Their pharmacokinetic (pk) behavior could be dependent not only on PTX excipient (polyethoxylated castor oil) interference, but even on different i.v. administration intervals between the two drugs. This study evaluated any possible administration interval-dependent pk interaction, when PLD infusion started 0, 1, 3, 12 or 24 h after PTX infusion end.
Materials and Methods: 30 patients, affected by recurrent cisplatin pre-treated squamous cellhead/neck cancer, were randomized to receive PTX 80 mg/m^2 q1w and PLD 12.5 mg/m^2 q2w at administration intervals of 0, 1, 3, 12 or 24 h. Pk parameters were evaluated during the first course by non-compartmental analysis, while statistical analysis was performed by non-parametric Kruskal Wallis test
Results: median pk parameters are reported in the table. The PTX pk profile is strongly affected by PLD administration. PTX total exposure is highly reduced, with a consequent increase in Cl_{tot}: this alteration is totally due to K_{el} modifications. On the other side, no statistically significant interactions affected PLD pk parameters. Some in vitro experiments indicate that PLD is able to partially absorb PTX, driving to PTX plasmatic concentration reduction, when PLD is administered at 0−1h interval.

Parameter	PTX						PLD					
	Administration interval					p	Administration interval					p
	0 h	1 h	3 h	12 h	24 h		0 h	1 h	3 h	12 h	24 h	
C_{max} (mg/l)	0.26	0.40	0.76	0.61	0.41	0.042	5.11	6.71	6.08	6.92	6.86	0.121
AUC_{tot} (mg/l*h)	0.87	1.57	4.67	4.29	3.36	0.005	676.4	606.8	749.6	723.8	739.6	0.515
K_{el} (h^{-1})	0.39	0.26	0.19	0.02	0.11	0.003	0.007	0.008	0.007	0.008	0.007	0.613
Cl_{tot} (l/h)	153.2	92.5	28.7	32.2	41.7	0.005	0.031	0.036	0.029	0.030	0.029	0.681

Conclusions: PLD liposomal components seem to be able to entrap PTX, therefore reducing PTX plasmatic concentrations: so, it is very important to choose the ideal administration interval. In order to avoid pk interaction, the i.v. administration interval between PTX and PLD had to be 3 h at least. For shorter interval, patients could be underexposed to PTX, with lesser clinical efficacy.

5523 POSTER

Risk of distant metastases after postoperative radiation therapy for locally advanced laryngeal cancer

A. Idasiak, S. Blamek, R. Suwinski. *M. Sklodowska-Curie Memorial Institute, Radiotherapy department, Gliwice, Poland*

Background: Laryngeal cancer is the most common head and neck malignancy. Postoperative radiotherapy in advanced laryngeal cancer reduces risk of local and regional recurrences. An improvement in local and regional control achieved by combined therapy results that distant metastases become an increasingly common case of treatment failure.
Objective: The aim of the study is to evaluate the risk of development distant metastases for patients with laryngeal cancer after postoperative radiotherapy. The particular aim of the study is:
1. To estimate the prognostic factors for the risk of distant metastases.
2. To construct theoretic algorithm of the relationship between clinical and pathological parameters and risk of distant metastases.

Material and Methods: Medical records of 267 patients (23 women, 244 men) with laryngeal cancer treated between 1997–2002 were analyzed. The age ranged from 37 to 78 (median 58). All patients had locally advanced squamous cell laryngeal cancer treated with surgery and postoperative radiotherapy. Locally advanced tumors (T3, T4) constituted 205 cases (77%). There were 62 (23%) patients in stage T1 and T2. Enlarged lymph nodes were found in 155 cases.
The survival plots were estimated using the Kaplan-Meier method. A multivariate Cox proportional hazard model and logistic regression model was used to evaluated influence of the following variables on MFS and the ultimate risk of metastases: age, sex, localization, TN stage, HGB before and at the end radiotherapy, total radiation dose, dose per fraction, overall treatment time, interval surgery-radiation time, pathological margins and positive nodes in surgical specimen. The effective doubling time of tumor clonogens has been estimated for local recurrences and distant metastases.
Results: The crude incidence of distant metastases was 12% (33/267 pts). One year, 3-year, 5-year actuarial metastases free survival were 95%, 85% and 84% respectively.
The Cox regression analysis revealed two variables, which had significant and independent influence on metastases-free survival: localization of cancer (glottic vs. supraglottic) and number of positive lymph nodes at pathological staging. The lungs and bones were the most common sites of metastases (58% and 33% respectively), whereas metastases to liver (6%) and brain (3%) were rare. The effective clonogen doubling time for loco-regional recurrence and distant metastases were estimated as 12.5 day and 16−32 days respectively.
Conclusion: Distant metastases rate is comparable with percentage of local treatment failure and in the presented group of patients was 12% vs. 16%. Number of positive lymph nodes in pathological specimen and site of primary cancer (glottic vs. supraglottic) significantly and independently predict a risk of distant metastases in combined modality treatment for laryngeal cancer.

