



Management of the Neck in Early Stage Oral Cancer

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Outline

- **Background on Elective Neck Dissection in Oral Cavity Cancer**
- **Recent Advances**
 - **Sentinel lymph node biopsy vs. END**
- **Ongoing NRG-HN006 trial**

Background

Elective Neck Dissection in early stage oral cavity cancer

Early Stage Oral Cavity Cancer

- Early Stage: T1-T2N0
- Clinically node negative
- Most recent AJCC 8th edition staging: includes DOI

T Category	T Criteria
TX	Primary tumor cannot be assessed
Tis	Carcinoma in situ
T1	Tumor ≤2 cm, ≤5 mm DOI
T2	Tumor ≤2 cm, DOI >5 mm and ≤10 mm or tumor >2 cm but ≤4 cm, and ≤10 mm DOI
T3	Tumor >4 cm or any tumor >10 mm DOI
T4	Moderately advanced or very advanced local disease
T4a	Moderately advanced local disease: (lip) tumor invades through cortical bone or involves the inferior alveolar nerve, floor of mouth, or skin of face (i.e., chin or nose); (oral cavity) tumor invades adjacent structures only (e.g., through cortical bone of the mandible or maxilla, or involves the maxillary sinus or skin of the face); note that superficial erosion of bone/tooth socket (alone) by a gingival primary is not sufficient to classify a tumor as T4
T4b	Very advanced local disease; tumor invades masticator space, pterygoid plates, or skull base and/or encases the internal carotid artery

1. Zanoni DK, Patel SG, Shah JP. Changes in the 8th Edition of the American Joint Committee on Cancer (AJCC) Staging of Head and Neck Cancer: Rationale and Implications. *Curr Oncol Rep.* 2019 Apr 17;21(6):52. doi: 10.1007/s11912-019-0799-x. PMID: 30997577; PMCID: PMC6528815.

Elective Neck Dissection for early oral cavity cancer

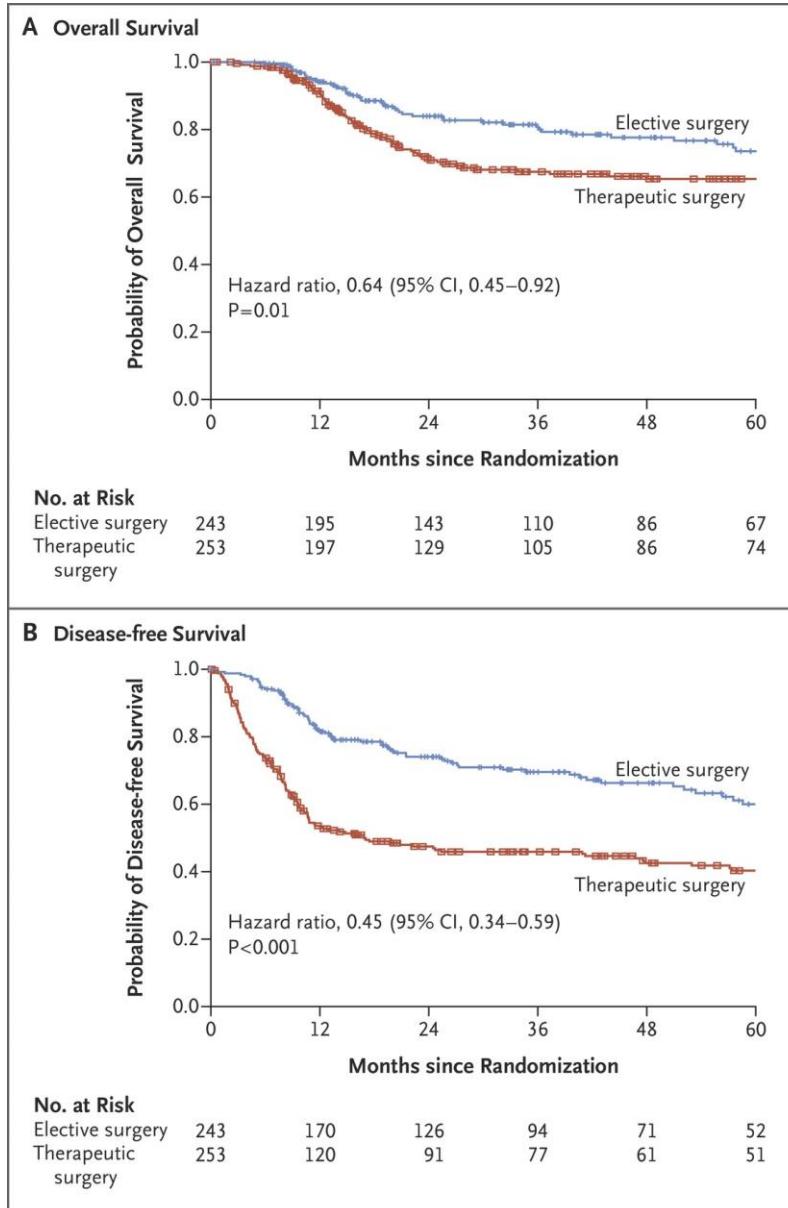
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ORIGINAL ARTICLE

