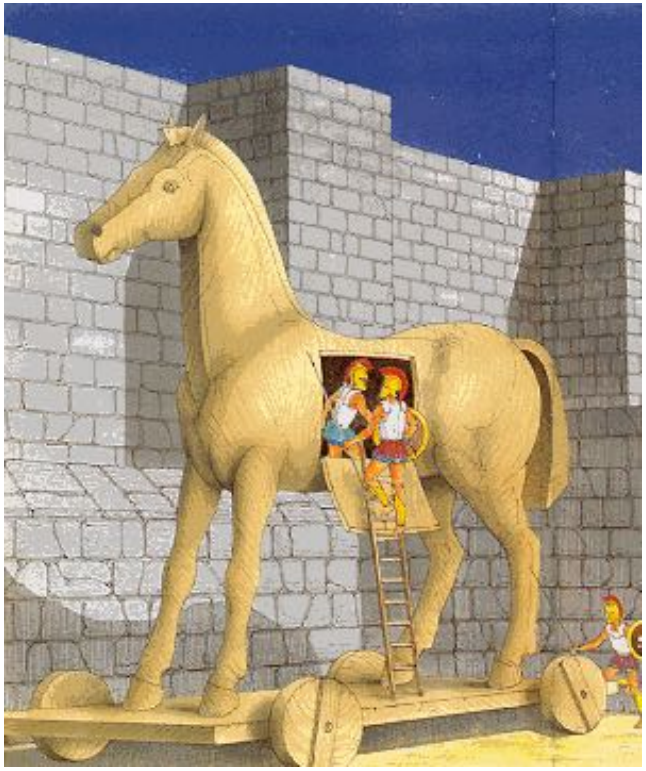

METASTASI LATEROCERVICALI DA FOCUS IGNOTO: LA GESTIONE DEGLI EFFETTI COLLATERALI.

Anna Merlotti
Radioterapia Busto Arsizio/Saronno (VA)

CASISTICHE DISOMOGENEE

- Only retrospective series.

- Treatment options range from surgical treatment of the neck alone to radiating bilateral necks, with or without radiation to possible primary sites as well ± chemotherapy.

TOSSICITA' POTENZIALMENTE MAGGIORE

- The radiation fields have classically covered all potential mucosal disease sites. Although this treatment has been effective, it has also been associated with significant long-term side effects, such as xerostomia and dysphagia

STRATEGIE PER RIDURRE LA TOSSICITA'

- Since the most common potential primary sites for HNCUP are located in oropharynx (base of tongue or tonsil), Mendenhall et al. at the University of Florida since 1997 (Am J Otolaryngol 2001;22:261-731) proposed to spare the larynx with opposed lateral fields matched at the thyroid notch to an anterior-posterior lower neck filed (AP field) with a midline laryngeal block.

- While this technique can reduce the doses to the larynx and hypopharynx that are critical for swallowing and speech, it delivers full dose to the parotids leading to xerostomia.

No. 4, pp. 1051–1058, 2007

-3016/07/$–see front matter

ELSEVIE

CLINICA and Neck

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Late toxicity (evaluated in 58 patients)*

Xerostomia	
Grade 0	23 (39.6)
Grade 1	15 (26.0)
Grade 2	16 (27.6)
Grade 3	4 (6.8)
Neck fibrosis	
Grade 0	40 (69.0)
Grade 1	10 (17.3)
Grade 2	16 (27.6)
Grade 3	4 (6.8)
Dysphasia	
Grade 0	51 (87.9)
Grade 1	6 (10.4)
Grade 2	1 (1.7)
Grade 3	0
Tooth decay	
Yes	6 (10.4)
No	52 (89.6)
Otalgia	1
Disgeusia	3

* Criteria of the Radiation Therapy Oncology Group/European Organization for Research and Treatment of Cancer.

risparmio laringe glottica

radiotherapy was delivered through two opposed lateral fields and an anterior–posterior field with midline split to the supraclavicular regions.

Int. J. Radiation Oncology Biol. Phys., Vol. 71, No. 4, pp. 1158–1166, 2008

0360-3016/08/$–see front matter

ELSEVIER

doi:10.1016/j.ijrobp.2007.11.059

CLINICAL INVESTIGATION **Head and Neck**

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

To compare the effectiveness of intensity-modulated radiotherapy (IMRT) and conventional (two-dimensional) radiotherapy in the treatment of cervical lymph node metastases from unknown primary cancer (UPC).

- Dose prescription involved multiple dose levels using a simultaneously integrated boost approach.

Table 1. Prescription dose levels to planning target volumes

Prescription dose level	Dose per fraction (Gy)	Total dose (Gy)
PTV_{69} = enlarged nonresected lymph nodes	2.16	69.1
PTV_{66} = putative mucosal sites + resected lymph nodes with capsule rupture	2.06	65.9
PTV_{62} = resected lymph nodes without capsule rupture	1.94	62.1
PTV_{56} = elective lymph nodes	1.75	56.0

Abbreviations: PTV = planning target volume; PTV_{69} = PTV receiving 69 Gy; PTV_{66} = PTV receiving 66 Gy; PTV_{62} = PTV receiving 62 Gy; PTV_{56} = PTV receiving 56 Gy.

