Abstract #132: Evaluation of Prognostic Factors for Oral Tongue Squamous Cell Carcinoma: Significance of Invasive Front Tumor Infiltrating Lymphocytes, Lymph Node Ratio, Tumor Size, and Depth of Invasion

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Background:

- Oral tongue squamous cell carcinoma (SCC) is recognized for its aggressive behavior and prognostic variability.
- Our study leveraged both traditional clinicopathological variables and advanced artificial intelligence (AI) techniques to assess prognostic factors in oral tongue SCC.

Methods:

- A retrospective cohort study was conducted on 140 patients who underwent surgical resection at Asan Medical Center between 2010 and 2017.
- Clinicopathological data, including age at diagnosis, American Joint Committee of Cancer (AJCC) 8th edition stages, depth of invasion (DOI), extranodal extension (ENE), lymphovascular invasion (LVI), margin status, metastatic-to-harvested lymph nodes ratio (LNR), number of metastatic lymph nodes, perineural invasion (PNI), sex, size, tumor budding, tumor differentiation, tumor-to-stromal ratio (TSR), and worst pattern of invasion (WPOI) were analyzed.
- An AI algorithm leveraging encode-decode network for tumor and stroma segmentation followed by YOLOv8 for lymphocyte and plasma cell detection was applied to calculate lymphocytes to stromal ratios in tumor invasive front (FLR), tumor center (CLR), and intratumoral areas (ILR).

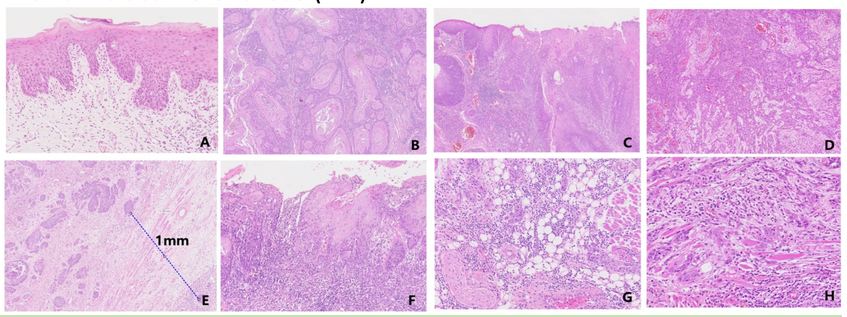

Figure 1: Measurement of histopathological parameters. (**A**) WPOI Grade 1: Tumor invasion in an expansile manner (100x) (B) WPOI Grade 2: tumor invading in solid cords and strands (100x), (**C**) WPOI Grade 3: invasive islands of the tumor with >15 cells cluster (100x), (**D**) WPOI Type 4: invasive tumor islands with <15 cells cluster (100x), (**E**) WPOI Type 5: tumor islands more than 1 mm away from the progressive end of the tumor (100x). (**F**) Isolated tumor cells or clusters of fewer than five cells at the invasive front, indicative of high-grade tumor budding (200x). (G) TILs at the invasive front stromal area (100x). (**H**) Tumor center TILs (100x).

Higher invasive front TILs, assessed by AI, predict a better survival probability in tongue cancer, especially in high stage groups along with factors DOI grade and LNR.

WPOI may have been overestimated in the literature .

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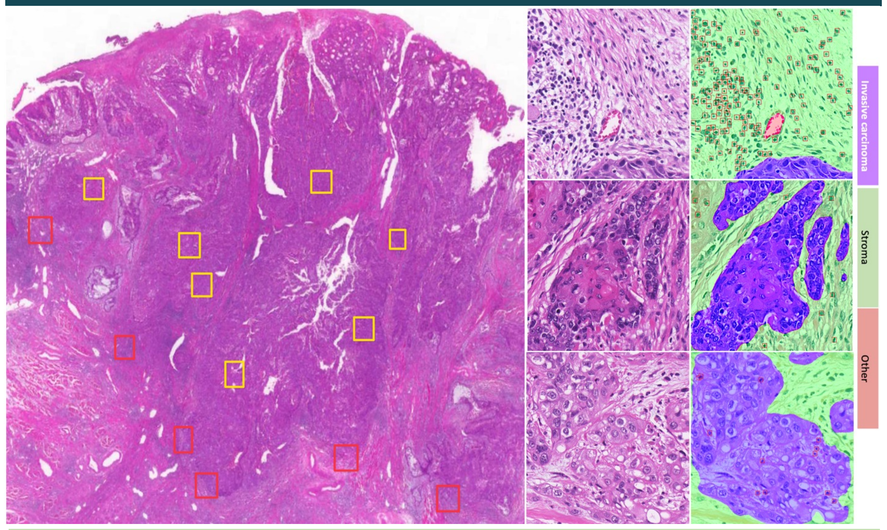