Elective versus Therapeutic Neck Dissection in Node-Negative Oral Cancer

Anil K. D'Cruz, M.S., D.N.B., Richa Vaish, M.S., Neeti Kapre, M.S., D.N.B.,
Mitali Dandekar, M.S., D.N.B., Sudeep Gupta, M.D., D.M.,
Rohini Hawaldar, B.Sc., D.C.M., Jai Prakash Agarwal, M.D.,
Gouri Pantvaidya, M.S., D.N.B., Devendra Chaukar, M.S., D.N.B.,
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- Prospective RCT
 - Arm 1: END at time of primary resection
 - Arm 2: Primary resection followed by therapeutic ND at later date
- Outcomes: DFS and OS



- 3 year OS: 80.0% in END group vs. 67.5% in TND group
 - 50 deaths in END group vs. 79 deaths in TND group
- 3 year DFS: 69.5% in END group vs. 45.9% in TND group
 - 81 recurrences in END group vs. 146 recurrences in TND group
- Enrollment stopped in trial early 2/2 safety committee finding the clear superiority of END

END for all early stage OC?



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Depth of invasion is the most significant histological predictor of
subclinical cervical lymph node metastasis in early squamous
carcinomas of the oral cavity

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1. van Lanschot CGF, Klazen YP, de Ridder MAJ, Mast H, Ten Hove I, Hardillo JA, Monserez DA, Sewnaik A, Meeuwis CA, Keereweer S, Aaboubout Y, Barroso EM, van der Toom QM, Bakker Schut TC, Wolvius EB, Baatenburg de Jong RJ, Puppels GJ, Koljenović S. Depth of invasion in early stage oral cavity squamous cell carcinoma: The optimal cut-off value for elective neck dissection. *Oral Oncol.* 2020 Dec;111:104940. doi: 10.1016/j.oraloncology.2020.104940. Epub 2020 Aug 5. PMID: 32769035.
2. Melchers LJ, Schuurings E, van Dijk BA, de Bock GH, Witjes MJ, van der Laan BF, van der Wal JE, Roodenburg JL. Tumour infiltration depth ≥4 mm is an indication for an elective neck dissection in pT1cN0 oral squamous cell carcinoma. *Oral Oncol.* 2012 Apr;48(4):337-42. doi: 10.1016/j.oraloncology.2011.11.007. Epub 2011 Nov 29. PMID: 22130455.
3. Kane, S. V., Gupta, M., Kakade, A. C., & D'Cruz, A. (2006). Depth of invasion is the most significant histological predictor of subclinical cervical lymph node metastasis in early squamous carcinomas of the oral cavity. *European Journal of Surgical Oncology (EJSO)*, 32(7), 795-803.

END for all early stage OC?



Depth of
subclinical



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Tumour infiltration depth ≥ 4 mm is an indication for an elective neck dissection in pT1cN0 oral squamous cell carcinoma

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Keywords: Elective neck dissection; Early stage oral cavity squamous cell carcinoma; Depth of invasion

