The International Federation of Head and Neck Oncologic Societies

Current Concepts in Head and Neck Surgery and Oncology 2017

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Oral Cancer: Principles of Management

Patrick Gullane

I have No Disclosures

Purpose of Presentation

- Review the Incidence, Etiology, Evaluation and Treatment Principles in Oral Cancer Management
- Understand the Prognostic Factors affecting selection of treatment
- Be Aware of the Oncologic Outcomes
- Understand Surgical Factors influencing Outcomes-
- Margins of Surgical Resection
- Management of the Neck
- Review the surgical approaches and Options for Soft tissue and Bony Reconstruction

Oral Cancer – Incidence/Epidemiology

- 6th most common cancer globally
- 24% of Head and Neck Canc
- Prevalence decreasing
  - 1974 3.6 / 100 000 / yr
  - 2009 2.7 / 100 000 / yr
- Improved survival
  - 5-year overall survival 53% to 57%
- But regional disease…
  - Decreased survival 49% to 43%

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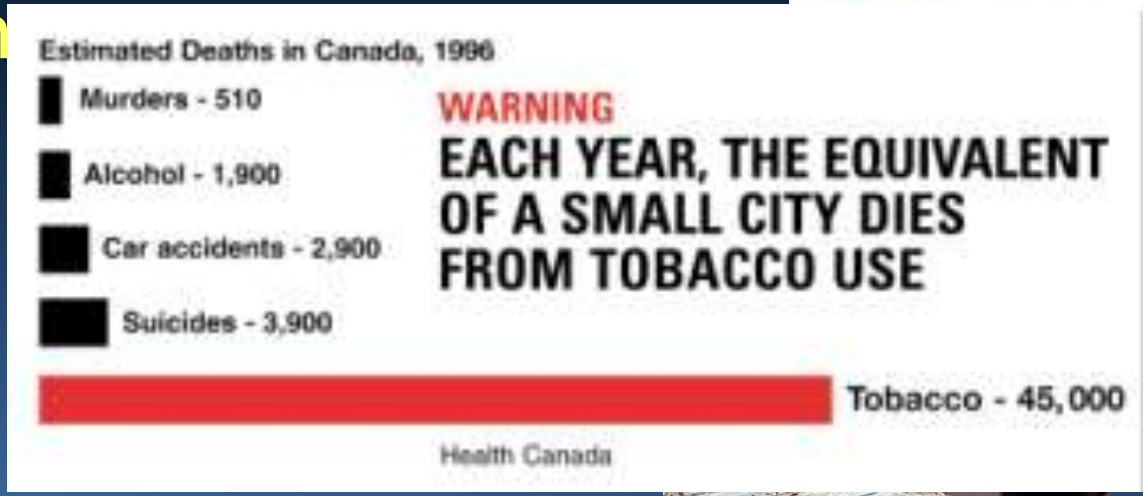
Carvalho AL et al. Trends in incidence and prognosis for head and neck cancer in the United States: A site specific analysis of the SEER database. Int. J Cancer (Advance of Publication)

Oral Cancer: *Etiology*

- Tobacco
- Alcohol
- Paan Chewing
- Betel Nut Chewin
- Poor oral hygiene
- Vitamin deficient
- Viruses
  - HPV
- Chemicals
- Immunosuppression
- Genetic



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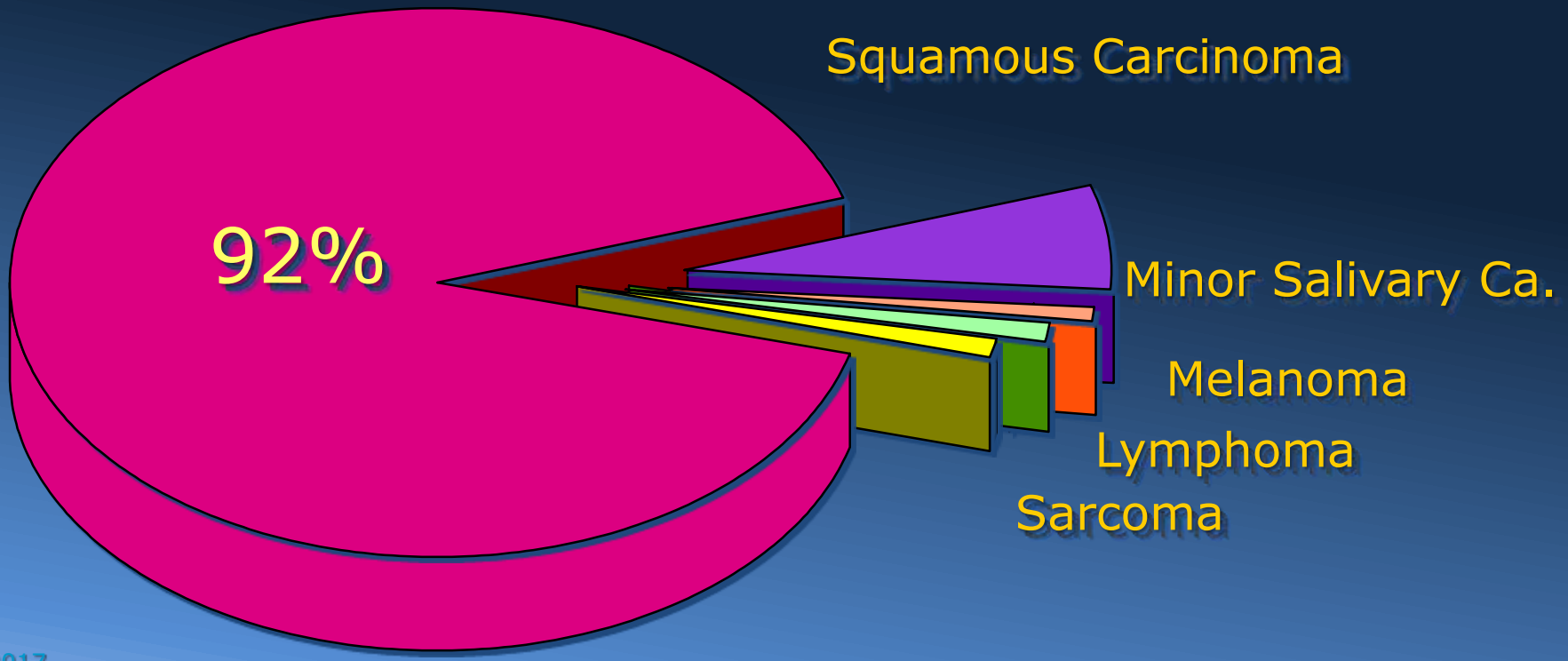
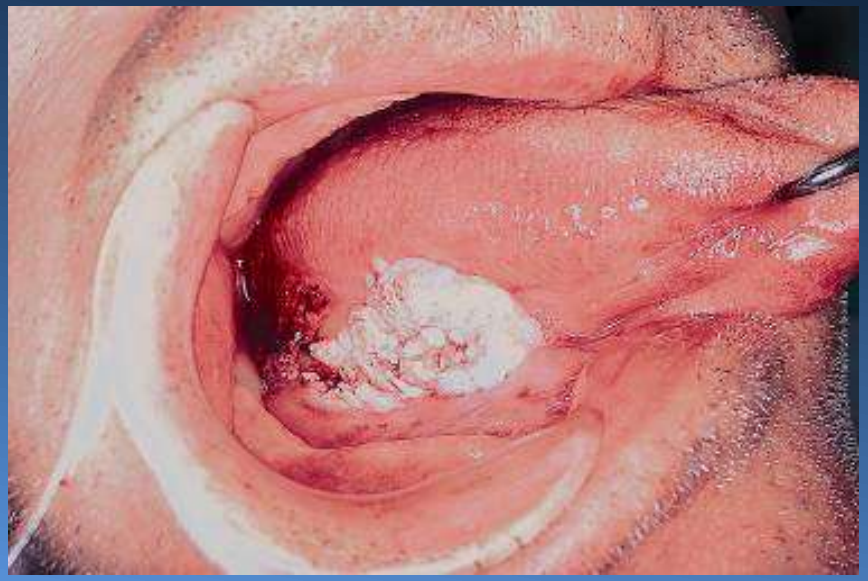
Cancer of Oral Cavity
Histological Distribution



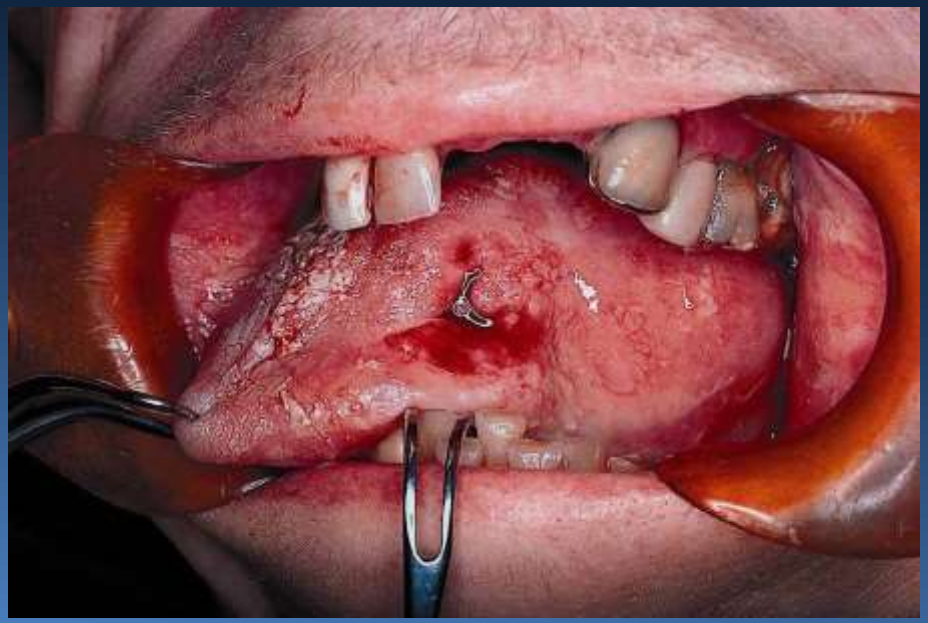
Oral Cavity is easily accessible

Exophytic tumor with distinct borders
Less risk of incomplete resection = better outcomes



Clinical Assessment

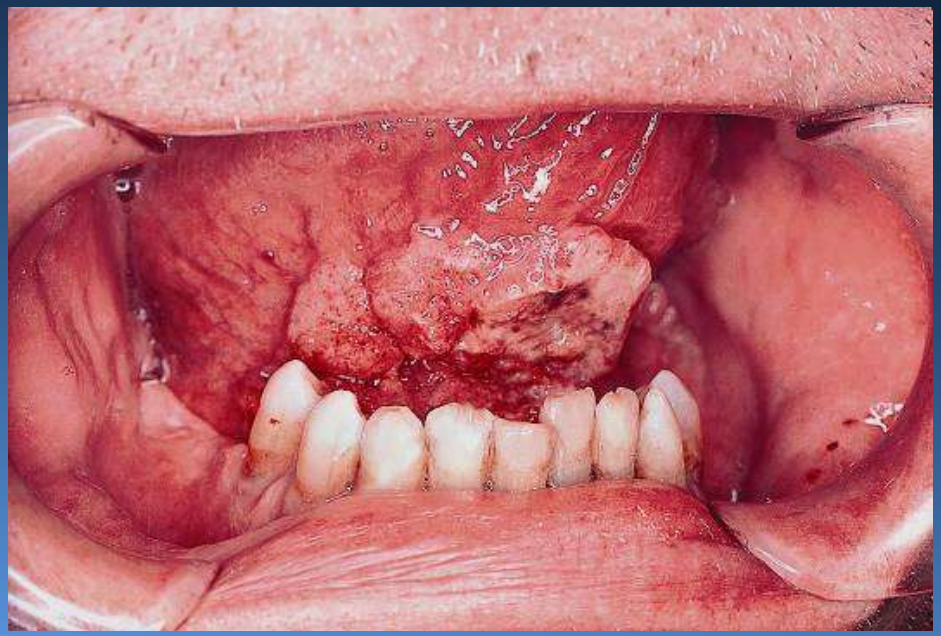
Endophytic tumor with diffuse borders
High risk of incomplete resection = worse outcomes



Clinical Assessment

Relationship to Salivary Duct Openings

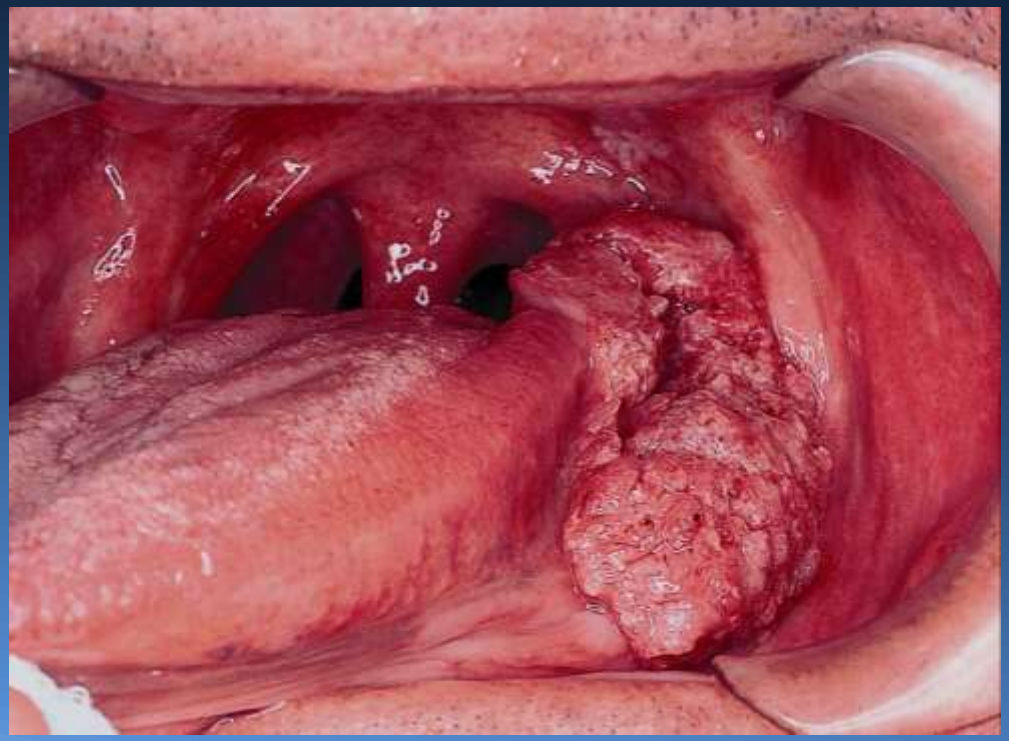
Translocation of duct/s if gland will be preserved



Clinical Assessment

Relationship to Bone

Plan resection & appropriate reconstruction



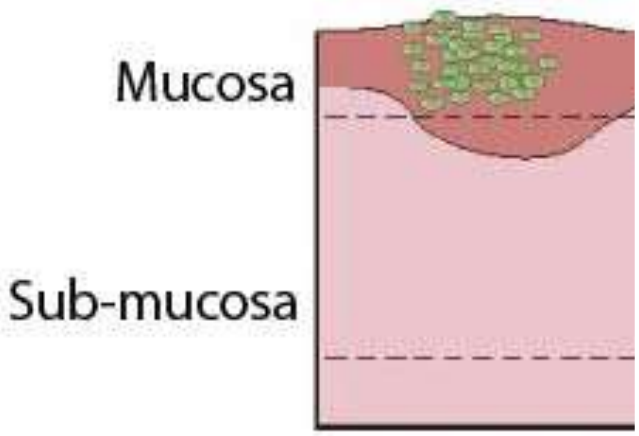
Depth of Invasion of the Primary Tumor and its Impact on Outcome

Impact of Tumour Thickness

Tumor Thickness	Nodal Metastases n = 38	%	χ^2 p
</= 2mm	0	0%	0.007
> 2mm	38	40%	(Fisher's exact test)
</= 3mm	1	7%	0.010
> 3mm	37	41%	
</= 4mm	2	9%	0.003
> 4mm	36	43%	
</= 5mm	3	10%	0.001
> 5mm	35	46%	
</= 6mm	6	18%	0.006
> 6mm	32	45%	
</= 8mm	8	19%	0.003
> 8mm	30	48%	
</= 2mm	**0**	**0%**	**0.004**
3–8mm	**8**	**26%**	
> 8mm	**30**	**48%**	

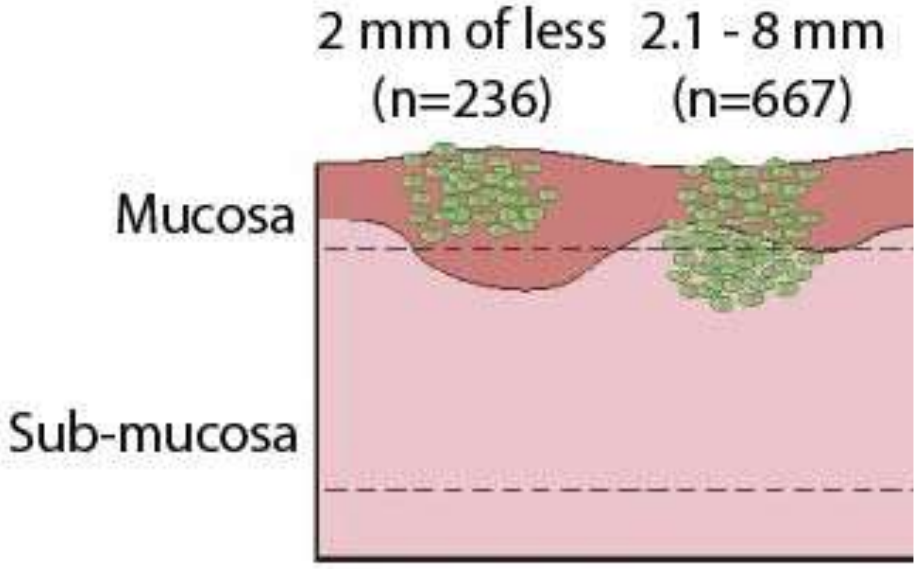
TUMOR THICKNESS, OCCULT METASTASES AND OTHER PROGNOSTIC VARIABLES IN ORAL CARCINOMA AND THE CLINICALLY NEGATIVE (N0) NECK
Jonathan R Clark, BSc(Med), MBBS, FRACS, Natalie Naranjo, MD, Patrick J Gullane, MD, FRCS(C), FACS

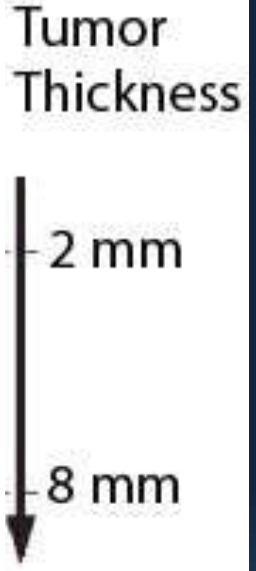
Depth of Invasion



Risk of occult nodal metastasis	8.9%
Overall incidence of nodal metastasis	5.5%
Cancer Specific Survival	94.5%

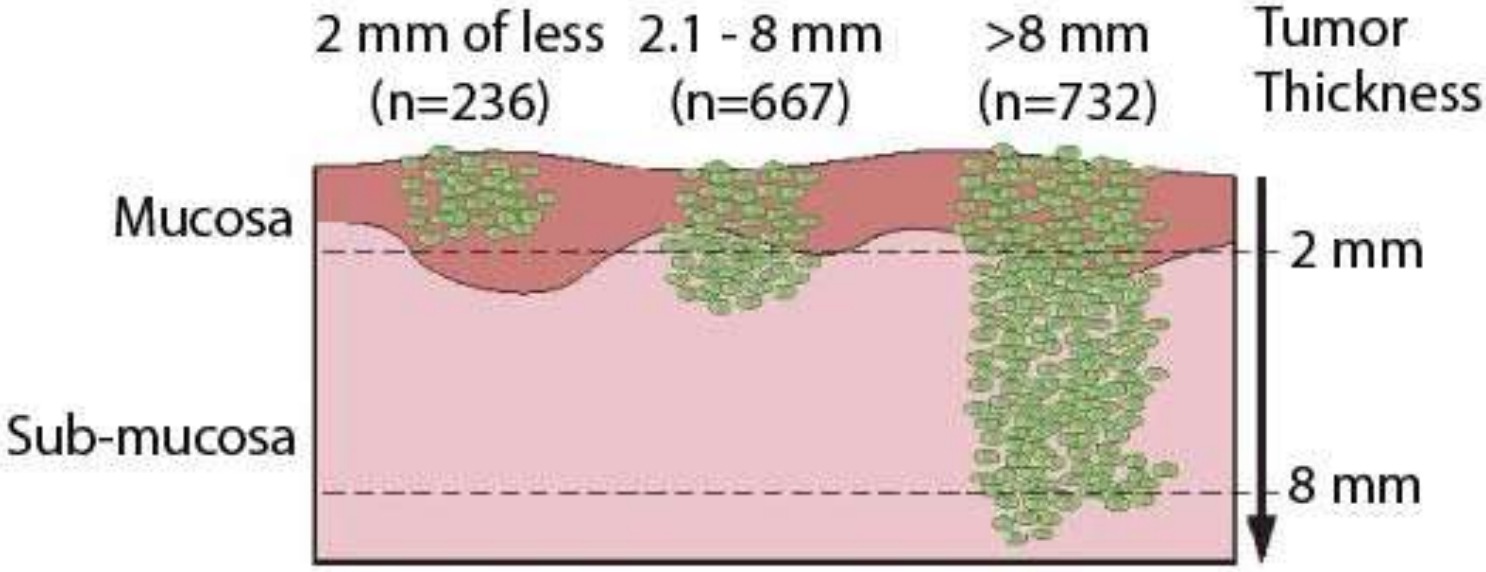
Depth of Invasion





Risk of occult nodal metastasis	8.9%	23.5%
Overall incidence of nodal metastasis	5.5%	24.4%
Cancer Specific Survival	94.5%	82.6%

Depth of Invasion



Risk of occult nodal metastasis	8.9%	23.5%	41.0%
Overall incidence of nodal metastasis	5.5%	24.4%	50.1%
Cancer Specific Survival	94.5%	82.6%	59.5%

