5519 POSTER

Proton beam therapy for nasal cavity and paranasal sinus malignancies

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Background: Advanced malignancy of nasal cavity and paranasal sinus shows high rate of local failure, and is difficult to deliver enough X-ray radiation doses by conventional technique because of its proximity to critical organs such as optic pathway and brain stem. Proton beam therapy (PBT) can provide better dose distribution because of its physical characteristics, and is deemed to be a feasible treatment modality. We retrospectively reviewed our experience to analyze the feasibility and efficacy of PBT for nasal cavity and paranasal sinus malignancies.
Materials and Methods: Between 1999–2006, 93 patients with nasal or paranasal sinus malignancies were treated with PBT. There were 51 men and 42 women, with median age of 58 years (ranged 17−88). The primary lesions were nasal cavity: 51, maxillary sinus: 15, ethmoid sinus: 14, sphenoid sinus: 7, and others: 6. Various histological types were present, squamous cell carcinoma: 27, olfactory neuroblastoma: 22, malignant melanoma: 18, adenoid cystic carcinoma: 13, and others: 12. T-stage was T2/T3/T4: 14/19/53, and there were 7 patients with recurrent tumors after surgery. PBT was done using 150–190 MeV of proton beam of which the relative biological effectiveness was estimated as 1.1. The optimization of dose distribution was performed with spread-out Bragg peak method. Adverse events were assessed according to the RTOG/EORTC acute and late radiation morbidity scoring criteria. Survivals were estimated by the Kaplan-Meier method.
Results: planned reduction surgery was performed in 24 patients, and induction chemotherapy was given in 18 patients. Median total PBT dose was 65 GyE with 2.5 GyE/fr. With a median follow-up period of 16 months (ranged 2−92), 2-year local control, overall survival, and disease-free survival rates were 78%, 69%, 58%, respectively. liquorrhea and hemorrhage were observed after shrinkage of tumor in one patient each. Cataract, asymptomatic brain necrosis, bone necrosis were developed in 3, 2, 1 patients, respectively. Two patients required surgical soft tissue repair. Visual impairment and other late adverse events equal to or greater than grade 3 were not observed.
Conclusions: The improved conformity of dose delivery by proton beam allows dose escalation leading superior local control and survival rates over those achieved with conventional forms of dose delivery. Toxicity appears acceptable in light of the considerable improvement in local control over conventional therapy.

5520 POSTER

Primary and post-operative radiation therapy for squamous cell carcinoma of the tonsil: a retrospective review of a single institution's experience during the CT simulation era

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Background: A review of patients with squamous cell carcinoma (SCCa) of the tonsil treated with definitive radiotherapy (RT) ± chemotherapy (C) or postoperative radiotherapy ± C (S+RT±C) during the CT simulation era at Mayo Clinic was performed to determine tumor control, survival, and functional outcome.
Materials & Methods: Between 1989–2004, 114 consecutive patients with SCCa of the tonsil were treated with RT±C (35) or S+RT±C (79). Local control (LC), neck control (NC), survival free of distant metastasis (DM), and overall survival (OS) were evaluated along with late effects of therapy including osteoradionecrosis (ORN), tracheostomy dependency, and percutaneous endoscopic gastrostomy (PEG) dependency.
Results: Median age of patients at diagnosis for the RT±C and S+RT±C group was 57 and 52 years, respectively. 11 patients were treated with RT only, 24 with concurrent C (platinum based) and RT, 78 patients with S+RT, and 1 patient with S+RT+C. In the RT±C, median treatment duration and dose was 43 days and 72 Gy, respectively. Median treatment duration and dose for the postoperative patients was 41 days and 60 Gy. In the definitive radiotherapy group, there was total of 10 patients who underwent neck dissection as part of their treatment either pre RT (3) or post RT (7). There were more advanced T and N stage patients in the RT±C group than the S+RT±C group ($p < 0.001$). Patients treated with RT+C had more advanced local and neck disease compared to RT alone ($p < 0.0001$).
Overall survival and survival free of distant metastasis was better for the S+RT±C group although there was no difference in local or neck control. There was an increased rate of PEG dependancy at last follow up with patients undergoing RT±C. PEG dependency was associated with advanced T stage (T3 & T4, $p = 0.0009$) and the addition of C as part of treatment ($p = 0.007$). There was no significant association between tracheostomy dependency rates or ORN with the type of treatment patients received.