Figure 2: AI-assisted lymphocyte assessment. The AI segments TIL patch regions into invasive carcinoma (purple), tumor-associated stroma (green), and other areas (red). Lymphocytes (red bounding boxes) within patches from the tumor invasive front (upper right) and tumor center (middle right) are detected. Additionally, lymphocytes inside the invasive carcinoma are separately quantified (lower right).

Results:

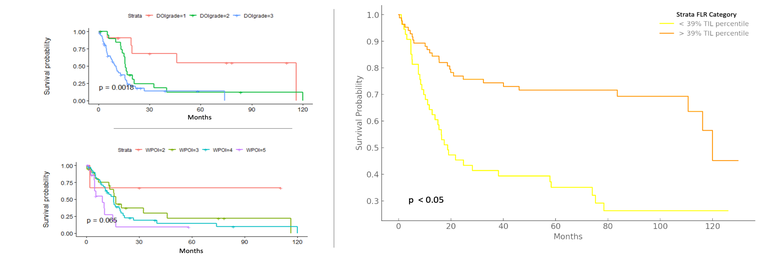

Figure 3: Kaplan Meier Curve. DOI grade (Left upper), AI-assessed FLR with 39% cutoff (Right) (all p <0.05). WPOI grade 1 to 5 (Left lower) does not show significant p-values (p=0.07)

Table. Cox proportional hazards ratio of clinicopathologic factors and AI-analysed TILs impacting tongue cancer survival (n=140)

Variable			Univariate (Hazard ratio, 95% CI, p-value*)	Multivariate (Hazard ratio, 95% CI, p-value*)
ENE[1]	Not identified	111 (79.3%)		
	Present	29 (20.7%)	**4.31 (2.57-7.21, p<.001)**	
DOI grade[3]	Mean ± SD	2.0 ± 0.8	**2.70 (1.88-3.86, p<.001)**	**1.53 (1.01-2.34, p=.047)**
Differentiation[4]	WD	78 (55.7%)		
	MD	53 (37.9%)	**1.71 (1.03-2.86, p=.039)**	
	PD	9 (6.4%)	1.86 (0.72-4.80, p=.203)	
LNR[5]	Mean ± SD	3.3 ± 5.6	**1.10 (1.07-1.14, p<.001)**	**1.10 (1.06-1.15, p<.001)**
Size	Mean ± SD	2.6 ± 1.4	**1.89 (1.59-2.25, p<.001)**	**1.39 (1.12-1.73, p=.003)**
PNI[6]	Not identified	105 (75.0%)		
	Present	35 (25.0%)	**2.66 (1.61-4.42, p<.001)**	
FLR[8]	Mean ± SD	5.9 ± 1.7	**0.69 (0.57-0.83, p<.001)**	**0.71 (0.57-0.89, p=.003)**
CLR[9]	Mean ± SD	4.9 ± 1.4	**0.68 (0.54-0.86, p=.001)**	

[1] ENE, Extranodal extension; [2] WPOI, Worst pattern of invasion; [3] DOI, Depth of invasion; [4] WD, Well differentiated; MD, Moderately differentiated; PD, Poorly differentiated; [5] LNR, Metastatic lymph node to harvested lymph node ratio multiplied by 100; [6] PNI, Perineural invasion; [7] ILR, Intratumoral lymphocyte ratio multiplied by 10,000; [8] FLR, Invasive front TIL ratio multiplied by 10,000; [9] CLR, Tumor center TIL (tumor-infiltrating lymphocyte) ratio multiplied by 10,000.

Future Directions for Research:

1. Further validation of the prognostic significance of TIL at the invasive front, LNR, and tumor size in larger, multi-institutional cohorts.
2. Investigating the biological mechanisms underlying the prognostic impact of invasive front TILs in oral tongue SCC.
3. Developing and validating AI-based algorithms for automated, quantitative assessment of invasive front TILs and other prognostic factors in oral tongue SCC.