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Impact of observer delineation variation on target coverage and dose to organs at risk in nasopharyngeal cancer patients

N. Pimentel Serra[1,2], B. van Asselen[2], R. Steenbakkers[2], J. Duppen[2], J. van de Geer[2], M. van Herk[2], C. Rasch[2]. [1]*Hospital Santa Maria, Serviço de Radioterapia, Lisboa, Portugal;* [2]*Antoni van Leeuwenhoek Ziekenhuis/Nederlands Kanker Instituut, Radiation Oncology Department, Amsterdam, The Netherlands*

Purpose: To provide a qualitative and quantitative correlation between inter-observer variation and dose coverage of targets and organs at risk (OAR) in Nasopharynx Patients (NPC).
Materials & Method: Ten nasopharyngeal patients' were included in this study. Ten Head & Neck radiation specialists delineated the Clinical target volumes (CTV) on CT with MRI and specific delineation instructions available. A median CTV was determined for each patient and accounted as the reference target volume. A 3D margin of 5 mm was applied to generate the planning target volume (PTV). The optical chiasm, brainstem, spinal cord and cerebellum were delineated for evaluation. The inverse planning module of ADAC Pinnacle^{3TM} was used to generate an IMRT plan for each CTV, resulting in eleven different dose distributions per patient.
In-house software package (Uncert$^{®}$) simulating random and systematic errors was used to calculate the dose to the median CTV and organs at risk (OAR) for each dose distribution, delineation and patient. The 95% and 90% dose volume to the median CTV was used to calculate the delineation effect on the CTV. The maximum dose was used to determine the impact of the inter-observer variation on dose to the OARs.
Results: a) The 95% dose coverage of the median CTV was 95.7% (sd 4.9). For the same volume, the 95% dose coverage dropped to 84.8% (sd 8.10) when the treatment plans designed for the individual observer PTVs were applied ($p < 0.05$). b) There was a direct impact of inter-observer variation on the maximum dose to the OAR's. For the chiasm, brainstem, spinal cord and cerebellum, the percentage of patients unable to fulfill both the pre-set PTV and OAR dose levels due to difference in observer PTV volumes, was 50%, 70%, 10% and 70% respectively.
Conclusion: Inter-observer delineation variation has a quantifiable direct impact on target dose coverage and influences dose to the OAR's. Interobserver variation leads to underdosage or avoidance of designated tumor volumes and/or unnecessary radiation dose to normal tissues. Delineation variation has to be addressed and minimized for accurate and objective target delineation and ultimately for highly conformal radiation treatments.
Keywords: Delineation Effect, IMRT, Inter-observer Variation, Nasopharynx, Radiotherapy;

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Impact of induction chemotherapy on treatment outcome in patients with early stage nasopharyngeal carcinoma

D.T.T. Chua[1], J. Ma[2], J.S.T. Sham[1], H. Mai[2], D.T.K. Choy[1], M. Hong[2], T. Lu[2], H. Min[2]. [1]*Queen Mary Hospital, Department of Clinical Oncology, Pokfulam, Hong Kong;* [2]*Cancer Center, Sun Yat-Sen University, Department of Radiation & Nasopharyngeal Carcinoma, Guangzhou, China*

Background: Prospective phase III studies failed to show any impact on survival with the addition of induction chemotherapy in patients with nasopharyngeal carcinoma (NPC). In order to evaluate the role of induction chemotherapy on survival and failure patterns in different patient subgroups according to T and N stage, we performed subgroup analysis of two phase III trials.
Materials and Methods: The pooled data from two phase III trials comparing induction chemotherapy (cisplatin/epirubicin or cisplatin/bleomycin/5-fluorouracil) followed by radiotherapy (CRT) with radiotherapy alone (RT) in NPC were reviewed and analyzed according to the following 4 subgroups based on T and N stage (1997 AJCC stage classification system): Group 1 with early T and N stage (T1–2N1), Group 2 with advanced N stage (T1–2N2–3), Group 3 with advanced T stage (T3–4N0–1) and Group 4 with advanced T and N stage (T3–4N2–3). A total of 784 patients were included for analysis based on intent-to-treat. Median follow-up for surviving patients was 67 months.
Results: No significant differences in survival, loco-regional control and distant metastases-free rates were observed between CRT arm and RT arm in Group 2, 3 and 4. On the contrary, significant differences in survival and distant metastases-free rates were observed in Group 1 favoring CRT arm.
Conclusion: Our pooled data analysis showed that patients with early stage NPC (T1–2N1 or stage IIb) treated by radiotherapy alone had a relatively poor long term survival due to distant metastases which could be improved by induction chemotherapy. Further studies to evaluate the role of adjunctive chemotherapy in early stage NPC are warranted.