- Patients in the historical control group were treated to a median dose of 66 Gy delivered in 33 fractions of 2.0 Gy. Nearby lymph node region to the involved lymph nodes received 56 Gy.

- Excluded laryngeal mucosa
- No Chemotherapy
- Historical controls 2 opposed fields

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	

Abbreviations: G0 = Grade 0 late toxicity; G1–2 = Grade 1–2 late toxicity; G3 = Grade 3 late toxicity; IMRT = intensity-modulated radiotherapy.

* Xerostomia and taste alteration were assessed in 17 patients.

† One patient with xerostomia Grade 0 was included.

- Approximately 70% of all patients evaluated had problems with swallowing solid and semi-solid food during follow-up. It is possible that a dose greater than 50 Gy to mucosal sites, as well as to nodal Levels Ib, II, III, and retropharyngeal lymph nodes that flank and even contain parts of the swallowing apparatus, could cause swallowing dysfunction

- Because there was no relapse in elective neck and because nodal failure occurred only in previously enlarged lymph nodes, dose reduction to elective nodal sites might be possible to preserve swallowing function and to reduce skin fibrosis without compromising treatment effectiveness.

TOSSICITA' ACUTE

Author	N° pts	tox acuta
Lu Oral Oncology 2009	18	5% PEG 6 mesi
Villeneuve IJROBP 2012	25	52% mucosite G>2, 28% dermatite G>2, 28% PEG
Frank IJROBP 2010	52	ND
Klem IJROBP 2008	21	14% mucosite G>2, 33% PEG, dermatite G>2 (5%), dehydration (10%), renal toxicity(5%), pulmonary tox(5%), infection (5%),pain(5%), and gastrointest. tox. (5%) hematol.toxicities (10%)
Madani IJROBP 2008	41	50% mucosite G3, 31.8% dermatite, disfagia G3 4.5%
Sher IJROBP 2011	24	75% mucosite G3, 29% G3-4 dermatite (100% cht, all mucosal sites included, 87% prophylactic PEG)
Grau R&O 2000	352	ND
Shoushtari IJROBP 2011	27	dermatite grado>2 15%, 7% PEG

TOSSICITA' CRONICHE

Author	N° pts	2D-3D RT	IMRT excl.	IMRT postop.	Oroph., nasoph.	larynx and hypoph.	PRE RT PEG	CHT	Xerostomia G>2	Dysphagia G>2	Neck fibrosis
Lu Oral Oncology 2009	18		33% 50.4 Gy	12 (66%) 66 Gy	16	1	6 (33%)	6 (33%)	ND	0 (stenosi esofagea)	
Villeneuve IJROBP 2012	25		68%7 50.4 Gy	8 (22%) 60-66 Gy	100%	100% risparmio laringe glottica		12% neoad, 72% conc,	8% a 1 anno	0 (stenosi esofagea o PEG)	
Beldì IJROBP 2007	113 (58)	113 (59% 50-56 Gy mucosa)			67 (59%)	59% (risparmi o laringe glottica		18% neoad, 9%conc	**9%**	0	9%
Frank IJROBP 2010	52		66% 54 Gy	33% 54 Gy	100%	66%		15% neoad, 27% conc	0	3.8% (stenosi o PEG)	
Klem IJROBP 2008	21		25% **54 Gy**	75% **54Gy**	100%, 90% nasopharynx	100%	25%	66% conc	0	**14% stenosi esofagea (dose media esofago 60 Gy)**	
Madani IJROBP 2008	41	44%	56% **66Gy**	44% **60Gy**	100%	100% 32% anche laringe			11,80%	**9% PEG**	
Sher IJROBP 2011	24		55% **60-64 Gy**	45% **56-64 Gy**	100%	100%	87.5%	100%		**46% stenosi**	
Shoushtari IJROBP 2011	27		81% 50-60 Gy	19% 50-60 Gy	1	no	no	30% neoad, 15% conc	0	7% (PEG , stenosi)	0,04

DISFAGIA

- Multifactorial (post-surgery scars, cyto/neurotoxic drugs, mucosal staminal depletion, xerostomia, edentulous patients, post RT fibrosis, atrophy from disuse)

- Different assessments of dysphagia in different series: aspiration and objective imaging, feeding tube dependency, patient-reported dysphagia, strictures, or observer-reported suchas RTOG, CTCAE, or PS Scale

- Different methods to delineate the organs (for example, drawing the PCs anatomically, results in different mean doses compared with drawing only the posterior pharyngeal wall).

