Title	Change in volumes and radiation doses of parotid and submandibular glands during intensity modulated radiation therapy (IMRT) for nasopharyngeal carcinoma
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modulated radiation therapy (IMRT) may improve the therapeutic ratio by reducing doses to normal tissue. The aim of this study is to address the efficacy and toxicity profile of 3D-CRT including IMRT for a cohort of patients with locally recurrent NPC.

Materials/Methods: Between May 1997 and June 2009, 212 patients diagnosed with locally recurrent NPC by biopsy and/or CT/MRI evidence of progressive skull base erosion and clinical symptoms were treated with 3D-CRT or IMRT. Median time to recurrence was 29 months (range 1 - 238 months) after the completion of conventional radiation to definitive dose. Fifty-three percent of the cases had rT3 - 4 classification. Minimum planned doses were 50 - 60 Gy in 1.8 - 2 Gy per daily fraction to the gross disease with margins, with or without chemotherapy.

Results: The median dose to the recurrent tumor was 64.2Gy (range 30 - 82Gy). Eleven patients received less than 50 Gy because of the severe acute side-effects, 57 patients received 50 - 60Gy. With a median follow-up of 25 months (range 3 - 135months), the locoregional recurrence-free survival (LRRFS), disease-free survival (DFS), and overall survival (OS) rates at 1-,3-,and 5 years were 79.1%, vs. 43.7% vs. 30.6%, 78.8% vs. 43.1% vs. 29.6% and 79.1% vs. 44.5% vs. 31.9%, respectively. Moderate to severe late toxicities were noted in 84 patients (39.6%), 24 patients (11.3%) had posterior nasal space ulceration, 38 (17.9%) developed cranial nerve palsies, 28 (13.2%) had trismus, and 32 (15.1%) suffered deafness. Advanced recurrent T- classification and long disease-free interval were adverse prognostic factors in multivariate analysis.

Conclusions: Re-irradiation with 3D-CRT provides reasonable long-term control in patients with locally recurrent NPC with acceptable profile of adverse-effects.

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2625 Treatment Outcome and Prognostic Factors for Nasopharyngeal Carcinoma with Cranial Nerve Palsy Treated by Conventional or Conformal Radiotherapy

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Purpose/Objective(s): To evaluate the therapeutic outcome for nasopharyngeal carcinoma (NPC) with cranial nerve (CN) palsy treated by conventional or conformal radiotherapy (RT), and to analyze the associated prognostic factors.

Materials/Methods: A total of 104 patients with NPC with CN palsy curatively treated by conventional (n = 44) or conformal (n = 60) RT from January 2000 to July 2007 were enrolled. Upper CN (II-VI) palsy was presented in 81 (78.9%) patients, lower CN (VII-XII) palsy in 4 (3.8%) patients, and both upper and lower in 19 (18.3%) patients. Sixty-three (60.6%) patients had CN palsy for more than 2 months before diagnosis. The median dose of RT was 73.9 Gy (range, 64.8 - 86.4 Gy). Concomitant cisplatin-based chemotherapy (C/T) was given to 78 (75%) patients.

Results: Complete recovery of CN palsy was observed in 74 patients (71.2 %). The interval of CN palsy more than 2 months before diagnosis was the independent adverse prognosticator for the CN recovery following treatment (43.9 % versus 88.9 %, $p < 0.001$). The actuarial 5-year loco-regional control (LRC), distant metastasis-free survival (DMFS), and overall survival (OS) rates were 58.2 %, 62.2 % and 38.4 %, respectively. No significant prognosticator was found for LRC. On the contrast, we observed patients with age $\geq$ 60 years, histology of WHO type I, and without receiving C/T had poorer OS; those with histology of WHO type I had worse DMFS. We did not observe any significant difference in the CN recovery, LRC, DMFS, and OS for patients treated by conventional versus conformal technique. However, significant reduction of grade 3 or greater toxicities was found in those treated by conformal technique. (odds ratio = 0.25, 95 % confidence interval = 0.10 - 0.61).

Conclusions: The recovery of CN palsy, LRC, and survival in NPC patients with CN palsy did not significantly change with the treatment evolution for conventional to conformal technique.

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2626 Change in Volumes and Radiation Doses of Parotid and Submandibular Glands during Intensity Modulated Radiation Therapy (IMRT) for Nasopharyngeal Carcinoma

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Purpose/Objective(s): To investigate the changes in volumes and radiation doses to parotid and submandibular glands during IMRT for nasopharyngeal carcinoma in an attempt to justify re-planning in the mid-course of IMRT to minimize radiation-induced xerostomia.

Materials/Methods: 33 consecutive patients with stage III to stage IVB nasopharyngeal carcinoma (AJCC Staging Manual 6th Edition) who received concurrent chemoradiation were included in this study. Computed tomography (CT) scans were performed for IMRT planning purposes (PLCT) and at mid-course of IMRT (MCCT) with head and neck immobilized by the same thermoplastic cast. Volumes of parotid and submandibular glands were outlined in these two set of CT images. Treatment plans were generated by planning systems for PLCT. PLCT of all patients were then co-registered with their corresponding MLCT. The treatment plans for PLCT were then copied to MCCT preserving the same beam shapes, angles and energies of PLCT. Dose distribution on MCCT was then re-calculated using this re-normalized plan so that differences in radiation dose will be due to anatomical and positioning changes rather than differences in dose calculation algorithms. Volumes of parotid and submandibular glands on PLCT and MCCT together with dosimetric parameters including D95, D50, D05, D01 and minimum, mean, maximum doses were compared by paired sample *t*-tests.

