XXII CONGRESSO NAZIONALE AIRO
Roma, 17-20 Novembre 2012

Associazione Italiana Radioterapia Oncologica

Strategie terapeutiche nelle metastasi laterocervicali da focus ignoto

I volumi clinici

F. **Paiar**

Focus Points

- Rare disease
- No randomized or prospective studies
- Poor knowledges on the molecular biology of cervical CUP

ORIGINAL ARTICLE

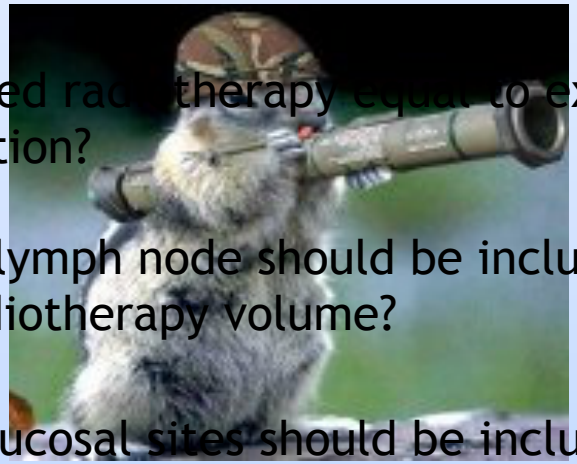
Metastatic Carcinoma of the Neck of Unknown Primary Origin

Evolution and Efficacy of the Modern Workup

Joshua D. Waltonen, MD; Enver Ozer, MD; Nathan C. Hall, MD, PhD; David E. Schuller, MD; Amit Agrawal, MD

had not undergone metabolic imaging. In contrast, after the introduction of PET-CT at our institution, primary tumors were detected in a significantly higher proportion of patients (31 of 52 [59.6%]) compared with those who did not undergo PET-CT (53 of 131 [40.5%]) ($P = .02$). These results would seem to indicate that fusion of PET with CT appears to allow more precise localization of small and often otherwise clinically undetectable tumors. As such, the combination of PET-CT with panendoscopy and directed biopsies (with or without tonsillectomy) appears to offer the most sensitive method of detecting occult primary tumor location. We believe it is advantageous to have the results of such imaging before panendoscopy, so that special attention can be directed toward identified suspicious sites. As the technology of metabolic imaging improves, we would expect that smaller and smaller lesions will be detectable by PET.

Is limited radiotherapy equal to extended irradiation?



Which lymph node should be included in the radiotherapy volume?

What mucosal sites should be included in the radiotherapy volume?

CERVICAL LYMPH NODE METASTASES FROM OCCULT SQUAMOUS CELL CARCINOMA: CUT DOWN A TREE TO GET AN APPLE?

CARSTEN [illegible] M.D.,* VINCENT GREGOIRE, M.D., PH.D.,† AND K. KIAN ANG, M.D., PH.D.‡

*Department of [illegible]y, Klinikum rechts der Isar, TU Munich, Munich, Germany; †St. Luc University Hospital, Bru[illegible] ‡The University of Texas M. D. Anderson Cancer Center, Houston, TX

NO IMPACT ON OVERALL SURVIVAL

Endpoint	[illegible]al RT	Comprehensive RT	Surgery alone (Coker et al , Coster et al, Grau et al)
Median mucosal primary emergence rate (range)	8% (5–[illegible]	[illegible].5% (2–13)	25%
Median neck relapse rate (range)	51.5% (31–63)	[illegible])	34%
Median distant metastases rate (range)	38%	19% (11–[illegible]	nr
Median 5-year overall survival rate (range)	36.5% (22–41)	50% (34–63)	

Int. J. Radiation Oncology Biol. Phys., Vol. 50, No. 3, 2001

ROLE OF RADIOTHERAPY IN THE TREATMENT OF CERVICAL LYMPH NODE METASTASES FROM AN UNKNOWN PRIMARY SITE: RETROSPECTIVE ANALYSIS OF 113 PATIENTS

	Univariate analysis									Multivariate analysis	
	5-year OS			5-year DFS			T onset			Cox	Stepwise
	n	%	*p* value	*n*	%	*p* value	*n*	%	*p* value	*p* value	
All patients	113	40.7	—	96	27.0	—					
Treatment intent											
Curative	91	52								NS	<0.05
Palliative	22	0	<0.05								
Margin status											
Negative	62										
Positive	6		NS								
Age											
≤60 years	61	35.9		54	28.4		61	50.8			
>60 years	52	46.2	NS	42	24.7	NS	52	42.3	NS		
N stage											
N1 N2a	33	60.8		29	41.5		33	60.1			
N2b-c N3	80	32.7	<0.05	67	18.5	<0.05	80	53.5	NS	<0.05	NS
Treatment type											
ND + EBRT	62	47.4		58	26.2		50	68.4			
EBRT alone	51	31.5	<0.01	38	24.7	NS	63	45.6	NS	NS	NS
Chemotherapy											
No	92	43.1		79	28.8		79				
Yes	21	26.5	NS	17	16.9	NS	17		NS		
EBRT Volume											
Mucosal + neck	70	54.2		63	36.5		70	58.9			
Neck only	43	20.2	<0.01	33	13.1	<0.01	43	42.9	NS	NS	<0.05
EBRT Technique											
2D-EBRT	53	26.3		53	15.2		64	45.5			
3D-EBRT	43	69.1	<0.01	43	48.3	<0.01	49	73.6	<0.05	NS	NS

Int. J. Radiation Oncology Biol. Phys., 2007

ORIGINAL ARTICLE

Squamous Cell Carcinoma From an Unknown Head and Neck Primary Site

A "Selective Treatment" Approach

Rajan S. Patel, MBChB, MD, FRCS ORL-HNS; Jonathan Clark, MBBS, BSc, FRACS; Rebecca Wyten, MBBS, BSc; Kan Gao, BEng; Christopher J. O'Brien, AM, MBBS, MS, MD, FRACS

Objective: To assess the efficacy of limiting treatment to the involved neck by way of neck dissection and adjuvant radiotherapy and reserving other therapies for salvage in the management of metastatic cervical squamous cell carcinoma from an unknown head and neck primary site.