AJCC – 8th Edition

DOI in T staging for Oral Cancer

T1 – Tumor ≤ 2 cms , ≤ 5 mm DOI

T2 – Tumor ≤ 2 cms, 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 - Same as 7th Edition

TNM Staging

- TNM staging is the current standard for predicting outcomes in an individual patient

Radiographic Imaging

- Essential for deep Extent & Bone involvement

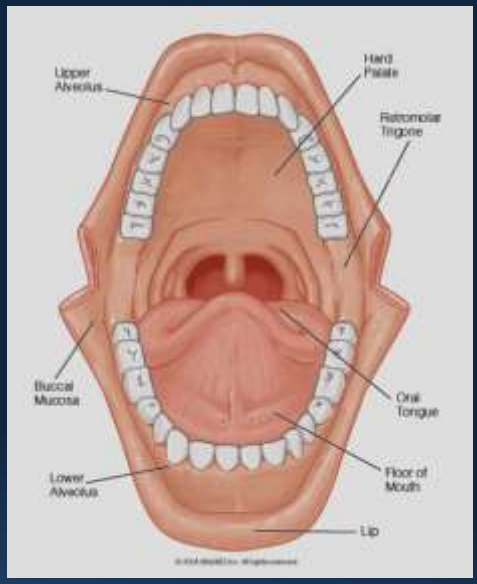
  Superior to palpation for lymph node assessment .
- CT is the workhorse
- MRI for specific questions:
  - Medullary bone invasion
  - Perineural spread
- PET scan generally not of added value over cross-sectional anatomic imaging

Oral Cancer: Factors Affecting Choice of Therapy

- Tumor factors
- Patient factors
- Provider/Physician factors

Oral Cancer- Tumour Factors

- Site
- Size (T stage)
- Location
- Multiplicity
- Proximity to bone
- Histology, grade, depth of invasion,
- Tumor type
- Status of cervical lymph nodes
- Previous treatment



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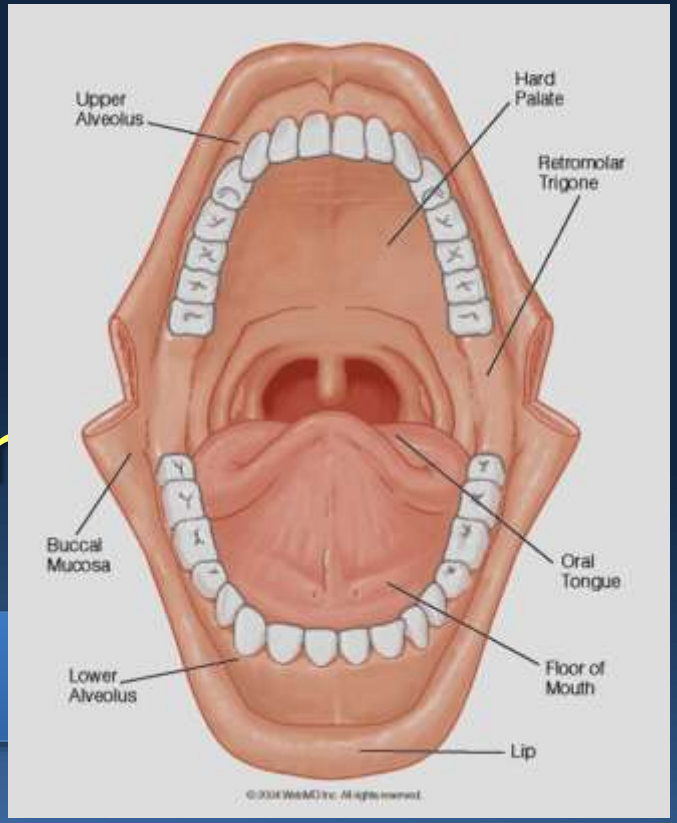
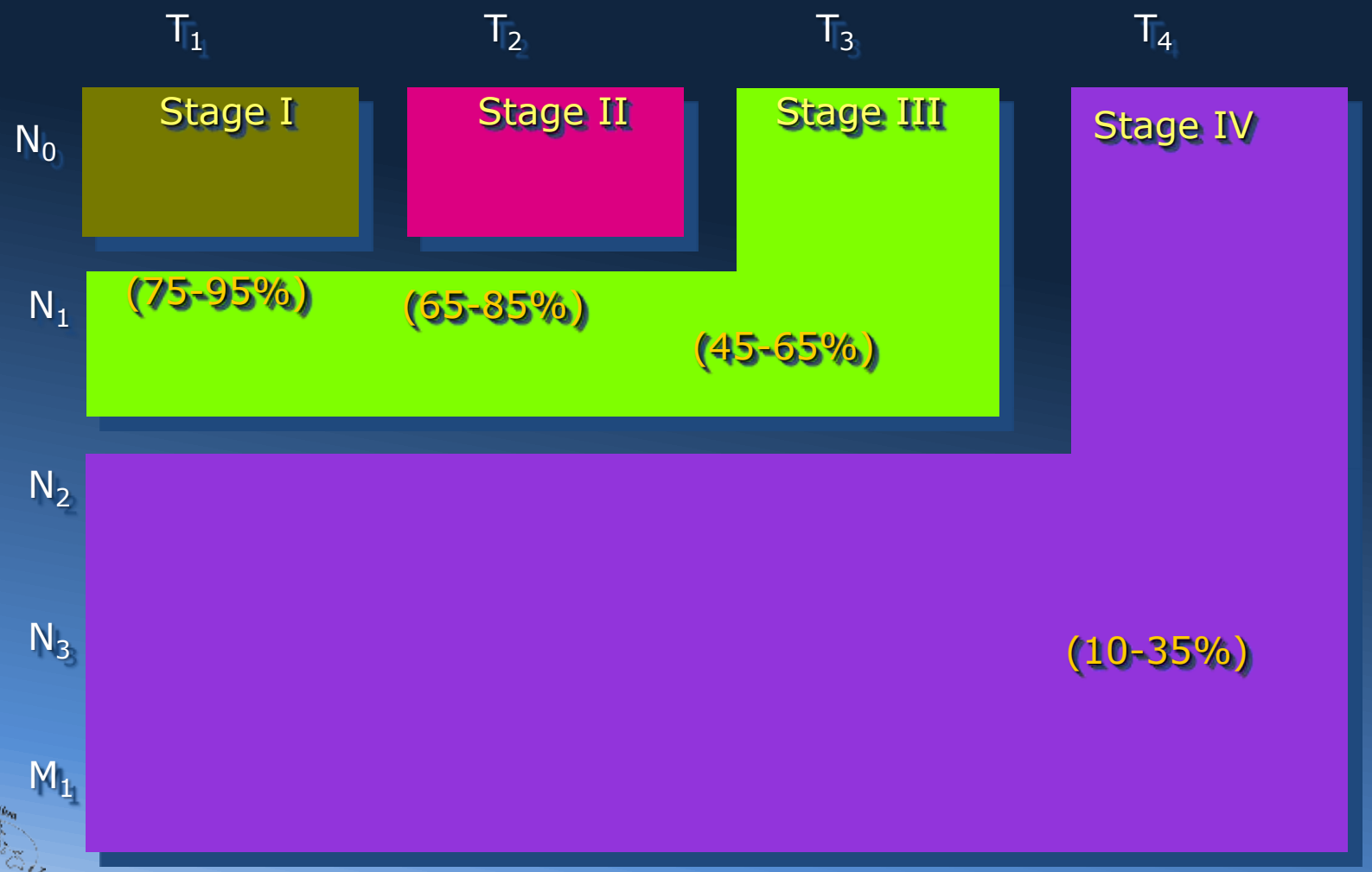
Prognostic Factors in Oral Cancer

- T –Stage-Size
- Histologic Grade
- Invasion pattern
- Lymphovascular Invasion
- Perineural Invasion
- Margin Status
- Nodal Stage and ECS



Cancer of Oral Cavity
5 yr. Survival by Stage



Head and Neck Cancers
Five year Survival

Farr and Arthur (MSKCC 1955-1969)

Oral Cavity:
Treatment Selection

- Dependant on multiple factors:
  - Tumor factors
    - Size (T stage), location, proximity to bone, nodal status, histology, depth of invasion
  - Patient factors
    - Functional status, age, tolerability, lifestyle, socioeconomic status, prior treatment (RT)
  - Resource factors
    - Competence, resources available

Oral Cancer:
Treatment Goals

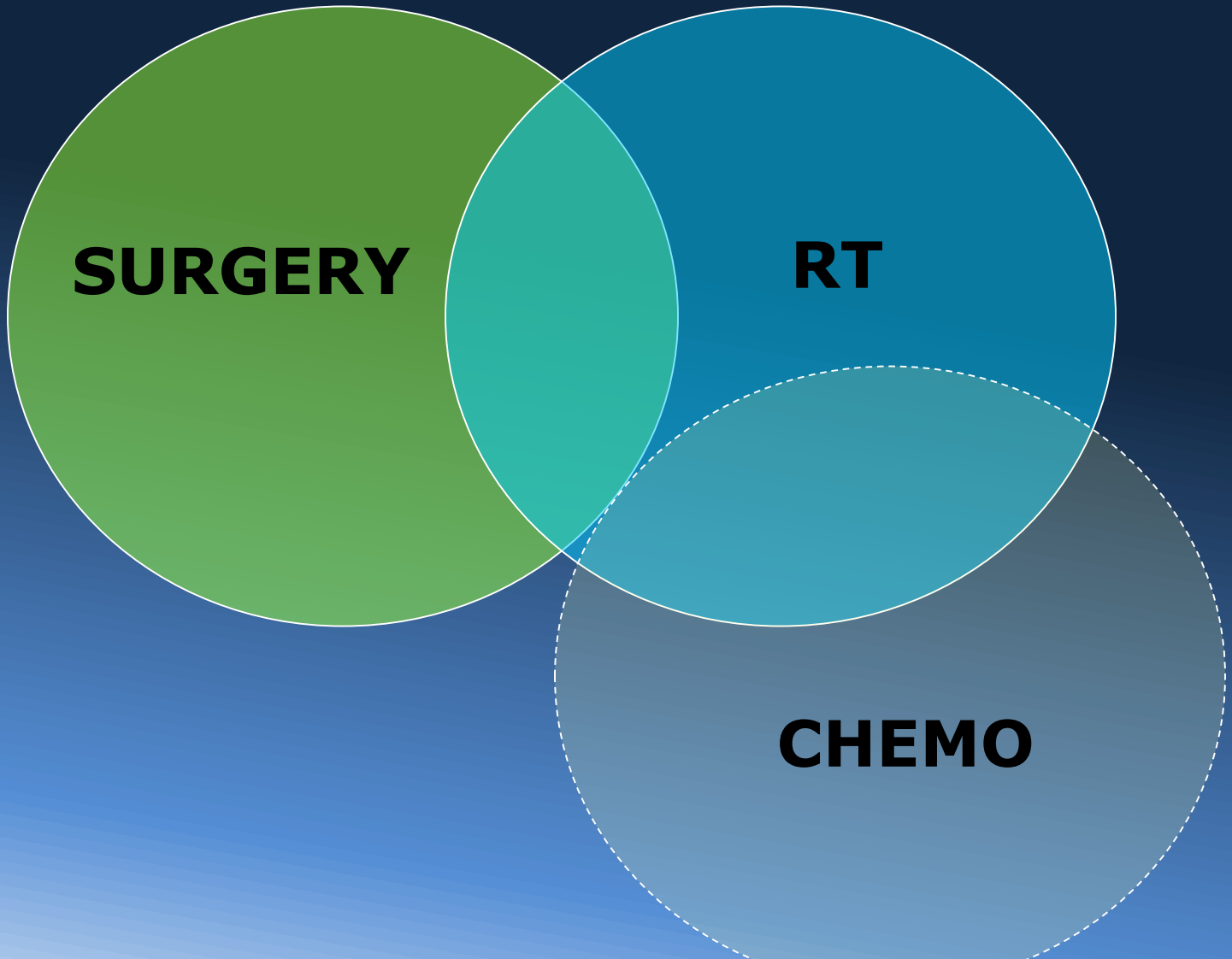
- Control of the cancer
- Preserve form and function
- Minimize complications of treatment
- Identify and prevent possible second primary cancers

Oral Cancer – Choice of Treatment

- Stage I & II single modality treatment is effective and preferable
- Stage III & IV multimodal therapy is essential

Single Modality for Early Stage Cancers

Combined Modality for Advanced Cancers



Indications for Adjuvant Treatment

Primary Tumor

- Advanced T stage:
- Positive surgical margins
- Lymphatic permeation
- Vascular invasion
- Perineural spread
- High histological grade
- Invasive islands of tumor

Indications for Adjuvant Treatment

Primary Tumor

- Advanced T stage:
- Positive surgical margins
- Lymphatic permeation
- Vascular invasion
- Perineural invasion
- High histological grade
- Invasive islands of tumor

Nodal Status

- ≥ 2 pN+ nodes
- pN+ node at > 1 level
- ≥ 3 cm node/s
- Extranodal Extension
- Residual neck disease:
  - Microscopic
  - Gross

Current Indications for ChemoRT

Primary Tumor

- Advanced T stage:
- Positive surgical margins
- Lymphatic permeation
- Vascular invasion
- Perineural invasion
- High histological grade
- Invasive islands of tumor

Nodal Status

- ≥ 2 pN+ nodes
- pN+ node at > 1 level
- ≥ 3 cm node/s
- Extranodal Extension
- Residual neck disease:
  - Microscopic
  - Gross

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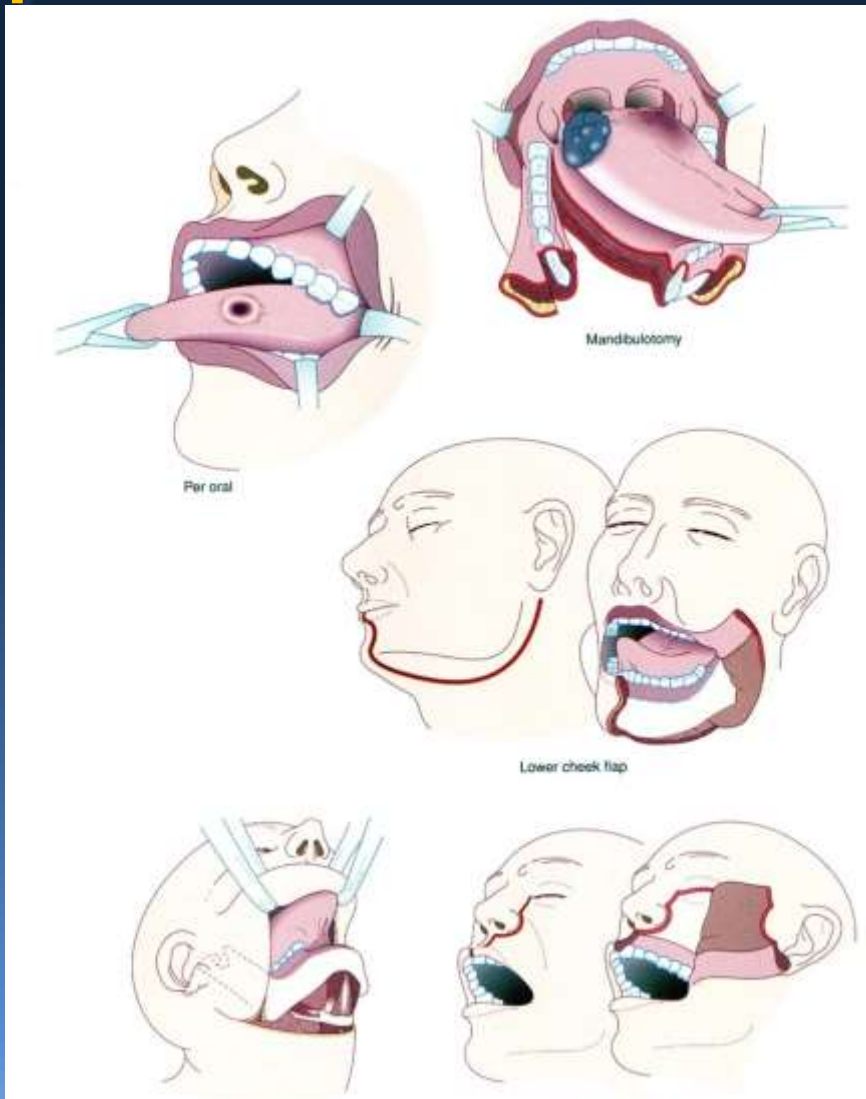
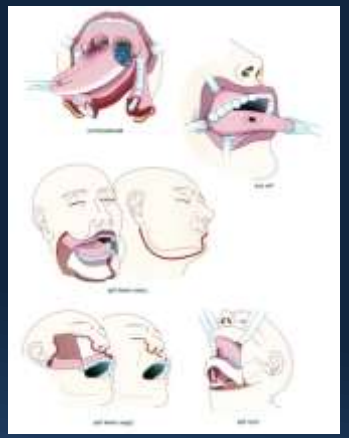
Oral Cancer
Surgical Approaches

- Per oral
- Pull through
- Lower cheek flap
- Upper cheek flap
- Visor flap
- Mandibulotomy



Oral Cancer

Surgical approach depends on:



- Tumor size
- Tumor site
- Tumor location
- Proximity to mandible or maxilla
- Need for neck dissection
- Need for reconstructive surgery

Surgical Approaches For the Management of Oral Cavity Tumors

- Issues in Surgical approaches
  - Which approach provides appropriate access and least morbidity?
    - Transoral Resection
    - Lingual Release
    - Mandibular Swing
    - Composite resection
  - Evidence Summary
    - No evidence that Approach Impacts Local Control or survival

Squamous Cell Cancer of the Oral Tongue- Mandible Uninvolved

46 year old healthy male
T2N0M0 carcinoma of the oral tongue

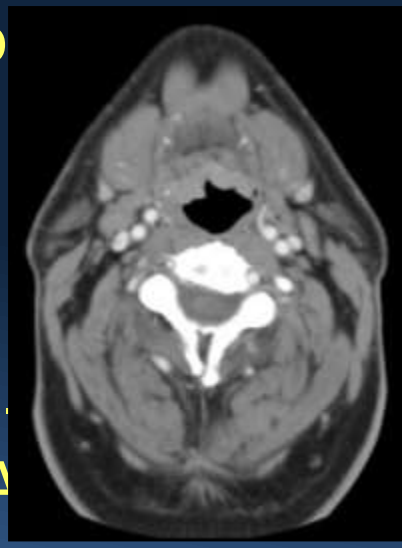
- T stage
  - clinical (p = 0.003)
  - pathological (p = 0.009)
- Tumor thickness
  - (p = 0.001 for 5mm cut-off)
- Multivariate analysis
  - tumor thickness was the only independent predictor for nodal metastases (p = 0.014 for 5 mm cut-off)

What tumour characteristics determine management of the primary and neck?

Diagnostic and Therapeutic Neck Controversy

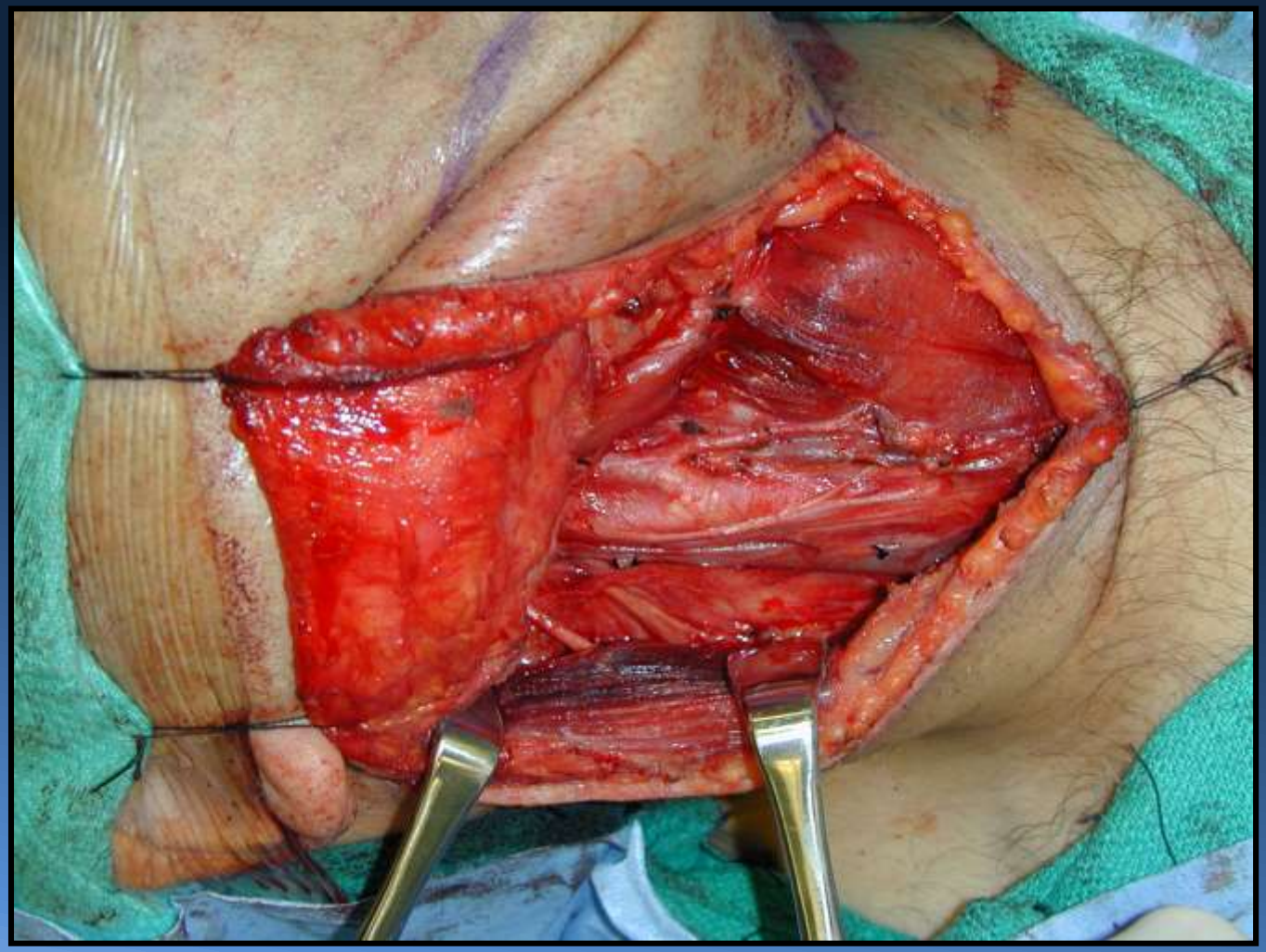
46 year old healthy male
T2N0M0 carcinoma of the oral tongue

- Clinical examinatio
- CT scan
- MRI
- Ultrasound
- Ultrasound-guided FNA
- PET/CT
- Sentinal Node

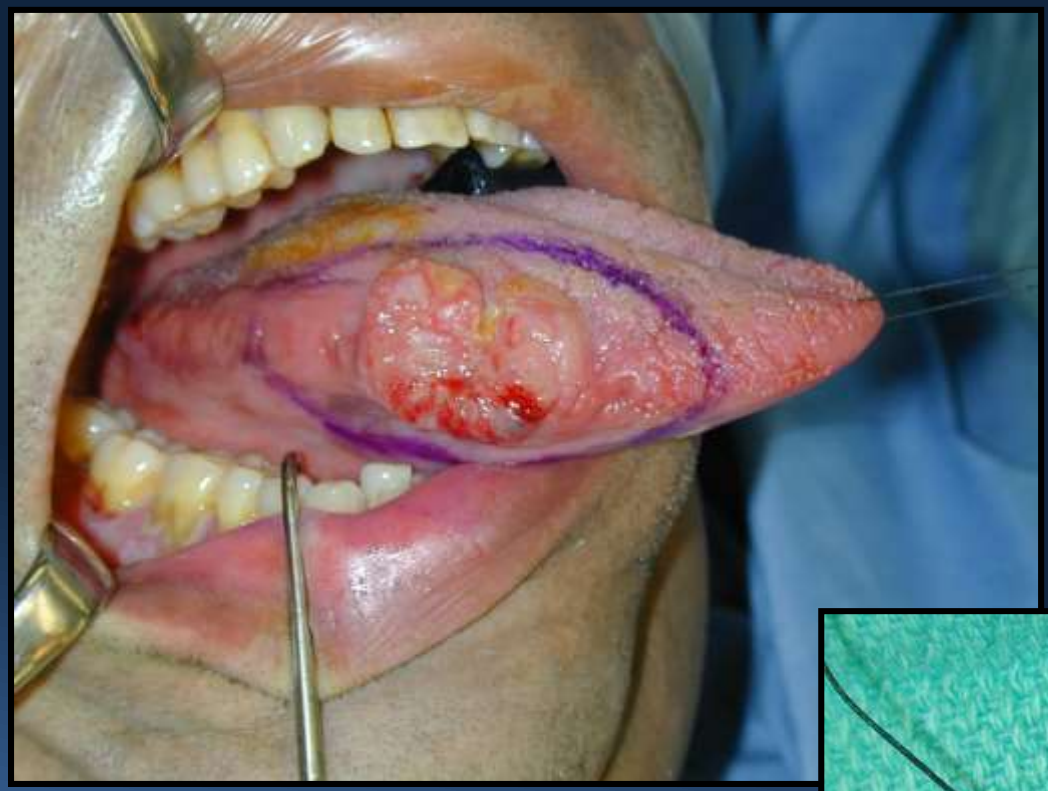


Would PET/CT help decide on therapy to the neck?
Would you offer elective neck dissection?
Would advocate for sentinel node mapping and biopsy?

