than 10 mm (7). However, how well this new staging system is able to act as a predictor for factors such as survival, occult metastasis, and recurrent disease is not fully established and is still up for debate.

In this perspective, a study recently published by Almangush *et al.* (8) aimed to evaluate the effectiveness of this new T category using a homogenous cohort of early oral tongue squamous cell carcinoma (OTSCC) has provided interesting information on the effectiveness of the

updated classification system and the applicability of DOI as a predictor of clinical behavior for early-stage OTSCC.

The AJCC 8<sup>th</sup> edition employs a cut-off value of 5 mm DOI for upstaging from stage T1 to T2 and 10 mm for upstaging to T3. This may be questionable as it has been shown that an invasion depth of more than 4 mm increases the risk of locoregional metastasis and is associated with a poor prognosis (9-11), but with the new staging system, a large number of invasive tumors in which the DOI is less than 10 mm will stay in stage T1 or T2. Thus, Almangush *et al.* while evaluating the effectiveness of the AJCC 8<sup>th</sup> edition staging system, also proposed a new system where the cut-off point for DOI was 2 and 4 mm for T2 and T3, respectively. In regards to the updated AJCC manual, they reported that in their study population, many previously T1-T2 OTSCCs with cN0 were reclassified to T3 (advanced stage) when using the 8<sup>th</sup> edition, and such cases had a significantly lower survival rate (8). When using the authors' proposed staging criteria, the results were similar as the survival analyses showed a significantly worse prognosis in the T3 cases compared to the T1 and T2 cases. However, using such a stringent DOI cut-off value resulted in a much higher percentage of previous T1, T2 cases being upstaged to T3 (161 out of 311 cases, compared to 20 cases when using the AJCC 8<sup>th</sup> edition). This may result in overtreatment and increased morbidity and mortality from unnecessary radiation therapy or radical neck dissections.

The 8<sup>th</sup> edition of the AJCC manual necessitates the measurement of DOI, and not tumor thickness for accurate staging. Strictly speaking, tumor thickness differs from DOI, although many clinicians use the two terms interchangeably.

DOI is defined as the extent of cancer expansion into the tissue beneath the epithelial basement membrane, while tumor thickness concerns the whole tumor dimension. DOI is known to be a better predictive parameter compared to tumor thickness (1). However, even though a new study suggests that DOI can be assessed with intraoral ultrasonography of the tongue using a T-shaped probe (12), it is still challenging to precisely measure DOI using just preoperative imaging (13). On the other hand, tumor thickness is relatively more easier to evaluate preoperatively with ultrasonography (14,15) and/or magnetic resonance imaging (16-18), and one study found that tumor thickness assessed on preoperative CT scans provided an accurate estimation of thickness measured histopathologically in OTSCC (19). A recent study revealed that there was similar stratification of disease-specific and overall survival in oral cavity cancer patients when using DOI or tumor thickness for AJCC 8<sup>th</sup> edition T staging (20). The authors also showed that in most cases the measurements of tumor thickness and DOI were not significantly different on histopathologic examination. Therefore, further research should analyze the benefit of integrating tumor thickness as measured by preoperative imaging in the T staging. This might be more clinically useful when deciding on a treatment plan than DOI, which can only be accurately measured postoperatively on histopathologic examination. Evaluation of DOI in preoperative biopsies may not be truly representative (21).

The AJCC 8<sup>th</sup> edition also made major modifications in regards to the staging of papillary thyroid cancer, such as the raising of the age cut-off from 45 to 55 years. Kim *et al.* reported the effectiveness of this change using the clinical and genetic data of 505 papillary thyroid cancer patients (22). Interestingly, genomic analysis revealed that patients  $\geq 55$  years had 103 differently expressed genes when compared with the other age groups and had altered signaling pathways associated with more aggressive thyroid cancer. Likewise, genomic analysis using mRNA expression according to DOI in oral tongue cancer may be helpful in examining the effectiveness of the new DOI criterion.

In conclusion, further studies are warranted to substantiate the prognostic value of OTSCC staging according to the 8<sup>th</sup> edition of the AJCC Cancer Staging Manual.

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