Design: Retrospective study of patients whose clinicopathological data had been prospectively collected in a comprehensive head and neck database.

Setting: A tertiary referral university hospital.

Patients: The study population comprised 70 patients with metastatic cervical squamous cell carcinoma from an unknown head and neck primary site.

Interventions: Neck dissection alone in patients with pN1 disease confined to the lymph node. All remaining patients received neck dissection and adjuvant postoperative irradiation of the involved (dissected) neck.

Main Outcome Measures: Incidence of primary, regional, and distant recurrence and disease-specific and overall survival.

Results: Nodal stage was pN1 in 5 patients (7%); pN2a in 13 (19%); pN2b in 30 (43%); pN2c in 4 (6%); and pN3 in 18 (26%). Neck dissection alone was performed in 10 patients (14%), while 60 patients (86%) underwent neck dissection and adjuvant irradiation. Median follow-up was 45 months. The primary tumor site emerged in 8 patients (11%). The 5-year control rates were 84% in the ipsilateral (dissected) neck and 93% in the contralateral (undissected) neck. The 5-year disease-specific and overall survival rates were 62% and 56%, respectively. Macroscopic extracapsular spread was the only statistically significant adverse prognostic factor ($P<.001$).

Conclusions: The results of our selective treatment approach compare favorably with the results of other reported protocols using comprehensive irradiation or concurrent chemoradiation. However, patients with extracapsular spread and pN2 or pN3 disease were at high risk of treatment failure and may benefit from adjuvant chemoradiation. Although our protocol spares patients of potentially morbid therapies, salvage is rarely successful.

Arch OtolaryngolHeadNeckSurg. 2007

ORIGINAL ARTICLE

Radiotherapeutic Management of Cervical Lymph Node Metastases From an Unknown Primary Site

Stephanie M. Perkins, MD; Christopher R. Spencer, MD; Rebecca D. Chernock, MD; Bruce H. Haughey, MB, ChB; Brian Nussenbaum, MD; Douglas R. Adkins, MD; David I. Kuperman, MD; Wade L. Thorstad, MD

Results: Overall survival at 2 years and 5 years was 87% and 77%, respectively. Cause-specific survival at 2 years and 5 years was 89% and 81%, respectively. There were no ipsilateral neck failures. There was no difference in overall survival between patients treated with IPSI or COMP radiation therapy. The contralateral neck was controlled in all patients receiving bilateral neck irradiation and in 95% receiving ipsilateral neck irradiation. Of the

tion therapy. Radiotherapy target volumes were categorized as either ipsilateral neck only (IPSI) or comprehensive (COMP), including both the potential mucosal surfaces and ipsilateral or bilateral neck. Human papillomavirus (HPV) status, as determined by p16 immunohistochemical analysis, was evaluated for 36 patients (74%).

p16-positive patients ($P = .06$).

Conclusion: IPSI radiation therapy demonstrated excellent locoregional control with no adverse effect on disease-free survival or overall survival.

Arch Otolaryngol Head Neck Surg. 2012

ORIGINAL ARTICLE

Radiotherapeutic Management of Cervical Lymph Node Metastases From an Unknown Primary Site

Stephanie M. Perkins, MD; Christopher R. Spencer, MD; Rebecca D. Chernock, MD; Bruce H. Haughey, MB, ChB; Brian Nussenbaum, MD; Douglas R. Adkins, MD; David I. Kuperman, MD; Wade L. Thorstad, MD

Table 4. Mean Radiation Dose to Nasopharynx and Oropharyngeal Structures

Structure	Radiation Dose, Mean, Gy: IPSI Treatment Group (n = 9)	Radiation Dose, Mean, Gy: COMP Treatment Group (n = 5)	*P* Value
Ipsilateral nasopharynx	58.0	59.0	.83
Ipsilateral tonsil	63.0	59.7	.72
Ipsilateral base of tongue	61.1	61.2	.18
Contralateral nasopharynx	36.9	59.3	<.05
Contralateral tonsil	35.7	60.0	<.005
Contralateral base of tongue	44.1	61.6	<.005

Abbreviations: COMP, comprehensive radiotherapy group as defined in the "Methods" section; IPSI, ipsilateral radiotherapy group as defined in the "Methods" section.

Arch Otolaryngol Head Neck Surg. 2012

METASTATIC CARCINOMA IN THE CERVICAL LYMPH NODES FROM AN UNKNOWN PRIMARY SITE: RESULTS OF BILATERAL NECK PLUS MUCOSAL IRRADIATION VS. IPSILATERAL NECK IRRADIATION

SARADA P. REDDY, M.D. AND JAMES E. MARKS, M.D.

Loyola University Chicago, Loyola-Hines Department of Radiotherapy, Maywood, IL

Table 4. Appearance of occult primary cancer

Treatment and technique	Number controlled/total number of patients				
	Patients with N1 nodes	Patients with N2a–N3 nodes		All patients	
Treatment					
*LND + †RT	2/3 (67%)	7/28 (25%)	$p = 0.11$	9/31 (29%)	$p = 0.09$
Biopsy + RT	1/6 (17%)	0/15 (0%)		1/21 (5%)	
Technique					
‡BT	1/4 (25%)	2/32 (6%)	$p = 0.002$	3/36 (8%)	$p = 0.0005$
§EB	2/5 (40%)	5/11 (46%)		7/16 (44%)	
Total	3/9 (33%)	7/43 (16%)		10/52 (19%)	

* LND—Lymph node dissection.
† RT—Radiotherapy.
‡ BT—Bilateral technique.
§ EB—Ipsilateral electron beam.