Extent of Neck Dissection



Levels 1-3 or levels 1-4?



Transoral Resection ?flap

Extent of Margin >5mm

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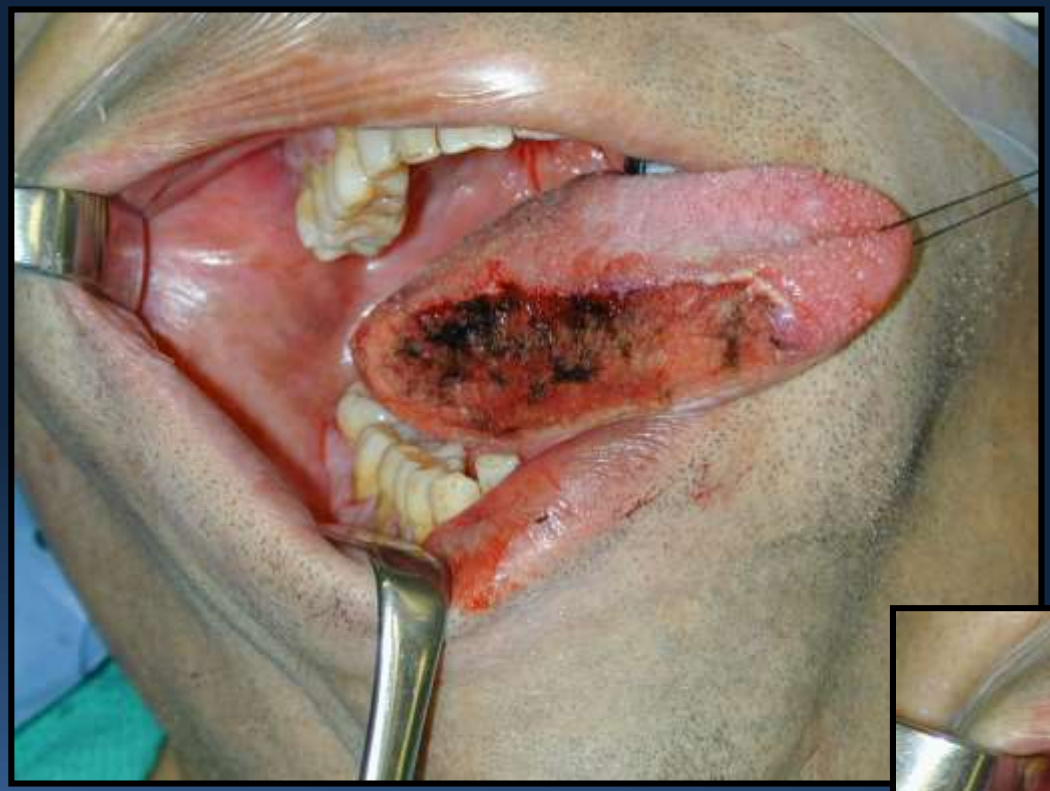

Final Pathology – margins clear
one positive node at 2a, no ecs

Is post operative radiotherapy necessary for the pathologically N1 (pN1) neck?
If so, what is the optimal dose?

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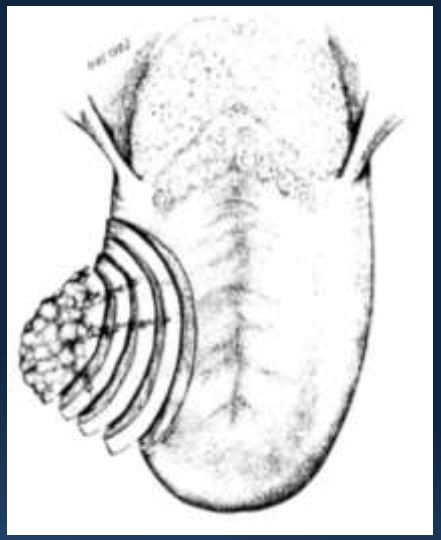
Oral Carcinoma : *Surgical Management*

- Does microscopic tumor cut-through matter and is it an indication for adjuvant treatment?



Oral Carcinoma : *Surgical Management*

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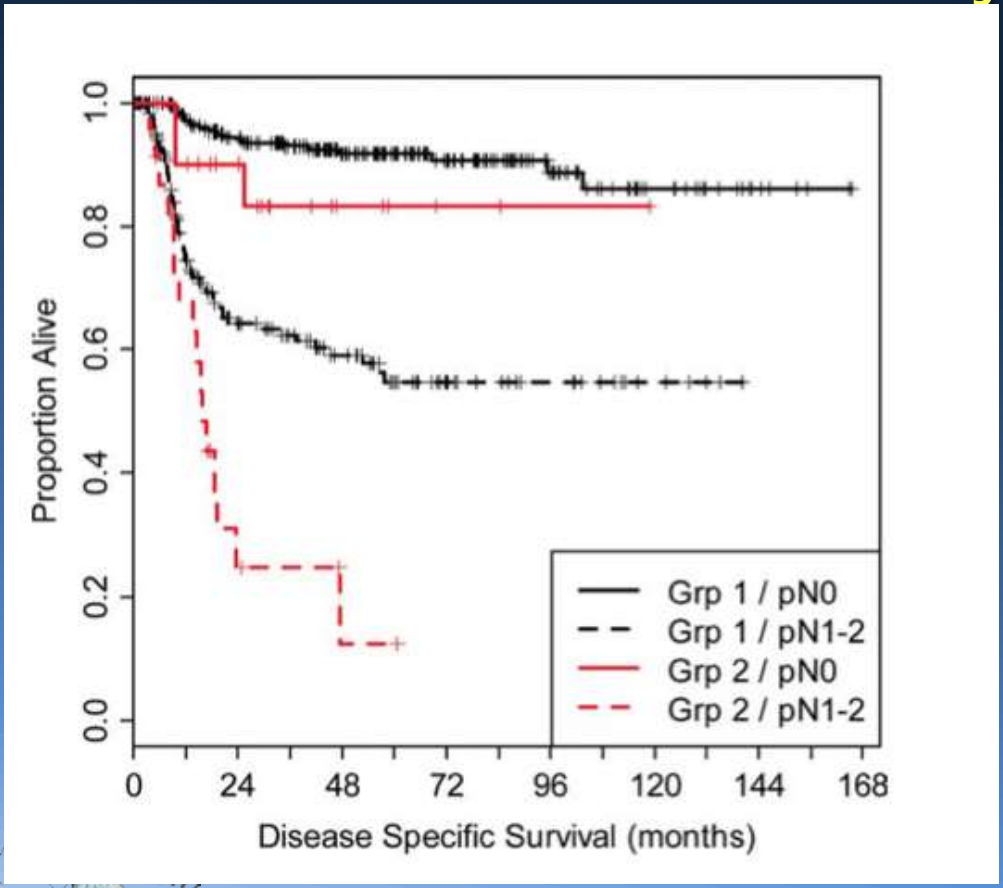

Grp 1 – No cut-through

Grp 2 –Cut-through

Head & Neck 32: 1444-1451,2010

Conclusion:

Microscopic tumour cut-through...

- in the presence of nodal disease is a powerful adverse prognosticator for cancer control and survival.

- in the absence of nodal disease it is not a poor prognosticator, and adjuvant therapy in these patients may be unnecessary.

Patel, Gullane ,Gilbert et al-Head and Neck 32;1444-1451, 2010

Surgical Approaches for the Management of Oral Cavity Tumors

Issues in Surgical approaches

- Which approach provides appropriate access and least morbidity?
  - Transoral Resections
  - **Lingual Release**
  - Mandibular Swing
  - Composite Resection
- Evidence Summary
  - No evidence that approach impacts local control or survival.

Oral Carcinoma : *Surgical Management*

- ***"The Oncologic Step Stool"***

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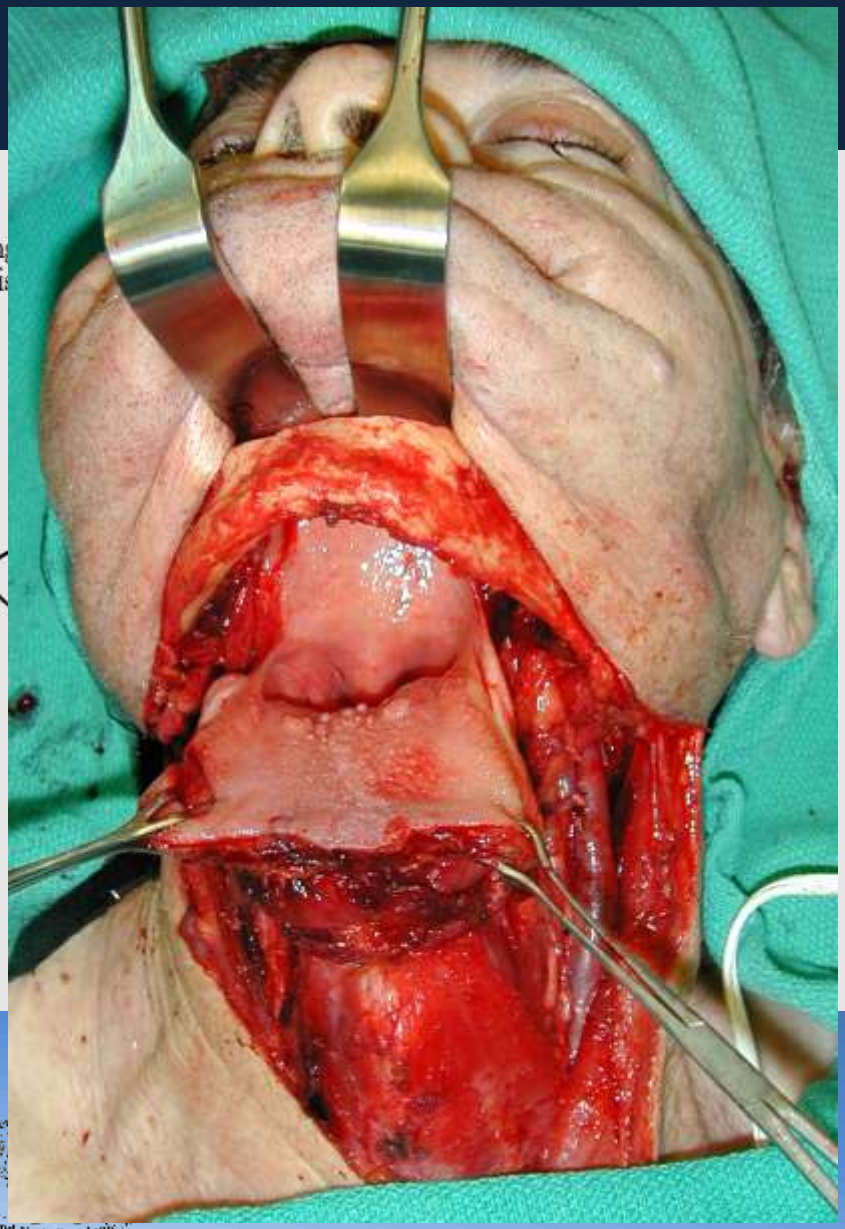
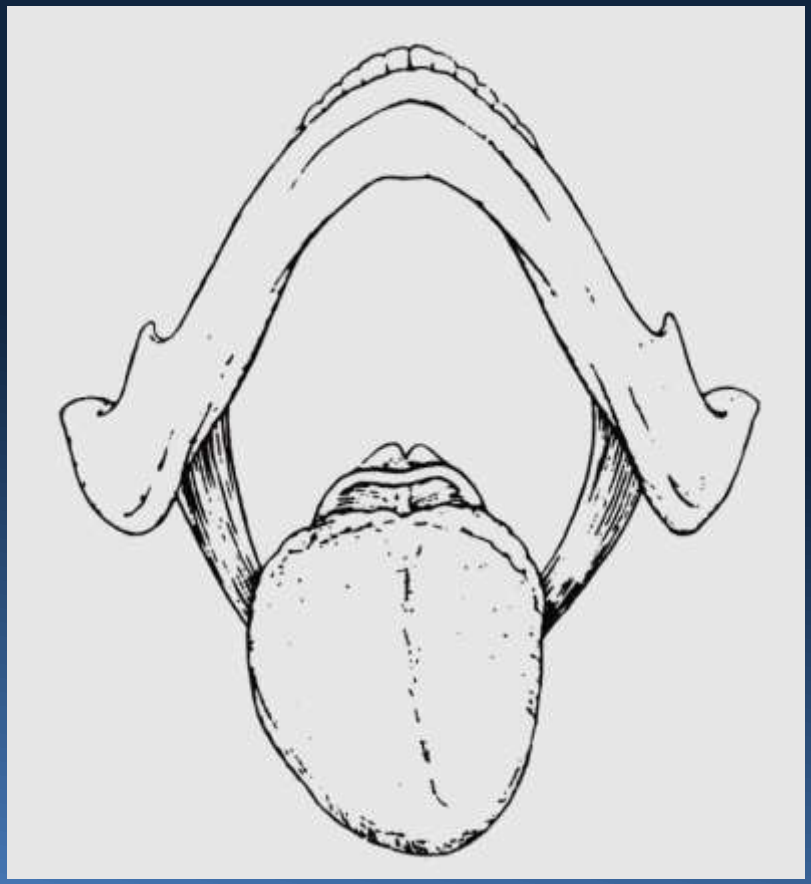
Lingual Release





Lingual Release vs Mandibular Swing
(Devine et al Int J of Oral and Maxillofacial Surgery-2001)

Subjective Outcome

Domain	Lip-split mandibulotomy			Mandibular lingual release			Analysis of variance
	Mean	SD	Range	Mean	SD	Range	*P*-value
Speech UW-QOL	79.00	14.5	60–100	59.5	22.9	20–80	0.035
Swallowing UW-QOL	90.00	21.1	60–100	60.0	31.6	40–100	0.022
Chewing UW-QOL	65.00	24.2	60–100	40.0	21.1	20–80	0.024
Disfigurement UW-QOL	75.0	11.8	60–100	70.0	15.8	60–100	0.430

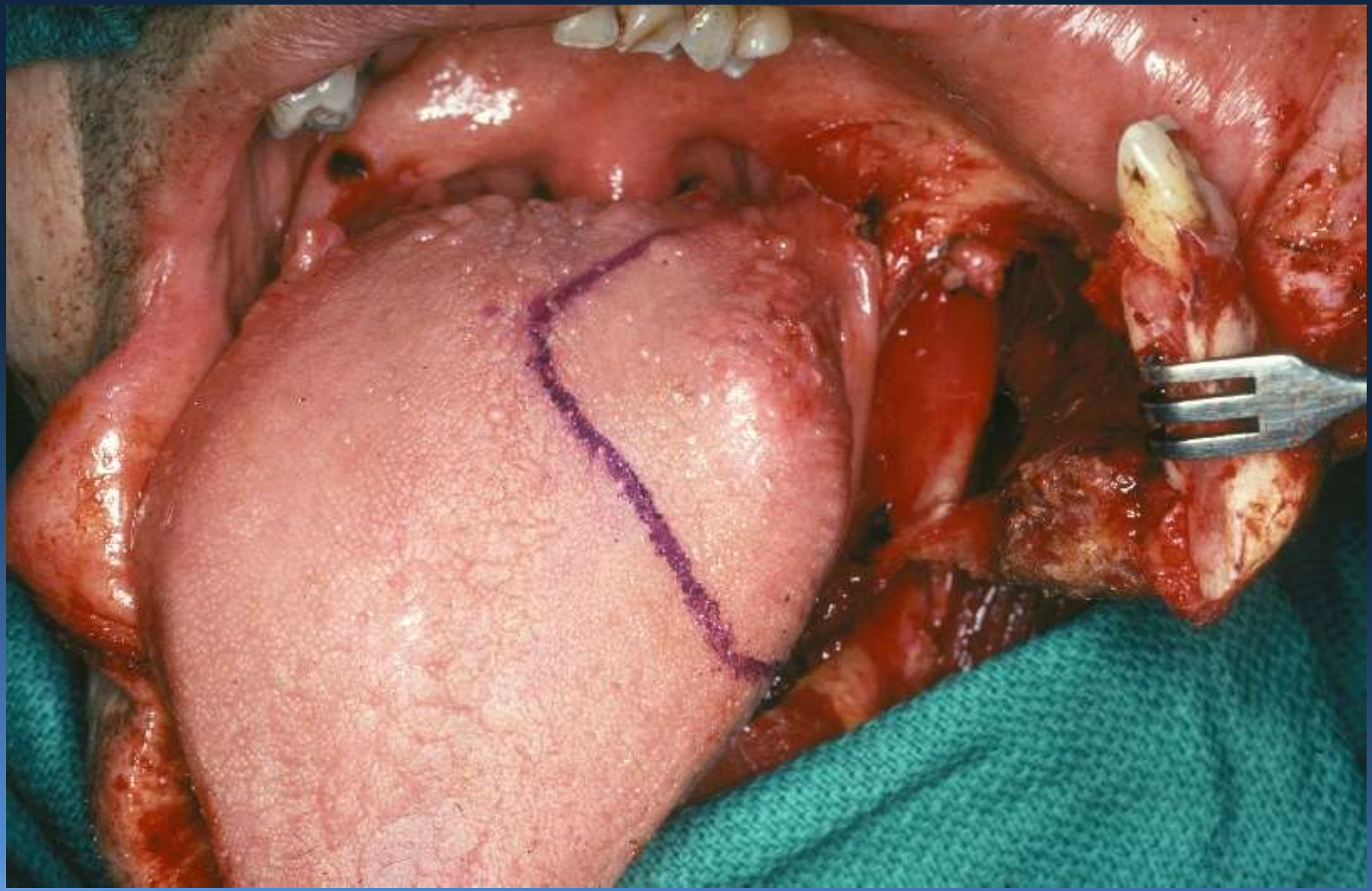
Higher score indicates better function.