Novità e Progressi nelle terapie di supporto nei tumori della testa collo
(a cura di Dott. Rampino e dott. Russi)

Raccomandazioni AIRO sulla valutazione e gestione della DISFAGIA

Prof. Maria Grazia Ruoredda

(1) Dysphagia evaluation general recommendation	All patients need to be clinically evaluated for researching signs and symptoms that herald dysphagia. The evaluation of more than one item, as listed in "Murphy's trigger symptoms" , is recommended (Recommendation D; level 4) (expert opinion based on bench research –neurological patients)
SLP	All patients at risk (based on Murphy's trigger symptoms) should be referred for a detailed swallowing evaluation to an SLP as soon as possible (Recommendation D; levels 4–5) (expert opinion mainly based on bench research – neurological patients) in order to (1) identify swallowing abnormality, (2) develop a treatment plan when indicated, (3) recommend additional testing to assess aspiration risk
Dysphagia tests	Water tests, with or without oxygen desaturation, with or without cough test29 during swallowing (endpoint: desaturation of >2%), can be performed in order to select patients to be further investigated or treated for dysphagia (Recommendation D) (expert opinion based on bench research – neurologic finding)
FEES vs. VFS/MBS	Both FEES and VFS/MBS are effective in predicting aspiration pneumonia in patients with dysphagia (Recommendation B, level 2b). VFS/MBS permits a superior evaluation of propulsive mechanism (the coordination of all pharyngeal events), velopalatinae closure, the patency of the hypopharyngeal lumen, UOES function, and the distal level of the aspiration26 (Recommendation D; level 5) (expert opinion based on physiology). FEES permits the detection of laryngeal penetration, aspiration, swallowing residue, and pharyngeal pooling in HNCPs. It does not assess UOES, but it permits the sensory deficits in the laryngopharynx to be evaluated (Recommendation B; level 2)

Radiotherapy and Oncology 90 (2009) 189–195

Contents lists available at ScienceDirect

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journal homepage: www.thegreenjournal.com

Swallowing dysfunction

A predictive model for swallowing dysfunction after curative radiotherapy in head and neck cancer

Johannes A. Langendijk [a,b,*], Patricia Doornaert [a], Derek H.F. Rietveld [a], Irma M. Verdonck-de Leeuw [c], C. René Leemans [c], Ben J. Slotman [a]

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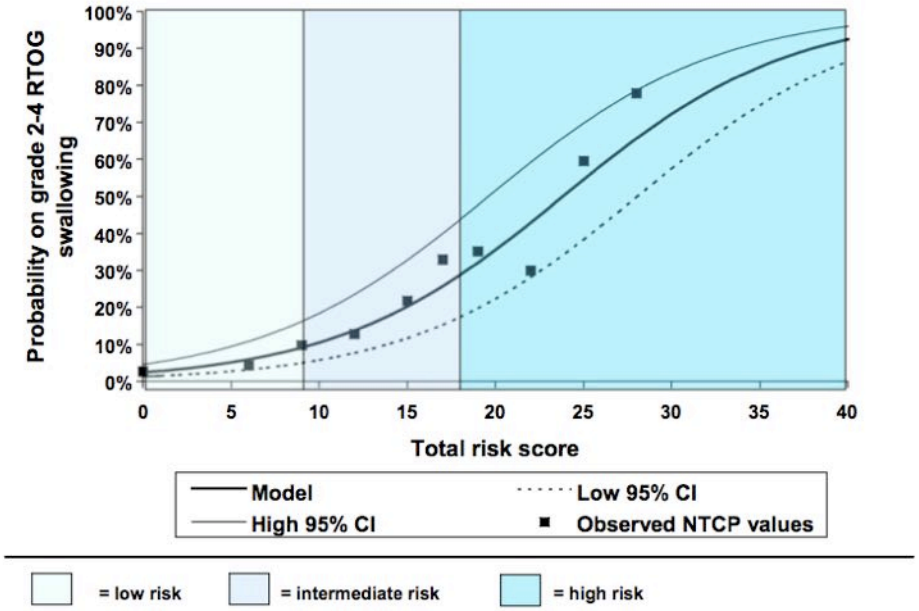


Fig. 1. Final model with probability on grade 2–4 RTOG swallowing dysfunction at 6 months as a function of the total risk score. The observed NTCP values all fall within the 95% confidence interval.