Contents lists available at ScienceDirect

Radiotherapy and Oncology

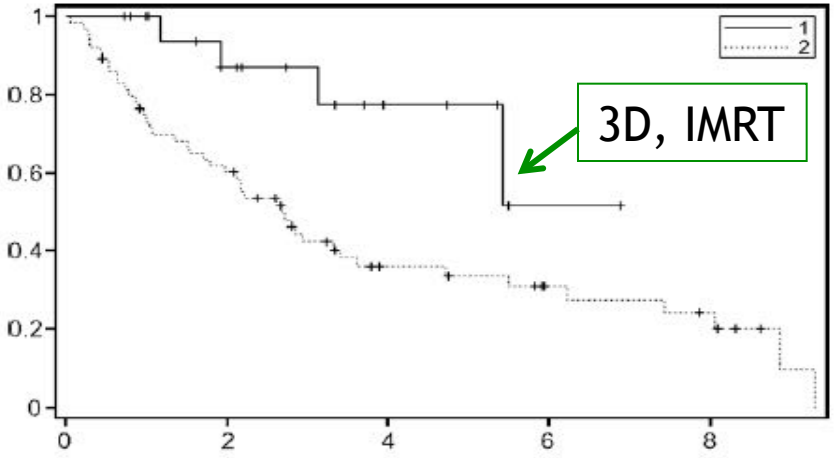
journal homepage: www.thegreenjournal.com

Neck node radiotherapy

Impact of target volumes and radiation technique on loco-regional control and survival for patients with unilateral cervical lymph node metastases from an unknown primary

A. Ligey [a,*], J. Gentil [b], G. Créhange [a], X. Montbarbon [c], P. Pommier [c], K. Peignaux [a], G. Truc [a], P. Maingon [a]

Regional control or recurrence	Unilateral irradiation $N = 59$	Bilateral irradiation $N = 36$	P
Regional control			
Yes	33 (56%)	27 (75%)	NS
No	20 (34%)	9 (25%)	
Neck node recurrence			
In-field	7 (12%)	7 (19%)	NS
Out-field	6 (10%)	0	
Mucosa or primary tumor emergence			
In-field	0	0	NS
Out-field	7 (12%)	2 (6%)	
Unknown	6 (10%)	–	

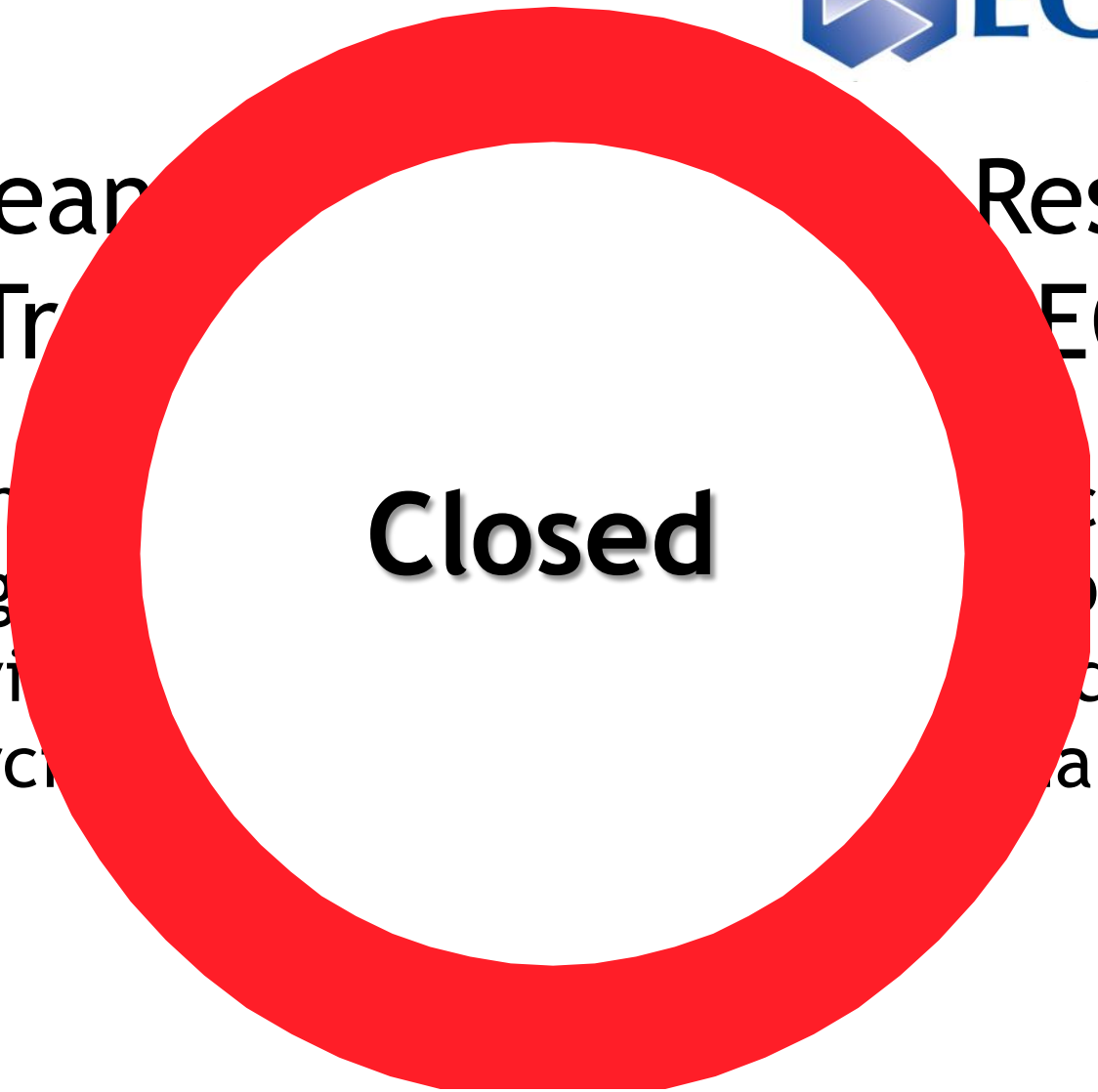


Nb of subjects in the survival analysis :

	At start	2 years (%)	6 years (%)	10 years (%)
Group 1 (3D or IMRT) :	20	12 (60)	1 (5)	1 (5)
Group 2 (2D) :	75	44 (59)	15 (20)	6 (8)

Conclusions: Retrospective comparisons between bilateral and unilateral neck radiotherapies did not show differences in terms of loco-regional control and survival. However, patient's local regional control and survival are significantly improved after 3D-CRT or IMRT.