Surgical Approaches Advanced Tumors

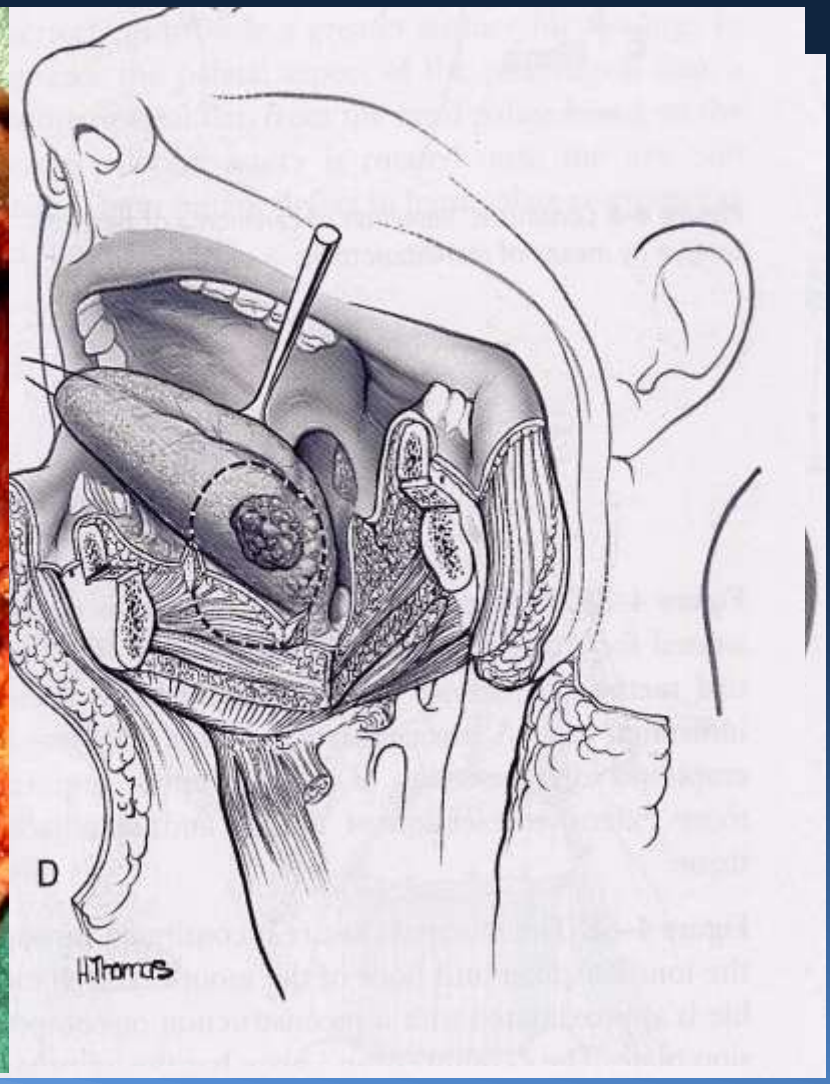
- Issues in Surgical approaches
  - Which approach provides appropriate access and least morbidity?
    - Transoral Resections
    - Lingual Release
    - Mandibular Swing
  - Evidence Summary
    - No evidence that approach impacts local control or survival

Paramedian Mandibulotomy: Advantages

- Wide exposure
- Preserves hyomandibular complex
- No denervation of skin
- No devascularization
- Easy fixation
- Out of radiation portals



Surgical Approaches for Advanced Tumors



Mandibular Swing-Approaches and Options

Surgical Approaches Advanced Tumors

- Issues in Surgical Approaches
  - –Extent of Mandibulectomy
    - Marginal vs Segmental
- Evidence Summary
  - Little published literature on this subject
  - data suggests that for limited involvement in dentate mandible rim mandibulectomy is adequate treatment

Marginal Mandibulectomy: Contraindications

- Gross tumor invasion
- Massive soft tissue disease
- Radiated, edentulous mandible

Defects of the Oral Cavity-Free Flap

- Soft Tissue repair
- Soft Tissue and bone

Menu of Options in Soft Tissue Repair

	Flap Thickness	Volume Adjustment	Sensate
Forearm	++++	++++	++++
Anterolateral Thigh	+++	++++	++
Lateral Arm	++	++++	++
DIEP	+++	++++	+

How do you determine whether you perform a Marginal or Segmental Mandibulectomy?

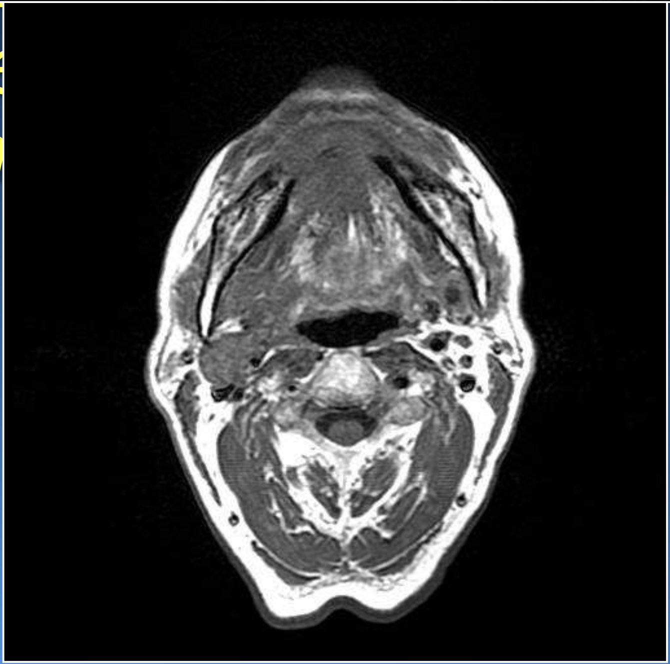
Indications for Segmental Resection Include:

- Gross invasion by Cancer
- Bone invasion
  - Inferior Alveolar Nerve Invasion

How do you determine the extent of Mandibulectomy to achieve adequacy of bony margins?

Investigations:

- CT scan
- MRI scan
- Metastatic survey clear.
- *Imaging revealed invasion the symphyseal region of the mandible, floor of mouth, an the mobile tongue with suspicious nodes at levels 2a,b bilaterally.*



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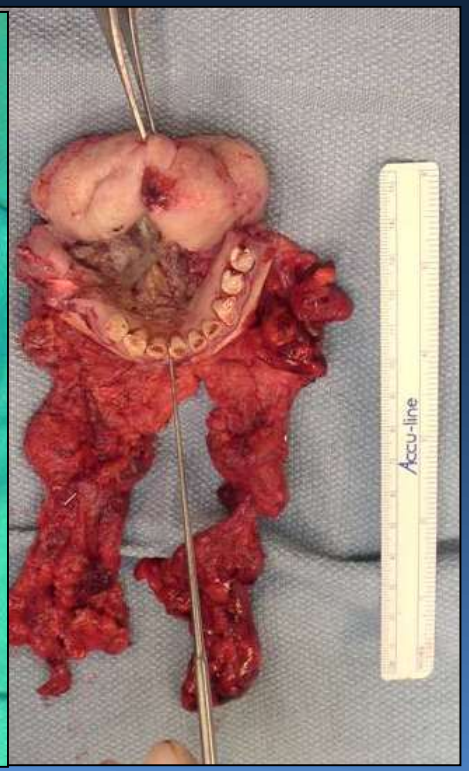
Management Options?

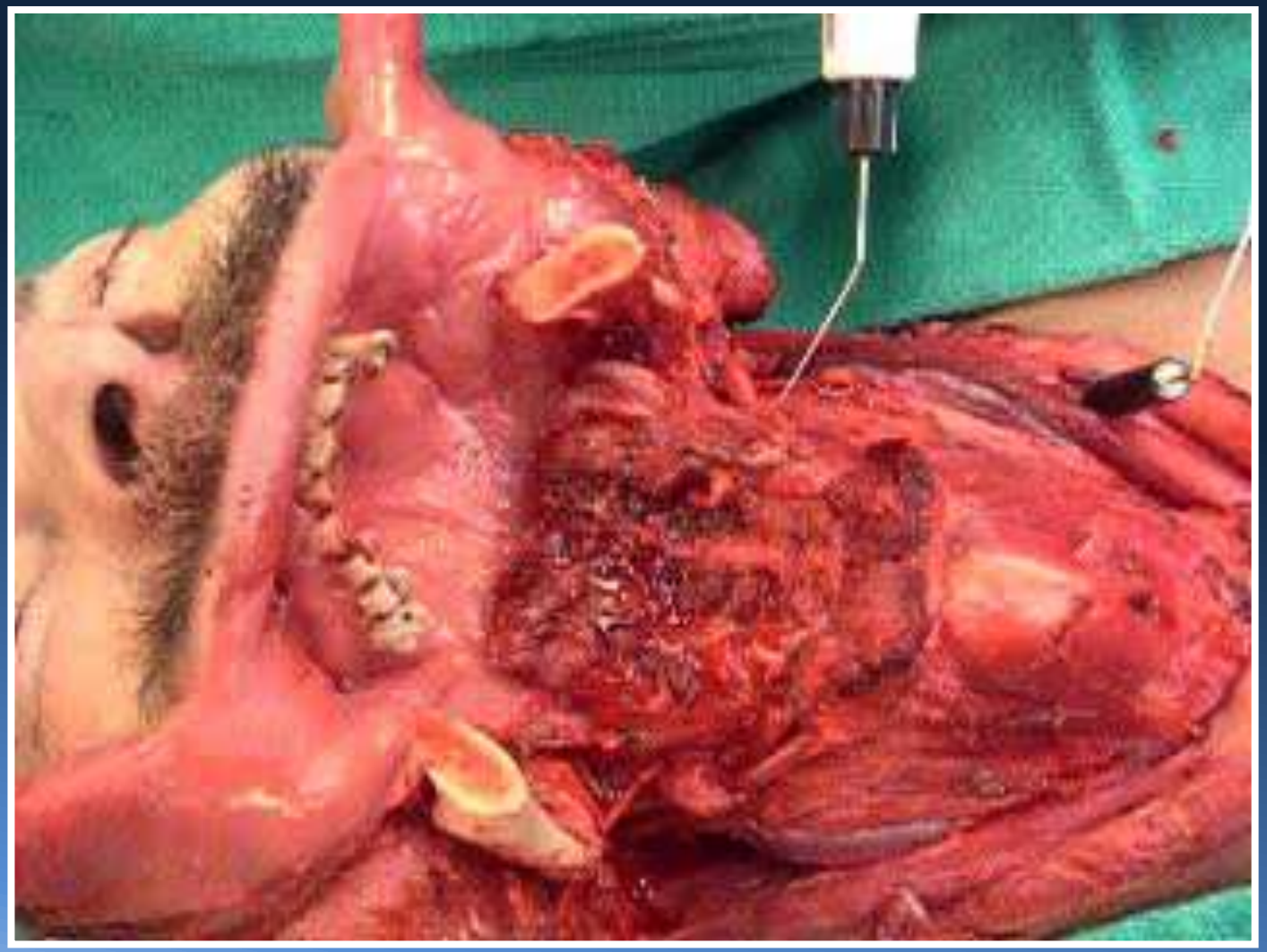
Segmental Mandibulectomy

Is required for:

- Gross invasion by cancer
- Bone invasion
- Inferior alveolar nerve invasion
- Osteoradionecrosis
- Proximity of oral cancer to irradiated edentulous mandible.



Nerve Stimulation Reveals Movement of the Right and Left Tongue Base from Preservation of the Posterior Branch of the Hypoglossal Nerves



Options in Reconstruction






Composite Flaps

Good bone

Menu

Radial forearm flap*
Scapular flap
Fibula flap*
Iliac crest flap

Good skin

* May be reinnervated

Defects of the Oral Cavity

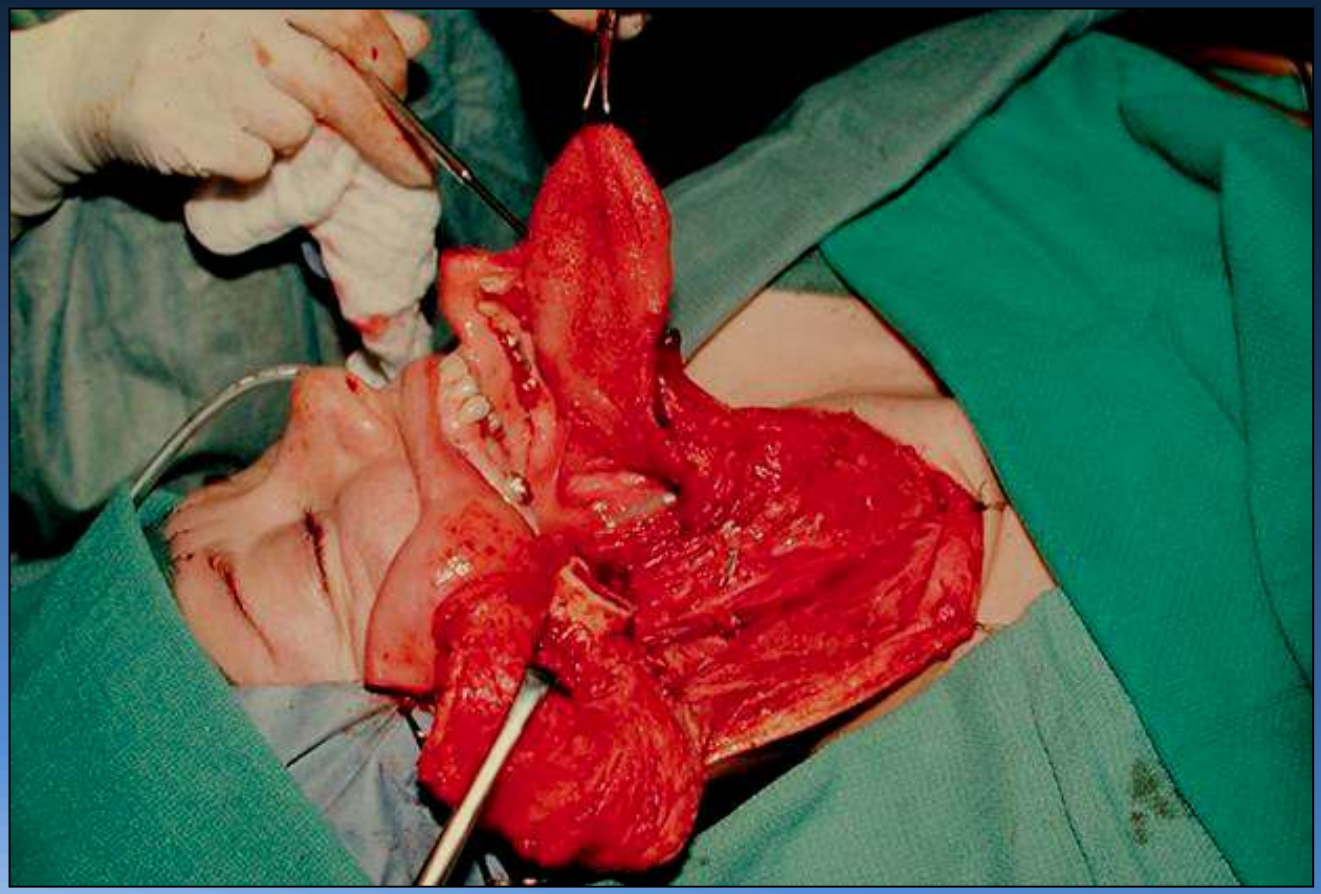
- Soft Tissue repair
- Soft Tissue and bone

Menu of Options in Soft Tissue and Bone Repair

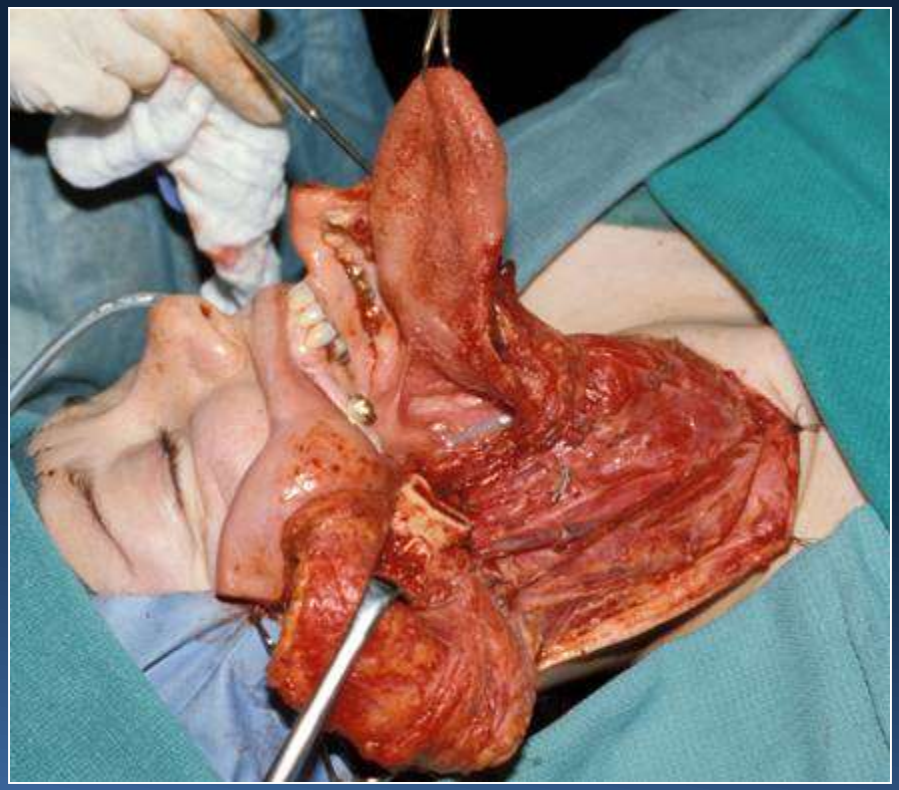
	Skin Paddle	Bone Length	Bone Quality	Donor Site	Favored Choice
Fibula	+++	++++	++++	++++	**Mandible**
Iliac Crest	+	+++	++++	++	
Scapula	++++	++	+++	++++	**Maxilla**
Forearm	++++	++	+	++	

Composite Resection

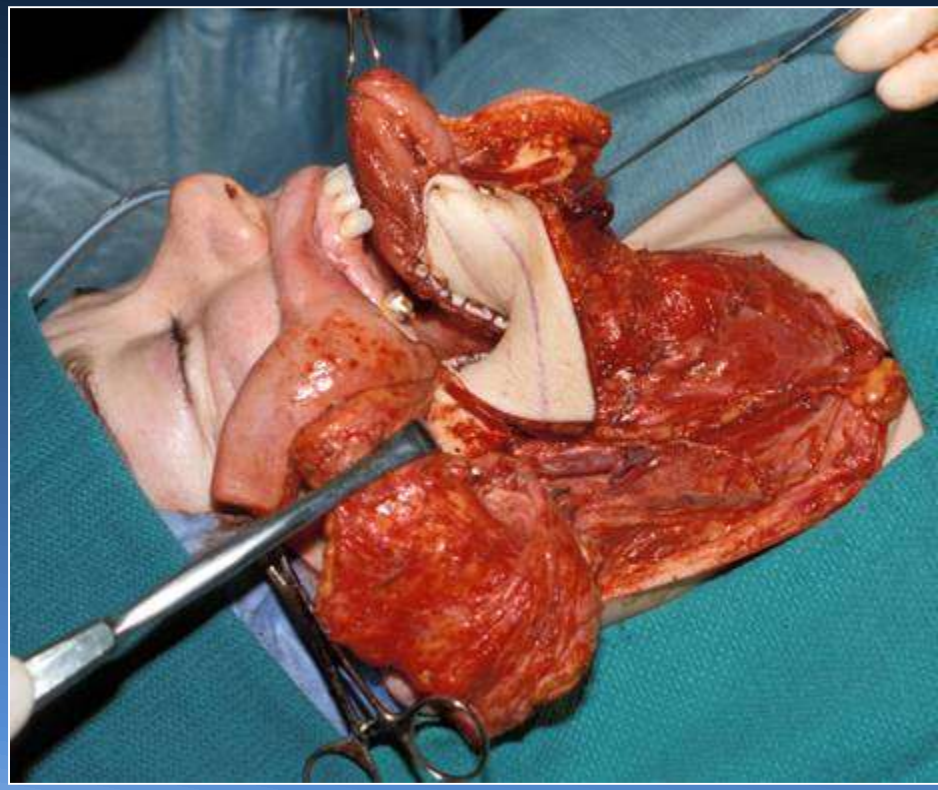
- What has changed?
- 2 flaps – soft tissue and bone



Double Flap: Radial Forearm and Fibula



Double Flaps
72 cases
1995 - 2007

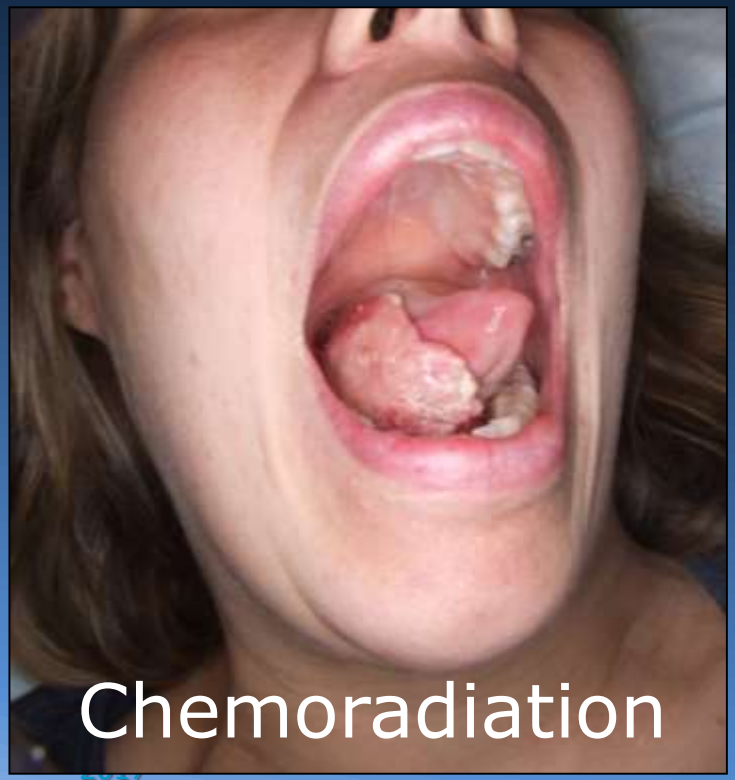


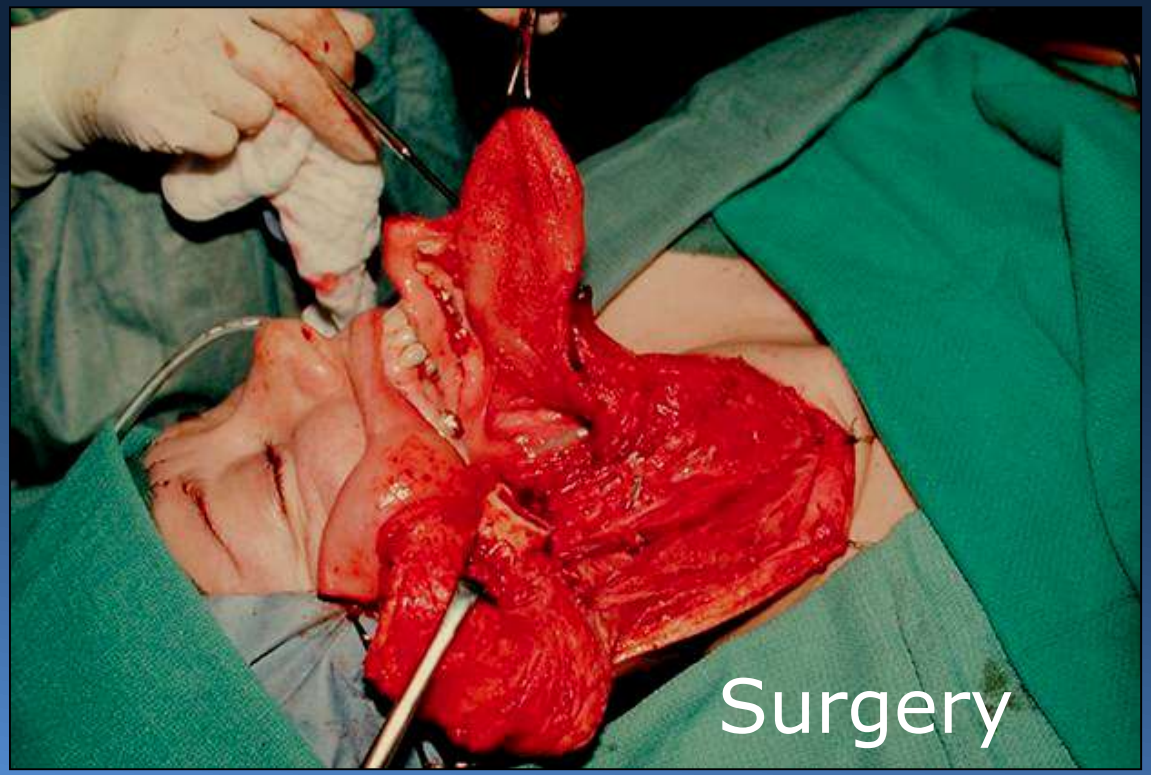
2 years post-op

Gullane et al "Leg morbidity and function following fibular free flap harvest." Ann Plast Surg. 1997 May;38(5):460-4.