5524 POSTER

Primary tumor volume predicts locoregional control and survival after concurrent chemoradiation with daily low dose cisplatin for advanced stage head and neck carcinoma

F. Hoebers[1], F. Pameijer[2], J. de Bois[1], W. Heemsbergen[1], A. Balm[3], J. Schornagel[4], C. Rasch[1]. *[1]The Netherlands Cancer Institute, Radiotherapy Department, Amsterdam, The Netherlands; [2]The Netherlands Cancer Institute, Radiology Department, Amsterdam, The Netherlands; [3]The Netherlands Cancer Institute, Department of Head and Neck Oncology and Surgery, Amsterdam, The Netherlands; [4]The Netherlands Cancer Institute, Department of Medical Oncology, Amsterdam, The Netherlands*

Background: To evaluate the prognostic value of tumor volume in patients with advanced HNSCC treated with concurrent cisplatin-chemoradiation.
Material and Methods: 46 patients were treated with radiotherapy (35×2 Gy) and cisplatin (6 mg/m^2 i.v. daily). Tumor sites were: oropharynx 72%, oral cavity 22%, hypopharynx 2%, and larynx 1%. Baseline primary tumor volume was recorded from diagnostic MRI-scan. In uni- and multivariate analysis, the prognostic impact of patient-, tumor-, and treatment-related factors was investigated, including primary tumor volume, for locoregional control and disease free survival.
Results: Mean follow up was 40 months (range 23−69) for patients alive at last follow-up. Mean tumor volume was 28 cm^3 (median 23, range 3–112). Oral cavity tumors were statistically significantly larger than oropharyngeal tumors (41 vs. 24 cm^3, p = 0.05). Tumor volume and T-stage were positively correlated: T3-tumors had a mean tumor volume of 19 cm^3, whereas the volume of T4-tumors was 40 cm^3 (p = 0.003). Locoregional (LR) control at 3 years was 72% for all patients. Disease free survival (DFS) was 36%. The LR control rate at 3-years was 81% for patients with tumor-volumes = median (p = 0.036). Oropharyngeal tumors had significantly better 3-year LR control rates compared to oral cavity tumors: 75% vs. 44% (p = 0.013). T3-tumors had significantly better 3-year LR control rates compared to T4-tumors: 78% vs. 44% (p = 0.033). In multivariate analysis, primary tumor site and larger tumor volumes were factors significantly associated with decreased LR control and DFS. T-stage was associated with LR control, but not DFS (Table).
Conclusions: In advanced HNSCC treated with concurrent chemoradiation, primary tumor volume is significantly associated with LR control and DFS and should therefore be incorporated in the staging system as a tool to guide treatment and predict outcome.

Variable	UV analysis, HR (95% CI)	p-value	MV analysis, HR (95% CI)	p-value
Disease free survival				
Site (oral cavity vs rest)	0.5 (0.2−1.0)	0.05	0.4 (0.2−1.0)	0.05
T-stage	1.4 (0.8−2.3)	0.2	-	
Tumor volume	1.02 (1.00−1.03)	0.01	1.02 (1.00−1.03)	0.05
Locoregional control				
Site (oral cavity vs rest)	0.3 (0.1−1.0)	0.04	0.2 (0.1−0.8)	0.02
T-stage	3.6 (1.2−10.7)	0.02	-	
Tumor volume	1.03 (1.00−1.04)	0.005	1.02 (1.00−1.05)	0.04
Level IV involvement yes/no	3.1 (1.0−10.0)	0.06	2.0 (0.4−9.9)	0.4
ASA (Co-morbidity score, 1−3)	2.1 (0.9−6.35)	0.02	1.6 (0.7−3.7)	0.2

5525 POSTER

Retropharyngeal nodal metastasis is related to a higher rate of distant metastasis in patients with nasopharyngeal cancer – results from a single centre retrospective study

I.W.K. Tham[1], S.P. Yap[1], J. Tuan[1], S.W. Hee[2], J. Wee[1]. *[1]National Cancer Centre, Department of Radiation Oncology, Singapore, Singapore; [2]National Cancer Centre, Department of Clinical Trials & Epidemiological Sciences, Singapore, Singapore*

Background: There is currently no consensus on how Retropharyngeal Lymph Nodes (RLN) in Nasopharyngeal Cancer (NPC) should be “staged”. A recent study showed a borderline significant difference of distant metastasis-free survival (DMFS) rates between patients with or without