	Group 1 (T1–2N1) n = 208	Group 2 (T1–2N2–3) n = 181	Group 3 (T3–4N0–1) n = 241	Group 4 (T3–4N2–3) n = 154
5-year survival rates				
CRT:	79%	55%	62%	44%
RT:	67%	60%	57%	43%
p:	0.048	0.98	0.16	0.51
5-year local relapse-free rates				
CRT:	86%	78%	65%	68%
RT:	83%	77%	56%	58%
p:	0.62	0.88	0.054	0.56
5-year nodal relapse-free rates				
CRT:	89%	77%	91%	74%
RT:	88%	73%	88%	70%
p:	0.81	0.96	0.58	0.80
5-year distant metastases-free rates				
CRT:	86%	61%	81%	55%
RT:	74%	70%	79%	49%
p:	0.0053	0.63	0.93	0.34

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Preliminary report of randomized phase II clinical study comparing standard radiotherapy with or without weekly oxaliplatin in treatment of locoregionally advanced nasopharyngeal carcinoma (NPC)

L. Zhang, C. Zhao, P.J. Peng, LX. Lu, P.Y. Huang, F. Han, S.X. Wu. *Cancer Center, Sun Yat-Sen University, Medical Oncology Department, Guangzhou, China*

Background: A prospective randomized phase II study was performed to evaluate the feasibility and efficacy of concurrent weekly oxaliplatin with radiotherapy in patients with locoregionally advanced nasopharyngeal carcinoma (NPC).
Material and methods: From Jan. 2001 to Jan. 2003, 115 locoregionally advanced nasopharyngeal carcinoma were randomized, to either radiotherapy alone (RT arm, 56 patients) or to concurrent chemo-radiotherapy (CCRT arm, 59 patients). All patients' characteristics were well balanced in both arms. Concurrent chemotherapy with oxaliplatin 70 mg/m^2 weekly was given for six doses from the first day of radiotherapy. All patients were treated in an identical method by definitive-intent radiation therapy in both arms.
Results: All patients were eligible for toxicity and response analysis. After a median follow-up of 24 months, there is a significant difference in overall survival (OS), relapse-free survival (RFS) and metastasis-free survival (MFS) in favor of the CCRT arm. The 2-year overall survival rates were 100% for the CCRT arm and 77% for the RT arm ($P = 0.01$). The 2-year metastasis-free survival rate was 92% for the CCRT arm versus 80% for the RT arm ($P = 0.02$). The 2-year relapse-free survival rate was 96% for the CCRT arm versus 83% for the RT arm ($P = 0.02$).
Conclusion: Concurrent chemo-radiotherapy with weekly oxaliplatin is feasible and improves the survival rate as well as the metastasis-free survival rate and relapse-free survival rate in the patients with locoregionally advanced nasopharyngeal carcinoma. Therefore, further randomized study including oxaliplatin is warranted.
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Results of nasopharynx cancer treated with high dose 3-dimensional conformal radiation therapy technique

Y.J. Park, Y.C. Ahn, S.G. Ju, W. Park, H.R. Nam, D.R. Oh, S.M. Yoon, Y.I. Han. *Samsung Medical Center, Radiation Oncology, Seoul, Korea*

Background: Authors have used a unique 3-dimensional conformal radiation therapy technique in treating nasopharynx cancer (NPC), and named it 'Samsung Medical Center (SMC) technique'. Herein, we would report the clinical outcomes of NPC patients treated with this method.
Material and methods: SMC technique is based on "serial shrinking field" concept by 1.8 Gy daily fractions. The initial radiation volume includes all gross lesions plus clinically negative lymphatics (36 Gy), the second volume typically eliminates the electively included lymphatics (54 Gy), and the final boost volume is confined to the gross lesions (72 Gy). The