Cancer of the R. Tongue

Without Mandible Invasion





How would you treat this patient in 2017? New discussion

Oncologic Outcomes

TONGUE CANCER THE PMH EXPERIENCE

Results: Demographic Data

- N= 319

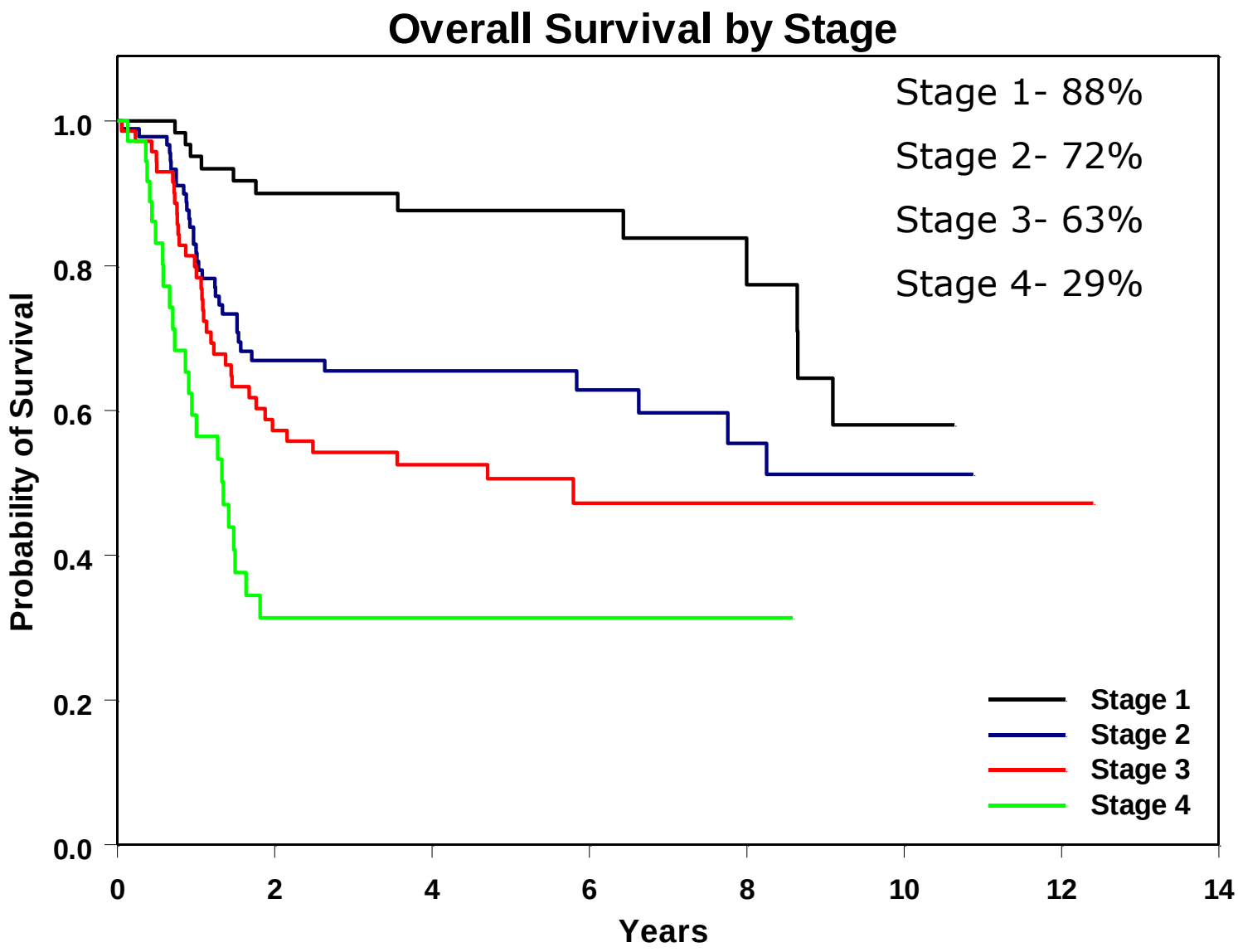
Age	Median (range)	59 years (22 ~ 92)
Gender	Male:Female	193 (60.5%):126 (39.5%)
Alcohol use	Moderate/Heavy	78 (24.5%)
Tobacco	Yes	209 (65.5%)
Clinical Stage	1	88 (35.7%)
	2	101 (34.9%)
	3	78 (15.5%)
	4	52 (11.6%)

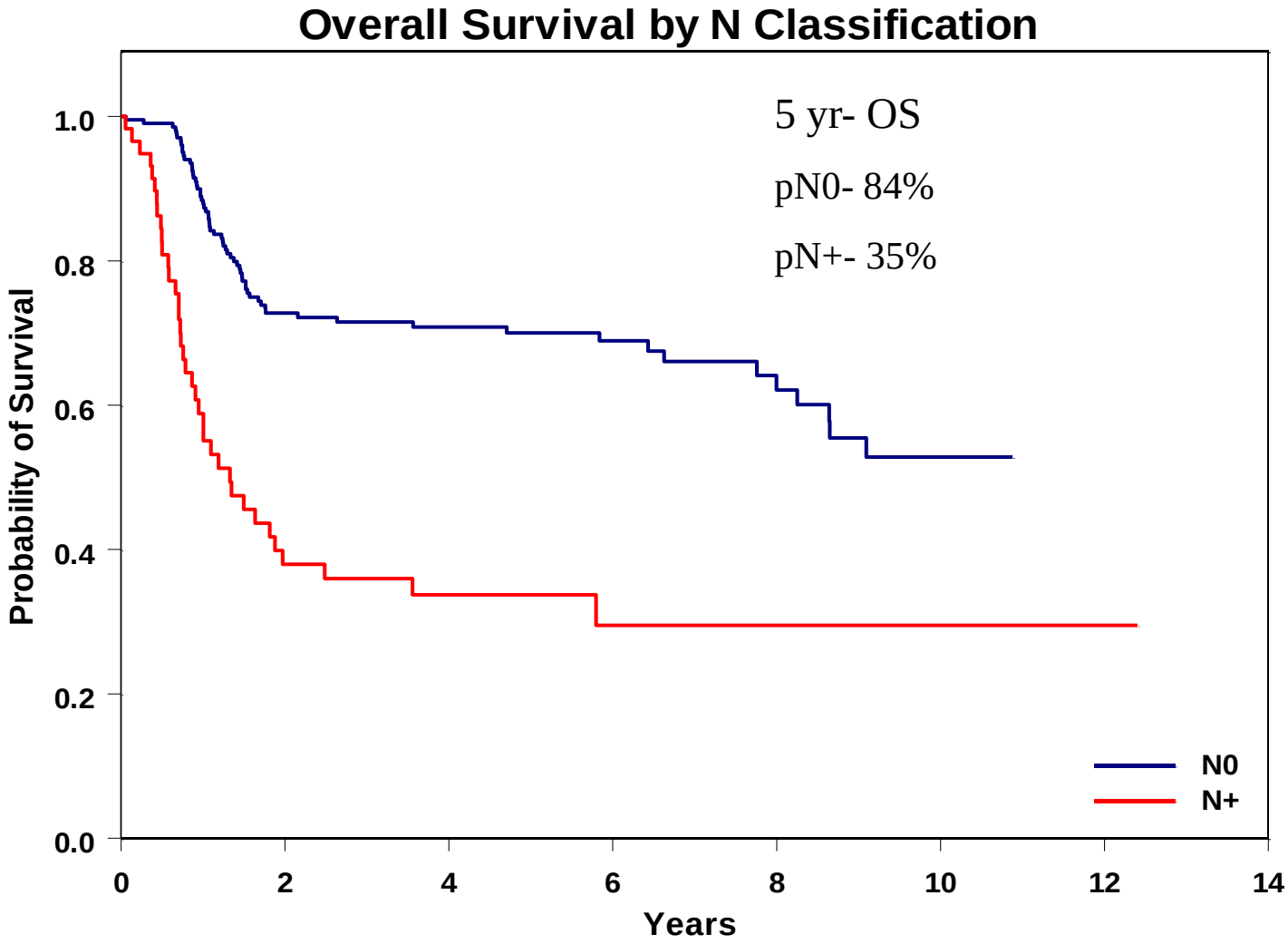
	N0	N1	N2a	N2b	N2c
T1	88	2	0	0	1
T2	101	14	3	4	1
T3	39	22	6	9	8
T4	6	2	1	6	6

Results: Treatment Data

Treatment	Primary Surgery	305 (96%)
	Primary Radiotherapy/chemorads	8 (4.9%)/6
Primary Surgery	Single Modality	242 (79%)
	Post-Operative RT	77 (21%)
Neck Dissection	Neck Dissection SND: MRND: RND	226/305 (74%) 184:90:14

Clinical T stage	Neck Dissection
T1	34 (37.7%)
T2	97 (80.8%)
T3	79 (96.3%)
T4	16 (94.1%)

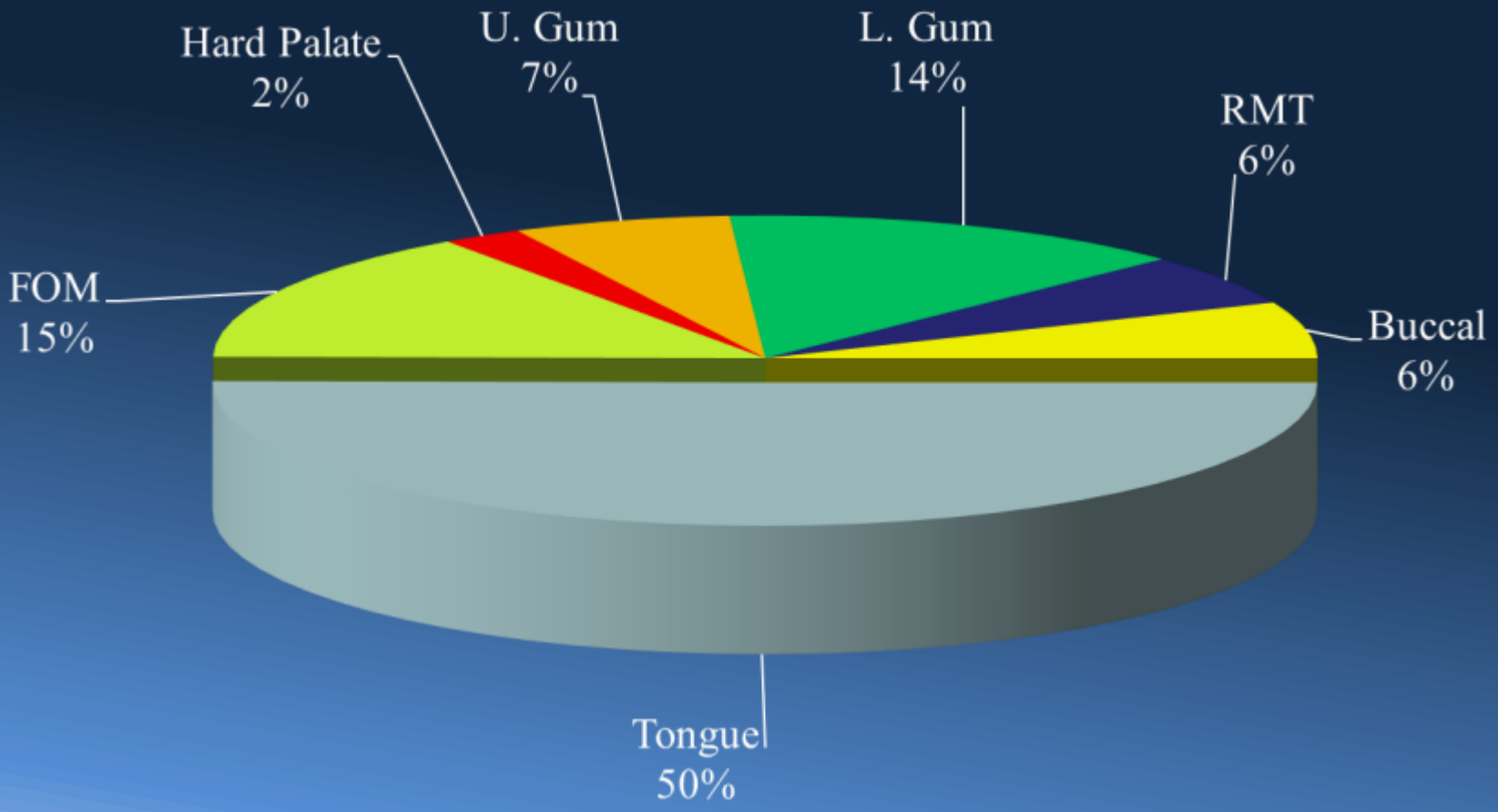

Overall Survival by Stage
Stage 1- 88%
Stage 2- 72%
Stage 3- 63%
Stage 4- 29%
Probability of Survival
1.0
0.8
0.6
0.4
0.2
0.0
0
2
4
6
8
10
12
14
Years
Stage 1
Stage 2
Stage 3
Stage 4


Overall Survival by N Classification
5 yr- OS
pN0- 84%
pN+- 35%
Probability of Survival
1.0
0.8
0.6
0.4
0.2
0.0
0
2
4
6
8
10
12
14
Years
N0
N+