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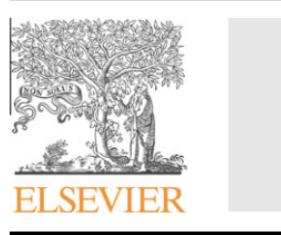
1. van Lanschot CGF, Klazen YP, de Ridder MAJ, Mast H, Ten Hove I, Hardillo JA, Monserez DA, Sewnaik A, Meeuwis CA, Keereweer S, Aaboubout Y, Barroso EM, van der Toom QM, Bakker Schut TC, Wolvius EB, Baatenburg de Jong RJ, Puppels GJ, Koljenović S. Depth of invasion in early stage oral cavity squamous cell carcinoma: The optimal cut-off value for elective neck dissection. *Oral Oncol.* 2020 Dec;111:104940. doi: 10.1016/j.oraloncology.2020.104940. Epub 2020 Aug 5. PMID: 32769035.
2. Melchers LJ, Schuuring E, van Dijk BA, de Bock GH, Witjes MJ, van der Laan BF, van der Wal JE, Roodenburg JL. Tumour infiltration depth ≥ 4 mm is an indication for an elective neck dissection in pT1cN0 oral squamous cell carcinoma. *Oral Oncol.* 2012 Apr;48(4):337-42. doi: 10.1016/j.oraloncology.2011.11.007. Epub 2011 Nov 29. PMID: 22130455.
3. Kane, S. V., Gupta, M., Kakade, A. C., & D'Cruz, A. (2006). Depth of invasion is the most significant histological predictor of subclinical cervical lymph node metastasis in early squamous carcinomas of the oral cavity. *European Journal of Surgical Oncology (EJSO)*, 32(7), 795-803.

END for all early stage OC?



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Depth of
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Tumour infiltration in pt1cN0 oral

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1. van Lanschot CGF, Klazen YP, de Ridder MAJ, Mast H, Ten Hove I, Hardillo JA, Monserez DA, Sewnaik A, Meeuwis CA, Keereweer S, Aaboubout Y, Barroso EM, van der Toom QM, Bakker Schut TC, Wolvius EB, Baatenburg de Jong RJ, Puppels GJ, Koljenović S. Depth of invasion in early stage oral cavity squamous cell carcinoma: The optimal cut-off value for elective neck dissection. *Oral Oncol.* 2020 Dec;111:104940. doi: 10.1016/j.oraloncology.2020.104940. Epub 2020 Aug 5. PMID: 32769035.
2. Melchers LJ, Schuurings E, van Dijk BA, de Bock GH, Witjes MJ, van der Laan BF, van der Wal JE, Roodenburg JL. Tumour infiltration depth ≥4 mm is an indication for an elective neck dissection in pT1cN0 oral squamous cell carcinoma. *Oral Oncol.* 2012 Apr;48(4):337-42. doi: 10.1016/j.oraloncology.2011.11.007. Epub 2011 Nov 29. PMID: 22130455.
3. Kane, S. V., Gupta, M., Kakade, A. C., & D'Cruz, A. (2006). Depth of invasion is the most significant histological predictor of subclinical cervical lymph node metastasis in early squamous carcinomas of the oral cavity. *European Journal of Surgical Oncology (EJSO)*, 32(7), 795-803.



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Contents lists available at [ScienceDirect](https://www.sciencedirect.com)