RLN metastasis. In N(0) disease, the presence of RLN metastasis was also a significant independent predictor for DMFS.
The aim of this report is to retrospectively review a cohort treated at our centre between 1992–1994, and to examine if the presence of RLN resulted in an increased incidence of distant metastases, especially in patients with otherwise N(0) disease.
Materials and Methods: A review was conducted on case records of 662 patients with histologically proven, non-metastatic NPC staged with CT scans and treated with radical radiotherapy (RT) alone on standard protocols. None received adjuvant chemotherapy.
Patients with obvious RLN on CT scans as well as patients with "parapharyngeal" extension to below C1/C2 level were deemed to have RLN. This criteria was based on our previous study comparing CT with MRI, where about 51% of RLNs were present below C1/C2 level. It has also been shown that most parapharyngeal involvement seen on CT appears to be retropharyngeal nodes on MRI. The AJCC/UICC Staging (6th edition) was retrospectively applied based on the original clinical and CT findings.
Results: Median follow-up for all patients was 5.1 years, and 11 years for patients alive at time of censorship. Median age was 48 years. 73% were male and 88.8% were of WHO Type 3 histology. 178 (24.7%) were staged N(0) of which 44 (24.7%) had RLN.
The 5-year DMFS after adjustment by age and sex were 91% for N(0) without RLN, and 78% for N(0) with RLN. The adjusted 5-year DMFS for N1 patients was 68%. The hazard ratios after adjustment by age, sex, and T-stage of N(0) with RLN, and N1 patients compared to the N(0) without RLN patients were 2.1 (95% CI, 0.9−4.7) and 3.6 (2.1−6.2) respectively.
Although the DMFS of N(0) with RLN patients was only marginally different than N(0) without RLN ($p = 0.071$), the DMFS of N(0) with RLN was not significantly different than N1 ($p = 0.101$).
Conclusion: Our study suggests that N(0) patients with RLN have a poorer DMFS compared to patients without RLN metastases, and have a similar outcome to N1 patients. Hence, we would recommend that the presence of RLN should now be considered as "N" disease in future staging systems for NPC.

5526 POSTER

Xerostomia and related quality of life in patients treated with intensity modulated radiation therapy for nasopharyngeal cancer: initial report of a prospective study

L. Marucci[1], S. Marzi[2], I. Sperduti[3], M. Benassi[1], G. Giovinazzo[1], M. Benassi[4], G. Arcangeli[1]. *[1]Regina Elena National Cancer Institute, Radiation Oncology, Rome, Italy; [2]Regina Elena National Cancer Institute, Medical Physics, Rome, Italy; [3]Regina Elena National Cancer Institute, Biostatistic, Rome, Italy; [4]Regina Elena National Cancer Institute, Mediacal Physics, Rome, Italy*

Purpose: To evaluate xerostomia and related quality of life in patients treated with Intensity Modulated Radiation Therapy (IMRT) for nasopharyngeal cancer.
Material and Methods: A prospective study was initiated in May 2003. The first 8 patients (Group I) were treated with a 5 field IMRT technique and the following 20 (Group II) with a 7 field technique. Salivary gland toxicity was evaluated using the RTOG scale, salivary flow (SF), and a xerostomia related questionnaire (XQ). The assessments were done before the beginning of therapy and at 3, 6, 12, 18 and 24 months after the end of radiotherapy.
Results: Twenty-eight patients with at least 6 months follow up are included in this initial report. The mean parotid dose was 35.8 Gy for the entire population, 45.5 Gy for Group I and 31.9 Gy for Group II. The difference between Group I and Group II parotid gland mean DVHs was statistically significant $p = 0.0001$. Using the RTOG scale, in group II there was no G3 toxicity and 28% of the patients were G0 at 18 months, while 25% of the patients in Group I were G3 and none was G0 at 18 months. Analysis of the SF showed that at 18 months, 80% of the patients in group II while only 53% in group I recovered at least 25% of their pre-therapy value. A strong trend toward correlation was observed between a mean parotid dose of less than 32 Gy and the stimulated SF recovery of more than 25% at 12 months ($p = 0.056$) A significant correlation was also found between the volume of the glands that received a dose of more than 25, 30, and 35 Gy (V25, V30 and V35) and the recovery of the SSF >25% at 12 months.
The XQ score showed a similar change in time as the SF. The stimulated SF showed a statistically significant correlation with the XQ score at any time (with a p value ranging from 0.018 to 0.036). Questions evaluating the sleeping and tasting functions and the need to sip water during the day, showed the greatest improvements (p ranging from 0.03 to 0.05).
Conclusion: The use of IMRT for the treatment of nasopharyngeal cancer allows a decrease in the parotid gland mean dose and reduces salivary gland toxicity. An increase in saliva translated into an improvement in the patients' perception of xerostomia related side effects.

