situation that provides the opportunity to link molecular biology of cancer with a known environmental exposure to a mutagen.
The aim of this study was to investigate whether the frequency of ret rearrangement and BRAF mutation in papillary carcinoma of the thyroid (PTC) is related to exposure to radiation or the age of the patient at clinical diagnosis. RNA extracted from 52 cases of PTC were obtained from the Chernobyl Tissue Bank. The cases were divided into 4 groups matched on age, sex and place of residence. Two groups of 13 cases were from the areas of Ukraine most heavily contaminated with radioiodine, one group was born before the accident (1A), and the other born after 1/1/87 (1B) and therefore not exposed to radioiodine. Two other groups of 13 cases were from areas of Ukraine not exposed to significant fallout, one born before the accident (2A) and the other after 1/1/87 (2B). All patients were aged under 16 at the time of operation. The expression of ret was determined by RT-PCR for the extracellular and intracellular regions of c-ret [1] and PTC1 and 3 rearrangements were identified by rearrangement specific RT-PCR. For BRAF, mutation at position 1746 was identified by PCR followed by restriction enzyme digestion [1].
There was no significant difference among the groups with respect to type or overall frequency of ret rearrangement. The most frequent rearrangement was PTC3, accounting for 16 of the 25 cases positive for ret rearrangement. Only one case (in group 2B) was positive for BRAF rearrangement. This study shows that contrary to other reports in the literature, there is no association of either ret rearrangement per se, or PTC3 rearrangement in particular, with radiation exposure. Thyroid cancer presenting in adults is typified by a higher frequency of BRAF mutation (58% in a series from Ukraine). We suggest that the pattern of molecular biological alterations observed in post Chernobyl thyroid cancer is related to the age of the patients under study, rather than to exposure to radioiodine. The Chernobyl experience suggests that age at diagnosis should be taken into account before conclusions are drawn regarding the relationship between molecular biology and radiation. This has implications for current studies in breast cancer following radiotherapy for Hodgkin's Disease.

References

[1] Powell et al., J Pathology (2005) 205: 558–564.

Poster presentations (Tue, 1 Nov)
Head and neck and endocrine cancer

1000 POSTER

Intensity modulation radiotherapy for nasopharyngeal carcinoma – an experience in Taiwan

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Introduction: To present the treatment result of intensity modulation radiotherapy (IMRT) in nasopharyngeal carcinoma (NPC) by intensity modulation radiotherapy technique and concomitant chemoradiotherapy.
Patients and methods: There were 180 consecutive M0 NPC patients received IMRT from March 2000 and December 2003. The median age was 48 (13–84). One hundred and thirty one patients were male. All patients received H&N MRI to evaluate the local and regional tumor extension and 126 patients received FDG-PET before radical treatment. The stage distrbution was stage I: 7; stage II: 67, stage III: 55 and stage IV 51. The gross tumor volume is defined based on the MRI T1 enhanced image with reference of FDG-PET image. Initial clinical tumor vloume is defined as gross tumor volume with 1 cm margins and whole neck. The boost clinical tumor volume is defined as primary tumor and initial gross neck node with 0.5 cm margins. Planning volume is defined as clinical tumor volume with 0.3 cm margins. The IMRT planning is planned by comercial planning system with co-planar 7 fields technique. The radiation dose was 72 Gy to T1-T3 gross tumor area and 76 Gy to T4 lesion. The radiation was delivered by 2 Gy per fraction and 5 freactions per week. The maximal radiation dose <110% and no simultaneous boost was used. Stage IIb to IVb patients received cocomitant chemotherapy with cisplatin, UFUR and leucovorin in outpatient clinic service. All patients with at least 16 months follow up or to death. The median follow up was 2.1 years.
Result: The 3 year overall survival (OS) was 91.7%. 3-year OS for stage I, II, III and IV was 100%, 100%, 91.7% and 80.6% respectively. There were 4 patients with local recurrence, 6 patients neck node recurrence and 12 patients with distant metastasis. The local tumor progression freel rate for T1, T2, T3 and T4 was 100%, 96.3%, 92.3% and 90.4%. The 3-year distant metastasis free survival was 86.8%. There were no grade IV comlications were noted. 2-year grade II xerostomia according to RTOG criteria was 14%.
Conclusion: With combined use of IMRT, concomitant chemothearpy and through staging workup can get good tumor control and survival.