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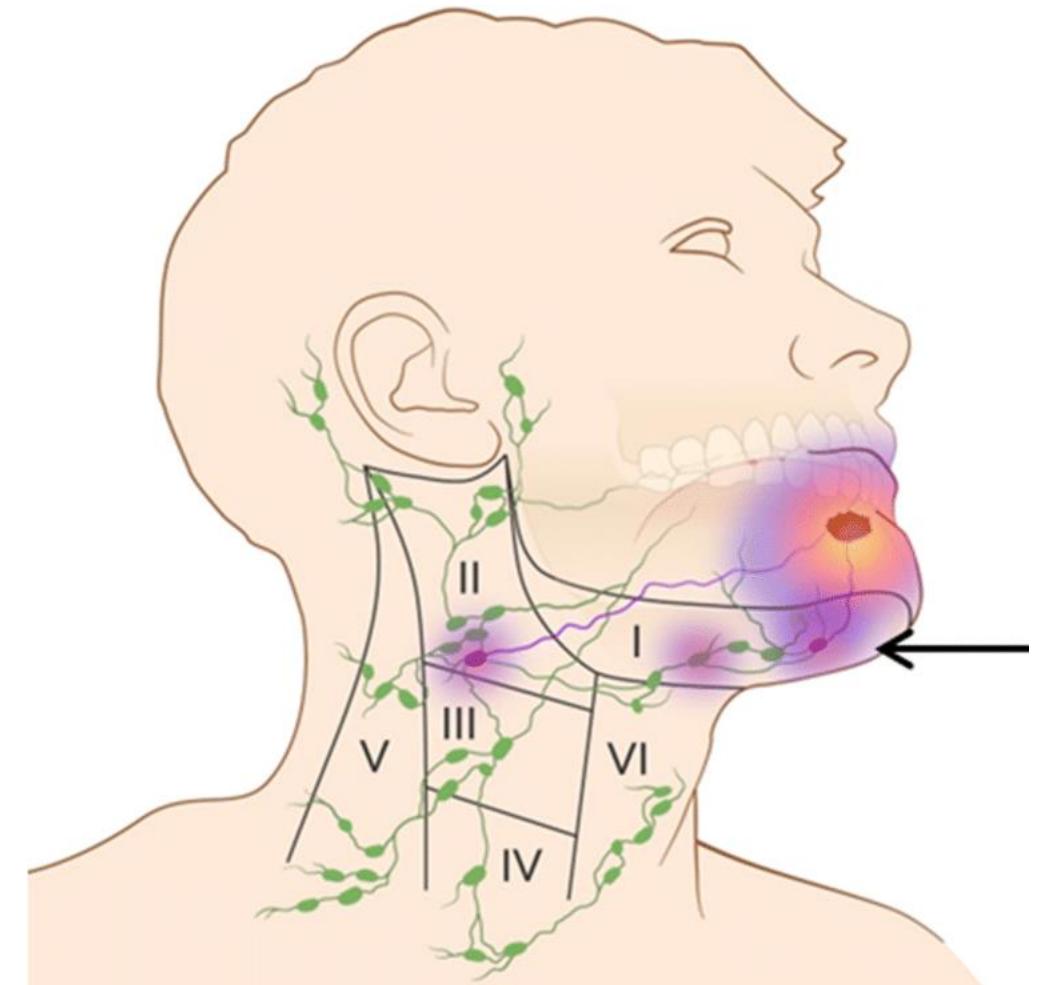


Surgical Management of the Neck

Recent Advances

Less invasive options?

- Sentinel lymph node biopsy (SNB)
 - Injection of methylene blue dye and/or a radiotracer to locate and dissect the lymph node that the primary cancer first drains into
 - Widely used in other cancers, and is a justifiable alternative to total lymph node dissection in breast, melanoma, vulval, and penile cancers
- Potential advantages over END:
 - Shoulder dysfunction
 - Scar length
 - Decreased hospital LOS



Saleem MI, Peng T, Zhu D, Wong A, Pereira LM, Tham T. Sentinel Lymph Node Biopsy Versus Elective Node Dissection in Stage cT1-2N0 Oral Cavity Cancer. *Laryngoscope*. 2022 May;132(5):989-998. doi: 10.1002/lary.29895. Epub 2021 Oct 12. PMID: 34637145.

Toom, Inne & Mahieu, Rutger & Rooij, Rob & Es, Robert & Hobbelink, Monique & Krijger, Gerard & Tijink, Bernard & Keizer, Bart & Bree, Remco. (2021). Sentinel lymph node detection in oral cancer: a within-patient comparison between [99mTc]Tc-tilmanocept and [99mTc]Tc-nanocolloid. *European Journal of Nuclear Medicine and Molecular Imaging*. 48. 10.1007/s00259-020-04984-8.

SENT trial: Sentinel European Node Trial

- EORTC 24021: prospective, observational study 2015
 - 14 European centers w/ 415 pts: radiologically staged T1-T2N0 SCC
 - SLNB with completion ND in pts with positive SLNB
- Results:
 - Positive SLN = 23% (94 in 415)
 - False-negative in 14% (15 in 109) → rescued by salvage therapy
 - Recurrence after +SLNB + ND: 22 pts, 73% in the neck
 - Only minor complications (3%) following SLNB
 - Disease-specific survival = 94% T
 - SLNB sensitivity = 86% , NPV 95%
- SNB is a reliable and safe oncological technique for staging the clinically N0 neck in patients with T1 and T2 oral cancer

Neck Dissections Based on Sentinel Lymph Node Navigation Versus Elective Neck Dissections in Early Oral Cancers: A Randomized, Multicenter, and Noninferiority Trial

