



**L'impatto dosimetrico e clinico del cambiamento dei volumi clinici
su 18 pazienti con neoplasia avanzata del testa collo trattati con
VMAT-Adaptive radiotherapy**

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UOC DI RADIOTERAPIA E MEDICINA NUCLEARE

I.O.V – I.R.C.C.S.

PADOVA

Adaptive Radiation Therapy (ART)

"Adaptive radiotherapy" is defined as changing the radiation treatment plan delivered to a patient during a course of radiotherapy to account for

- **Temporal changes in anatomy** (e.g. tumor shrinkage, weight loss or internal motion)
- **Changes in tumor biology/function** (e.g. hypoxia).



Deformable registration of the planning image (kVCT) and the daily images (MVCT) for adaptive radiation therapy*

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Published 15 August 2006 • 2006 IOP Publishing Ltd • Physics in Medicine and Biology, Volume 51,



Identification of volumetric and geometric changes occurring during fractionated radiotherapy for head-and-neck cancer using an integrated CT linear accelerator system

For poster discussion presentation at the 45th Annual Meeting of the American Society for Therapeutic Radiology and Oncology, Salt Lake City, UT, October 19–23, 2003.

Barkley J. Cole, Adam S. Garden, M.D., K.Kian Ang, M.D., Ph.D., Jennifer C. O'Daniel, M.S., Heung Sik Park, Ph.D., Lawrence E. Court, Ph.D., William H. Morrison, M.D., David I. Rosenthal, M.D., K.S.Clifford Brown, M.D., Susan L. Tucker, Ph.D., Radhe Mohan, Ph.D., Lei Dong, Ph.D.



Adaptive Radiotherapy of Head and Neck Cancer

Pierre Castadot, MD, John A. Lee, Eng, PhD, Xavier Geets, MD, PhD, and Vincent Grégoire, MD, PhD, FRCR

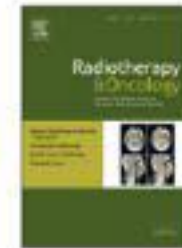
Intensity-modulated radiation therapy (IMRT) in head and neck cancer takes advantage of the capability to generate steep dose gradients, leading to an improved therapeutic index. IMRT plans are typically based on a pretreatment computed tomography scan that provides a snapshot of the patient's anatomy. Nevertheless, interfractional patient variations may occur because of setup error and anatomical modifications. Therefore, the accuracy of IMRT delivery for H&N cancer may be compromised during the treatment course, potentially affecting the therapeutic index. In this framework, adaptive radiotherapy is a potential solution, which consists of the explicit inclusion of the temporal changes in anatomy during the imaging, planning, and delivery of radiotherapy. Adaptive radiotherapy has brought an additional dimension to the management of patients with H&N cancer and has the potential to surmount the effects of positioning errors and anatomical changes. This article reviews the causes and discusses potential solutions to circumvent the discrepancies between the planned dose and the actual dose received by patients treated for H&N cancer.

Semin Radiat Oncol 20:84-93 © 2010 Elsevier Inc. All rights reserved.



Assessment of Parotid Gland Dose Changes During Head and Neck Cancer Radiotherapy Using Daily Megavoltage Computed Tomography and Deformable Image Registration

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Adaptive RT in head and neck cancer

Adaptive functional image-guided IMRT in pharyngo-laryngeal squamous cell carcinoma: Is the gain in dose distribution worth the effort?

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QUESTIONI APERTE

- Clinical benefit of adaptive strategy will have to be evaluated both in terms of patients outcome and cost-effectiveness
- In the mean-time, owing to the complexity of the procedure, **ART should not be used in routine clinical base**



Clinical Investigation

Replanning During Intensity Modulated Radiation Therapy Improved Quality of Life in Patients With Nasopharyngeal Carcinoma

This work was presented in part at the 54th Annual Meeting of the American Association of Physicists in Medicine, Charlotte, NC, July 29-Aug 2, 2012. The manuscript received final approval from Hai-Hua Yang, Wei Hu, Wang Wei, Pei-Fang Chen, Weijun Ding, and Wei Luo.