5527 POSTER

High dose rate brachytherapy as a boost to radio-chemotherapy in base of tongue cancer

J. Vock[1], B. Isaak[1], J. Curschmann[1], E.E. Friedrich[1], F. Behrensmeier[1], R.H. Greiner[1], D.M. Aebersold[1], C. Kolotas[2]. *[1]University of Bern, Radiation oncology, Bern, Switzerland; [2]Hirslanden Klinik Aarau, Radiation oncology, Aarau, Switzerland*

Background: Interstitial boost to external beam irradiation (EBI) with low dose rate (LDR) BT in cancer of the base of tongue results in improved local control without additional toxicity compared to EBI alone. Data for HDR BT are scarce; however, compared to LDR BT this technique has the advantage of less radiation exposure for medical staff. The purpose of this study was to assess feasibility and short term clinical outcome of interstitial HDR BT and radio-chemotherapy in cancer of base of tongue.
Materials and Methods: Between 02/2003 and 02/2006, 20 patients (pts) with cancer of base of tongue were treated with HDR BT followed by EBI and concurrent chemotherapy. Their median age was 59 (46−83) years. AJCC stage was I/II in two pts, III in six and IVa in twelve pts. Fourteen pts had positive cervical lymph nodes. Neck dissection was carried out in 7/20 pts. Concomitant platinum based chemotherapy was given in all but one patient. A median number of five (2−9) applicators were implanted under general anaesthesia. After CT based treatment planning, HDR BT was delivered by an afterloading unit with an iridium-192 source. The median planning target volume was 37 (12–118) ccm. The median coverage (V100) was 92 (86−97)% of the target volume. The median HDR target dose was 24 (9−32) Gy, the median EBI dose 60 (50−72) Gy.
Results: At a median follow-up of 18 (5−41) months, 17 pts (85%) were alive, 14 pts (70%) without evidence of disease. One patient had died due to regional, one due to distant progression and one from unclear reason. Local control at the base of the tongue at time of death or last follow-up was 90% (two pts with initial T3/4 disease locally relapsed), Regional control 70%, two pts developed distant metastases.
There were no perioperative complications due to the implant. Two pts suffered radionecrosis of mandible during follow-up.
Conclusions: These preliminary data suggest that HDR BT as a boost prior to radio-chemotherapy results in excellent local control, regional control comparable to literature and acceptable toxicity.

5528 POSTER

Non-surgical treatment of the neck in cN+ oropharyngeal squamous cell carcinoma

W. Duthoy, C. Goor, I. Jacobs, P. Meijnders, S. Vanderkam, D. Van Gestel, D. Van den Weyngaert. *ZNA Middelheim, Department of Radiotherapy, Antwerp, Belgium*

Background: Squamous cell carcinoma (SCC) of the oropharynx often presents with lymph node metastases. The treatment of the clinically positive neck (cN+) can be primarily surgical or with radiotherapy (RT) or concomitant radio-chemotherapy (RChT). A R(Ch)T approach might result in lower chronic morbidity, like neck fibrosis, but possibly at the cost of a higher regional failure rate.
Materials and Methods: Between 2000 and 2004, 157 patients (pts) with oropharyngeal SCC were treated at our institution. Of these, 94 pts had cN+ disease. 31 pts were excluded for various reasons (previous neck dissection, palliative intent, etc.), leaving 63 pts for this retrospective analysis. 28 of them (44%) received neo-adjuvant ChT (N-ChT), followed by RChT in 11 and RT only in 17 pts. Fourteen pts (22%) were treated with RChT, and 21 (33%) received RT only. Median RT dose was 70 Gy. Response evaluation (RE) was performed at 2 months after the end of RT. The endpoints were: RE of the primary tumour and the involved neck, overall survival (OS), local control (LC), regional control (RC) and distant recurrence (DR). When less than a complete response (CR) was achieved, the date of RE was used as event date for LC and RC.
Results: T- and N-classification are shown in Table 1. Median follow-up (FU) in survivors was 46 months. A CR was obtained in 49 pts (78%) for the primary tumour, and in 50 (79%) for the neck. Median OS was 31 months, with a 2-year (2Y) and 4-year (4Y) OS of 60% and 43%, respectively. LC rates were 70% at 68% at 2Y and 4Y, respectively. The 2Y and 4Y LC rates raised to 87% and 84% for pts who achieved a CR for the primary tumour. The 2Y and 4Y RC were both 66%, with a 1Y RC of 74%. There were no regional relapses occuring after 24 months of FU. In pts achieving a CR in the neck, RC was 90% at 1 year, while the 2Y RC was 80%. No significant difference was found in RC between pts receiving N-ChT (1Y RC 77%) or not (1Y RC 71%). The 1Y RC for pts who had received RChT was 84%, while this was 67% in those not receiving RChT. Isolated regional recurrence as first site of relapse was seen in 5 pts (8%), of whom 2 could be salvaged surgically. During FU, DR was diagnosed in 13 pts (21%), 5 of whom had received N-ChT.