Yasuhide Hasegawa, MD, PhD¹; Kiyoaki Tsukahara, MD, PhD²; Seiichi Yoshimoto, MD, PhD³; Kouki Miura, MD, PhD⁴; Junkichi Yokoyama, MD, PhD⁵; Shigeru Hirano, MD, PhD⁶; Hirokazu Uemura, MD, PhD⁷; Masashi Sugasawa, MD, PhD⁸; Tomokazu Yoshizaki, MD, PhD⁹; Akihiro Homma, MD, PhD¹⁰; Kazuaki Chikamatsu, MD, PhD¹¹; Mikio Suzuki, MD, PhD¹²; Akihiro Shiotani, MD, PhD¹³; Takashi Matsuzaka, MD, PhD^{1,14}; Naoyuki Kohno, MD, PhD¹⁵; Masakazu Miyazaki, MD, PhD¹⁶; Isao Oze, MD, PhD¹⁷; Keitaro Matsuo, MD, PhD¹⁷; Shigeru Kosuda, MD, PhD¹⁸; and Yasushi Yatabe, MD, PhD³; for the HNCMM Research Group

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- RCT: Selective ND vs. SLN directed ND
 - T1-2N0 SCCa, with ≥ 4 mm
- 3-year OS: SLNB group (87.9%) vs. ND group (86.6%) P for noninferiority $< .001$
- 3-year DFS: SLNB 78.7% vs. ND 81.3%
- Neck functionality in SLNB group significantly better than ND group

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Equivalence Randomized Trial to Compare Treatment on the Basis of Sentinel Node Biopsy Versus Neck Node Dissection in Operable T1-T2NO Oral and Oropharyngeal Cancer

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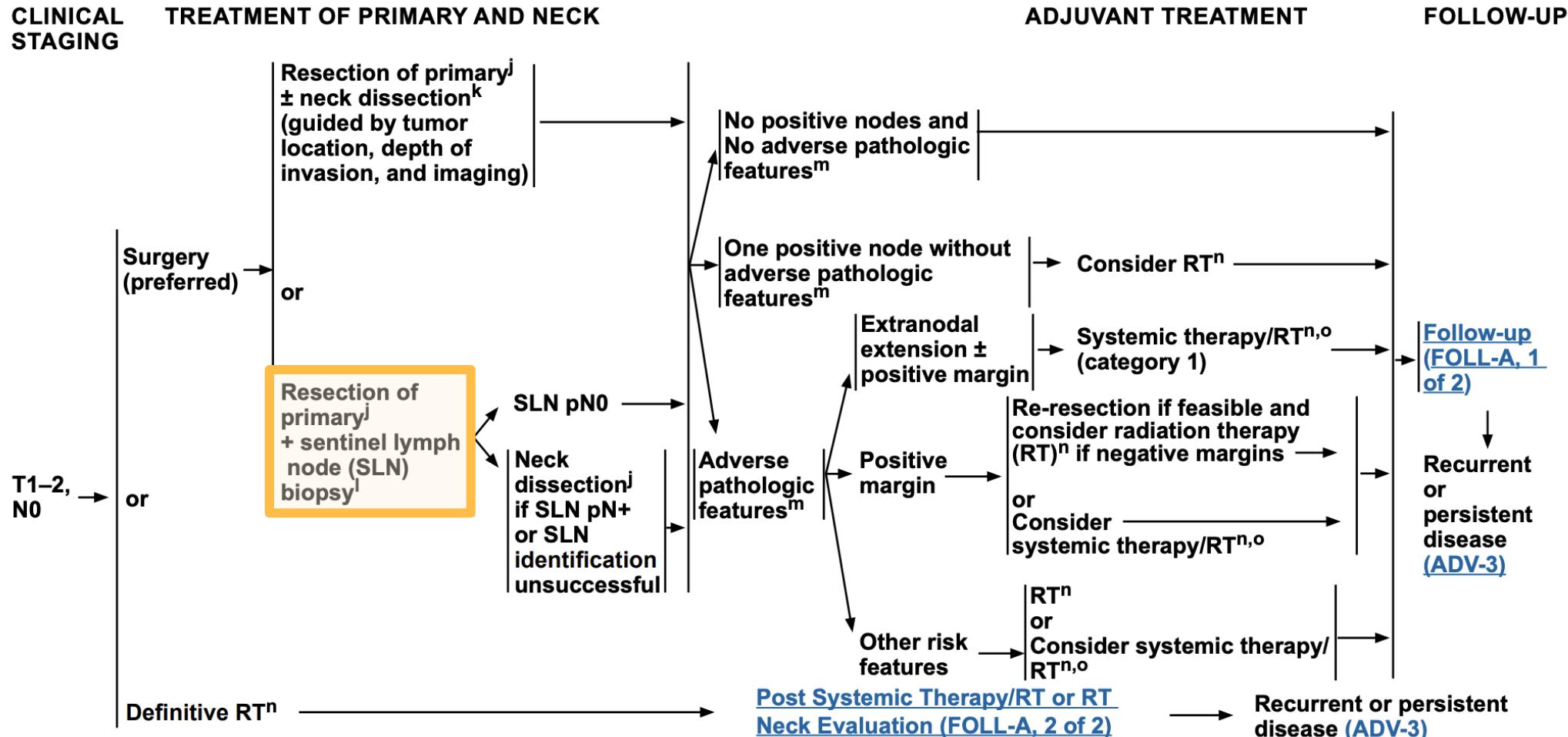
- RCT: Selective ND vs. SLN directed ND (intraop w/ completion same day)
 - Also assessed: hospital LOS, neck and shoulder morbidity, and # PT Rx in 2 yr s/p sx
- 2-year RFS: SLNB group (90.7%) vs. ND group (89.6%) P for noninferiority < .01
- Hospital LOS: SLNB 7 days, ND 8 days ($P<0.01$)
- Functional outcomes significantly worse in ND until 6 months post-op



