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Table of Contents – [click the page number to go to the summary and full article link.](#)

| | |
|--|---------------|
| <i>Nomenclature Revision for Encapsulated Follicular Variant of Papillary Thyroid Carcinoma: A Paradigm Shift to Reduce Overtreatment of Indolent Tumors</i> | <i>page 1</i> |
| <i>Fluorescence Visualization–Guided Surgery for Early-Stage Oral</i> | <i>page 2</i> |
| <i>How Does Depth of Invasion Influence the Decision to Do a Neck Dissection in Clinically N0 Oral Cavity Cancer?</i> | <i>page 3</i> |
| <i>PET-CT Surveillance versus Neck Dissection in Advanced Head and Neck Cancer</i> | <i>page 4</i> |

[Nomenclature Revision for Encapsulated Follicular Variant of Papillary Thyroid Carcinoma: A Paradigm Shift to Reduce Overtreatment of Indolent Tumors](#)

Nikiforov YE, Seethala RR, Tallini G, Baloch ZW, Basolo F, Thompson LD, Barletta JA, Wenig BM, Al Ghuzlan A, Kakudo K, Giordano TJ, Alves VA, Khanafshar E, Asa SL, El-Naggar AK, Gooding WE, Hodak SP, Lloyd RV, Maytal G, Mete O, Nikiforova MN, Nosé V, Papotti M, Poller DN, Sadow PM, Tischler AS, Tuttle RM, Wall KB, LiVolsi VA, Randolph GW, Ghossein RA.

from JAMA Oncology, April 2016

Many retrospective studies have demonstrated that a non-invasive and encapsulated follicular variant of papillary thyroid carcinoma (EFVPTC) carries a very indolent prognosis with a negligible risk of recurrence, even without completion thyroidectomy and radioactive iodine ablation. Despite this, noninvasive EFVPTCs are often overtreated with further surgery and adjuvant therapy, leading to increased morbidity, psychosocial stress, and increased financial burden for both the patient and health care system. Nikiforov et al convened an international, multidisciplinary experts to look at over 200 cases of EFVPTC with long follow-up to establish standardized diagnostic criteria and identify terminology that would appropriately address the biological and clinical characteristics of this lesion.

For this retrospective study, pathologists from 13 institutions contributed a total of 268 tumors diagnosed as EFVPTC using current histologic criteria for inclusion into 2 groups. After review utilizing consensus criteria, data on 109 patients with non-invasive EFVPTC and 101 with invasive EFVPTC were gathered. Among group 1 patients who were observed for at least 10 years (10-26), all were alive with no evidence of recurrent or metastatic disease. Sixty-seven of these patients were treated with lobectomy only, and none of the 109 received RAI. In group 2, 85/101 patients were treated with RAI. Patients were observed for 1 to 18 years with 12 patients (12%) registering an adverse event: 5 patients developed distant metastases (lung and/or bone), 2 of whom died of disease, 1 patient had a lymph node recurrence, 1 had persistent disease, and 5 had detectable serum thyroglobulin levels.

The authors developed a diagnostic nuclear score that showed a sensitivity of 98.6% (95%CI, 96.3% - 99.4%), specificity of 90.1% (95%CI, 86.0%-93.1%), and overall classification accuracy of 94.3% (95%CI, 92.1%-96.0%). Based on these results, the authors proposed changing the name to non-invasive follicular type neoplasm with papillary-like nuclear features (NIFTP) to remove the work carcinoma from the diagnosis and de-escalate therapy for these patients.

Strengths

- timely and crucial article that seeks to de-escalate treatment for approximately 20% of the patients diagnosed with “thyroid cancer” each year. Results can have a significant impact on morbidity and costs for tens of thousands of patients each year
- Well designed study with long follow up in both the invasive and non-invasive groups showing distinct differences in outcomes

Limitations

- Retrospective study with possible selection bias
- Panel of experts with high-volume thyroid pathology practices and extensive experience may lead to issues of external validity. Will require further study to see if the accuracy can carry over to more community-based settings

[back to top](#)