Radiother. and Oncol. 2009



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Right Decision
Wrong Decision


COSTS
BENEFITS

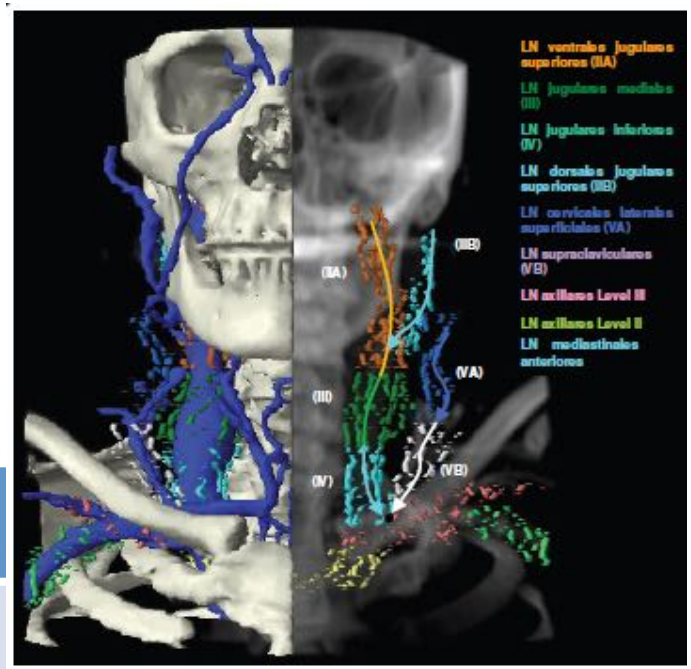
CERVICAL CUP: RADIOTHERAPY

MUCOSA PRIMARY
TUMOR EMERGENCE

REGIONAL CONTROL

ACUTE AND LATE
MORBIDITY
QUALITY OF LIFE

Which lymph node should be included in the radiotherapy volume?



Primary tumor	N0-N1	N2b
Oral cavity	I-IV	I-V
Oropharynx	II-IV+ retropharyngeal	I-V+ retropharyngeal
Hypopharynx	II-IV (+VI for esophageal extension)	I-V+ retropharyngeal (+VI for esophageal extension)
Larynx	II-IV (+VI for transglottic and subglottic tumors)	II-V(+VI for transglottic and subglottic tumors)
Nasopharynx	II-V+ retropharyngeal	II-V+ retropharyngeal

Gregoire V Radiother and Oncol 2000

Int. J. Radiation Oncology Biol. Phys., Vol. 37, No. 4, pp. 797–802, 1997

0360-3016/97 $17.00 + .00

PII S0360-3016(97)00025-4

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● *Clinical Investigation*

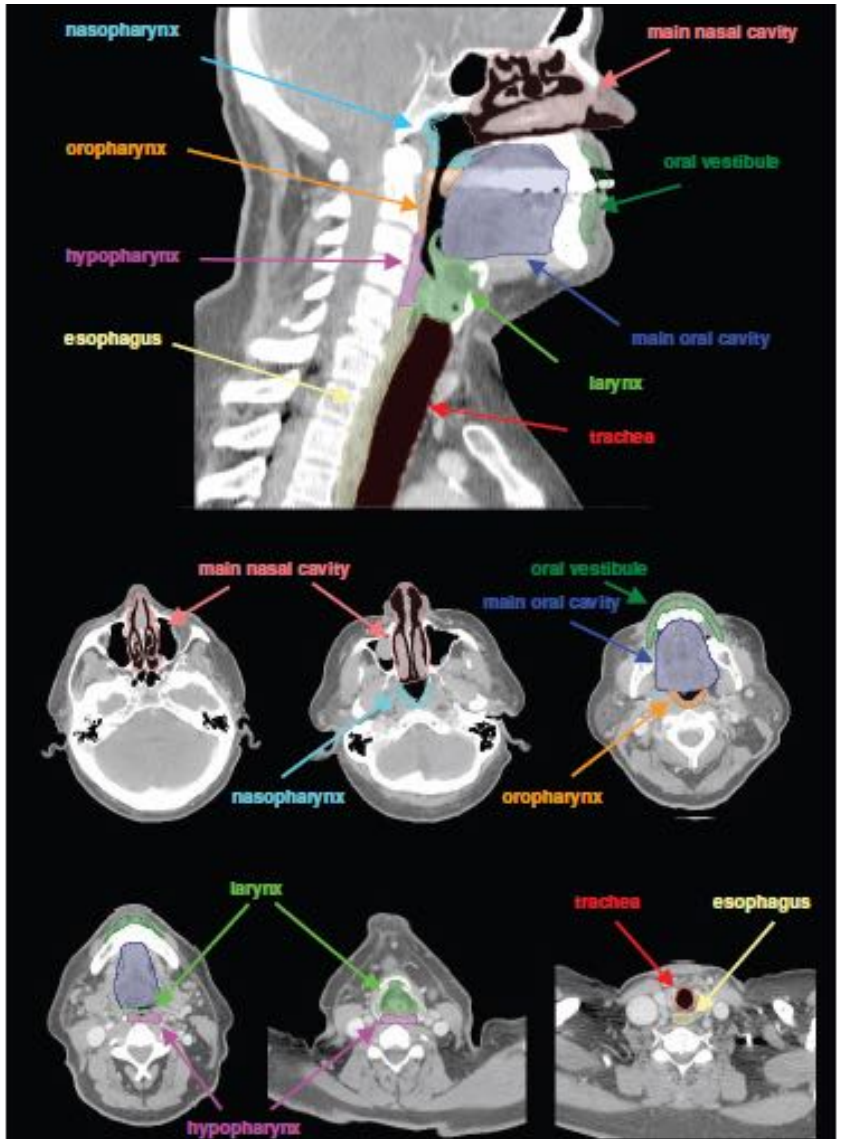
METASTATIC CARCINOMA IN THE CERVICAL LYMPH NODES FROM AN UNKNOWN PRIMARY SITE: RESULTS OF BILATERAL NECK PLUS MUCOSAL IRRADIATION VS. IPSILATERAL NECK IRRADIATION

SARADA P. REDDY, M.D. AND JAMES E. MARKS, M.D.