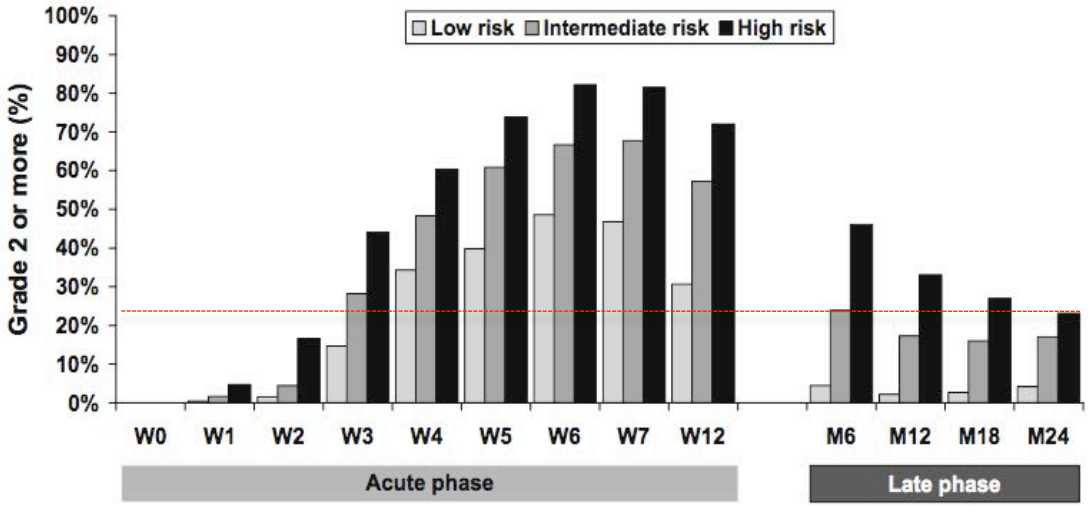
CALCULATION OF THE TOTAL DYSPHAGIA RISK SCORE TDRS

TDRS = risk points (T-classification) + risk points (neck irradiation) + risk points (weight loss) + risk points (primary tumour site) + risk points (treatment modality).

Risk. points

T-classification (T3 = 4 points; T4 = 4 points).
Neck irradiation (bilateral neck irradiation = 9 points).
Weight loss (1–10% = 5 points; >10% = 7 points).
Primary tumour site (oropharynx = 7 points; nasopharynx = 9 points).
Treatment modality (accelerated radiotherapy = 6 points; concomitant chemotherapy = 5 points).

TDRS=30



low risk was defined as a NTCP value of 6–10%, corresponding to a TDRS of 0–9; intermediate risk was de- fined as a NTCP value >10–30%, corresponding to a TDRS of 10–18, and high risk was defined as a NTCP value of >30%, corresponding to a TDRS of >18 points

Raccomandazioni AIRO sulla valutazione e gestione della DISFAGIA

Prof. Maria Grazia Ruoredda

(1) Dysphagia evaluation general	All patients need to be clinically evaluated for researching signs and

preventing, where possible:

- oral mucosa V9.5–V10 Gy/w > 50–60 cm3
- anterior oral cavity V30 exceeding 65%
- anterior oral cavity V35 exceeding 35%.

(Recommendation B; level 3)

	FEES permits the detection of laryngeal penetration, aspiration, swallowing residue, and pharyngeal pooling in HNCPs. It does not assess UOES, but it permits the sensory deficits in the laryngopharynx to be evaluated (Recommendation B; level 2)

Raccomandazioni AIRO sulla valutazione e gestione della DISFAGIA

Prof. Maria Grazia Ruoredda

Table 9 QUANTEC Summary: Approximate Dose/Volume/Outcome Data for Main DARS Following Conventional Fractionation (From (Marks et al. 2010)

ORGAN	VOLUME	RT TYPE	ENDPOINT	DOSE (GY) OR D/V PARAMETER	RATE (%)	NOTE
Pharynx	Whole organ	3D-CRT	Symptomatic dysphagia and aspiration	Mean dose < 50	< 20	
Larynx	Whole organ	3D-CRT	Vocal disfunction	Mean dose < 66	< 20	With chemotherapy based on single study
	Whole organ	3D-CRT	ASPIRATION	Mean dose < 50	< 30	With chemotherapy based on single study
	Whole organ	3D-CRT	edema	Mean dose < 44	< 20	Without chemotherapy based on single study, no larynx cancer
		3D-CRT	edema	V50< 27%	< 20	

