

Novel CT Imaging Characteristics to Detect Occult Nodal Metastasis in Oral Cavity Squamous Cell Carcinoma

Megan Morisada, MD¹; Abdisalam Hassan, BPH²; Roberto Solis, MD¹; Marianne Abouyared, MD¹; Andrew Birkeland, MD¹; D. Greg Farwell, MD³; Reza, Assadsangabi, MD⁴; Vladimir Ivanovic, MD⁴; Arnaud Bewley, MD¹

¹Department of Otolaryngology – Head and Neck Surgery, University of California Davis, Sacramento, CA; ²University of California Davis School of Medicine, Sacramento, CA; ³Department of Otolaryngology – Head and Neck Surgery, University of Pennsylvania, Philadelphia, PA; ⁴Department of Radiology, University of California Davis, Sacramento, CA

Introduction

Nodal metastasis is an important prognostic indicator for patients with oral cavity squamous cell carcinoma (OCSCC). For patients with clinically positive nodal (cN+) metastasis, a modified radical neck dissection is the standard treatment. Patients without radiographic or clinical evidence of nodal metastasis (cN0) can be managed with elective neck dissection (END) or clinical surveillance. The decision as to whether to proceed with END is typically based on characteristics of the primary tumor, such as depth of invasion. Despite evolving imaging techniques, the risk of occult disease remains high.

We sought to identify novel CT imaging characteristics of regional sub-centimeter lymph nodes that would enhance our ability to detect occult nodal metastases over that provided by conventional criteria.

Methods

From July 2014 to December 2019, we identified 143 patients with OCSCC who were cN0 and underwent END at a tertiary academic center. 38 of these patients were identified as having occult cervical metastasis on pathologic analysis of their neck dissection specimens. A 1:1 mix of 38 cN+ and 38 matched cN0 controls were analyzed by a blinded neuroradiologist. 54 of these patients had adequate pre-operative CT imaging and were included in the final analysis. CT imaging was performed within 3 months of surgery with a slice thickness of 3 millimeters or less. Clinical and pathologic data were collected.

Mixed effects logistic regression models, where patients were considered as random effects to account for the correlation of the multiple measures from the same patients, were used to study radiographic characteristics include the following: presence of lymph node cortical nodule, disrupted or absent fatty hilum, flat/oval lymph node shape, lobulations, asymmetric number of lymph nodes, asymmetric clustering, asymmetric size of lymph nodes.

Analysis

Associations between novel radiographic characteristics and the presence of regional disease were evaluated with a logistic regression and chi-squared analysis. The positive predictive value (PPV) and negative predictive value (NPV) of tests developed from these imaging characteristics was calculated.

Results

Table 1	pN+ (n=26)	pN0 (n=28)	p-value
Age at diagnosis, years; mean (SD)	63 (9.5)	66 (12.7)	0.333
Gender; % female	42.3	39.3	0.821
Smoking status; %			0.251
Never	30.8	46.4	
Former	42.3	42.9	
Current	26.9	10.7	
Subsite			
Tongue	17	19	
Floor of mouth	4	4	
Mandibular alveolus	1	4	
Maxillary alveolus	4	1	
Tumor size, cm; mean (SD)	3.0 (1.4)	3.0 (1.0)	1.000
Perineural invasion present; %	32.0	81.5	<0.001
Lymphovascular invasion present; %	34.6	7.4	0.014
Bone or cartilage invasion present; %	23.1	17.9	0.063

Table 1 Patient demographics and tumor pathology

Table 2	Odds Ratio	p-value
Side of lymph node	1.76	0.1707
Lymph node short axis	0.57	<0.0001
Lymph node cortex nodule size	0.71	0.0028
Lymph node presence of cortex nodule	0.13	0.0003
Asymmetric size of lymph nodes	0.09	<0.0001
Asymmetric number of lymph nodes	0.05	<0.0001
Round/ oval hilar loss	0.08	<0.0001
Lymph node index	2.04	0.1320

Table 2 Univariate analysis of nodal characteristics

Table 3	Odds Ratio	p-value
Asymmetric size of lymph nodes	0.24	0.0188
Asymmetric number of lymph nodes	0.10	0.0102
Lymph node presence of cortex nodule	0.24	0.0392
Lymph node index (lymph node level > 2)	1.00	0.9941

