Materials and Methods: Between May 2001 and December 2005, 16 patients with skull base tumor and 43 patients with head-and-neck cancer with intra cranial invasion were treated with particle radiotherapy. Patient characteristics were as follows; median age: 59 (range, 23−81), male/female: 25/34. Single protocol for proton therapy (65 GyE in 26 fractions using 150 or 190 MeV), and single protocol for carbon ion therapy (57.6 GyE in 16 fractions using 250 or 320 MeV) were employed in the period. Pathologic subtypes of tumor included adenoid cystic carcinoma in 17 patients, chordoma in 9, malignant melanoma in 7, squamous cell carcinoma in 7, others in 19, respectively. Among these 59 patients, 43 patients received proton therapy and 16 patients received carbon ion therapy, respectively. Patients underwent MRI every 3 month during the first 2 years and every 3 to 6 month intervals thereafter. Adverse events were assessed according to the National Cancer Institute Common Terminology Criteria for Adverse Events (CTCAE, v3.0) grading system. Incidence rate of adverse event and survivals were estimated with Kaplan-Meier methods.
Results: Three (7%) of 43 patients who treated with proton therapy and 5 (31%) of 16 patients who treated with carbon ion radiotherapy had certain degree of MRI findings on CNS necrosis. One (2%) of the patients had some clinical symptoms, such as vertigo and headache (CTCAE Grade 2). The other 7 (12%) patients had no symptoms. Actuarial occurrence rate of grade 1 or greater CNS necrosis at 2 year and 3 year was 7% and 10%, respectively. There was no statistically significant difference between the patients underwent proton radiotherapy and carbon ion radiotherapy.
Conclusions: Particle therapies were administered to the patients with skull base tumors or head-and-neck cancers, resulting in minimum symptomatic CNS toxicities. However, our sequential evaluation with MRI detected higher incidence of abnormal intensities. This discrepancy between symptom and MRI as for CNS damage may bring important information for the era of particle therapies. Further accumulation of patients and longer follow-up should be warranted.

5536 POSTER

A non-randomized single-centre comparison of induction chemotherapy followed by chemoradiation versus chemoradiation for locally-advanced squamous cell carcinoma of the head and neck

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Background: Gemcitabine (GEM) is a potent radiosensitizer with activity in squamous cell carcinoma of the head and neck (SCCHN). Chemoradiation (CRT) is still the standard treatment for locally advanced (LA) SCCHN. CRT improves local control and overall survival (OS) when compared to radiotherapy (RT) alone. Induction chemotherapy (IC) reduces the risk of distant metastases (DM) and improves OS by 5% when the analysis is restricted to the cisplatin/5 fluorouracil (PF) combination. Adding a taxane to PF clearly confers a better outcome. The concept of sequential treatment of IC followed by CRT (ST) is under active investigation in multiple phase III trials.
Methods: We compared the outcome of two cohorts of patients with LA-SCCHN treated at our institution respectively by CRT (December 1998-September 2005) or ST (March 1998-January 2005). Treatment: CRT: GEM 100 mg/m^2 weekly + conventional RT (70 Gy); ST: same CRT preceded by IC, which included DIP (docetaxel, ifosfamide + P [16/23]), TPF (docetaxel + PF [5/23]) or PF [2/23]
Results: Patient characteristics are summarized in the table.

Cohort	#pts	M	Age	OP	HP	L	Other	T3	T4	N2	N3
CRT	27	22	55	8	16	1	2	4	16	14	5
ST	23	19	56	10	7	4	2	6	13	15	5

num; pts: number of patients; M: male; Age = median age in years; OP = oropharynx, HP = hypopharynx, L = larynx

Response to IC: complete: 5, partial 16, stable 1, progressive 1. Median follow up (FUP) of the surviving patients is 60 months in the CRT cohort and 29 months in the ST cohort. In the CRT cohort, median time to local failure (TLF) was not reached. Median time to distant metastasis (TDM) was 23 months and median OS was 20 months. Median TLF, TDM and OS were not reached in the ST cohort. There was a (not significant) trend to better survival in the ST cohort, while the TLF showed a (not significant) trend in favor of the CRT cohort. TDM was significantly longer in the IC cohort ($p = 0.009$).
Conclusion: TDM was significantly longer in the ST cohort. There was a trend in favor of the ST cohort for OS and a trend in favor of the CRT cohort for TLF. These data are to be interpreted with extreme caution as this is a non-randomized single-centre comparison of two rather small cohorts of SCCHN patients. However, the observations are in line with preliminary data suggesting a better outcome with sequential therapy.

