

Electronic Poster: Clinical track: Head and neck

EP-1136

Adaptive radiotherapy for nasopharyngeal carcinoma

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Purpose/Objective: This study is to investigate the body contour changes and tumor regression in intensity modulated radiotherapy (IMRT) for nasopharyngeal carcinoma (NPC) after 1-month of treatment and to identify factors associated with body contour changes.

Materials and Methods: Thirty-eight newly diagnosed NPC patients were enrolled in this study and were treated with IMRT; computer-assisted tomography (CT) of head and neck for IMRT planning were performed twice, the 1st CT at one week before radiotherapy (Plan 1) and the 2nd CT at 22 radiation treatments (Plan 2). Same physician outlined all target volumes and organs at risk. The physical objective and dose constraints were optimized with same criteria. Principle component analysis and clustering were used for body contour changes. We tried to identify variables associated with body contour changes before and after treatments.

Results: Patient weight decreased remarkably after 1-month of radiotherapy. The average weight decreased by 3.0% (2.3kg, range 1.5-3.2kg). Comparing Plan 1 to Plan 2, the parotid gland volume was significantly reduced by 15.7% (10.8cc, ranged from 7.5-14.2cc); the submandibular gland volume by 15.8% (3.4cc, ranged from 2.14-4.65cc); GTV by 15.5% (3.8cc, ranged from 2.4-5.3cc); and GTV-LN by 41.8% (15.1cc, ranged from 8.7-21.6cc). The separation distance in each slice of head and neck CT images reduced by average of 0.32-0.89 cm (1.9%-6.0%), especially at the transverse diameter in the level of 3rd cervical spine (0.9cm). The GTV volume on average shrank 2.23cc and 6.91 cc as comparing T1-3 with T4 disease (p = 0.0013); The GTV-LN volume shrank on average 8.59 cc, 38.93 cc (p = 0.0208) as comparing N1-2 with N3 disease. The transverse diameter changes of head and neck contours were correlated significantly with N stage and body weight loss.

Conclusions: For NPC patients treated with IMRT, weight loss, volume reduction of salivary gland and body contour changes are common. The salivary glands on average reduced volume by 16% and GTV-LN by 42% after one-month treatment. The most significant factor associated with body contour changes is weight loss. We recommend repeat simulation after one-month of radiotherapy in order to reduce the dose to the normal organs and avoid missing treatment targets.

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IMRT treatment plan dosimetry as a predictor for loco-regional control in head-and-neck cancer

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Purpose/Objective: To retrospectively assess the loco-regional disease control in head-and-neck cancer (HNC) patients treated with Intensity Modulated Radiation Therapy (IMRT) and estimate the role of treatment plan dosimetry as a predictor for loco-regional control (LC).

Materials and Methods: Between February 2012 and February 2014, 30 consecutive patients with HNC were treated with Simultaneous Integrated Boost (SIB) IMRT. Their demographic and clinical variables, such as age at the time of diagnosis, gender, T and N stage and chemotherapy data were collected and analyzed. Planning CT images of all patients with loco-regional failures were retrospectively reviewed and dosimetric data of the treatment plans investigated, seeking for a possible correlation between an eventual loco-regional disease relapse and the dose delivered to the area where the relapse occurred. Dose-Volume-Histograms (DVH) were used to extract D_{95%}, D_{98%} and D_{mean} values. Because DVH does not provide spatial information about hot and cold spots, Equivalent Uniform Dose (EUD) was considered too. As the dose varied among patients, for analysis we used values of D_{95%}, D_{98%}, D_{mean} and EUD normalized to the prescribed dose. Correlation of the available variables with LC was assessed by a logistic regression test and a p value of < 0.05 was considered significant.

Results: After a median follow-up of 12 months (range: 1-28 months), 8 (26%) patients presented loco-regional relapse and 22 (64%) were free of disease. During this time, 3 (10%) patients died from the disease; all of them were tongue cancer cases.

Table 1. Patient and tumor characteristics (n=30).