NCCN Guidelines Version 5.2024

Cancer of the Oral Cavity (Including Mucosal Lip)

Buccal mucosa, floor of mouth, oral tongue, alveolar ridge, retromolar trigone, hard palate^a



Is it being utilized in practice?

- SNB is an uncommon modality for neck management: used in approximately 2.9% of stage I to II OCSCC cases captured by the NCDB between 2012 and 2015

Ongoing Trial

NRG-HN006 Trial in US for SLNB

NRG- HN006

- Randomized to SLNB group vs. Elective ND group
- Primary Outcomes:
 - Patient-reported neck and shoulder function (Neck Dissection Impairment Index)
 - Disease-Free Survival
- Secondary Outcomes:
 - Overall Survival, Pattern of failure: Loco-regional Failure vs. Distant metastasis, Patient-reported shoulder-related QOL, General QOL, Nodal metastasis detection rate, Pathologic false omission rate, Post-surgery patient-reported outcome
- Opened 7/2020, still recruiting

Key Points

- The neck should be addressed for Oral Cavity SCCa \geq 4mm DOI
- Traditionally recommendation was for END
- SLNB has become more widely used and has data to back its safety and efficacy
- Awaiting results of NRG-HN006 Trial

Thank you

Questions?

References

- Zanoni DK, Patel SG, Shah JP. Changes in the 8th Edition of the American Joint Committee on Cancer (AJCC) Staging of Head and Neck Cancer: Rationale and Implications. *Curr Oncol Rep.* 2019 Apr 17;21(6):52. doi: 10.1007/s11912-019-0799-x. PMID: 30997577; PMCID: PMC6528815.
- D'Cruz AK, Vaish R, Kapre N, Dandekar M, Gupta S, Hawaldar R, Agarwal JP, Pantvaidya G, Chaukar D, Deshmukh A, Kane S, Arya S, Ghosh-Laskar S, Chaturvedi P, Pai P, Nair S, Nair D, Badwe R; Head and Neck Disease Management Group. Elective versus Therapeutic Neck Dissection in Node-Negative Oral Cancer. *N Engl J Med.* 2015 Aug 6;373(6):521-9. doi: 10.1056/NEJMoa1506007. Epub 2015 May 31. PMID: 26027881.
- van Lanschot CGF, Klazen YP, de Ridder MAJ, Mast H, Ten Hove I, Hardillo JA, Monserez DA, Sewnaik A, Meeuwis CA, Keereweer S, Aaboubout Y, Barroso EM, van der Toom QM, Bakker Schut TC, Wolvius EB, Baatenburg de Jong RJ, Puppels GJ, Koljenović S. Depth of invasion in early stage oral cavity squamous cell carcinoma: The optimal cut-off value for elective neck dissection. *Oral Oncol.* 2020 Dec;111:104940. doi: 10.1016/j.oraloncology.2020.104940. Epub 2020 Aug 5. PMID: 32769035.
- Melchers LJ, Schuuring E, van Dijk BA, de Bock GH, Witjes MJ, van der Laan BF, van der Wal JE, Roodenburg JL. Tumour infiltration depth ≥ 4 mm is an indication for an elective neck dissection in pT1cN0 oral squamous cell carcinoma. *Oral Oncol.* 2012 Apr;48(4):337-42. doi: 10.1016/j.oraloncology.2011.11.007. Epub 2011 Nov 29. PMID: 22130455.