Int. J. Radiation Oncology Biol. Phys., Vol. 80, No. 5, pp. 1405–1411, 2011

0360-3016/$–see front matter

ELSEVIER

doi:10.1016/j.ijrobp.2010.04.029

Sher IJROBP 2011

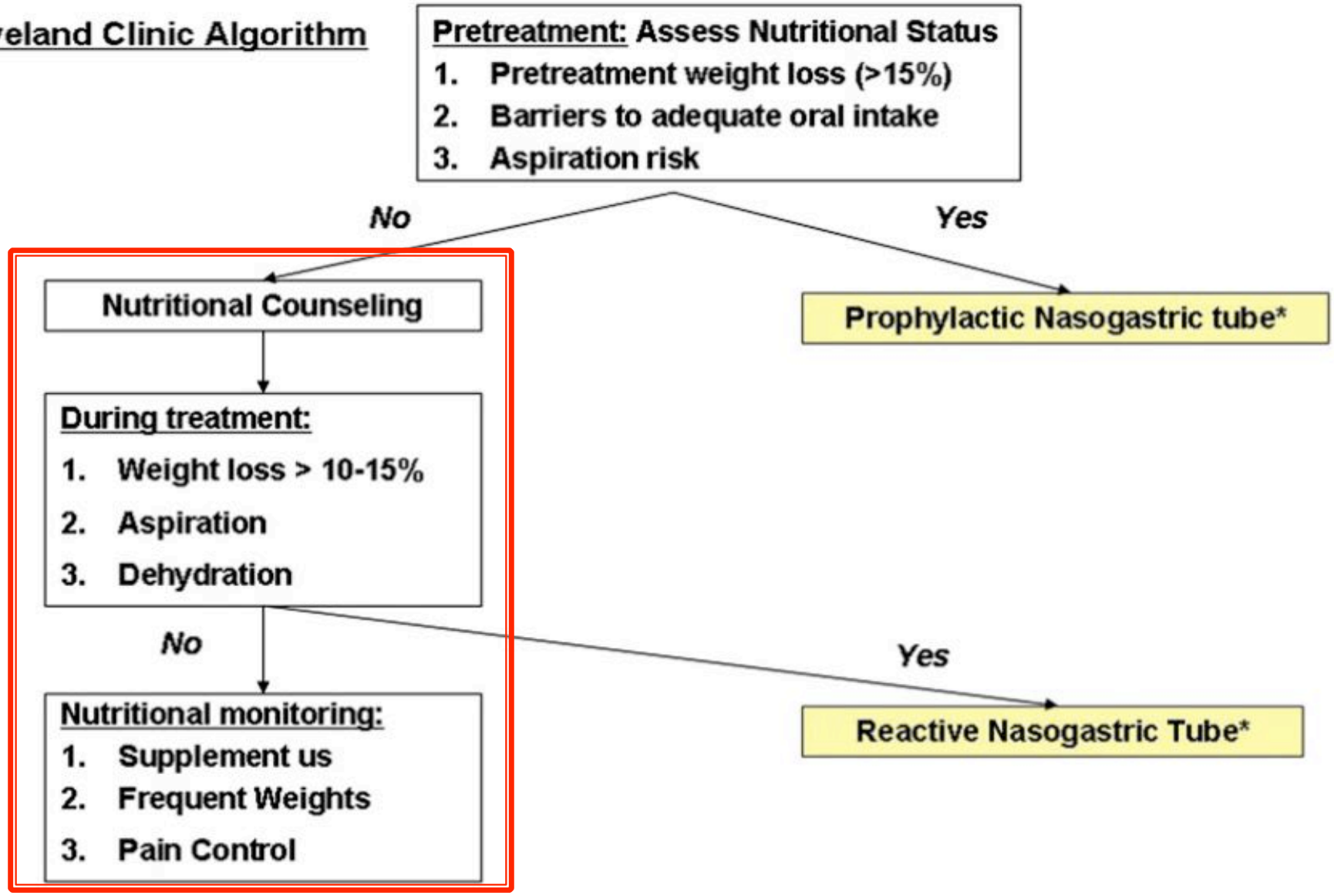
CLINICAL INVESTIGATION **Head and Neck**

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

24 pts, FUP a 2aa
46% stenosi

- Mucosal dose was lowered over time, because the first patients in our experience were treated to 60–64 Gy and then to 60 Gy as the standard. More recently, the dose has been decreased to 56 Gy.
- Given the near universal use of chemotherapy, we prioritized homogeneity and keep the hot spots out of the oral cavity, larynx, and oropharynx; however, the latter two structures and postcricoid space could not be kept to<50 Gy because the prescription dose was generally 60–64 Gy.

Cleveland Clinic Algorithm



*Indications for PEG (vs. NG tube): 1. Frequent NG tube dysfunction

2. Anatomic barrier (e.g. nasal cavity obstruction)

3. No expectation for restoration of normal swallowing

Royal Brisbane & Women's Hospital: Swallowing and Nutrition Management Guidelines

Multi-Disciplinary Team Assessment:

HIGH RISK

Oral + bilateral chemoradiotherapy
Midline oropharyngeal/nasopharyngeal/ pharyngeal + chemoradiotherapy

OR

Dysphagia at presentation or prior to radiotherapy/chemoradiotherapy

OR

Severe malnutrition at presentation:
- Unintentional weight loss > 10% in 6 months
- BMI < 18.5
- BMI < 20 with unintentional weight loss 5-10% in 6 months
- Dietitian assessment SGA C
- Poor oral intake (minimal intake > 5days and/or unlikely to improve > 5days)

MEDIUM RISK

All other head and neck cancers which do not fit into high or low risk category

OR

Moderate malnutrition at presentation:
- Unintentional weight loss > 5% in 6 months
- BMI < 20 with unintentional weight loss up to 5% in 6 months
- Dietitian assessment SGA B