Loyola University Chicago, Loyola-Hines Department of Radiotherapy, Maywood, IL

Patients	RT Tecniques	Controlateral failure	Control rate in controlateral neck	P-Value
52	36 BT+M	14%	86%	P=0.03
	16 IT (electron)	44%	56%	

What mucosal sites should be included in the radiotherapy volume?



If comprehensive radiation therapy to putative mucosal sites is decided, it is possible to tailor the radiotherapy volumes according to the location of the metastatic lymph node.

Vorwerk and Hess Radiation Oncology 2011

Distribution of clinical metastatic neck nodes from HNSCC

Tumor site	Patients with N+ (%)	Distribution of metastatic lymph nodes per level (percentage of the node- positive patients)					
		I	II	III	IV	V	Other[b]
Oral cavity ($n = 787$)	36	42/3.5[c]	79/8	18/3	5/1	1/0	1.4/0.3
Oropharynx ($n = 1479$)	64	13/2	81/24	23/5	9/2.5	13/3	2/1
Hypopharynx ($n = 847$)	70	2/0	80/13	51/4	20/3	24/2	3/1
Supraglottic larynx ($n = 428$)	55	2/0	71/21	48/10	18/7	15/4	2/0
Nasopharynx ($n = 440$)	80	9/5	71/56	36/32	22/15	32/26	15/10

[a] Redrawn from Refs. [3,28,49].
[b] Parotid, buccal nodes.
[c] Ipsilateral/contralateral nodes.

V. Gregoire et al. Radiotherapy and Oncology 2000

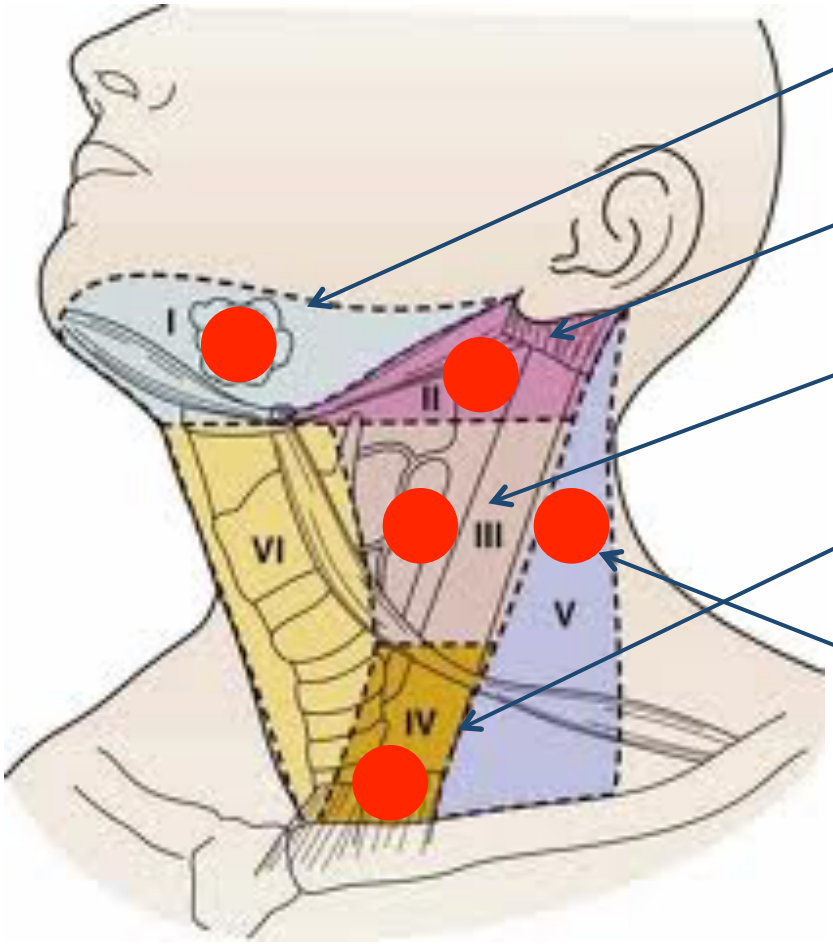
Incidence of retropharyngeal lymph nodes in HNSCC

Authors	Primary site	Incidence of retropharyngeal lymph nodes (percentage of the total number of patients)		
		Overall	N0 neck[a]	N+ neck[b]
McLaughlin et al. [33]	Oropharynx			
	Pharyngeal wall	18/93 (19[c])	6/37 (16)	12/56 (21)
	Soft palate	7/53 (13)	1/21 (5)	6/32 (19)
	Tonsillar fossa	16/176 (9)	2/56 (4)	14/120 (12)
	Base of tongue	5/121 (4)	0/31 (0)	5/90 (6)
	Hypopharynx (pyriform sinus or postcricoid area)	7/136 (5)	0/55 (0)	7/81 (9)
	Supraglottic larynx	4/196 (2)	0/87 (0)	4/109 (4)
	Nasopharynx	14/19 (74)	2/5 (40)	12/14 (86)
Chua et al. [14]	Nasopharynx	106/364 (29)	21/134 (16)	85/230 (37)
Chong et al. [12]	Nasopharynx	Not stated	Not stated	59/91 (65)

[a] Clinically negative nodes in levels I–V.
[b] Clinically positive nodes in levels I–V.
[c] Numbers in parentheses are in percentages.