5537 POSTER

Prospective evaluation of oral health parameters and quality of life in HNSCC patients submitted to radiation therapy

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Background: Treatment-related oral complications are a major problem in HNSCC patients (pts) submitted to RT. We prospectively measured oral health parameters and quality of life (QoL) in HNSCC pts during RT and explored their relationship to treatment-related complications.
Methods: Histologically-proven HNSCC pts candidates to RT were consecutively included, after signing an informed consent. Pretreatment oral/dental stabilization was performed, potential sources of infection were eliminated, adequate prophylaxis was made, and pts were followed every week until the end of RT. Salivary flux (Guebur et al, 2004), a dental plaque index (WHO 1999), an evaluation of the periodontal health (PSR: Periodontal Screening & Recording System, WHO 1999) and a dental morbidity score (NCI) were all measured before/after RT. Mucositis, dysphagia and xerostomia before/after treatment were classified using the NCI-CTCAE v3.0. QoL was evaluated using EORTC QLQ-C30/HN35 questionnaires.
Results: 70 pts were included, median age 57 y, 44 male. Primary site: oral cavity 33, pharynx 20, larynx 12, lip 5. Staging: 4 T1, 35 T2, 24 T3, 7 T4, 39 N0, 23 N1, 5 N2, 3 N3, 1 M1. All pts received once a day, conventionally delivered RT (median dose: 70 Gy in the primary site), 40 pts received chemotherapy and 44 pts were submitted to surgery. Mean salivary flux decreased from 0.46 mL/min to 0.12 mL/min ($p = 0.00$, t-test). Mean dental plaque index increased from 14.42 to 23.65 ($p = 0.014$). An increase of the PSR ($p = 0.003$, Wilcoxon) and also of the dental morbidity ($p = 0.00$) scores were observed. As expected, more severe mucositis ($p = 0.00$), dysphagia ($p = 0.00$) and xerostomia ($p = 0.00$) occurred after RT. The association of chemotherapy to RT significantly worsened the PSR index ($p = 0.025$) and the morbidity score ($p = 0.014$), as compared to exclusive RT, as well the abuse of alcohol ($p = 0.014$) and tobacco ($p = 0.005$). Accordingly, significant worsening in the physical condition, swallowing, senses, speech, pain, xerostomia, viscous salivation and cough QoL modules were detected at the end of RT, but global QoL, emotional and social contact modules showed improvements.
Conclusions: Oral health and QoL are affected by RT in HNSCC pts and its objective evaluation can help us to better detect, treat and prevent the RT-related adverse events.

5538 POSTER

Womens's squamous cell carcinoma of the head and neck: retrospective analysis of two cohorts

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Background: Changing patterns have been observed in women's head and neck squamous cell carcinoma (SCC), probably related with increasing smoking habits in women and changes in sexual habits, with HPV infection as a recently recognised risk for this disease.
Objective: to analyse if there are changing patterns in women's head and neck SCC, concerning age, topography, risk factors and referral to Medical Oncology Services between two retrospective cohorts. All patients were treated in our centre, the main referral centre for these cancers in the south of the country.
Methodology: Retrospective analysis of two cohorts: all women with head and neck SCC (excluding lip) treated in this centre between 1995–1999 (cohort 1) and 2000–2004 (cohort 2). Data were obtained from the Portuguese Southern Cancer
Results: Cohort 1: Two hundred and nine women, medium age of 66 years (median 68). Topography: Oral cavity-59%; Larynx-13%; Oropharynx-13%; and others (Hypopharynx; Queratinizing Nasopharingeal; Pharynx NOS; Nasal Fossa)-10%. Smoking and alcohol consumption were identified as a risk factor in 37 (18%) and 20 (10%) of these women and clearly denied in 89 (44%) and 95 (47%) of them. No information was registered concerning sexual habits or risk factors for HPV infection. Ten of these women (5%) had other cancers, mostly breast.
Cohort 2: Two hundred eighty four women, medium age of 66 years (median 68). Topography: Oral cavity-65%; Larynx-12%; Oropharynx-8%; and others (Hypopharynx; Queratinizing Nasopharingeal; Pharynx NOS; Nasal Fossa)-15%. Risk factors were assessed in only eighty one of the two hundred eighty four patients from our cohort, smoking and alcohol consumption were identified as a risk factor in 18 (22%) and 11 (14%)