LOW RISK

Surgery alone, no radiotherapy required
Unilateral radiotherapy alone
All salivary tumours
All tumours of skin in temple region and above

High Risk

- **Severe malnutrition**
  - >10% in 6 months
  - BMI<18.5 Kg/m2
  - Minimal intake>5d and unlikely to improve
  - Lean Body mass

OR

- **Dysphagia at presentation**

OR

- **Midline (/oral) + Bilateral + CT/RT**

BMI = Body Mass Index
PEG = Percutaneous Endoscopic Gastrostomy
SGA = Subjective Global Assessment
MBS = Modified Barium Swallow
NGT = Nasogastric Tube

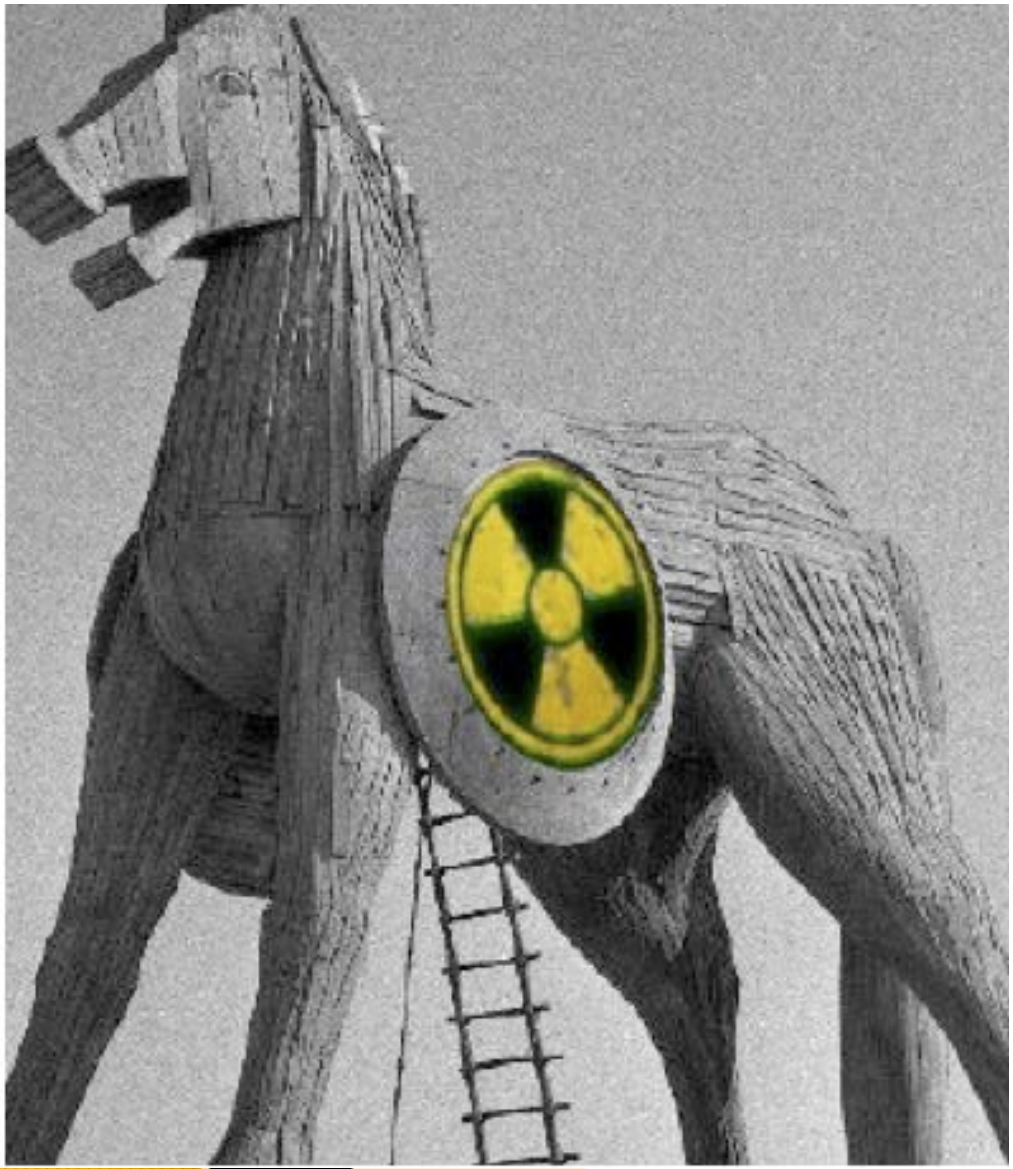
- dysphagia
- Inadequate dentition
- Significantly reduced appetite/taste alterations

- Inadequate dentition
- Stricture formation
- Presence of tracheostomy

March 2007
Developed by the Departments of Nutrition and Dietetics and Speech Pathology and endorsed by the Combined Head and Neck Clinic, Royal Brisbane and Women's Hospital, Brisbane, QLD, Australia