Table 3 Multivariate-adjusted mixed effects analysis of nodal characteristics

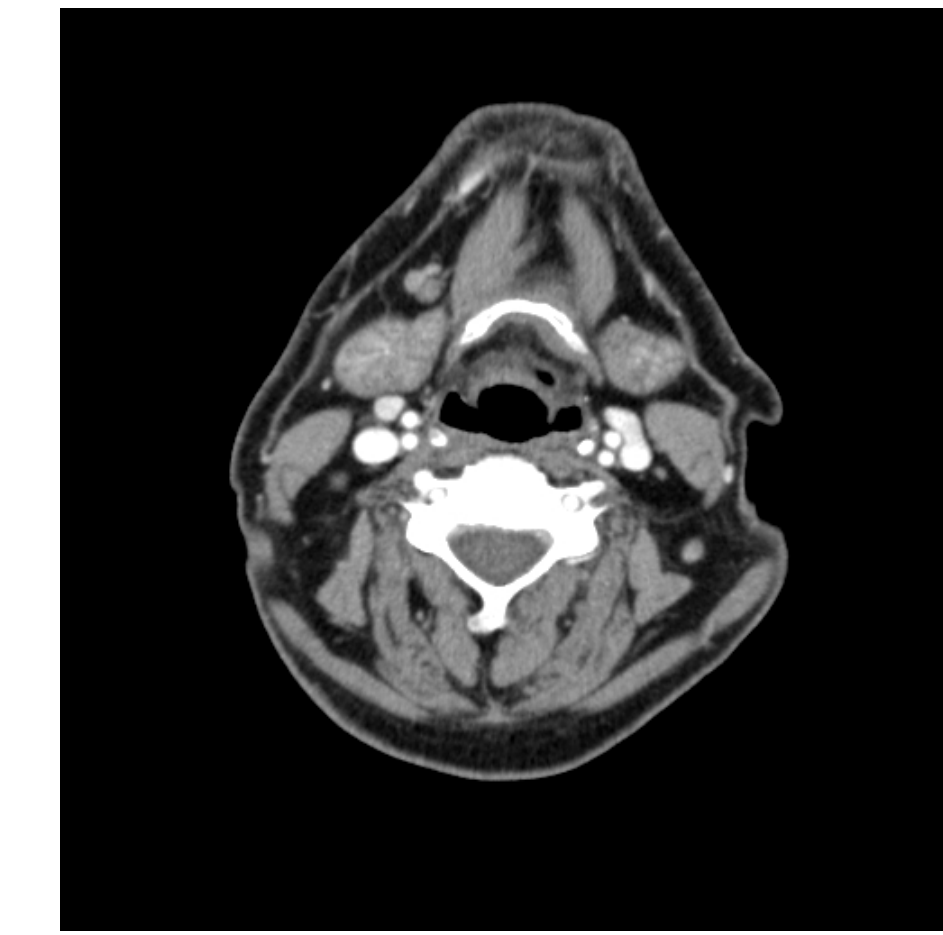


Figure 1 Cortical nodule

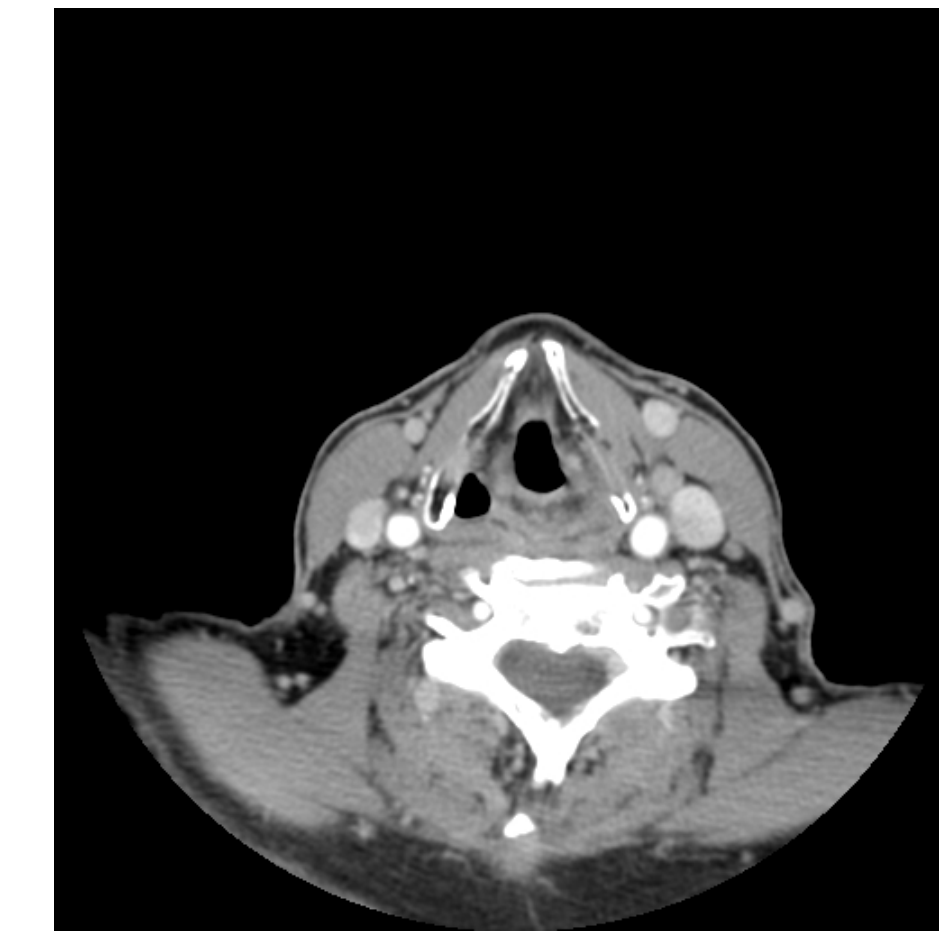


Figure 2 Asymmetric size

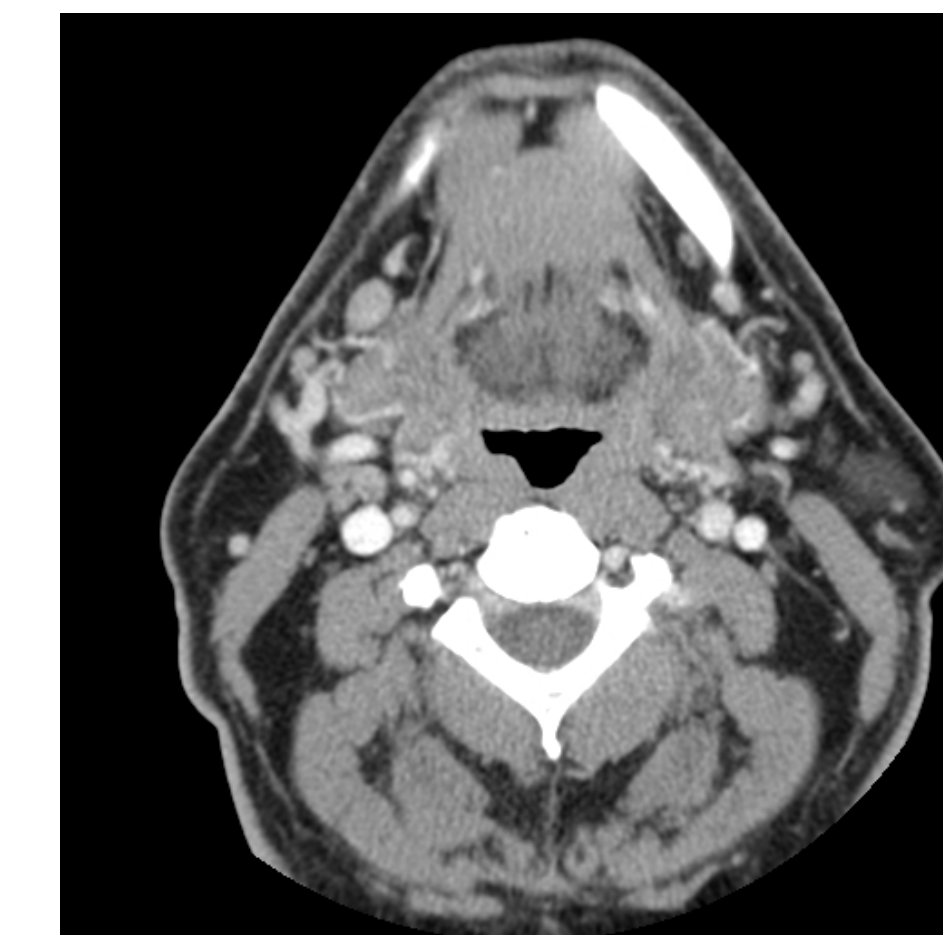


Figure 3 Asymmetric size

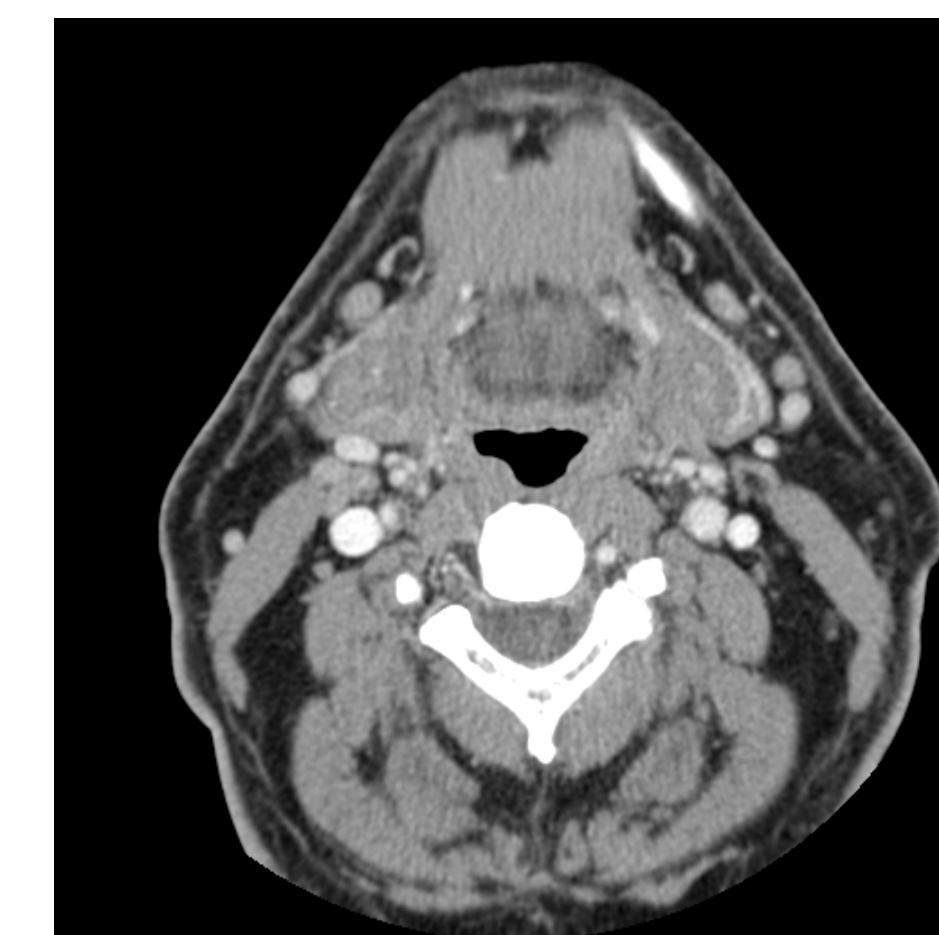


Figure 4 Asymmetric number of LNs

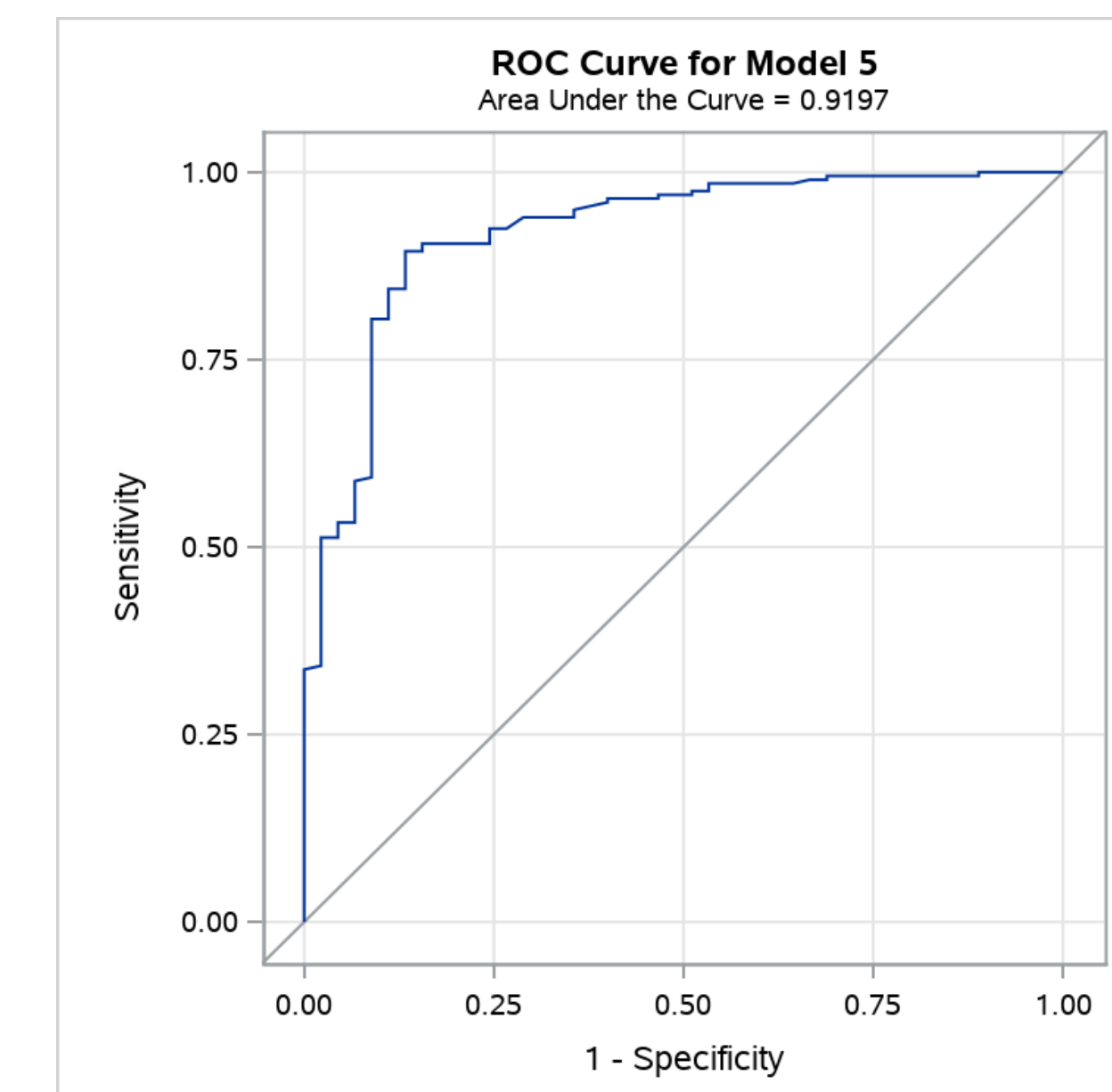


Table 4	Estimate	95% Confidence Limits
Sensitivity	0.5327	0.4633 - 0.6020
Specificity	0.9556	0.8953 - 1.0000
Positive predictive value	0.9815	0.9561 - 1.0000
Negative predictive value	0.3162	0.2380– 0.3943

Table 4 Sensitivity and specificity of our model (90% threshold)