Results: All 33 patients had their volumes of parotid and submandibular glands significantly reduced on MCCT (Table 1). The minimum and mean doses, D50, D05 and D01 of both parotids were significantly increased during mid-course while there was no difference of the dosimetric parameters of both submandibular glands before and during mid-course.

Conclusions: The major salivary glands shrank and the parotids received a higher radiation dose during IMRT for nasopharyngeal carcinoma. This signifies that adaptive radiotherapy with re-planning should be seriously considered during course of IMRT as normal organs can receive an unexpected higher dose leading to more profound complications.

Table. Change in volumes of parotid and submandibular glands at mid-course of IMRT for NPC

Parameter	Right parotid (PLCT/MCCT)	*p*-value	Left parotid (PLCT/MCCT)	*p*-value	Right submandibular (PLCT/MCCT)	*p*-value	Left submandibular (PLCT/MCCT)	*p*-value
Mean volume (cm^3)	27.25/21.23	0.000	24.43/18.56	0.000	8.16/5.42	0.000	7.73/5.41	0.000
Mean change (%)	-22.09		-24.03		-33.58		-30.01	

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2627 Dosimetric Evaluation Of Less-than-daily IGRT Regimens In The Treatment Of Nasopharyngeal Carcinoma

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Purpose/Objective(s): For head and neck cancers, less-than-daily image guided radiotherapy (IGRT) has been proposed as an alternative to daily IGRT as a means of reduce imaging dose while maintaining treatment accuracy. The aim of this study was to determine the dosimetric effects of less-than-daily IGRT on tumor volumes and critical structures in the treatment of nasopharyngeal cancer (NPC) with intensity-modulated radiotherapy (IMRT).

Materials/Methods: Positioning and dosimetric data were collected from 10 NPC patients treated with IMRT to a prescription dose of 70 Gy to 95% of the PTV in 33 fractions, in accordance with guidelines proposed by RTOG trial 0615. Using megavoltage CT data obtained daily per a prospective institutional registry protocol, three less-than-daily IGRT regimens were hypothetically simulated: (1) imaging on the first fraction only, (2) weekly imaging with 3mm action threshold, and (3) imaging on alternating days. To evaluate the dosimetric effect of these less-than-daily IGRT regimens, we shifted the planned dose matrices according to simulated positional errors, discounting changes in anatomy. The following daily and cumulative endpoints were then analyzed: dose to 95% (D_{95}) and 99% (D_{99}) of the gross tumor volume (GTV), clinical target volume (CTV) and planning target volume (PTV), as well as the maximum doses to the brainstem, spinal cord, optic nerves, and optic chiasm.

Results: Initial results (n = 5) suggested that D_{95} and D_{99} for the GTV and CTVs met the planned dose for all patients, regardless of IGRT regimen. For the GTV, daily D_{95} <95% of the planned dose occurred 7%, 4% and 1% of the time for regimens 1, 2, and 3; and daily D_{99} < 95% of the planned dose occurred 14%, 10% and 5% of the time, respectively. Similarly, for the CTV, daily D_{95} and D_{99} <95% of the planned dose occurred on 2%, 1% and 0%, and on 12%, 4% and 2% of fractions, respectively. The cumulative dose to the spinal cord exceeded dose constraints in 20% of patients with the first IGRT regimen. Using simulated IGRT regimens 1, 2, and 3, the daily doses exceeded dose constraints on 12%, 21%, and 6% of fractions for the brainstem, 30%, 12%, and 7% of fractions for the spinal cord, 9%, 12%, and 3% of fractions for the chiasm, and 18%, 21%, and 12% of fractions for optic nerves, respectively.

Conclusions: Planned dose objectives to the GTV and CTV were satisfied with each of the less-than-daily IGRT regimens, but cumulative overdose to the brainstem, spinal cord and optic nerves were observed with IGRT on the first fraction and IGRT weekly. IGRT on alternating days eliminated cumulative overdose and minimized fractional overdose to the brainstem, spinal cord, optic chiasm and optic nerves. This suggests that less-than-daily IGRT may be clinically acceptable, provided sufficient PTV margins are incorporated.

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2628 Brachytherapy, a Highly Focused Technique for Applying High Booster Doses of Radiation. Question: Can it be of Value in Reducing the Local Relapse Rate in Advanced Cancer of the Nasopharynx?

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Purpose/Objective(s): Mainstay of treatment of NPC is Intensity Modulated Radiation Therapy (IMRT). Except for T1N0 tumors, a dose of 70/2 Gy is given to the primary tumor and neck nodes, combined with concomitant chemotherapy (cCHT). However, particularly with advanced T-stages (T3,4), patients remain to fail locally. Thus applications of conformal boosts using RT doses beyond 70 Gy, might be appropriate. To enable boosting by endocavitary brachytherapy (BT) in limited T-stages (T1,2N0), a Nasopharyngeal Applicator (NA) was designed. Whether the NA is as effective in early (T1,2) as in more advanced T3,4 NPC categories is the purpose of this investigation.

Materials/Methods: The database for advanced NPC stages T1,2N+ and T3,4N0,+ consists of patients treated by 70 Gy and BT boost (B) in the Erasmus MC (Rotterdam, n = 94), by 70 Gy and cCHTin the AvL/NKI (Amsterdam, n = 89) (C), and according to