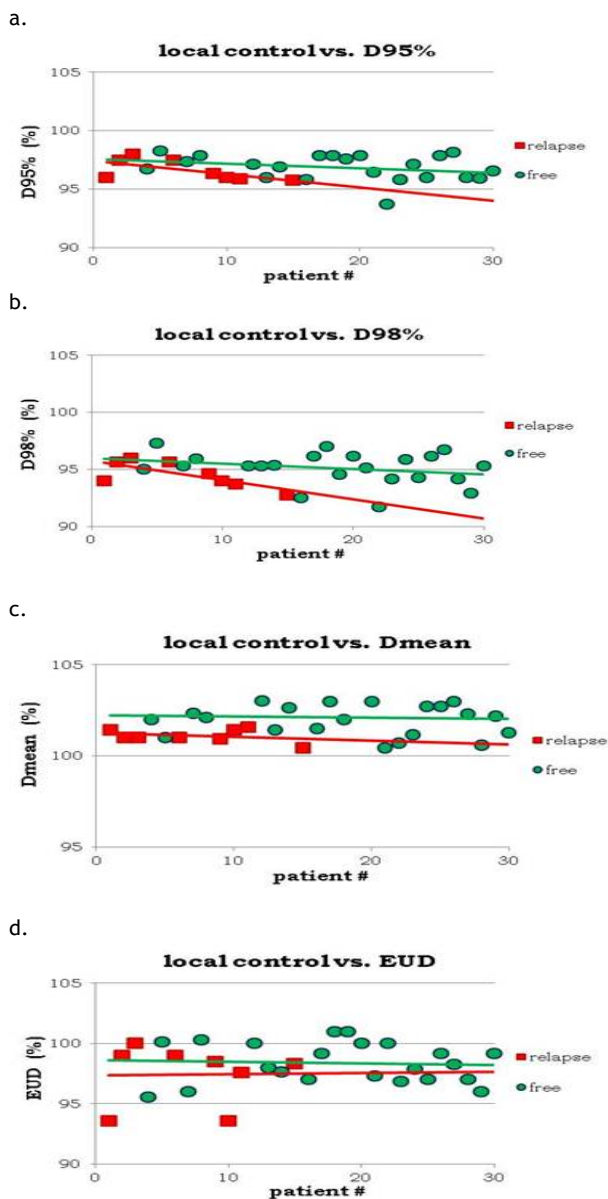
Characteristic	n (%)	Loco-regional relapse (n=8)	Free of disease (n=22)
Age			
median	44	57	42
range	21-78	36-78	21-67
Gender			
females	11	4 (36%)	7 (64%)
males	19	4 (21%)	15 (79%)
Diagnosis			
nasopharynx	14 (47%)	0 (0%)	14 (100%)
larynx	3 (10%)	1 (33%)	2 (66%)
buccal mucosa	3 (10%)	1 (33%)	2 (66%)
tongue	3 (10%)	3 (100%)	0 (0%)
maxilla	3 (10%)	1 (33%)	2 (66%)
hypopharynx	2 (7%)	2 (100%)	0 (0%)
others	2 (7%)	0 (0%)	2 (100%)
T stages			
T1	4 (13%)	0 (0%)	4 (100%)
T2	10 (33%)	1 (3%)	9 (97%)
T3	3 (10%)	0 (0%)	3 (100%)
T4	13 (44%)	7 (53%)	6 (47%)
N stages			
N0	7 (23%)	2 (28%)	5 (72%)
N1	6 (20%)	1 (16%)	5 (84%)
N2	15 (50%)	5 (33%)	10 (67%)
N3	2 (7%)	0 (0%)	2 (100%)
Concomitant chemotherapy			
	11 (36%)	0 (0%)	11 (100%)

Significantly improved LC of the disease was associated with nasopharyngeal diagnosis (p=0.0004), early stages (T1, p=0.0454; N0, p=0.0024), and the use of concomitant chemotherapy (p=0.0028).

Treatment plans evaluation showed that all loco-regional relapses occurred within the 95% isodose line inside the Planning-Target-Volume (PTV) of the primary disease. Dosimetric parameters analysis showed a weak correlation

between LC and $D_{95\%}$ and $D_{98\%}$, but a strong dependence on D_{mean} ($p=0.0274$) and EUD ($p=0.0483$) was noticed.

Fig. 1. The correlation between loco-regional control and $D_{95\%}$ (a), $D_{98\%}$ (b), D_{mean} (c) and EUD (d). Values of $D_{95\%}$, $D_{98\%}$, D_{mean} and EUD are normalized to the prescribed dose.



Due to the small number of patients, multivariate analysis of correlation between LC and patients' clinical and dosimetric data was not possible, and further studies are needed to identify the most predictive variable.

Conclusions: LC for HNC patients treated with SIB IMRT significantly correlates with pathology, stage and the use of concomitant chemotherapy. Treatment plan dosimetric data such as D_{mean} and EUD appear to be useful predictors of LC for this group of patients.

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Reirradiation, cetuximab and itraconazole in locally recurrent and unresectable head and neck cancer

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Purpose/Objective: Locoregional inoperable recurrence of previously irradiated head and neck carcinoma (HNC) remain a therapeutic challenge. In our previous study, we combined re-RT with cetuximab, with the aim to inhibit epidermal growth factor receptor EGFR and consequently increase tumor radiosensitivity, but this therapeutic approach did not influence patient survival in the comparison to standard therapy. [Hedgehog \(HH\) signaling pathway, which plays important role in embryogenesis, carcinogenesis und radioresistance, can mediate therapeutic resistance to EGFR targeted therapies.](#) Itraconazole is well known antimicotic agent which inhibits HH signaling. In patients with advanced basal cell carcinoma, itraconazole inhibited this pathway and caused promising clinical response. We propose that inhibition of HH signaling with itraconazole will avoid development of resistance to cetuximab and that simultaneous inhibition of these two pathways which interfere with radioresistance may lead to better tumor response and consequently prolonged survival in patient with recurrent HNC treated with re-RT.

Materials and Methods: Between March and November 2014, we reirradiated (59.4 Gy, 5 X 1.8 Gy/Week) 5 patients with inoperable, previously irradiated, recurrent HNC. Cetuximab was given initially at 400 mg/m² two days prior to re-RT and weekly (250 mg/m²) thereafter. Patients were treated with first dose itraconazole (100 mg) two days prior to re-RT and continued to take this drug daily two weeks after finishing re-RT.

Results: Itraconazole did not increase toxicity of re-RT and cetuximab expecting for induction of acne-like skin rash. 3 patients developed grade III and 1 grade II of this complication. Until now, three patients had a first follow-up investigation - two partial responses (1 patient with grade I and one with grade III skin rash) and 1 with grade III and one stable disease were documented.

Conclusions: Promising antitumor responses were observed. To determine if this therapeutic strategy may influence survival in patients with recurrent HNC treated with re-RT, larger clinical studies are necessary.

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Hypofractionated radiation therapy for nasopharyngeal carcinoma: preliminary results

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Purpose/Objective: To evaluate the efficacy and toxicity in a group of patient with non-metastatic nasopharyngeal carcinoma (NPC) treated with a hypofractionated radiation therapy with or without chemotherapy.