Results

Novel nodal characteristics that were associated with occult nodal disease included, lymph node short axis, lymph node cortex nodule size, lymph node presence of cortex nodule, asymmetric size of lymph nodes, asymmetric number of lymph nodes, and round/oval hilar loss. On multivariable-adjusted mixed effects logistic regression, only the presence of a cortical nodule (OR 0.24, p = 0.0188), asymmetric number of lymph nodes (OR 0.10), and asymmetric size of lymph nodes (OR 0.24, p = 0.0188) maintained an independent association with the presence of occult disease.

Assuming a 95% threshold to predict the absence of nodal disease (1 = no cancer) in the neck, a model with 4 covariates had a sensitivity of 0.5327, specificity of 0.9556, positive predictive value of 0.9815, negative predictive value of 0.3162 and area under the curve of 0.9197.

Summary

We describe novel CT imaging characteristics of regional nodes that are highly predictive of the presence of occult nodal disease in cN0 OCSCC patients undergoing END. A model incorporating the presence of cortical nodules, asymmetric number of lymph nodes, and asymmetric size of lymph nodes could be used to predict with high specificity a true positive outcome of no cancer. Patients without these findings are very unlikely to have occult disease and may be able to avoid END. These imaging characteristics may be integrated into current END decision-making paradigms.

Conclusions/Further Study

- Patients without cortical nodules of the lymph node capsule, lymph node number asymmetry, and lymph node size asymmetry are very unlikely to have occult cervical disease.
- Future directions include matching of pN+ and pN0 patients by tumor subsite and T stage and addition of a 2nd radiologist reviewed for inter-rater and intra-rater reliability

References available upon request.

Contact Information:
Megan Morisada, MD
Email: mvmorisada@ucdavis.edu