Haihua Yang, MD*, Wei Hu, MD* · 👤 · ✉, Wei Wang, BS*, Peifang Chen, BS*, Weijun Ding, MD*, Wei Luo, PhD†

Results

IMRT replanning had a profound impact on the QoL of NPC patients, as determined by statistically significant changes in global QoL and other QoL scales. Additionally, the clinical outcome comparison indicates that replanning during IMRT for NPC significantly improved 2-year local regional control (97.2% vs 92.4%, respectively, $P=.040$) but did not improve 2-year OS (89.8% vs 82.2%, respectively, $P=.475$).



Clinical outcomes among patients with head and neck cancer treated by intensity-modulated radiotherapy with and without adaptive replanning

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Article first published online: 22 JAN 2014

DOI: 10.1002/hed.23477

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Issue



Head & Neck

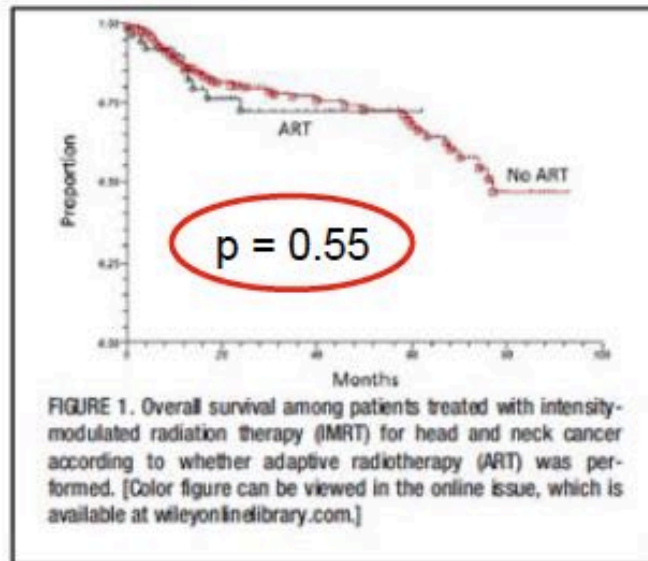
Volume 36, Issue 11, pages
1541–1546, November 2014

Three hundred seventeen patients underwent IMRT with daily image-guidance for newly diagnosed squamous cell carcinoma of the head and neck to a median dose of 66 Gy (range, 60–74 Gy). Of these 317 patients, 51 (16%) underwent adaptive radiotherapy with modification of the original IMRT midway during treatment.

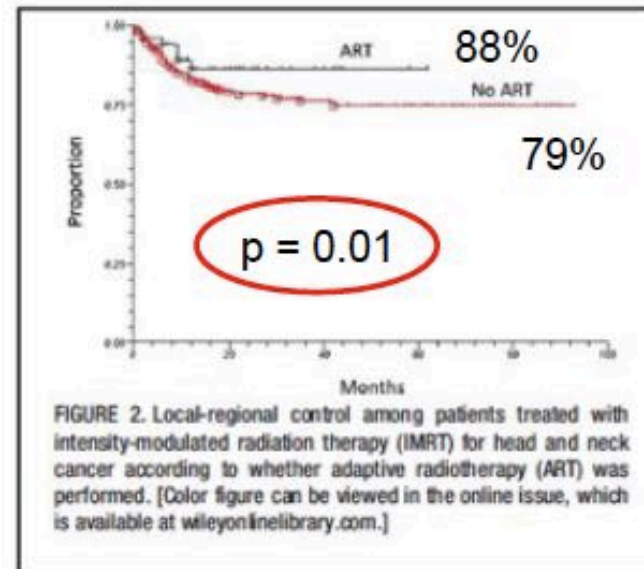


Head & Neck
Volume 36, Issue 11, pages
1541–1546, November 2014

2-year OS



2-year LRC



The 2-year local-regional control was 88% for patients treated with adaptive replanning compared with 79% for patients treated without ($p = .01$). The median time to local-regional recurrence for the 4 patients treated by adaptive radiotherapy was 7 months (range, 3–15 months) with all failures occurring within the high-dose planning target volume (PTV).