- Kane, S. V., Gupta, M., Kakade, A. C., & D'Cruz, A. (2006). Depth of invasion is the most significant histological predictor of subclinical cervical lymph node metastasis in early squamous carcinomas of the oral cavity. *European Journal of Surgical Oncology (EJSO)*, 32(7), 795-803
- Saleem MI, Peng T, Zhu D, Wong A, Pereira LM, Tham T. Sentinel Lymph Node Biopsy Versus Elective Node Dissection in Stage cT1-2N0 Oral Cavity Cancer. *Laryngoscope.* 2022 May;132(5):989-998. doi: 10.1002/lary.29895. Epub 2021 Oct 12. PMID: 34637145.
- Schilling C, Stoeckli SJ, Haerle SK, Broglie MA, Huber GF, Sorensen JA, Bakholdt V, Krogdahl A, von Buchwald C, Bilde A, Sebbesen LR, Odell E, Gurney B, O'Doherty M, de Bree R, Bloemena E, Flach GB, Villarreal PM, Fresno Forcelledo MF, Junquera Gutiérrez LM, Amézaga JA, Barbier L, Santamaría-Zuazua J, Moreira A, Jacome M, Vigili MG, Rahimi S, Tartaglione G, Lawson G, Nolleaux MC, Grandi C, Donner D, Bragantini E, Dequantier D, Lothaire P, Poli T, Silini EM, Sesenna E, Dolivet G, Mastronicola R, Leroux A, Sassoon I, Sloan P, McGurk M. Sentinel European Node Trial (SENT): 3-year results of sentinel node biopsy in oral cancer. *Eur J Cancer.* 2015 Dec;51(18):2777-84. doi: 10.1016/j.ejca.2015.08.023. Epub 2015 Nov 18. PMID: 26597442.
- Hasegawa Y, Tsukahara K, Yoshimoto S, Miura K, Yokoyama J, Hirano S, Uemura H, Sugawara M, Yoshizaki T, Homma A, Chikamatsu K, Suzuki M, Shiotani A, Matsuzuka T, Kohno N, Miyazaki M, Oze I, Matsuo K, Kosuda S, Yatabe Y; HNCMM Research Group. Neck Dissections Based on Sentinel Lymph Node Navigation Versus Elective Neck Dissections in Early Oral Cancers: A Randomized, Multicenter, and Noninferiority Trial. *J Clin Oncol.* 2021 Jun 20;39(18):2025-2036. doi: 10.1200/JCO.20.03637. Epub 2021 Apr 20. PMID: 33877855.

References

- Garrel R, Poissonnet G, Moyà Plana A, Fakhry N, Dolivet G, Lallemand B, Sarini J, Vergez S, Guelfucci B, Choussy O, Bastit V, Richard F, Costes V, Landais P, Perriard F, Daures JP, de Verbizier D, Favier V, de Boutray M. Equivalence Randomized Trial to Compare Treatment on the Basis of Sentinel Node Biopsy Versus Neck Node Dissection in Operable T1-T2N0 Oral and Oropharyngeal Cancer. *J Clin Oncol.* 2020 Dec 1;38(34):4010-4018. doi: 10.1200/JCO.20.01661. Epub 2020 Oct 14. PMID: 33052754.
- Cramer JD, Sridharan S, Ferris RL, Duvvuri U, Samant S. Sentinel Lymph Node Biopsy Versus Elective Neck Dissection for Stage I to II Oral Cavity Cancer. *Laryngoscope.* 2019 Jan;129(1):162-169. doi: 10.1002/lary.27323. Epub 2018 Oct 3. PMID: 30284248.