Head & Neck
pages n/a–n/a, 13 SEP 2012 DOI: 10.1002/hed.23146
http://onlinelibrary.wiley.com/doi/10.1002/hed.23146/full#fig1

MALNUTRIZIONE



Symptom Control Issues and Supportive Care of Patients With Head and Neck Cancers

Clin Adv Hem Oncol 2007

Barbara A. Murphy, MD, Jill Gilbert, MD, Anthony Cmelak, MD, and Sheila H. Ridner, RN, PhD

Cumulative Weight Loss and Time Course		
Time Course	**Significant Weight Loss**	**Severe Weight Loss**
1 week	≤2%	>2%
1 month	≤5%	>5%
3 months	≤7.5%	>7.5%
6 months	≤10%	>10%

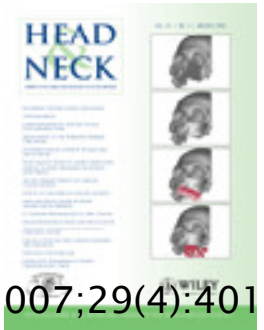
Patients with a critical weight loss should be seen quickly by a dietician to formulate an aggressive intervention strategy. Nutritional assessments should continue on a frequent basis throughout the treatment and periodically to ensure adequate nutritional intake. This generally requires the expertise of a dietician versed in facing patients with head and neck cancer.

Table 2. Diagnosis of cancer cachexia.

Test	Finding
Clinical	
Body weight	Unintentional weight loss (>5% during
Skeletal muscle mass	Decreased biceps, quadriceps muscle mass
Food intake recall or diary	Anorexia and/or decreased food intake
Fatigue	Increased
Range of motion	Usually impaired
Quality-of-life surveys	Decreased scores
Karnofsky Performance Scale	Decreased scores
Serum:	
Serum CRP	Increased (acute-phase response)
Serum fibrinogen	Increased (acute-phase response)
Serum hematocrit	Decreased (anemia)
Serum albumin	Decreased
Nutritional assessment	
Indirect calorimetry	Increase in REE
DXA	Decrease in LBM

Abbreviations: CRP, C-reactive protein; REE, resting energy expenditure; DXA, dual X-ray absorptimetry; LBM, lean body mass.

TREATMENT



Head & Neck. 2007;29(4):401–1

Valutazione iniziale

SIRS

Almeno due dei seguenti criteri

1. Frequenza cardiaca > 90/ min
2. Frequenza respiratoria > 20/min o paCO2<32 mmHg
3. Temperatura > 38° o <36°
4. WBC >12.000/mm3 o < 4.000/mm3

Non aspettare la febbre per sospettare l'infezione

Valutazione l'origine della sepsi

Non aspettare la febbre per sospettare l'infezione

Clinica

- Polmonite CAP senza neutropenia o HAP o da aspirazione
- Mucosite
- CVC
- Dermatite

Laboratorio

- Emocolture e colture prelievi aree sospette
- EGA
- Rx torace
- Ricerca degli indici di flogosi: PCR e procalcitonina

COURTESY DR RUSSI

Arkader et al Arch Dis. Child 2006

XEROSTOMIA

Int. J. Radiation Oncology Biol. Phys., Vol. 82, No. 5, pp. 1866–1871, 2012

0360-3016/$ - see front matter

ELSEVIER

doi:10.1016/j.ijrobp.2011.02.031

CLINICAL INVESTIGATION **Gynecologic Cancer**

CERVICAL LYMPH NODE METASTASES FROM UNKNOWN PRIMARY CANCER: A SINGLE-INSTITUTION EXPERIENCE WITH INTENSITY-MODULATED RADIOTHERAPY

Hugo Villeneuve, M.D.,* Philippe Després, Ph.D.,* Bernard Fortin, M.D., M.Sc.,* Edith Filion, M.D.,* David Donath, M.D.,* Denis Soulières, M.D.,† Louis Guertin, M.D.,‡ Tarek Ayad, M.D.,‡ Apostolos Christopoulos, M.D.,‡ and Phuc Felix Nguyen-Tan, M.D.*

Departments of *Radiation Oncology, †Medical Oncology, and ‡Head and Neck Surgery, Centre hospitalier de l'Université de Montréal, Montréal, QC, Canada