La nostra esperienza



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**ADAPTIVE RADIOTHERAPY (A.R): RISULTATI DOSIMETRICI IN 10
PAZIENTI CON CARCINOMA DEL RINOFARINGE E
DELL'OROFARINGE TRATTATI CON TECNICA VMAT**

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TO
2

	Istologia	Sesso	Eta	Stadio	CT concomitante	Kg.persi	
	SCC	M	70	T3N2c	NO	16	
	NPC	M	70	T3N1	SI	7	
3	SCC	F	67	T3N0	SI	7	
4	SCC	M	58	T2N2b	SI	14	
5	NPC	M	36	T2N1	SI	6	
6	NPC	M	63	T2N1	SI	5	
7	NPC	M	68	T3N2	SI	9	
8	NPC	F	69	T1N2	SI	4	
9	NPC	F	59	T2N2	SI	6	
0	NPC	M	40	T2N2	SI	10	
1	SCC	M	65	T2N2b	SI	5	
2	SCC	M	70	T3N1	SI	7	
3	SCC	M	57	T3N2c	SI	14	
4	SCC	F	61	T2N2b	SI	4	
5	SCC	F	47	T3N3	SI	13	
6	SCC	M	63	T1N2c	SI	8	
7	SCC	M	59	T2N2b	SI	5	

MATERIALI E METODI

- VMAT a 2 archi(360 gradi)
Varian Unique

-Pianificazione con Eclipse TPS

-5mm di margine per il PTV
66Gy-60-54/30f SIB per Orofaringe
69.9Gy-60-54/33f SIB per Rinofaringe

-TC settimanale di controllo

-Registrazione elastica con la TC di pianificazione
(Raystation TPS)

MATERIALI E METODI

- Follow up medio 14 mesi
- Follow up ogni 3 mesi per i primi 2 aa in ambito multidisciplinare
- Valutazione della risposta clinica con videolaringoscopia prima dell'inizio della RT e dopo 1 mese dalla fine del trattamento
- Prima valutazione radiologica 8 settimane dopo la fine del trattamento



MATERIALI E METODI

Valutazione della tossicità acuta e tardiva

RTOG ACUTE Radiation Morbidity

Tissue	Grade 1	2	3	4
Skin	Follicular, faint or dull erythema / epilation / dry desquamation / decreased sweating	Tender or bright erythema, patchy moist desquamation / moderate edema	Confluent, moist desquamation other than skin folds, pitting edema	Ulceration, hemorrhage, necrosis
Mucous membrane	Injection / may experience mild pain not requiring analgesic	Patchy mucositis that may produce an inflammatory serosanguinous discharge / may experience moderate pain requiring analgesia	Confluent fibrinous mucositis / may include severe pain requiring narcotic	Ulceration, hemorrhage or necrosis
Eye	Mild conjunctivitis w/ or w/o scleral injection / increased tearing	Moderate conjunctivitis w/ or w/o keratitis requiring steroids and/or antibiotics / dry eye requiring artificial tears / iritis with photophobia	Severe keratitis with corneal ulceration / objective decrease in visual acuity or in visual fields / acute glaucoma / panophthalmitis	Loss of vision (uni or bilateral)
Ear	Mild external otitis with erythema, pruritus, secondary to dry desquamation not requiring medication. Audiogram unchanged from baseline	Moderate external otitis requiring topical medication / serous otitis media / hypoacusis on testing only	Severe external otitis with discharge or moist desquamation / symptomatic hypoacusis / tinnitus, not drug related	Deafness
Salivary gland	Mild mouth dryness / slightly thickened saliva / may have slightly altered taste such as metallic taste / these changes not reflected in alteration in baseline feeding behavior, such as increased use of liquids with meals	Moderate to complete dryness / thick, sticky saliva / markedly altered taste	(none)	Acute salivary gland necrosis
Pharynx & esophagus	Mild dysphagia or odynophagia / may require topical anesthetic or non-narcotic analgesics / may require soft diet	Moderate dysphagia or odynophagia / may require narcotic analgesics / may require puree or liquid diet	Severe dysphagia or odynophagia with dehydration or weight loss > 15% from pretreatment baseline requiring NG feeding tube, IV fluids, or hyperalimentation	Complete obstruction, ulceration, perforation, fistula
Larynx	Mild or intermittent hoarseness / cough not requiring antitussive / erythema of mucosa	Persistent hoarseness but able to vocalize / referred ear pain, sore throat, patchy fibrinous exudate or mild arytenoid edema not requiring narcotic / cough requiring antitussive	Whispered speech, throat pain or referred ear pain requiring narcotic / confluent fibrinous exudate, marked arytenoid edema	Marked dyspnea, stridor or hemoptysis tracheostomy or intubation necessary