of these women and clearly denied only in 21% and 26% respectively. In 5 (6%) patients surrogate markers of HPV infection were registered (sexually transmitted disease or cervix disease including cancer). Sixteen women had other cancers.
Conclusion: With the data assessed until now, no change in clinical and epidemiological changes or women with head and neck SCC refered to our institute could be detected.

5539 POSTER

Different predictors of asymptomatic carotid artery stenosis in patients having received radiotherapy for head and neck cancers

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Background and Purpose: Carotid artery stenosis (CAS) is one of the major complications of external irradiation (radiotherapy, RT) to the head and neck cancers. Few large-scale studies of CAS after radiotherapy were reported. We try to predict the severity, extent and progression of radiation-induced CAS in these patients and discuss its related factors.
Methods: In a cross-sectional study, CAS was detected by color-coded carotid duplex. We enrolled 290 consecutive Taiwanese patients of head and neck cancers with (RT group, 192 patients) or without (control group, 98 patients) receiving RT. Detailed review of cerebrovascular risk factors was documented. Multivariate regression was performed for analysis of independent factors for CAS.
Results: The mean duration after radiotherapy in the RT group was 4.9±3.9 years (median 3.8 years) and the mean dosage of irradiation was 6225±906 (median 6600) cGy on the neck. There was no statistically significant difference of age and common risk factors of cerebrovascular diseases between RT and control groups. The majority (82.3%) of CAS had more than one atherosclerotic plaques of any degree of stenosis in the RT group, and was significantly more than that of the control group ($p < 0.001$). Significant (⩾50%) stenosis was observed only in the RT group (19.8%, $p < 0.001$). In all segments of carotid arteries, the summation of plaque scores was statistically significant higher in the RT group with highest score at both bulb bifurcations ($p < 0.001$). Multiple linear regression analysis showed the increase of total plaque scores was independently associated with dosage of RT, age, time interval after RT and male gender.

5540 POSTER

Papillary thyroid microcarcinoma: prognostic factors, management and treatment outcome in 228 patients

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Background: Within the group of patients with papillary thyroid microcarcinoma (PTMC), the prognostic factors have not been well defined and the optimal treatment has not been proved. The aim of this study was to find out the factors associated with the tumor recurrence in patients with PTMC.
Material and Methods: A total of 228 patients with PTMC (189 females, 39 males; age 14−85 years, median 46 years) were treated at our Institute between 1975 and 2006; among them 98 patients had incidental PTMC. The data on patients' gender, age, extent of disease, pathomorphological characteristics, therapy, locoregional control, disease-free survival and disease specific survival were collected. Statistical correlation between possible prognostic factors and tumor recurrence was analyzed by chi-square analysis.
Results: The tumor diameter ranged from 0.1 to 10 mm (mean 6.1 mm). Initially, lymph node metastases were present in 56 patients (25%) and distant metastases in 1 patient (0.4%). Pathology revealed that, in 211 patients (92.5%), PTMC was confined to the thyroid and, in 17 (7.5%), the tumor invaded into surrounding tissue. The tumor was multifocal in 60 patients (26%). Primary surgical treatment consisted of total or near-total thyroidectomy in 189 patients (83%), lobectomy in 25 (11%) or subtotal thyroidectomy in 14 patients (6%), lateral lymph nodes dissection in 51 (22%) and central lymph nodes dissection in 23 (10%) patients. Radioiodine ablation of the thyroid remnant was performed in 111 patients (49%). During the follow-up period, the recurrence was diagnosed in 7 patients (6 locoregional and 1 distant). None of the patients with the tumor diameter of 6 mm or less had recurrent disease. There was no cancer related mortality. The median length of observation was 84 months (range 1–385). The 5-year, 10-year and 20-year disease-free survival was 98.5%, 98% and 93%, respectively. None of the patients died of disease. Incidentally diagnosed PTMC, tumor size, tumor differentiation and presence of lymph node metastases were the factors which correlated with tumor recurrence. Neither the extent of thyroid surgery nor radioiodine ablation of thyroid remnant correlated with tumor recurrence.
Conclusions: Patients with PTMC have a favorable long term prognosis. Lower recurrence rate was found in the patients with incidentally diagnosed PTMC, and those with the tumor diameter ⩽6 mm, with well differentiated tumor and without lymph-node metastases.