Summary of treatment results

Median Follow Up	RT±CT 42 months	S+RT±CT 67 months	P Value
3 year Local Control	91%	97%	0.12
3 year Neck Control	97%	96%	0.86
3 year Survival Free of DM	78%	93%	0.01
3 year Overall Survival	70%	83%	<0.01
Trach at Last Follow Up	9%	3%	0.15
PEG at Last Follow Up	26%	9%	0.02
ORN at any time	14%	9%	0.51
Surgery for ORN	3%	5%	0.17

Conclusions: Based on our analysis, RT±C provides local and regional control equivalent to S+RT±C even though the disease was more advanced (T and N). Patients with more advanced local or regional disease were more commonly treated with RT±C. This may have led to a higher rate of distant metastasis and lower overall survival compared to the surgery group. Higher rate of PEG dependency was associated with more advanced primary tumors and the addition of chemotherapy to the patient's treatment.

5521 POSTER

The anthology of outcomes: prospective point-of-care outcomes for head and neck cancer patients

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Background: The Head and Neck (HN) Radiation Oncology Site Group at our quaternary care comprehensive cancer hospital has established an Anthology of Outcomes (AO) to record outcomes prospectively at point-of-care for all new HN cancer referrals. During each clinic, clinicians indicate the following outcome events: attendance, recurrence (local/regional/distant), second malignancy, and late RTOG grade 3/4 toxicity.
Methods: All patients registered in the AO since July 2003 to Dec 2006 were retrospectively reviewed. Descriptive data, treatment strategy, and vital status were recorded.
Results: Over 3.5 years, 1866 patients were registered; of these, 1763 (F: 504, M: 1259) were treated and followed. Mean age was 62 (range: 15−93) years. Most common cancer diagnoses included: larynx (n = 394), oropharynx 379, oral cavity 357, nasopharynx 156, salivary gland 128, and unknown primary 109. Excluding patients with benign lesions, complex skin cancers and unknown primary cancers, and malignant tumours lacking TNM staging criteria, staging was available for 1585/1622 (98%) patients; 1063/1622 (65%) had advanced disease (stages III/IV), including 26 with distant metastases. Treatment intent was curative in 1688 and palliative in 75. Of patients treated with curative intent, primary surgery was used in 521 (alone, 186; with post-op RT, 284; pre-op RT, 17; post-op chemoradiation [CRT], 34), primary RT in 1167 (alone, 747; CRT 420). The most common RT dose-fractionation schemas were: 70/35 (155 RT alone, 411 CRT), 60/25 (304), 60/30 (162 RT, 18 CRT), 64/40 bid (151), 51/20 (130). IMRT (standard of care since September 2005) was used to treat 860/1577 (54%) radiotherapy patients. At a median follow-up of 16.4 months, 1379 patients (78%) are alive with ongoing follow-up, 160 have died and 224 are no longer being followed by radiation oncology.
Conclusion: Approximately 500 patients per year have been prospectively captured; about 13% are lost to follow-up. The AO allows ongoing quality assurance, rapid feasibility assessment for specific research questions, and represent a resource for outcomes research.

5522 POSTER

Paclitaxel and pegylated liposomal doxorubicin association: effects of different administration intervals on the pharmacokinetics

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Background: The paclitaxel (PTX) and pegylated liposomal doxorubicin (PLD) association is a promising schedule for recurrent head/neck cancer.

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

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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

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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

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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