1001 POSTER

Neoadjuvant docetaxel (Taxotere) and cisplatin followed by concurrent cisplatin-radiotherapy in locally advanced nasopharyngeal carcinoma: a randomized phase II study

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Background: The current standard treatment for locally advanced nasopharyngeal carcinoma (NPC) is concurrent chemotherapy and radiotherapy (RT) *(JNCI 2005: 97: 536–9)*. The current study aimed to compare the toxicities and tumor response of advanced NPC patients treated with concurrent cisplatin-RT +/− neoadjuvant docetaxel and cisplatin.
Methods: Previously untreated NPC of UICC 1997 stage III/IVA/IVB. Randomized (stratified by stage 3 vs 4) to one of two arms: (1) Neoadjuvant chemotherapy arm: docetaxel 75 mg/m^2 on D1 and cisplatin 75 mg/m^2 on D1 q 3 wks x 2 cycles, followed by cisplatin 40 mg/m^2 weekly x 6–8 concurrent with RT (66 Gy in 2-Gy fractions), or (2) Control arm: concurrent cisplatin-RT as arm 1 without neoadjuvant chemotherapy. All treatments were delivered as outpatients. Planned accrual was 30 patients (pts) per arm to detect 20% difference of toxicity on one side of a 95% confidence interval.
Results: 60 pts were randomized from 11/2002 to 11/2004. Toxicity and response data of the first 53 pts were complete for this analysis (complete data for all 60 pts will be available at meeting). NCI-CTC grade 3 and 4 toxicities in the two arms were summarized in Table 1. All pts in the neoadjuvant arm completed the planned two cycles of chemotherapy and all pts in both arms completed RT to the prescribed dose. In the neoadjuvant arm, 86%, 71%, 43%, 7%, 3% completed 4, 5, 6, 7 and 8 weeks of concurrent cisplatin during RT. The corresponding numbers for control arm were 84%, 76%, 48%, 20%, 0%. Response rate to neoadjuvant chemotherapy: nasopharynx (NP) 86% (CR 22%, PR 64%), nodal 80% (CR 50%, PR 30%). Response after cisplatin-RT: (a) neoadjuvant arm: NP 100% (CR 96%, PR 4%), nodal 95% (CR 80%, PR 15%); (b) control arm: NP 100% (CR 84%, PR 16%), nodal 100% (CR 65%, PR 35%).
Conclusions: Neoadjuvant docetaxel and cisplatin was well tolerated and produced high response rate. The higher haematological toxicities in the neoadjuvant arm were manageable and did not compromise the delivery of full dose concurrent cisplatin-RT. This neoadjuvant strategy warrants a phase 3 study to determine its impact on the overall survival in advanced NPC.

Table 1: NCI-CTC Grade 3 and 4 toxicities during treatment.

	Neoadjuvant arm (n = 28)		Control arm (n = 25)		P-value
	G3	G4	G3	G4	
(a) During neoadjuvant chemotherapy					
Hematological					
Neutropenia	6 (21%)	21 (75%)			
Febrile Neutropenia	4 (14%)	0			
Non-haematological:					
Fatigue	2 (7%)	0			
Nausea/Vomiting	3 (11%)	0			
(b) During cisplatin-RT					
Hematological					
Anaemia	3 (10%)	0	5 (20%)	0	0.31
Thrombocytopenia	1 (4%)	1 (4%)	0	1 (4%)	0.11
Neutropenia	6 (21%)	22 (79%)	3 (12%)	1 (4%)	**<0.0001**
Febrile neutropenia	0	0	1 (4%)	0	0.29
Non-hematological					
Anorexia/nausea/vomiting	3 (10%)	0	3 (12%)	0	0.36
Dehydration/renal	5 (18%)	0	7 (28%)	0	0.58
Fatigue	2 (7%)	0	2 (8%)	0	0.91
Electrolytes	4 (14%)	0	0	0	0.07
Mucositis/odynophagia	10 (36%)	1 (4%)	11 (44%)	1 (4%)	0.24
Transfusion	4 (14%)	0	4 (16%)	0	0.86