5541 POSTER

Treatment for the patients with clinically lymph node-negative squamous cell carcinoma of the oral cavity

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Introduction: Oral cavity is cosmetically and functionally important structure. It is not easy to find phase III study about oral cavity cancer in the literature, because the incidence is relatively low. There are still many debates concerning the optimal treatment of oral cavity cancer. A retrospective analysis for the patients with clinically lymph node-negative squamous cell carcinoma of the oral cavity was performed to evaluate treatment outcome and determine optimal treatment strategy.
Materials and Methods: From January 1990 through December 2004, 227 patients with squamous cell carcinoma of the oral cavity including mobile tongue, floor of mouth, gingiva, retromolar trigone, hard palate, and buccal mucosa received radiotherapy with curative intent. We retrospectively analyzed 69 patients with clinically lymph node-negative disease. There were 46 patients (67%) presented with early stage disease (T1 or T2). Forty-four patients (64%) had well-differentiated disease. The patients were divided into two groups according to the treatment modalities for local disease: those treated with surgery plus external beam radiotherapy (EBRT) ($n = 43$) and those with EBRT alone ($n = 26$). The median doses were 63.0 Gy (range; 45.0−70.2 Gy) in the former group and in 70.2 Gy (range; 61.2−72.0 Gy) in the latter, respectively.
Results: The incidences of occult metastasis were 60% for T1, 69% for T2, 100% for T3, and 39% for T4, respectively. Contralateral occult metastasis occurred only in two patients. After median follow-up of 27 months (range; 6−170), 24 patients had failed treatment as follows: local ($n = 10$); regional ($n = 10$); distant ($n = 1$); local plus regional ($n = 2$); and regional plus distant ($n = 1$). Of the 10 patients who received salvage treatment with curative intent for loco-regional failure, 50% were salvaged. The 5-years overall survival (OS), disease free survival (DFS), local control (LC), and regional control (RC) rates for patients analyzed were 56%, 48%, 67%, and 78%, respectively. The 5-years OS, DFS, LC, and RC rates were 63%/ 42% ($p < .01$), 65%/ 16% ($p < .01$), 91%/ 21% ($p < .01$), and 73%/ 88% ($p = 0.12$) for surgery plus EBRT group/ EBRT alone group, respectively. Similarly, significant differences in OS, DFS, and LC between the treatment groups were found for patients with early stage disease. There were fewer regional failures in patients treated with neck dissection than in those without neck dissection, but the differences were not significant (21% vs. 23%, $p = 0.70$).
Conclusion: The risk for occult metastasis in ipsilateral neck is high in patients with early squamous cell carcinoma of the oral cavity as well as advanced disease and therefore, elective treatment for ipsilateral neck should be considered. Excellent regional control can be achieved with EBRT alone for subclinical disease of the neck. However, EBRT alone for primary tumor treatment resulted in poor local control and combined treatment with surgery and EBRT appeared to be better treatment strategy.

5542 POSTER

Impact of nuclear factor kappa B activity for local tumor controllability by radiotherapy in patients with T1/T2N0 laryngeal cancer

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Background: External radiotherapy (ERT) plays a critical role in organ preservation in patients with early stage laryngeal cancer. From previous reports, 5-year local control rates were 80−90% in patients with stage I, and 65−85% in patients with stage II laryngeal cancer. Although surgical salvages have been developed in the latest decade, it seems to be unfortunate that local controllability by radiotherapy has not been improved in these two decades. Aberrant NF-kappa B activity has been associated with inflammatory disorders, carcinogenesis, and response to chemotherapy and radiotherapy. The purpose of this study are to investigate whether the NF-kappa B activity affects local tumor controllability and to assess that NF-kappa B could be a predictive marker for the radioresistant laryngeal cancer.