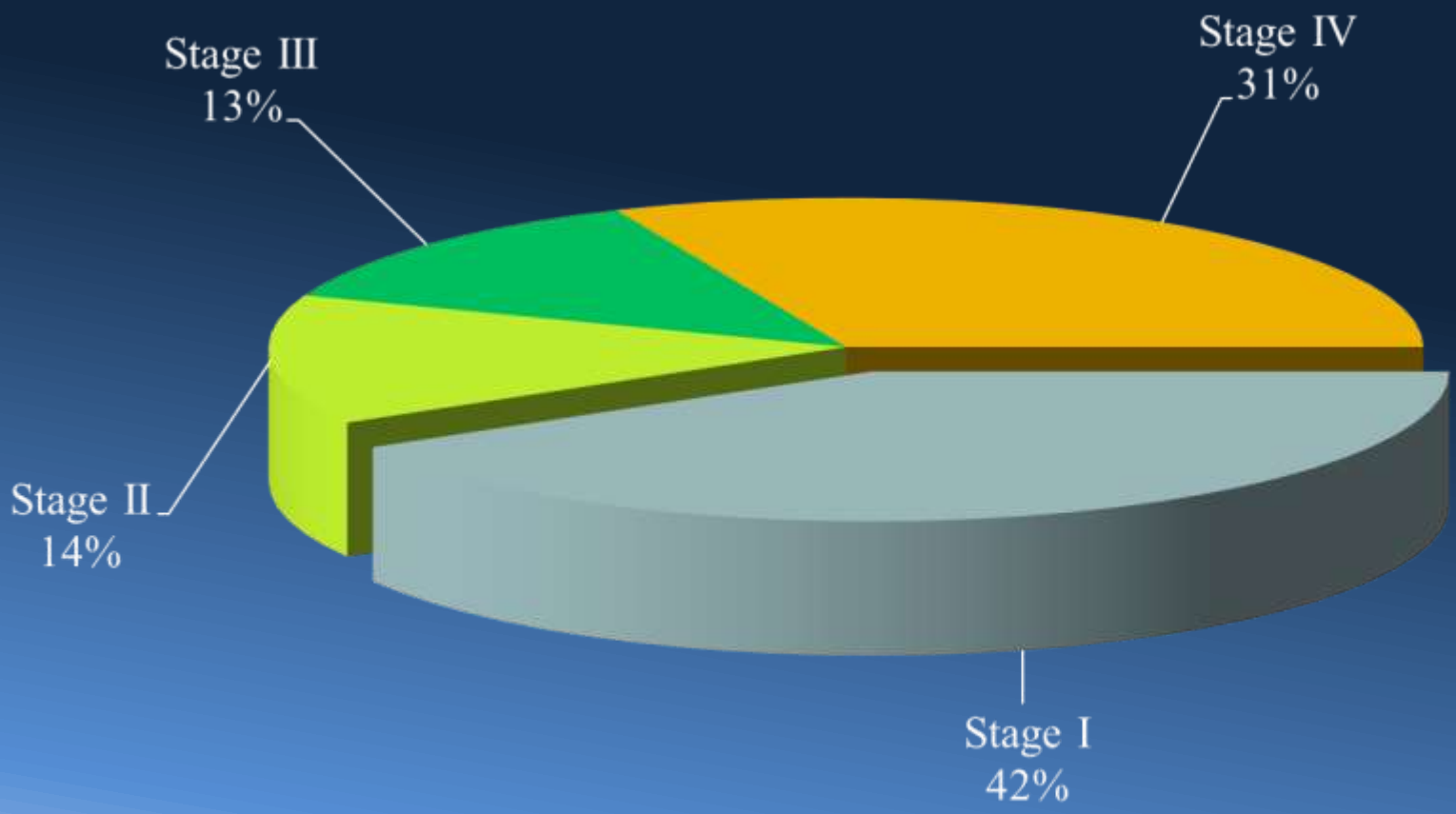
MSKCC Data

- n = 1,866
- Previously untreated patients
- 1985 - 2012

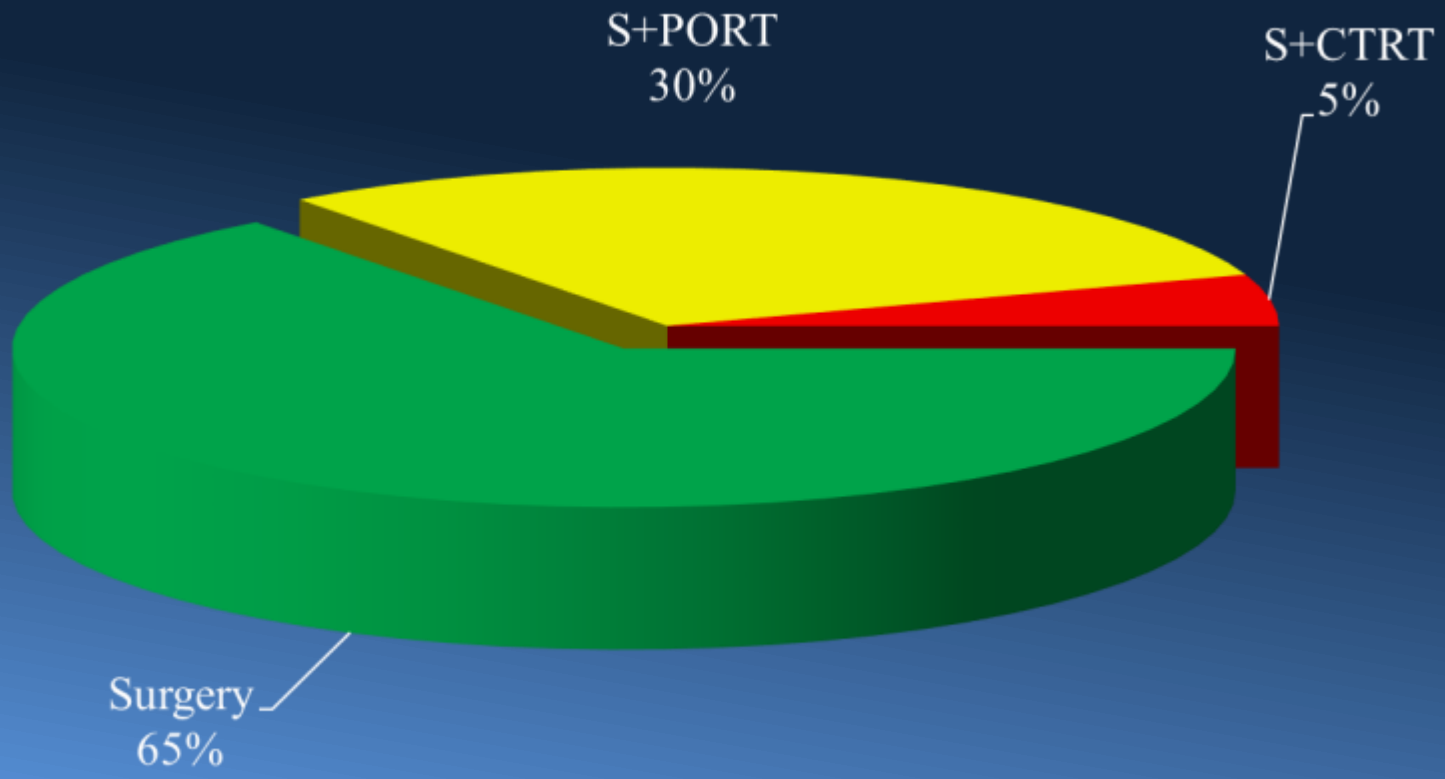
Site of Primary Tumor



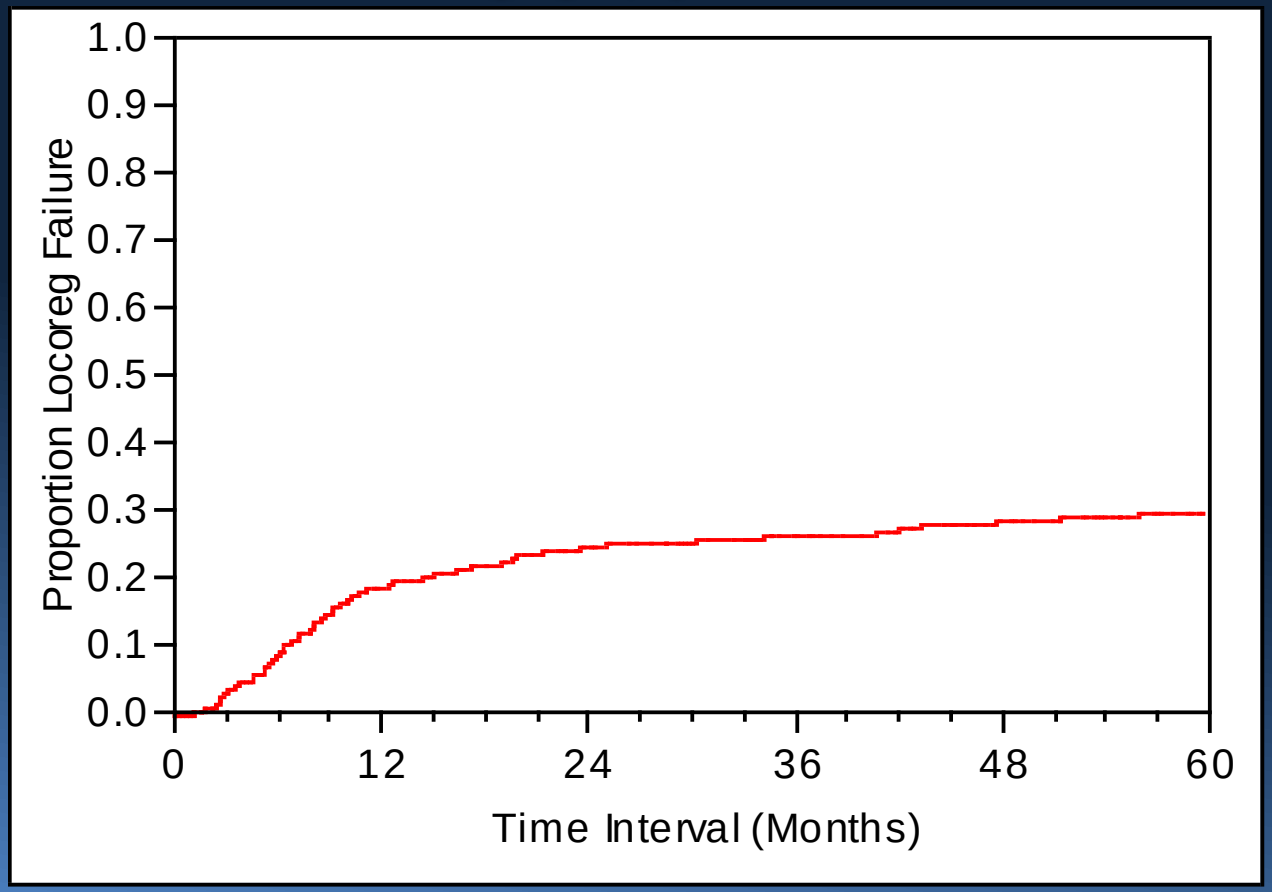
TNM Stage Groups



Postoperative Adjuvant Treatment

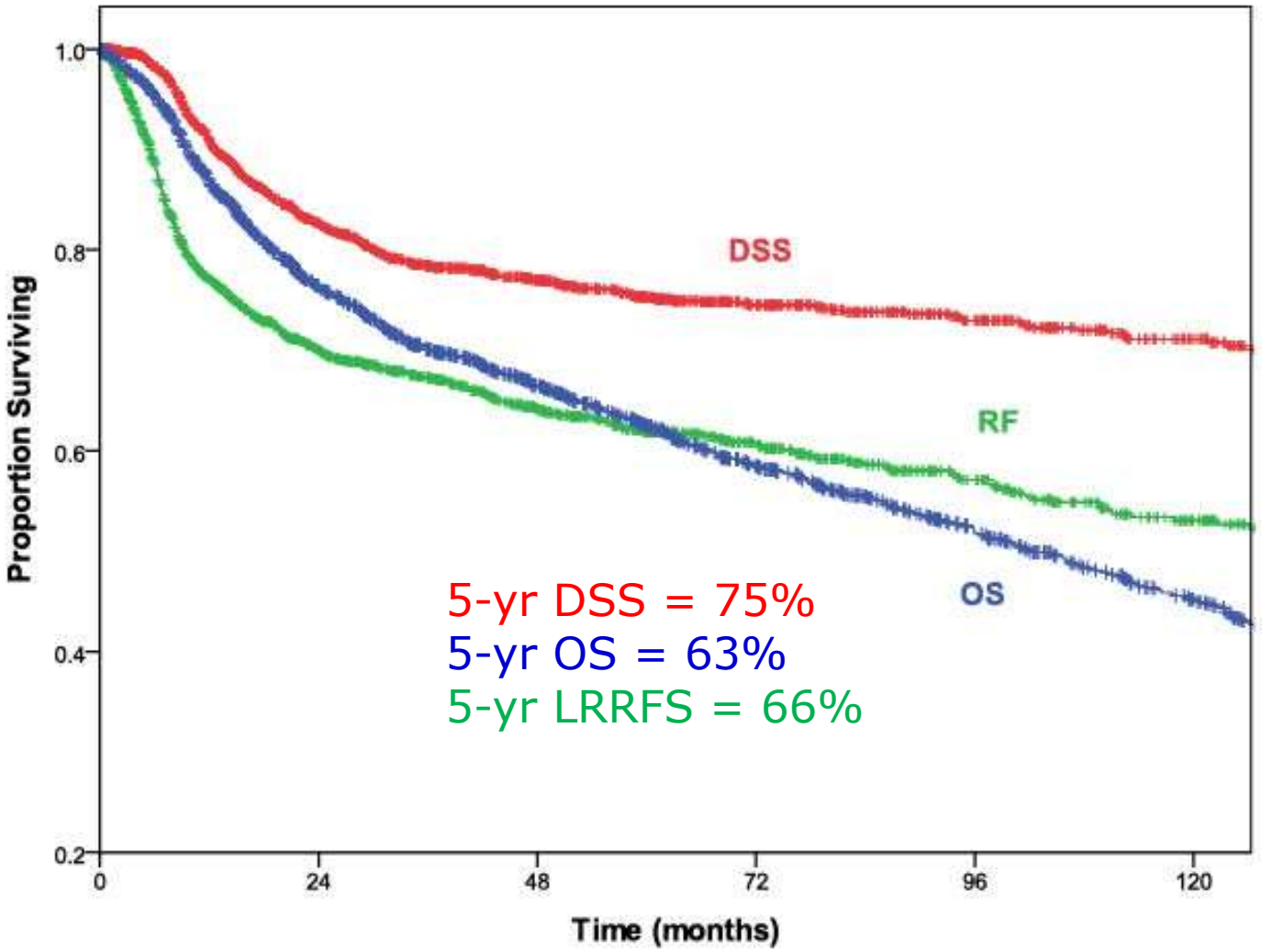


5-yr Locoregional Recurrence Rate = 30%



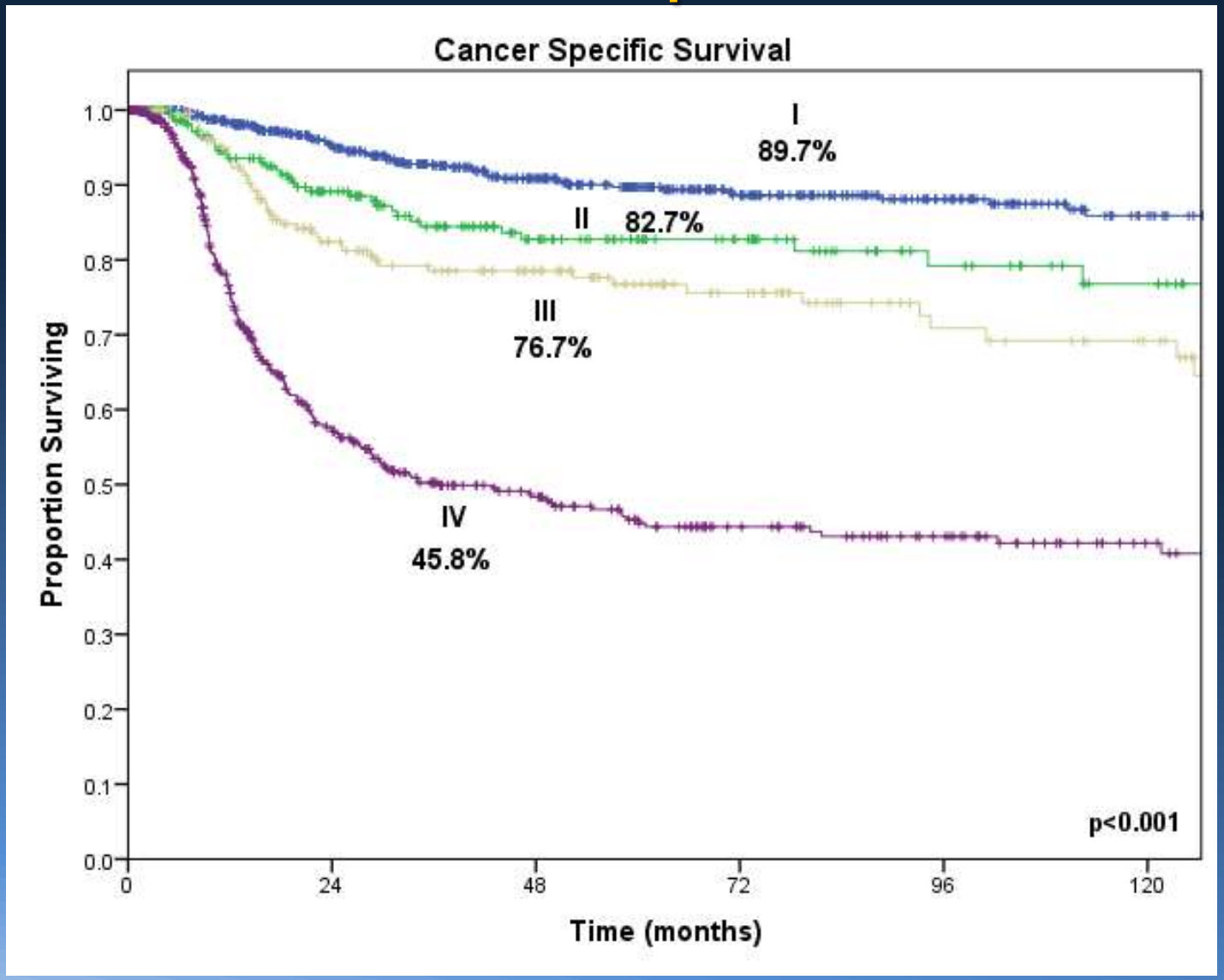
Median time to recurrence 9 months (Range 1 – 141)

75% quartile 19.6 m

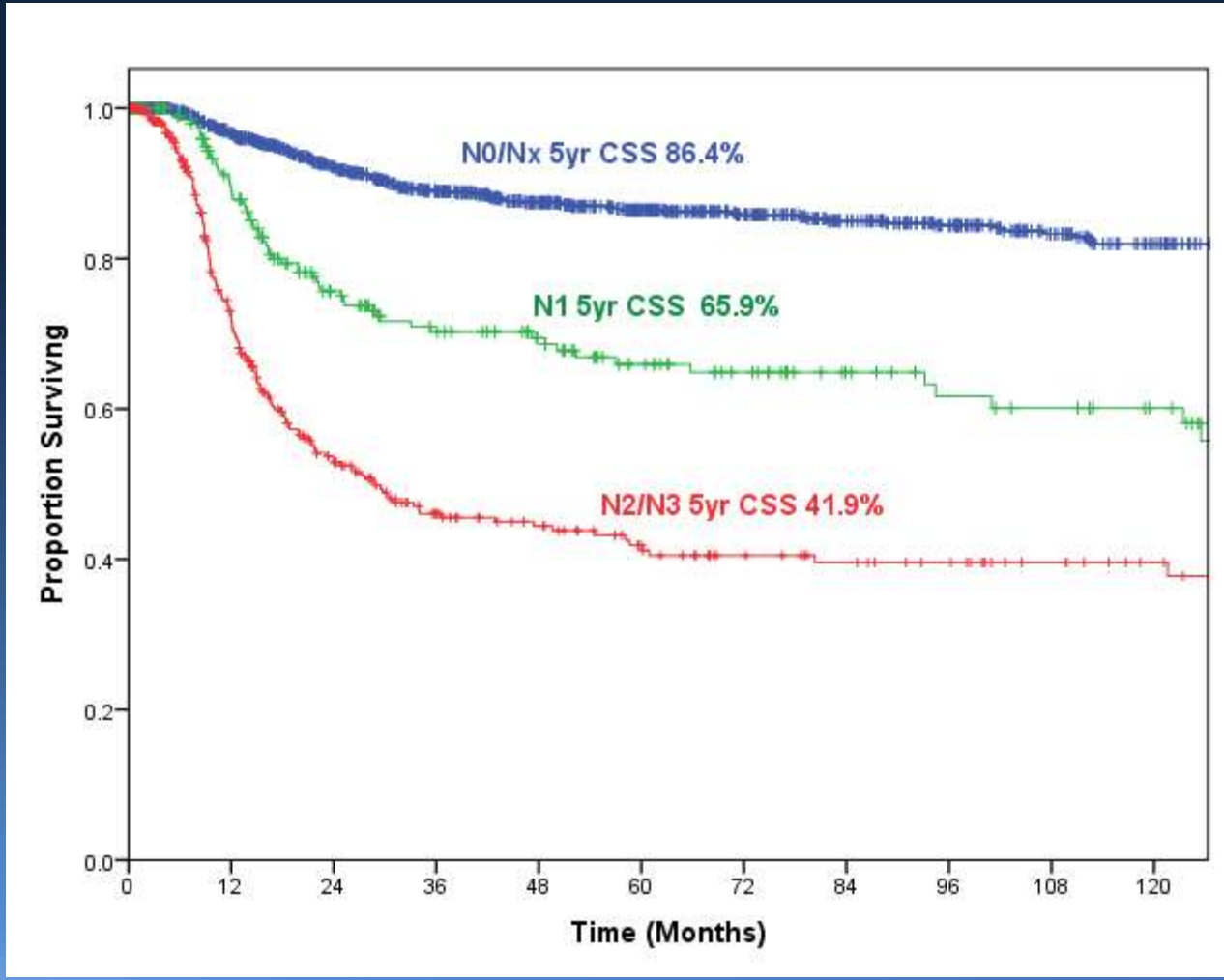


Median follow-up of 56 months (Range 1 – 343)