MATERIALI E METODI

Valutazione della tossicità acuta e tardiva

RTOG/EORTC LATE Radiation Morbidity

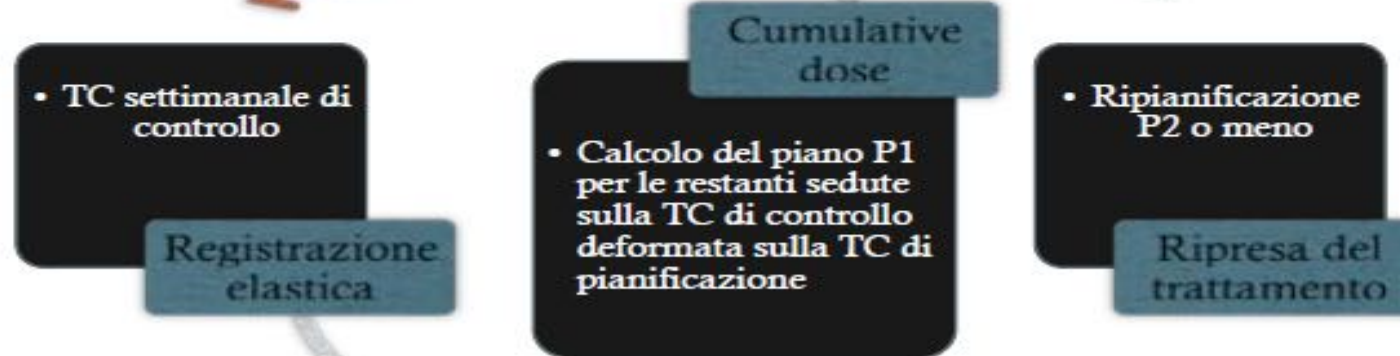
Tissue	Grade 1	2	3	4
Skin	Slight atrophy; pigmentation change; some hair loss	Patch atrophy; moderate telangiectasia; total hair loss	Marked atrophy; gross telangiectasia	Ulceration
Subcutaneous tissue	Slight induration (fibrosis) and loss of subcutaneous fat	Moderate fibrosis but asymptomatic; slight field contracture; <10% linear reduction	Severe induration and loss of subcutaneous tissue; field contracture > 10% linear measurement	Necrosis
Mucous membrane	Slight atrophy and dryness	Moderate atrophy and telangiectasia; little mucous	Marked atrophy with complete dryness	Ulceration
Salivary glands	Slight dryness of mouth; good response on stimulation	Moderate dryness of mouth; poor response on stimulation	Complete dryness of mouth; no response on stimulation	Fibrosis