V. Gregoire et al. Radiotherapy and Oncology 2000

Can the location of the lymph node indicate the site of origin of the primary tumor? IMPACT ON CLICAL TARGET VOLUME



LIVELLO I : cavo orale

LIVELLO II: rinofaringe, orofaringe, ipofaringe, laringe

LIVELLO III: rinofaringe, orofaringe, ipofaringe, laringe

LIVELLO IV: ipofaringe, laringe,

LIVELLO V: rinofaringe, ipofaringe

EPSTEIN-BARR VIRUS DETECTION IN NECK METASTASES BY IN-SITU HYBRIDIZATION IN FINE-NEEDLE ASPIRATION CYTOLOGIC STUDIES: AN AID FOR DIFFERENTIATING THE PRIMARY SITE

Wen-Ying Lee, MD,[1] Jenn-Ren Hsiao, MD,[2] Ying-Tai Jin, DDS, MS,[1] Sen-Tien Tsai, MD[2]

[1] Department of Pathology, National Cheng Kung University Medical College, Tainan, Taiwan.
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HEAD & NECK

ORIGINAL ARTICLE

Detection of Epstein-Barr Virus in Metastatic Lymph Nodes of Patients With Nasopharyngeal Carcinoma and a Primary Unknown Carcinoma

Kazunari Nakao, MD; Tadashi Yuge, MD; Masato Mochiki, MD; Ken-ichi Nibu, MD; Masashi Sugasawa, MD

Archives of
Otolaryngology–Head & Neck Surgery

ORIGINAL PAPER

Histologic Identification of Human Papillomavirus (HPV)-Related Squamous Cell Carcinoma in Cervical Lymph Nodes: A Reliable Predictor of the Site of an Occult Head and Neck Primary Carcinoma

Samir K. El-Mofty · Megan Q. Zhang · Rosa M. Davila

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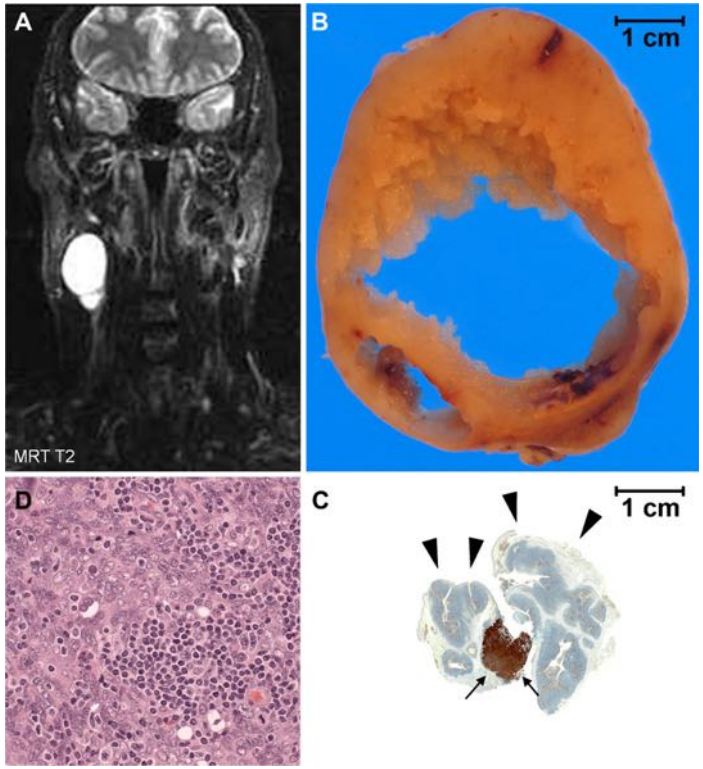
Virchows Arch (2012) 461:283–290
DOI 10.1007/s00428-012-1290-3

ORIGINAL ARTICLE

Cancer of unknown primary originating from oropharyngeal carcinomas are strongly correlated to HPV positivity

Pamela Zengel · Gerald Assmann · Martin Mollenhauer · Andreas Jung · Karl Sotlar · Thomas Kirchner · Stephan Hofler



- No classical risk factors (smoke, alchool)
- cystic transformation of nodal metastases
- atypical histological differentiation (lymphoepithelial and basaloid)

Human Pathology (2010) 41, 431–437

ELSEVIER

Human PATHOLOGY

www.elsevier.com/locate/humpath

Original contribution

The use of an immunohistochemical diagnostic panel to determine the primary site of cervical lymph node metastases of occult squamous cell carcinoma☆

Jung Mee Park MS[a], Chan Kwon Jung MD, PhD[b,*], Yeong Jin Choi MD, PhD[b], Kyo Young Lee MD, PhD[b], Jin Hyoung Kang MD, PhD[c], Min Sik Kim MD, PhD[d], Hae Jin Hu PhD[e]

Table 4 Expression patterns of variable markers according to primary tumor location in 101 metastatic squamous cell carcinomas

Markers	Oral cavity (n = 16)	Oropharynx (n = 38)	Hypopharynx (n = 26)	Larynx (n = 21)	*P*
CK5/6	16 (100%)	37 (97.4%)	26 (100.0%)	20 (95.2%)	.469
CK8/18	3 (18.8%)	15 (39.5%)	6 (23.1%)	8 (38.1%)	.309
CK10	10 (62.5%)	4 (10.5%)	5 (19.2%)	7 (33.3%)	.001
CK13	11 (68.8%)	30 (78.9%)	18 (69.2%)	15 (71.4%)	.790
CK14	14 (87.5%)	22 (57.9%)	21 (80.8%)	12 (57.1%)	.053
CK19	6 (37.5%)	28 (73.7%)	18 (69.2%)	13 (61.9%)	.079*
p16	3 (18.8%)	25 (65.8%)	3 (11.5%)	1 (4.8%)	<.001
pRb altered	8 (50.0%)	27 (71.1%)	15 (57.7%)	6 (28.6%)	.017

A comparison of the relationship between oral cavity (n = 28, 37.5%), oro- and hypopharynx (n = 46, 71.9%), and larynx (n = 13, 61.9%) primary tumors revealed significant differences in the level of CK19 ($P = .036$).