Cancer Specific Survival: Stage Groups

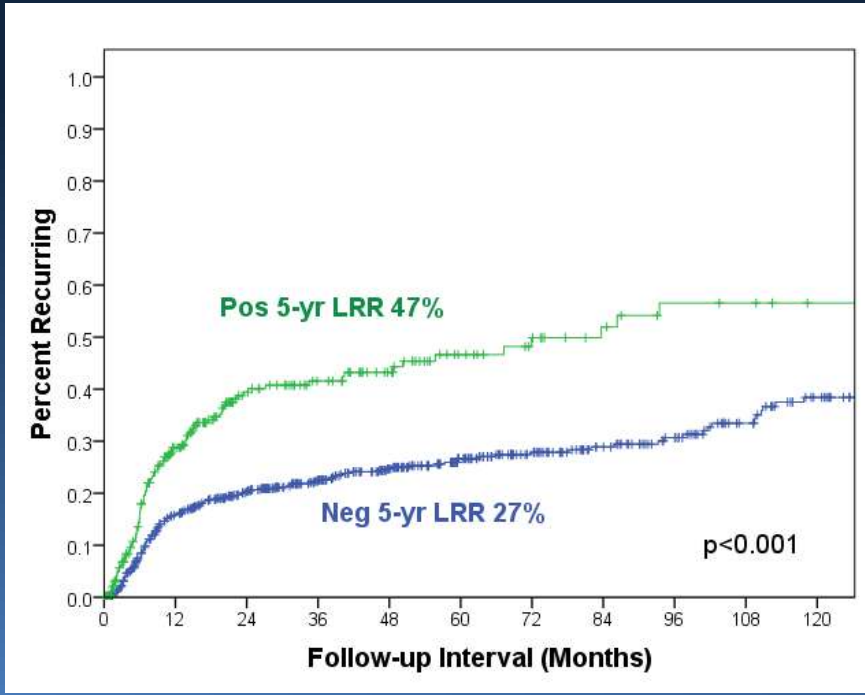


Cancer Specific Survival: N Stage

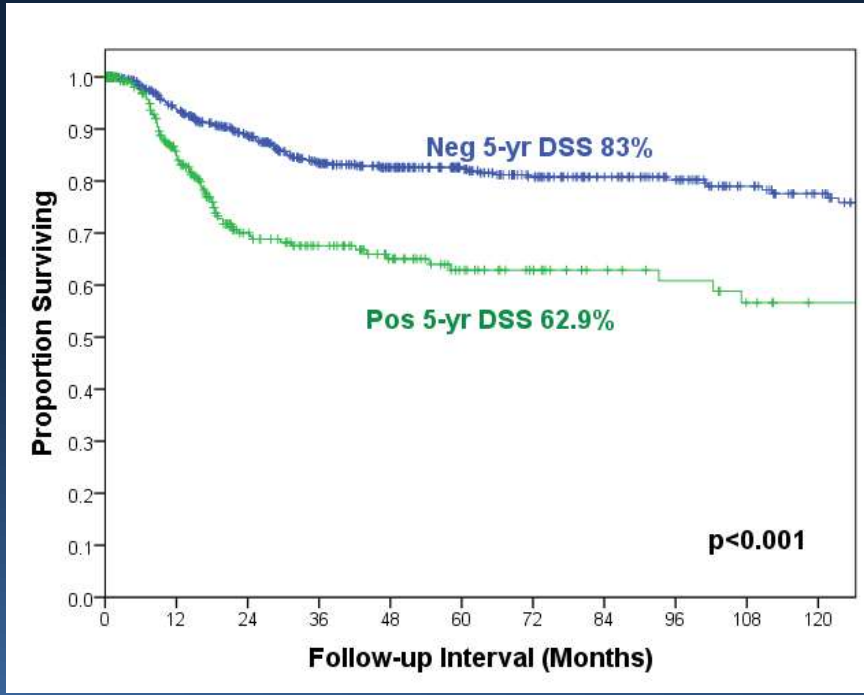


Margins of Surgical Resection

Margin Status in Tongue Cancer



LR Recurrence



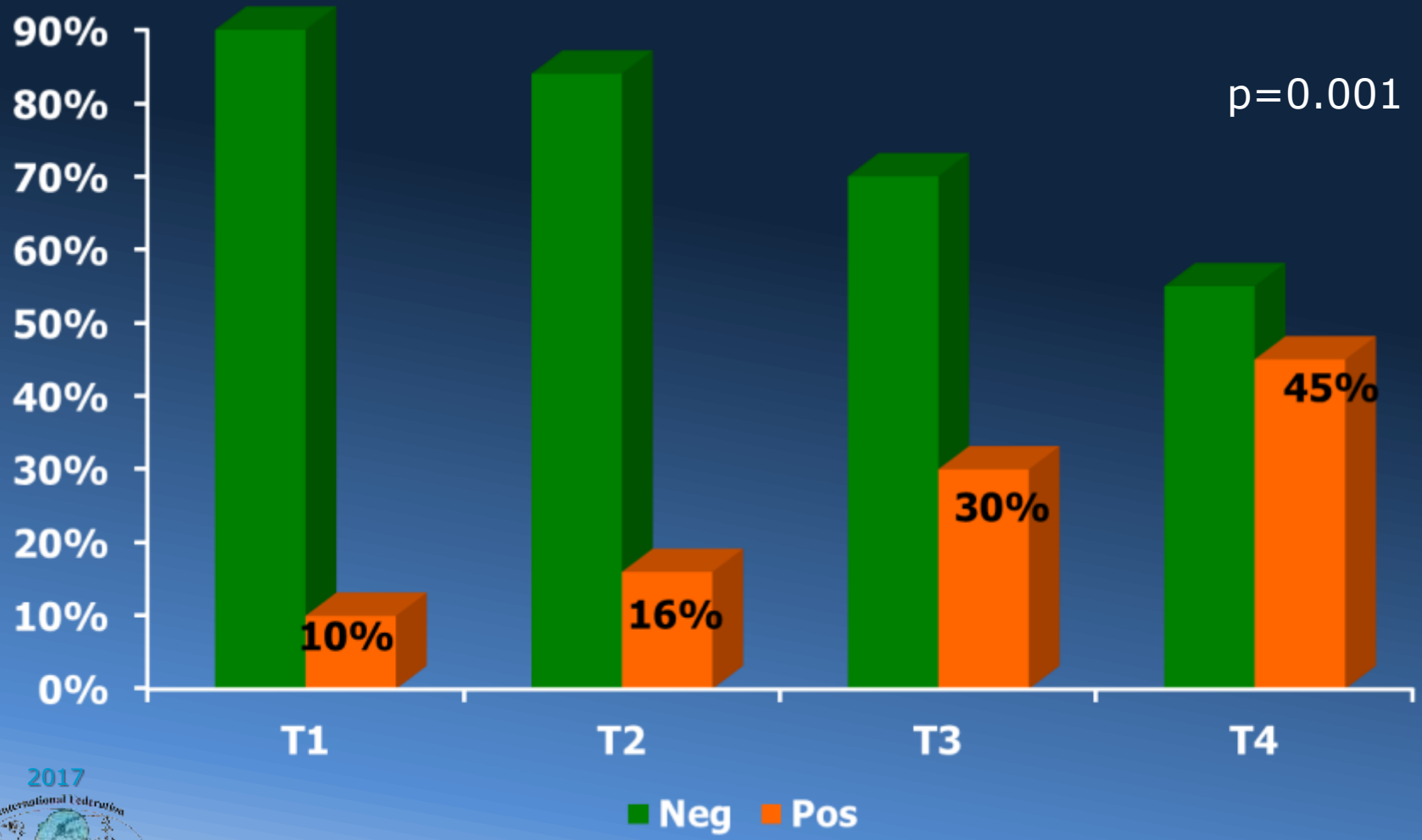
DSS

Patients with positive surgical margins have significantly worse outcome

2017

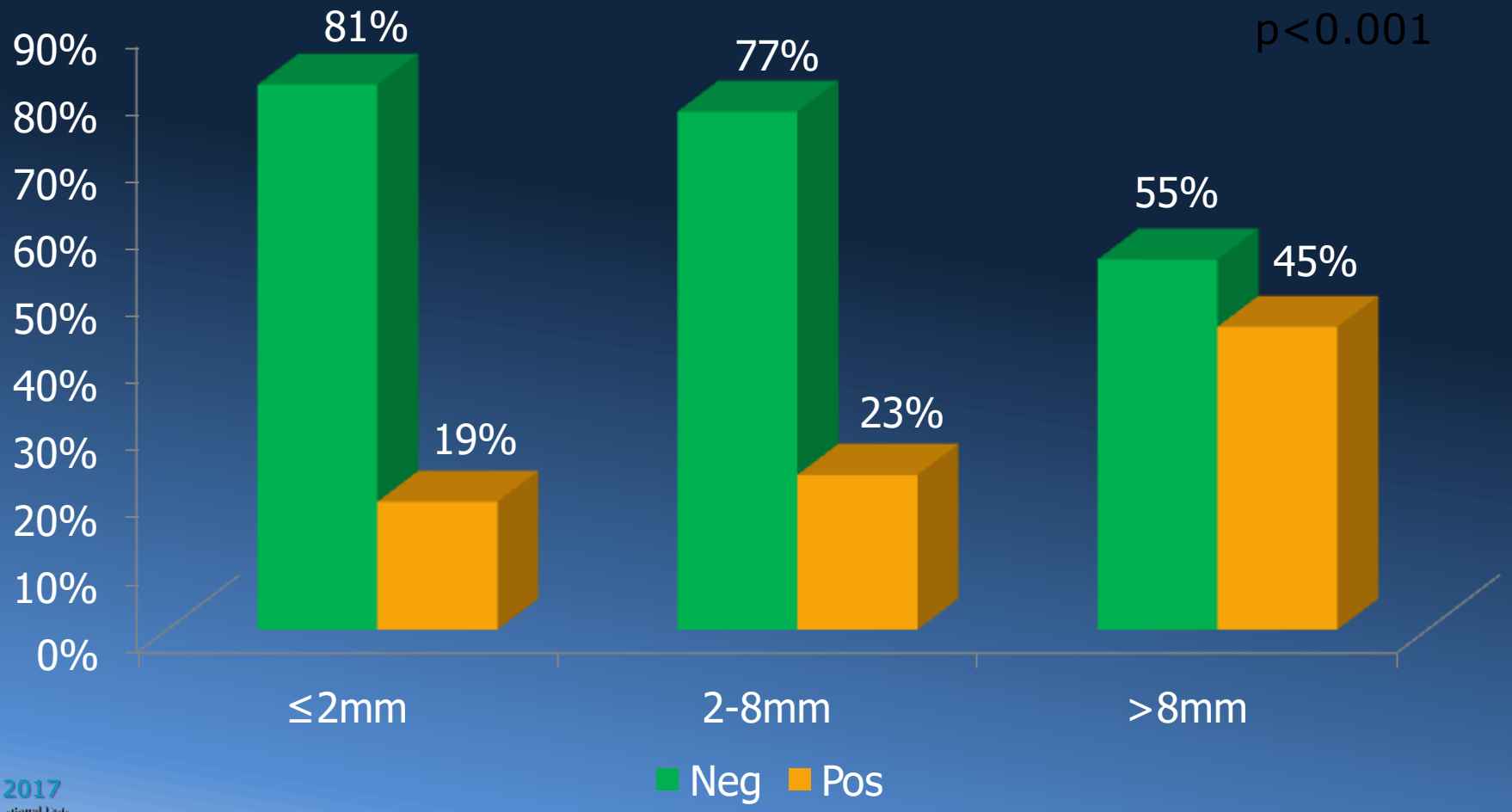
MSKCC Outcomes; 1985-2012

Risk for positive margins: T Stage



MSKCC Outcomes; 1985-2012

Thicker Tumors Are at Higher Risk for Positive Margins

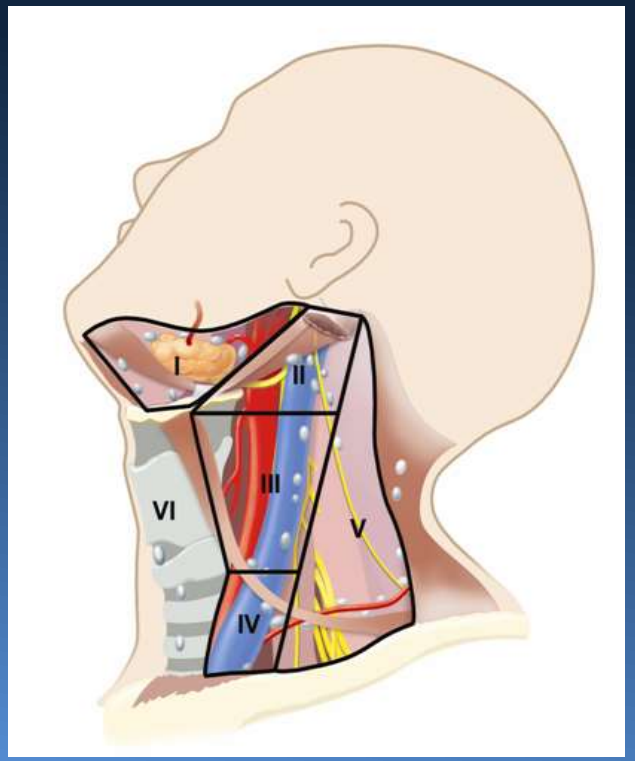


MSKCC Outcomes; 1985-2012

Margin status as surrogate for biological behavior of tumor

Positive Margin → Aggressive Tumor → Escalate Treatment

Management of the Neck

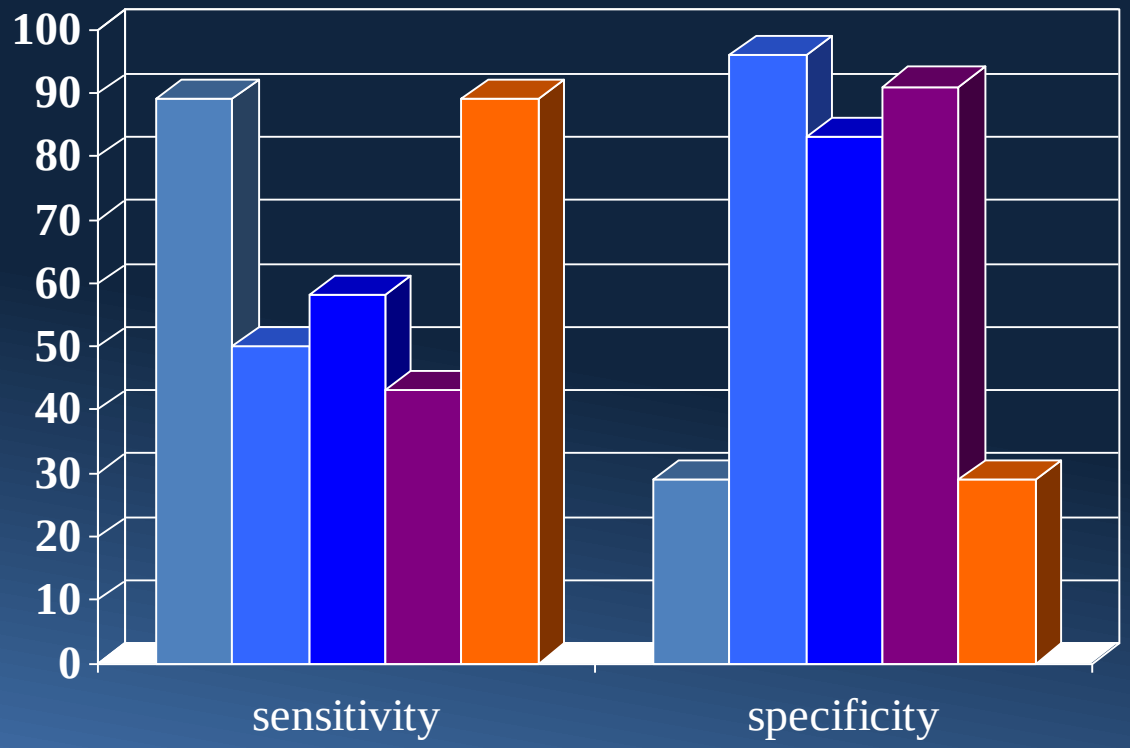


Controversy: Management of the Neck in Oral Cancer

- Cervical node involvement is the most significant prognostic factor in mucosal SCC
- Management of the neck should be part of a comprehensive treatment plan
- Should selection of patients for neck treatment be based on clinical criteria alone?
  – tumour site and stage

Leemans CR, Tiwari R, Nauta JJ, van der Waal I, Snow GB. Regional lymph node involvement and its significance in the development of distant metastases in head and neck carcinoma. Cancer 1993;71:452–456.

Histopathological Parameters as Predictors of Metastasis



Ross et al Ann Surg Oncol Feb 2004

Risk of Nodal Involvement by Site and T Stage

	T1	T2	T3	T4
Oral Cavity	5-20%	17-30%	43-60%	50-76%

O'Brien et al, ANZ J Surg, 1987

Multivariate predictors of occult neck metastasis in early oral tongue cancer

ANTHONY SPARANO, MD, GREGORY WEINSTEIN, MD, ARA CHALIAN, MD, MIKE YODUL, MD, and RANDAL WEBER, MD,
Philadelphia, Pennsylvania

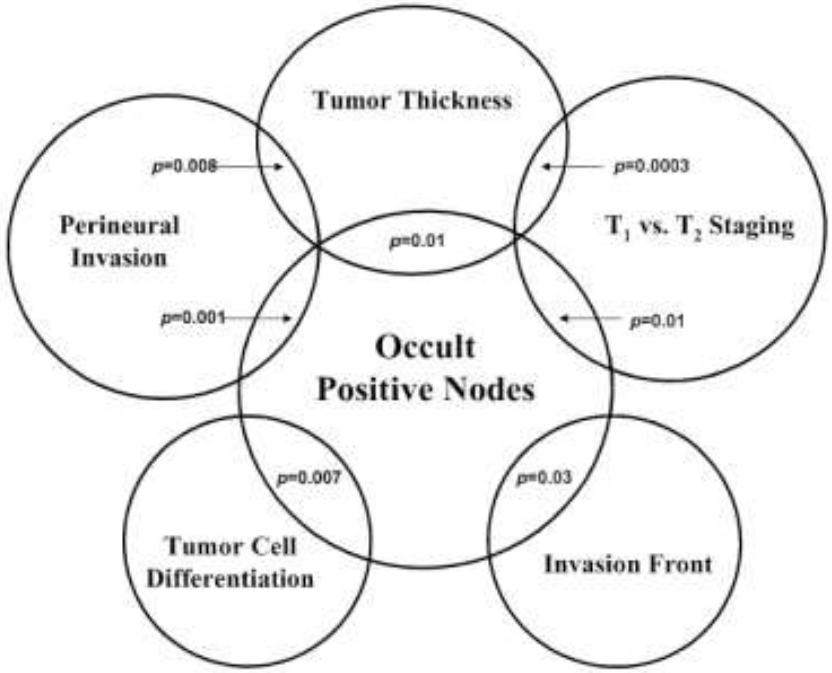
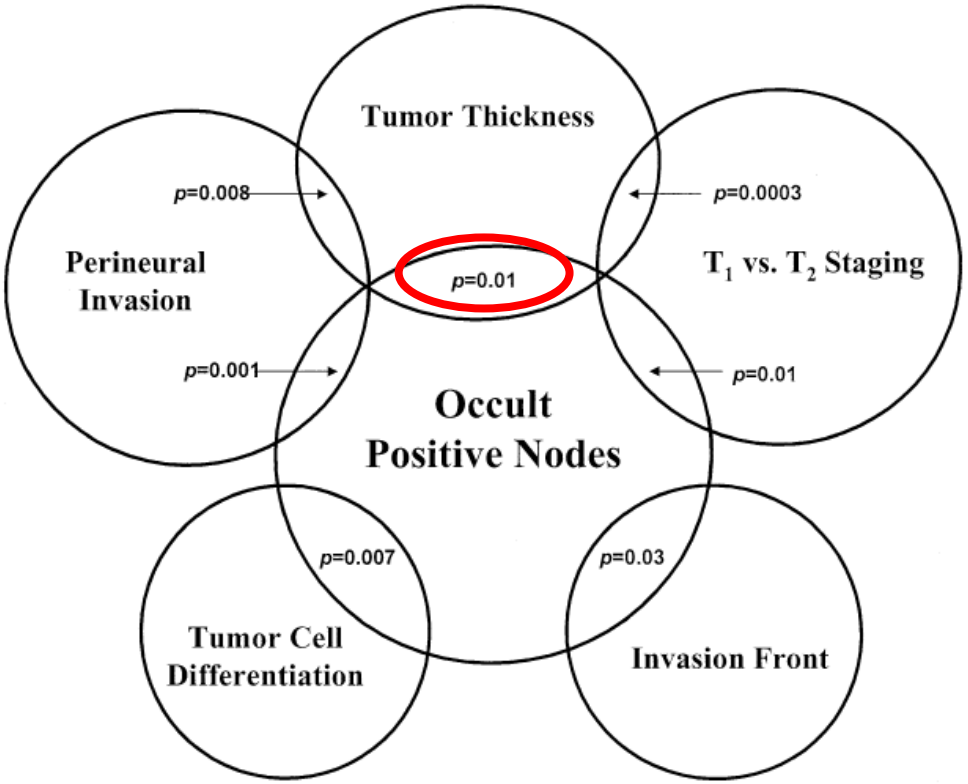


Fig 1. Relationships of correlates retained in the multivariate model with each other, as well as with the presence of neck micrometastasis by univariate analysis.

2017

Sparano A, Weinstein G, Chalian A, Yodul M, Weber R. Multivariate predictors of occult neck metastasis in early oral tongue cancer. Otolaryngol Head Neck Surg. 2004 Oct;131(4):472-6.

Tumor Thickness



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Decision Making: Elective Neck Dissection

Table 4. Multivariable model for occult neck metastasis

Correlates	Coefficients	Standard error	Odds ratio	*P* value
Tumor thickness (mm)	0.43	0.25	1.54	0.08
Perineural invasion	3.33	1.44	28.03	0.02
Infiltrating invasion front	6.26	2.85	525.57	0.02
Poorly differentiated	2.23	1.37	9.33	0.10
T_2 stage	2.13	1.31	8.38	0.10

- Perineural invasion and infiltrating front most predictive
- Tumor thickness important to the model
- Differentiation and stage improve fit and reduce error

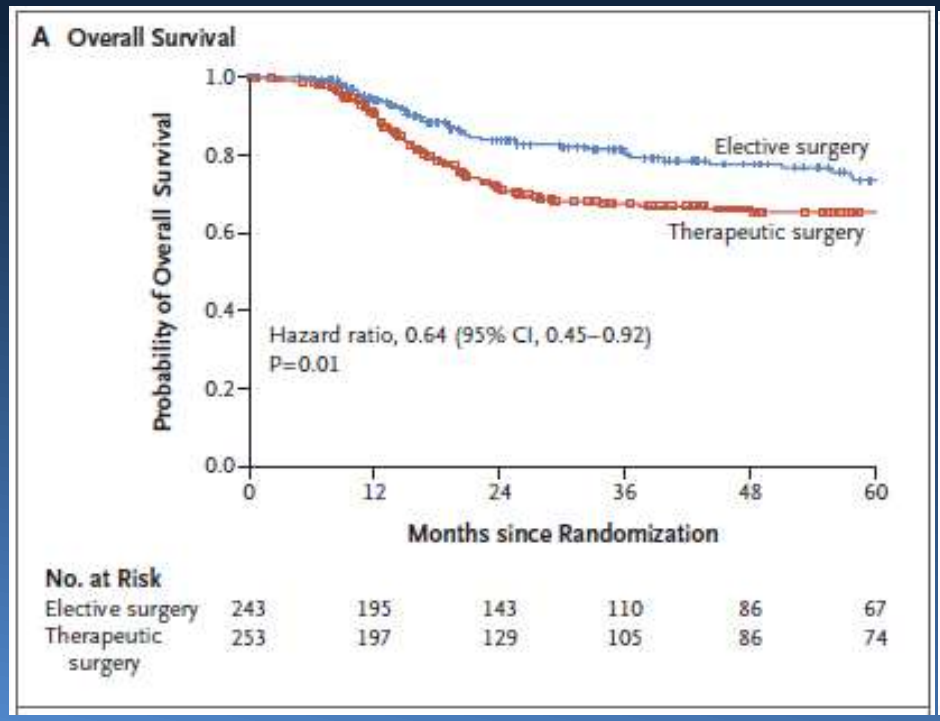
Sparano A, Weinstein G, Chalian A, Yodul M, Weber R. Multivariate predictors of occult neck metastasis in early oral tongue cancer. Otolaryngol Head Neck Surg. 2004 Oct;131(4):472-6.

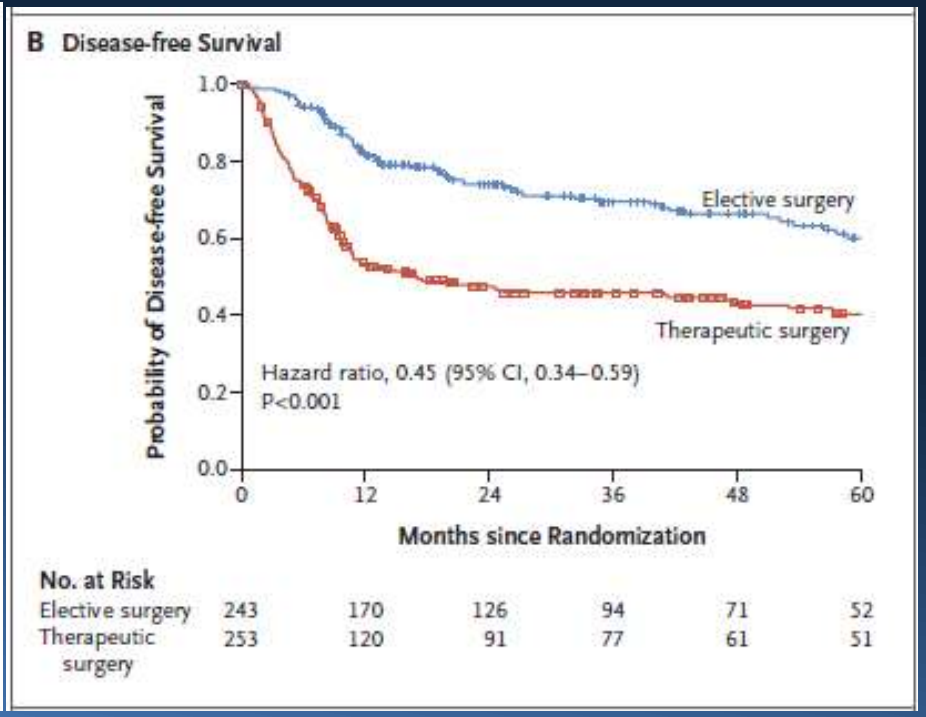
ORIGINAL ARTICLE

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., Anuja Deshmukh, M.S., D.L.O., D.O.R.L., Shubhada Kane, M.D., Supreeta Arya, M.D., D.N.B., D.M.R.D., Sarbani Ghosh-Laskar, M.D., D.N.B., Pankaj Chaturvedi, M.S., F.A.I.S., Prathamesh Pai, M.S., D.N.B., D.O.R.L., Sudhir Nair, M.S., M.Ch., Deepa Nair, M.S., D.N.B., D.O.R.L., and Rajendra Badwe, M.S., for the Head and Neck Disease Management Group

Overall Survival and Disease-free Survival





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. Elective versus Therapeutic Neck Dissection in Node-Negative Oral Cancer. N Engl J Med. 2015 May 31. Epub ahead of print.

Pattern of Recurrence

Table 2. Pattern of Recurrence.

Recurrence	Elective-Surgery Group (N=81)	Therapeutic-Surgery Group (N=146)
	number (percent)	
Nodal*	25 (30.9)	108 (74.0)
Local	23 (28.4)	7 (4.8)
Distant metastasis	3 (3.7)	3 (2.1)
Combination of above†	4 (4.9)	8 (5.5)
Second primary tumor	16 (19.8)	11 (7.5)
Not known	10 (12.3)	9 (6.2)

* In the elective-surgery group, nodal recurrence was defined as any recurrence in the neck. In the therapeutic-surgery group, nodal recurrence was defined as the development of first nodal disease after the excision of the primary tumor.

† Four patients in elective-surgery group and 6 patients in the therapeutic-surgery group had cervical lymph-node metastasis in combination with recurrence at a local or distant site.

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. Elective versus Therapeutic Neck Dissection in Node-Negative Oral Cancer. N Engl J Med. 2015 May 31. Epub ahead of print.