Workflow

Simulazione

Pianificazione
P1

Trattamento



RISULTATI

-10 pazienti sono andati incontro ad ART1

-Tempo medio tra TC e ART1 :1,9 giorni

-Media 1[^] ripianificazione: 12[^]frazione

-6 pazienti sono andati incontro ad ART2

-Media 2[^]ripianificazione:20[^]frazione

RISULTATI

- Volume del CTV ad alto rischio diminuisce del ordine del 35% durante le prime 3 settimane di trattamento
- Volume medio parotideo diminuito dell 11%
- ART 1 riduce la dose media alle parotidi del 3,2%
- ART 2 nei casi Ca orofaringe riduce la dose media al cavo orale del 10%

RISULTATI/TOSSICITA' ACUTA

Acute side effects	Any Grade N	Grade 0 N/%	Grade 1 N/%	Grade 2 N/%	Grade 3 N/%	Grade 4 N/%
Skin	11	-	8(44)	7(39)	3(17)	-
Mucosal	18	-	9(50)	4(23)	5(27)	-
Salivary Glands	16	-	10(55)	6(34)	-	-
Faringo-esofageal	14	-	3(16)	7(39)	4(22)	-
Laryngeal	7	-	5(28)	2(11)	-	-

RISULTATI/TOSSICITA' TARDIVA

Late side effects	Any Grade N	Grade 0 N/%	Grade 1 N/%	Grade 2 N/%	Grade 3 N/%	Grade 4 N/%
Skin	7	-	7(39)	-	-	-
Mucosal	8	-	3(16)	5(27)	-	-
Salivary Glands	10	-	4(23)	6(34)	-	-
Faringo-esofageal	4	-	4(23)	-	-	-
Laryngeal	1	-	1	-	-	-

RISULTATI/ TOSSICITA' ACUTA

ADAPTIVE

Acute side effects	Any Grade N	Grade 1 N/%	Grade 2 N/%	Grade 3 N/%	Grade 4 N/%
Skin	11	8(44)	7(39)	3(17)	-
Mucosal	18	9(50)	4(23)	5(27)	-
Salivary Glands	16	10(55)	6(34)	-	-
Faringo- esophageal	14	3(16)	7(39)	4(22)	-
Laryngeal	7	5(28)	2(11)	-	-

NO ADAPTIVE

Any Grade N	Grade 1 N/%	Grade 2 N/%	Grade 3 N/%	Grade 4 N/%
18	4(20)	10(50)	4(20)	-
20	1(5)	11(27)	8(40)	-
19	8(40)	11(55)	-	-
15	4(20)	8(40)	3(15)	-
11	1(10)	10(50)	-	-

RISULTATI/ TOSSICITA' TARDIVA

ADAPTIVE

Late side effects	Any Grade N	Grade 1 N/%	Grade 2 N/%	Grade 3 N/%	Grade 4 N/%
Skin	7	7(39)	-	-	-
Mucosal	8	3(16)	5(27)	-	-
Salivary Glands	10	4(23)	6(34)	-	-
Faringo-esophageal	4	4(23)	-	-	-
Laryngeal	1	1(5)	-	-	-

NO ADAPTIVE

Any Grade N	Grade 1 N/%	Grade 2 N/%	Grade 3 N/%	Grade 4 N/%
10	10(50)	-	-	-
13	6(30)	7(35)	-	-
14	4(23)	10(50)	-	-
4	4(23)	-	-	-
5	5(25)	-	-	-

RISULTATI/ CONTROLLO LOCALE DELLA MALATTIA

-Con un follow up medio di 14 mesi abbiamo osservato una risposta parziale in 15% dei pazienti e una risposta completa nel restante 85% dei casi.

-Nessuna recidiva locale di malattia

-3 pazienti sono deceduti dopo la fine del trattamento
(median survival =13 mesi)

CONCLUSIONI

- L'A.R. mostra un trend di riduzione della tossicità acuta e tardiva
- Non sembrano esserci delle differenze nel controllo locale della malattia
- L'impatto clinico di questa tecnica deve essere ancora confermato da futuri trials.