Squamous Cell Carcinoma Metastatic to the Neck from an Unknown Head and Neck Primary Site

William M. Mendenhall, MD, Anthony A. Mancuso, MD,†*
Robert J. Amdur, MD, Scott P. Stringer, MD,‡ Douglas B. Villaret, MD,‡*
and Nicholas J. Cassisi, DDS, MD‡

SEDE T PRIMITIVO	N° PAZ (%)
Tonsilla	25 (43)
Base lingua	23 (39)
Seno piriforme	5 (9)
Parete posteriore del faringe	2 (3)
Parete laterale del faringe	1 (2)
Vallecula	1 (2)
Epiglottide sopraioidea	1 (2)

Am J Otolaryngol 2001

AMERICAN JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL ARTICLE

Larynx-Sparing Radiotherapy for Squamous Cell Carcinoma From an Unknown Head and Neck Primary Site

Christopher A. Barker, BS, Christopher G. Morris, MS, and William M. Mendenhall, MD

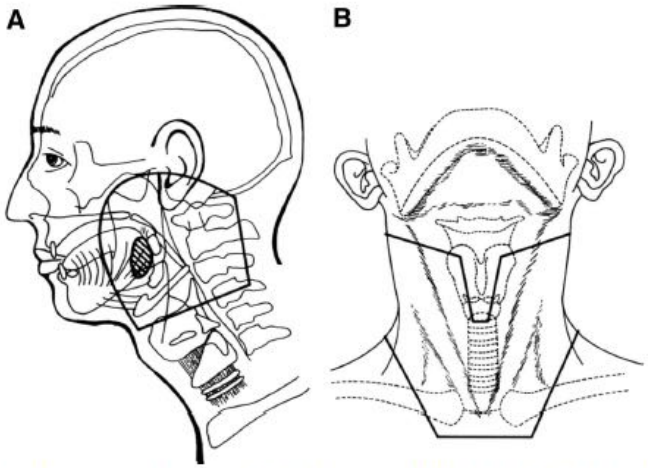
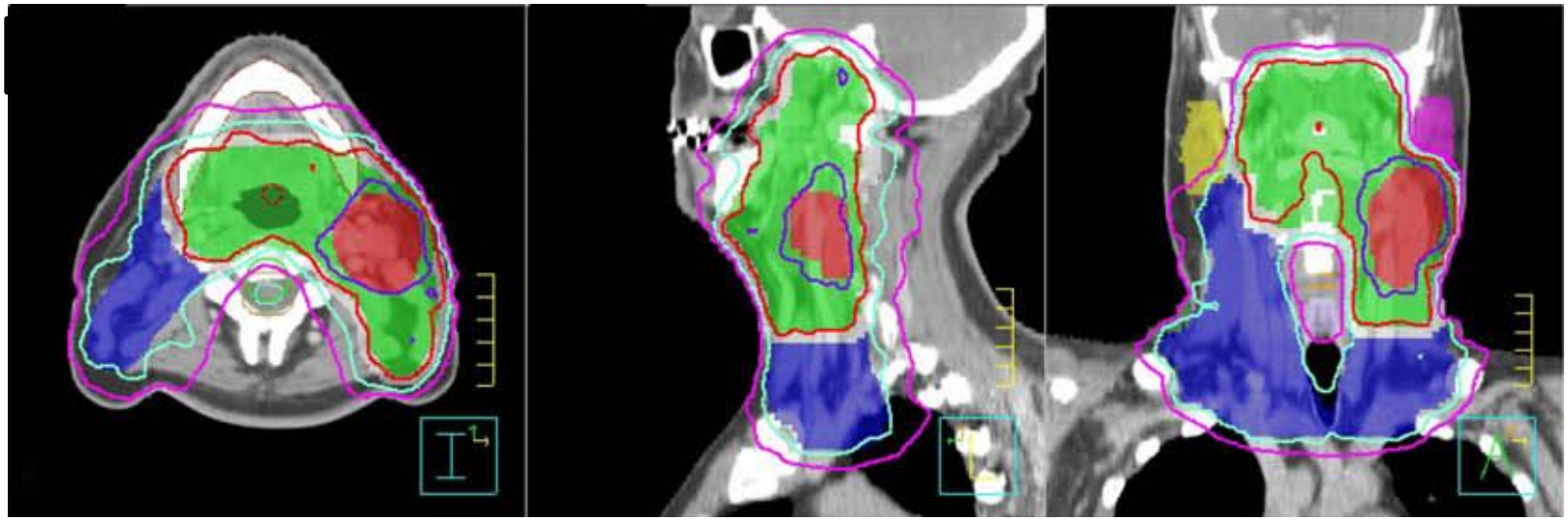


FIGURE 1. (A, B) Radiation portals sparing the larynx. A, Parallel-opposed fields include the primary lesion with a 2- to 3-cm inferior margin. The lower border of the field is placed at the thyroid notch and slants superiorly as the junction line proceeds posteriorly. This substantially reduces the amount of mucosa, larynx, and spinal cord included in the primary treatment portals. B, *En face* low-neck portal with tapered midline larynx block. It is not necessary to treat the supraclavicular fossa unless clinically positive nodes are found in that particular hemineck. A 5-mm midline tracheal block may be placed in the low-neck portal (dashed line). Reprinted with permission from Mendenhall WM, Parsons JT, Million RR. Unnecessary irradiation of the normal larynx. *Int J Radiat Oncol Biol Phys.* 1990;18:1531–1533 (Fig. 2A–B, p. 1533).

Is IMRT beneficial for cervical CUP patients?