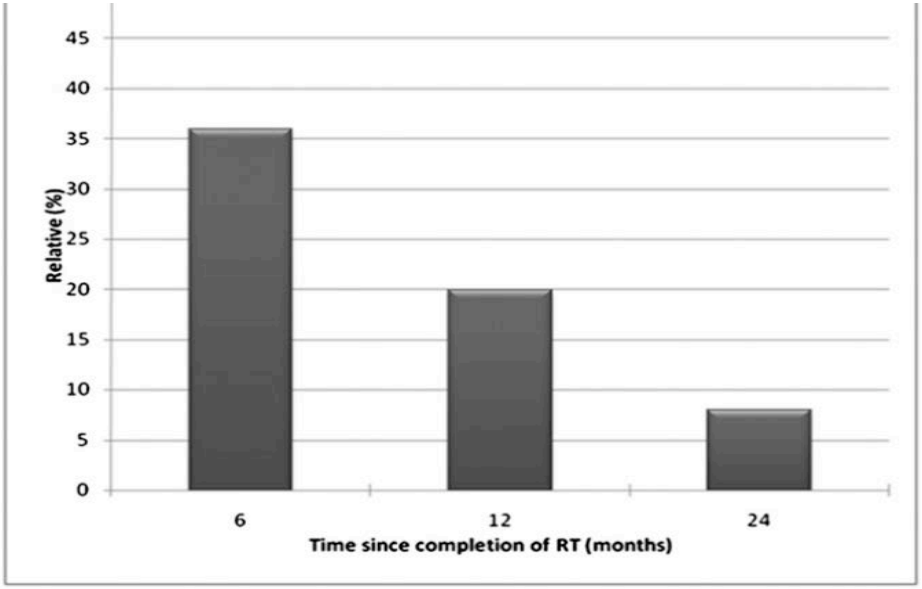


Fig. Xerostomia Grade 2 or greater since radiotherapy completion.

Int. J. Radiation Oncology Biol. Phys., Vol. 70, No. 4, pp. 1100–1107, 2008

0360-3016/08/$–see front matter

ELSEVIER

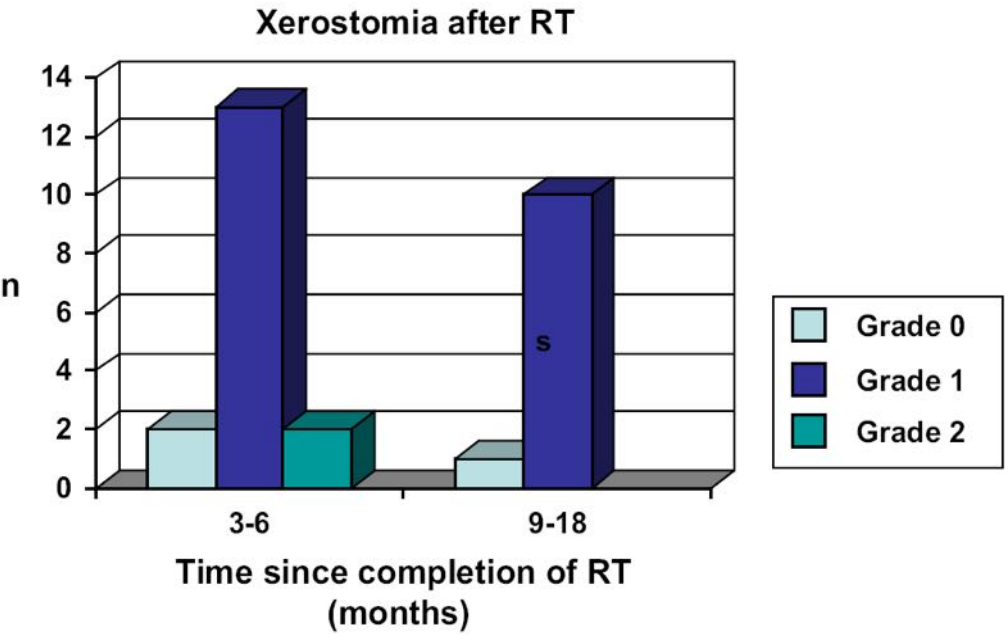
doi:10.1016/j.ijrobp.2007.07.2351

CLINICAL INVESTIGATION **Head and Neck**

INTENSITY-MODULATED RADIOTHERAPY FOR HEAD AND NECK CANCER OF UNKNOWN PRIMARY: TOXICITY AND PRELIMINARY EFFICACY

MICHELLE L. KLEM, M.D.,* JAMES G. MECHALAKOS, PH.D.,† SUZANNE L. WOLDEN, M.D.,*
MICHAEL J. ZELEFSKY, M.D.,* BHUVANESH SINGH, M.D., PH.D.,‡ DENNIS KRAUS, M.D.,‡
ASHOK SHAHA, M.D.,‡ JATIN SHAH, M.D.,‡ DAVID G. PFISTER, M.D.,§ AND NANCY Y. LEE, M.D.*

Departments of *Radiation Oncology, †Medical Physics, ‡Surgery, and §Medical Oncology, Memorial Sloan-Kettering Cancer Center, New York, NY



- Xerostomia improved with the time from RT. All patients experienced Grade 1 or 2 xerostomia during treatment, but, by 6 months, only 1 patient had greater than Grade 1 xerostomia.
- No patient (0/21) had Grade 3 or 4 xerostomia at any point.

GRAZIE PER L'ATTENZIONE