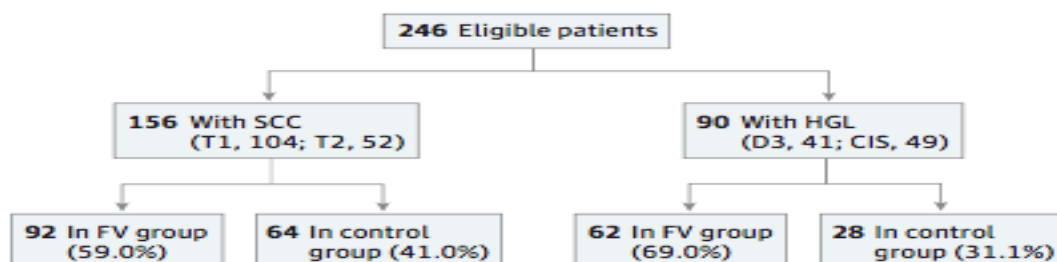
Fluorescence Visualization–Guided Surgery for Early-Stage Oral Cancer

Catherine F. Poh, DDS, PhD; Donald W. Anderson, MD; J. Scott Durham, MD; Jiahua Chen, PhD; Kenneth W. Berean, MD; Calum E. MacAulay, PhD; Miriam P. Rosin, PhD

from *JAMA Otolaryngology Head and Neck Surgery*, March 2016

This is a retrospective observational study of Fluorescence Visualized (FV) guided surgery in 246 patients treated with curative intent for high grade lesions (CIS and Severe dysplasia) and T1 and T2 SCC of the oral cavity treated in 2004-2009 and with follow up until 2013. A Total of 154 patients underwent surgery performed under FV guidance (FV group); the other 92 were treated with conventional surgery (control group). The decision to use FV-guided surgery was based on the availability of a of surgeon who was a FV specialist. Loss of tissue auto fluorescence is believed to reflect a complex mixture of alterations to intrinsic tissue fluorophore distribution, which has been associated with neoplastic development and angiogenesis and the use of this technology has been published as a pilot study prior.

Figure 1. Study Schema



The numbers of patients, their diagnoses, and the types of treatment they received are shown. CIS indicates carcinoma in situ; D, dysplasia; D3, severe dysplasia; FV, fluorescence visualization; HGL, high-grade lesions; and SCC, squamous cell carcinoma.



The overall rates of local recurrence, regional treatment failure, and disease-free survival in the SCC group were 20.5% (32 of 156 patients), 19.2% (30 of 156 patients), and 84.0% (131 of 156) respectively; the local recurrence rate of the HGL group was 17.8% (16 of 90 patients). FV guided surgery showed significantly lower local recurrence in the SCC (6 of 92 patients [6.5%] vs (26 of 64) [40.6%]; $P < .001$). FV guided surgery showed significantly lower local recurrence in the HGL arm approximately 8% vs 40%. The data also indicated that the FV-guided approach had less regional failure (14 of 92 patients [15.2%] vs 16 of 64 [25.0%]) and death (12 of 92 [13.0%] vs 13 of 64 [20.3%]) in the SCC group, although these differences were not statistically significant. The data also indicated that the FV-guided approach had less regional failure (14 of 92 patients [15.2%] vs 16 of 64 [25.0%]) and death (12 of 92 [13.0%] vs 13 of 64 [20.3%]) in the SCC group, although these differences were not statistically significant ($P = .08$ and $P = .22$, respectively).

When comparing the FV and control subgroups 3-year local recurrence rates there was significant reductions from from 35.9% (23 of 64 patients) to 4.3% (4 of 92 patients), respectively ($P < .001$) favoring the FV group. The rate of regional treatment failure for the patients with SCC was reduced in the FV subgroup (15.2%)

Strengths

- Compelling retrospective data
- Given the improvement in local recurrence rates demonstrated using this technology supports its role for improved margin determination, prospective studies are pending.
- Provides data regarding local recurrence rates for HGL and early stage oral cancers
- A randomized control trial is pending which will help further understand the benefits of FV surgery

Weakness

- Single site retrospective study

[back to top](#)

[How Does Depth of Invasion Influence the Decision to Do a Neck Dissection in Clinically N0 Oral Cavity Cancer?](#)