IMRT IN CUP

			OS	CL
Klem et al 2008 (16 postop)	21	Omolateral mucosa+bilateral neck	85% (2 yrs)	90%
Lu et al 2008 (12 postop)	22	Extensive Rt Without hipopharinx and larynx	74.2% (2yrs)	88.5%
Madani 2008 (19 postop)	23	Extended putative mucosal and bilateral nodal sites (Without larynx in 60%)	74.8% (2yrs)	nr
Frank 2010 (13 postop)	52	Extensive Rt (Without hipopharinx and larynx in 33%)	89% (5yrs)	94% (5yrs)
Villeneuve 2012 (8 postop)	25	bilateral neck and ipsilateral putative pharyngeal mucosa	100% (3yrs)	100% (3yrs)

INTENSITY-MODULATED RADIOTHERAPY FOR CERVICAL LYMPH NODE METASTASES FROM UNKNOWN PRIMARY CANCER

INDIRA MADANI, M.D.,* LUC VAKAET, M.D., PH.D.,* KATRIEN BONTE, M.D.,† TOM BOTERBERG, M.D., PH.D.,* AND WILFRIED DE NEVE, M.D., PH.D.*

* Department of Radiotherapy and † Division of Head and Neck Surgery, Ghent University Hospital, Ghent, Belgium

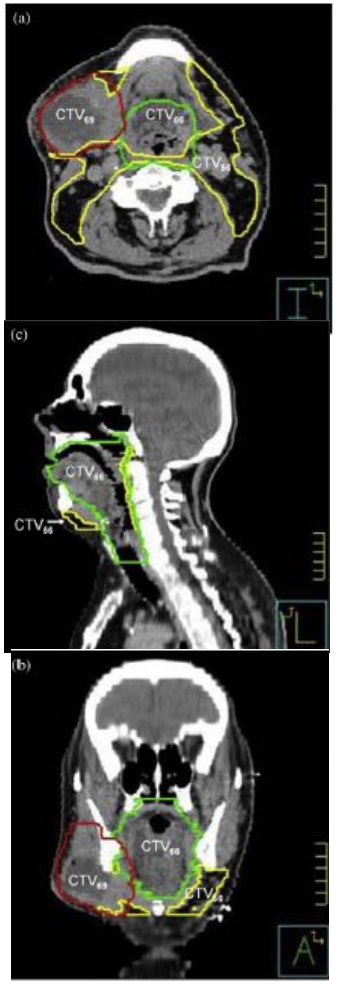


Table 5. Incidence of acute toxicity by grade in patients receiving intensity-modulated radiotherapy (IMRT) and in historical control patients

	Dysphagia		Mucositis†		Radiation dermatitis‡	
Treatment	G≤2	G3	G≤2	G3	G≤2	G3
IMRT patients ($n = 22$)	21 (95.5%)	1 (4.5%)	11 (50%)	11 (50%)	15 (68.2%)	7 (31.8%)
Historical controls ($n = 18$)	9 (50%)	9 (50%)*	7 (41.2%)	10 (58.8%)*	5 (33.3%)	10 (66.7%)*
p Value	0.003		0.82		0.08	

Table 6. Late toxicity by grade scored after at least 6 months of follow-up

	Dysphagia			Xerostomia*		Taste alteration	Skin		
Treatment	G0	G1–2	G3	G1–2	G3	G3	G0	G1–2	G3
IMRT patient ($n = 18$)	5 (27.8%)	13 (72.2%)	0	15 (88.2%)	2 (11.8%)	0	11 (61.1%)	7 (38.9%)	0
Historical control ($n = 15$)	7 (46.6%)	4 (26.7%)	4 (26.7%)	7† (46.6%)	8 (53.4%)	1 (6.7%)	4 (26.7%)	7 (46.6%)	4 (26.7%)
p Value		0.01		0.03				0.03	

CONCLUSIONS

In our study, use of IMRT for UPC resulted in 2-year overall survival and distant disease–free probability of 74.8% and 76.3%, respectively. The rates of acute (dysphagia) and late (dysphagia, xerostomia, and skin fibrosis) toxicity were significantly less compare with those in the historical control group. Re-evaluation of mucosal sites and dose reduction to elective nodal sites might further improve treatment outcomes. High rate of distant relapse over a short time warrants a combined treatment approach.

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EFFICACY AND TOXICITY OF CHEMORADIOTHERAPY USING INTENSITY-MODULATED RADIOTHERAPY FOR UNKNOWN PRIMARY OF HEAD AND NECK

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Late	
Esophageal stenosis	
Grade 2	2 (8)
Grade 3	11 (46)
Grade 4	0
Trismus	
Grade 1	3 (13)
Grade 2	0
Grade 3	0
Xerostomia	
Grade 1	12 (50)
Grade 2	6 (25)
Grade 3	0
Fibrosis	
Grade 1	2 (8)
Grade 2	1 (4)
Grade 3	0

CONCLUSION

Our experience using aggressive chemoradiotherapy with IMRT for HNCUP has demonstrated excellent local and distant tumor control with this approach. No locoregional failures developed, and no primaries emerged during a median of 2 years of follow-up. The rate of swallowing toxicity was significant, however, because almost one-half of the patients required esophageal dilation. These complications illustrate that as the oncologic outcomes in head-and-neck cancer patients continue to improve, patients are living longer with life-altering long-term toxicities. Additional strategies to optimize the therapeutic ratio in these patients are therefore urgently required, including reducing the mucosal target doses and/or omitting low-risk mucosal targets with high treatment-related toxicity, such as the larynx.

TAKE HOME MESSAGES

- The wide-field irradiation reduces the risk of tumor recurrence. However, it also causes significant morbidity. Therefore, the accurate identification of occult primary sites is to improving therapeutic efficacy.

- The type of treatment can be individualised depending on the patient's age, site, histology and extent of metastatic lymph node involvement of the tumour to decrease toxicity.

- IMRT compared with the conventional technique allows excellent bilateral neck and putative pharyngeal mucosa coverage, with few late salivary function toxicities

Grazie per l’attenzione!