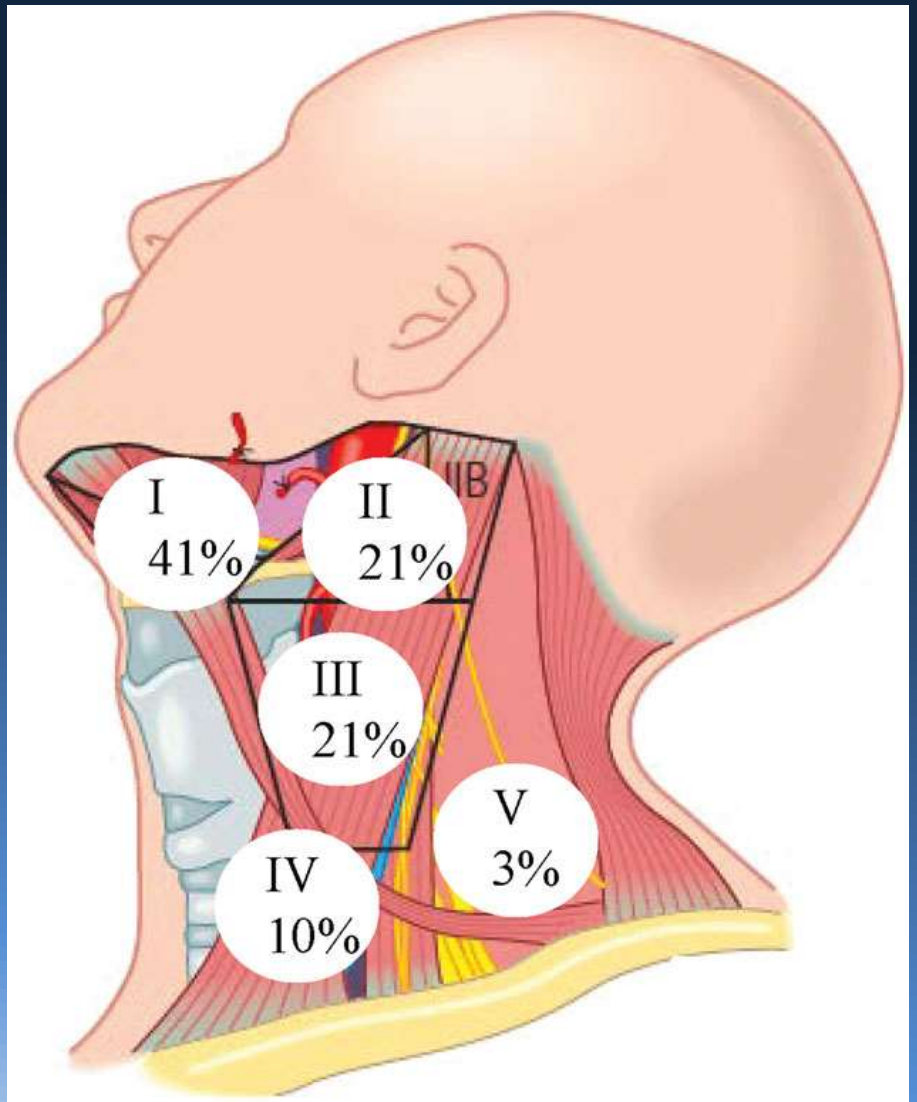
Long-Term Regional Control and Survival in Patients With "Low-Risk," Early Stage Oral Tongue Cancer Managed by Partial Glossectomy and Neck Dissection Without Postoperative Radiation

The Importance of Tumor Thickness

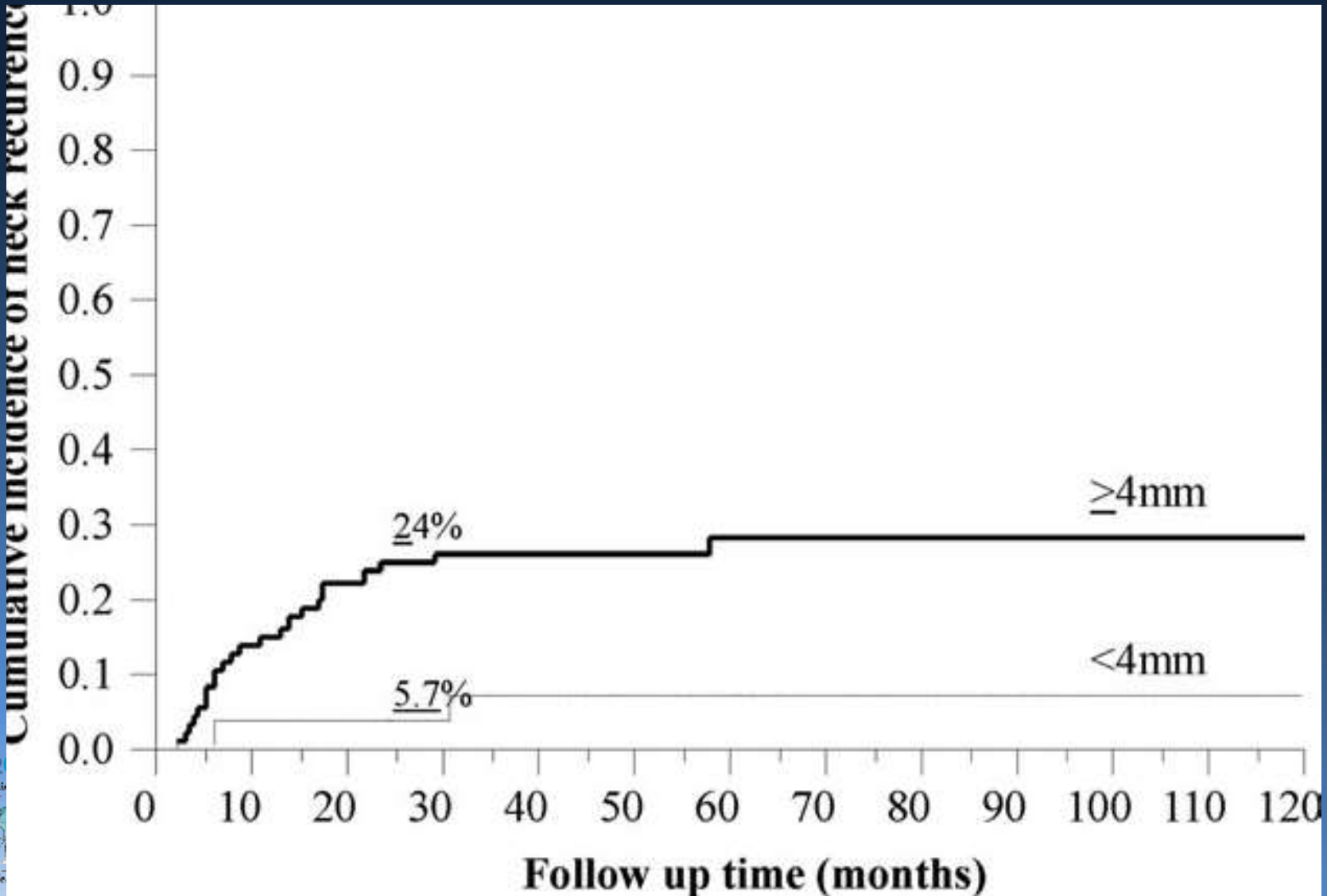
Ian Ganly, MD, PhD1;
David Goldstein, MD4;
Diane L. Carlson, MD3;
Snehal G. Patel, MD1;
Brian O'Sullivan, MD5;
Nancy Lee, MD2;
Patrick Gullane, MD4;
Jatin P. Shah, MD1

Cancer March 2017 Pages 1168-1178.

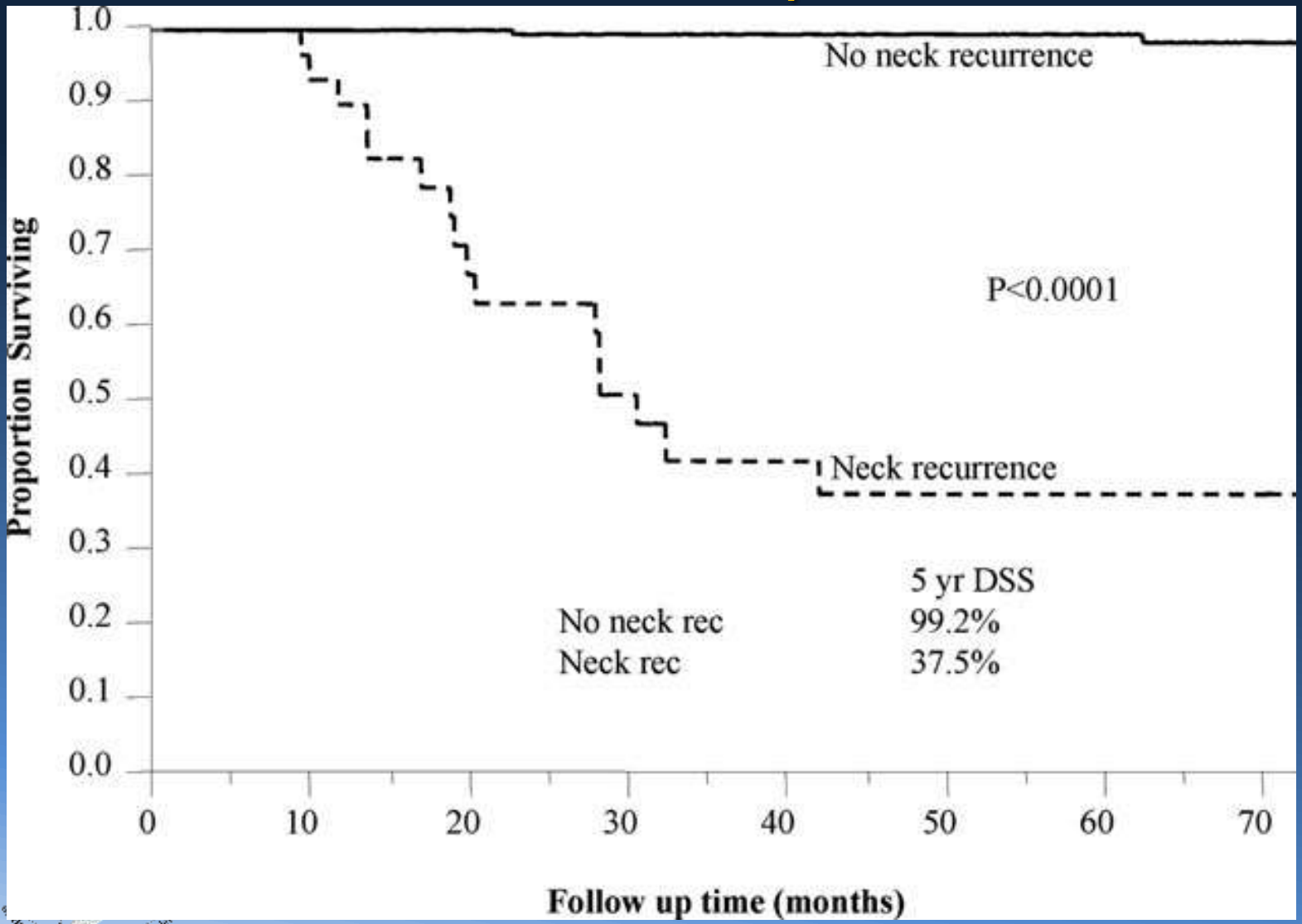
The Sites and levels of neck recurrence are illustrated in patients with pathologic T1-T2N0 oral tongue cancer who underwent partial glossectomy and ipsilateral elective neck dissection without postoperative radiation



The rate of neck recurrence is illustrated in patients who had pathologic T1-T2N0 oral tongue cancer stratified according to thickness of the primary tumour >4mms <4mm



Disease-specific survival (DSS) is illustrated for patients who had pathologic T1-T2N0 Oral Tongue Cancer Stratified by Neck recurrence

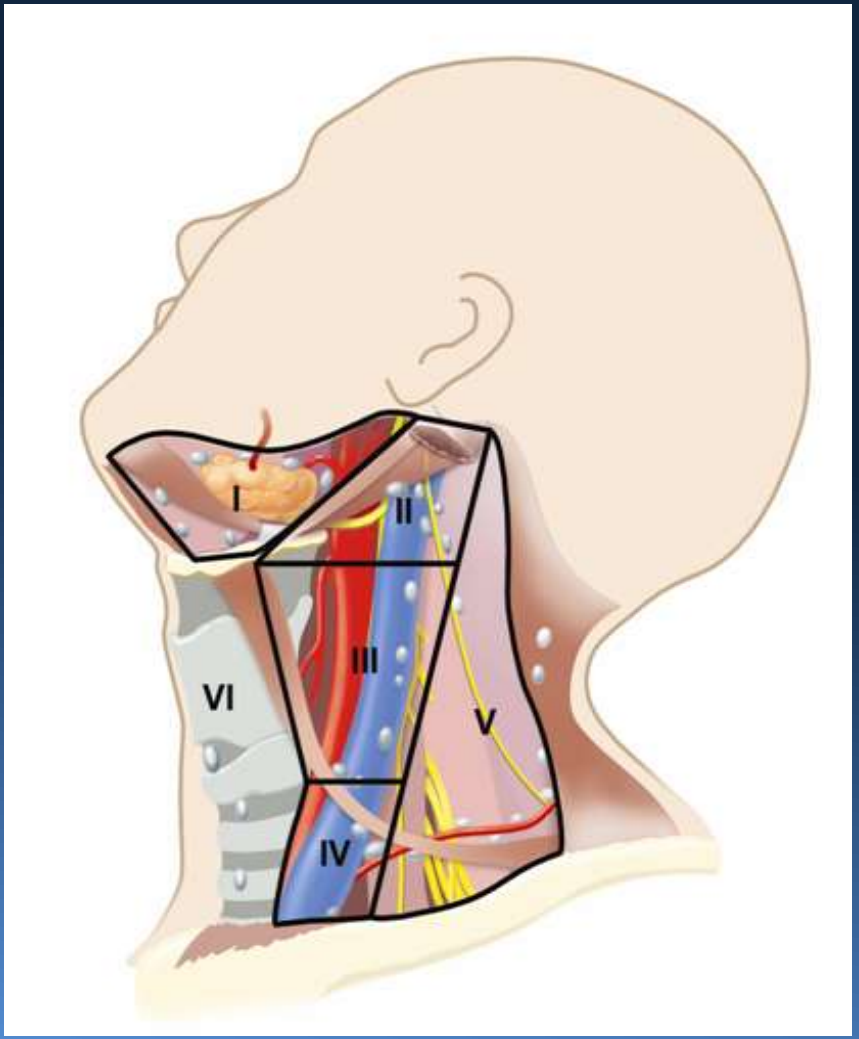


Conclusions

- Patients with low-risk, pathologic T1-T2N0 OTSCC had a greater than expected rate of neck
- Failure, with contralateral recurrence accounting for close to 40% of recurrences.
- Failure occurred predominantly in patients who had primary tumors that were 4 mm thick.
- Cancer 2013;119:1168-76.
- *V*C 2012 American Cancer Society.

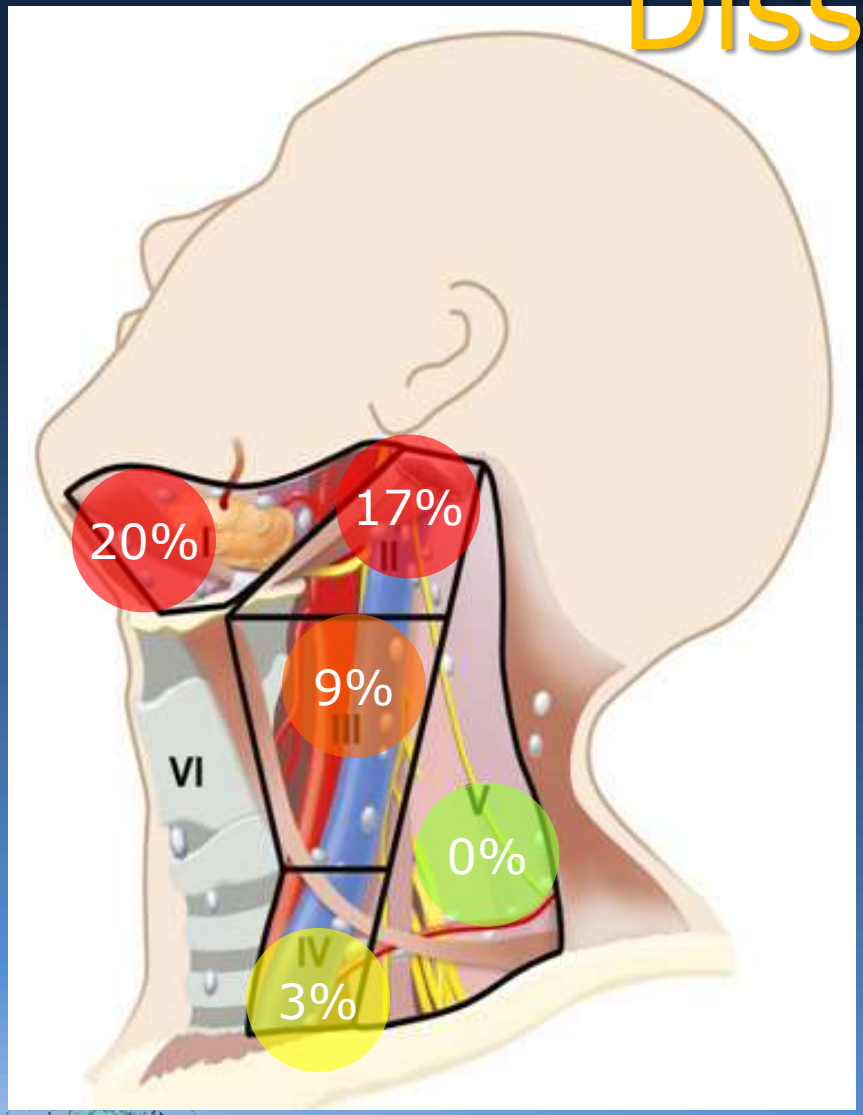
The Clinically Positive Neck

- Comprehensive neck dissection including levels I-V (sparing VA)
- Postop adjuvant treatment as indicated



Therapeutic Options for management of the cN0 Neck

Extent of Elective Neck Dissection



Levels I-III are at highest risk

- Level I = 20%
- Level II = 17%
- Level III = 9%
- Level IV = 3%
- Level V = 0%

- Level IV involved in 2-6%
  RMT 6% > BM 4% > OT 2%

Shah JP et al. *Cancer* 1990; 66: 109-113

Arguments against END

- Routine END over-treats the majority of patients since only 20-30% have occult metastases
- Increased contralateral neck failure
  END disrupts normal lymphatic channels & diverts "in transit" mets to other lymphatic basins
- Added initial cost and morbidity
- No survival advantage for END over observation in 4 prospective RCCTs

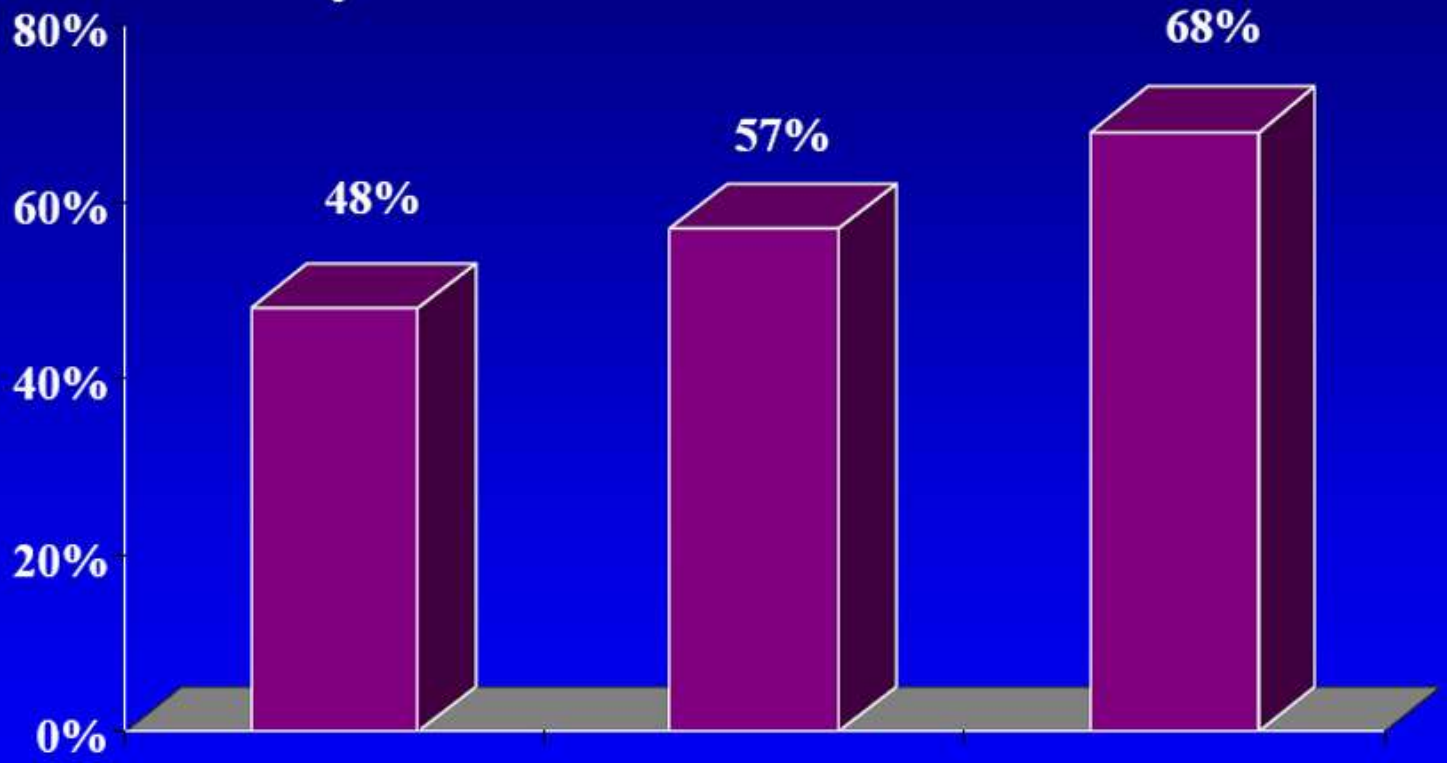
Vandenbrouck et al. Cancer 1980; 46: 386-90
Fakih et al. Am J Surg 1989; 158: 308-13
Kligerman et al. Am J Surg 1994; 168: 391-4
Yuen et al. Head Neck 1997; 19:583-8

Conclusion

- Changing distribution of primary tumor:
  - Oral tongue 48% of all oral ca: The highest reported from our institute
- Improved Outcome: 5-year overall survival
  - 1960~1964: 48%
  - 1979~1983: 57%
  - 1986~1995: 68%
- Significant predictors:
  - Disease-specific survival: surgical margins and pathologic N stage

Oral Cancer
Changing Trends in Outcome at MSKCC

5-year Overall Survival



J. Shah

Oral Cancer Results

Improvement in results is seen due to:

- Early identification and treatment of nodal metastases
- Employment of adjuvant therapy

Oral Cancer Improvement in quality of life is seen due to

- Contemporary surgical techniques
- Preservation or reconstruction of mandible and soft tissues
- Osseointegrated implants