Kuan EC, Mallen-St Clair J, Badran KW, St John MA

from *Laryngoscope*, March 2016

The risk of occult cervical metastasis in a patients with early stage (T1-2) squamous cell carcinoma of the oral cavity is reported to be $\geq 40\%$. Cervical metastasis predicts a decreased survival with 5 year survival rates reduced by approximately 50%. Treatment of the No neck has thus been a topic of significant debate. Depth of invasion has been studied specifically as a potential predictor of cervical metastasis. In this study Kuan et al perform a review of the literature with the goal of clarifying the appropriate depth of invasion for which an elective neck dissection should be recommended. The appropriately identify biases in comparing such studies in the literature such as: variation in reporting/measuring the depth of invasion makes studies difficult to compare, the need to access this by permanent section makes intra operative decision making difficult, and combining all subsites of the oral cavity knowing some convey a different risk of cervical metastasis than others. After review of the major articles available on the topic to date the



author's recommendation is for elective neck dissection in patients with early stage (T1-2) squamous cell carcinoma of the oral cavity (especially oral tongue) when the primary lesion demonstrates a depth of invasion of ≥ 3 mm. On the contrary, there is no recommendation for elective neck dissection in patients with a depth of invasion of less than 3 mm.

[back to top](#)

PET-CT Surveillance versus Neck Dissection in Advanced Head and Neck Cancer

Hisham Mehanna, Ph.D., Wai-Lup Wong, F.R.C.R., Christopher C. McConkey, Ph.D., Joy K. Rahman, M.Sc., Max Robinson, Ph.D., Andrew G.J. Hartley, F.R.C.R., Christopher Nutting, Ph.D., Ned Powell, Ph.D., Hoda Al-Booz, F.R.C.R., Martin Robinson, F.R.C.R., Elizabeth Junor, F.R.C.R., Mohammed Rizwanullah, F.R.C.R., Sandra V. von Zeidler, Ph.D., Hulya Wiesmann, F.R.C.R., Claire Hulme, Ph.D., Alison F. Smith, M.Sc., Peter Hall, Ph.D., and Janet Dunn, Ph.D., for the PET-NECK Trial Management Group

from New England Journal of Medicine, March 2016

Chemoradiotherapy is widely used to treat advanced squamous cell carcinoma of most subsites of the head and neck. Post treatment management of the N2-3 neck in these patients is controversial. On one hand, studies have suggested 40% of the patients will harbor persistent disease post treatment and thus argue in favor in a planned neck dissection. On the other hand, other studies suggest low (<10%) recurrence rates in patients whom demonstrate complete responses in the neck when accessed by cross sectional imaging thus arguing for an observational approach in these patients. In this study, Mehanna et al conducted a prospective, randomized, controlled trial to compare the clinical usefulness and health economic outcomes of planned neck dissection versus PET-CT-guided surveillance in patients with nodal stage N2 or N3. Patients were randomized into two groups; group one, planned neck dissection group (control) or group two, who 12 weeks post treatment underwent a PET/CT. Those demonstrating a complete response (no remaining neck disease uptake or anatomic abnormality) underwent observation by clinical exam and imaging over a 24 month period, those with equivocal or persistent disease underwent a neck dissection. Those in the control group had surgery within 4 weeks before or within 4 to 8 weeks after completion of chemoradiotherapy. In this study most patients had N2b ds (61%), oropharyngeal primaries (84%), and 75% had tumor specimens that stained positive for the p16 protein (no significant difference between the groups with respect to p16 expression). The 2-year overall survival rate was 84.9% in the surveillance group and 81.5% in the planned-surgery group. Quality of life was similar in the two groups. In regards to the economic outcomes, PET-CT-guided surveillance, as compared with neck dissection, resulted in savings of \$2,190 per person over the duration of the trial. The authors concluded survival was similar among patients who underwent PET-CT-guided surveillance and those who underwent planned neck dissection with surveillance resulting in considerably fewer operations and proving more cost-effective. Potential biases of this study include the lack of calibration of SUV among various scanning systems thus limiting interpretation of the SUV results. A retrospective re review of this is underway. It should also be noted that this study included primaries of multiple subsites including oropharynx, hypopharynx, larynx, oral cavity, or an unknown primary site in the head or neck. This may also present some bias to the study design. Lastly, as the authors



pointed out, there were only 9 patients with N3 disease in the observation group thus caution should be taken in justifying this observational recommendation in this subset of patients with N3 disease.

[*back to top*](#)
