comparison with pts treated with the same chemotherapy alone until PD suggests that it may be detrimental to stop chemotherapy after 6 cycles if disease did not progress.

8528 POSTER

Epstein-Barr virus quantification and aberrant host DNA methylation pattern as marker for nasopharyngeal carcinoma in non-invasive nasopharyngeal brushings

S.H. Hutajulu[1], L.P.L. Indrawati[1], S.R. Indrasari[1], A. Harijadi[1], A.E. Greijer[2], S. Mubarika[1], R.D.M. Steenbergen[2], J.M. Middeldorp[2]. *[1]Faculty of Medicine, Gadjah Mada University, Yogyakarta, Indonesia; [2]Department of Pathology, VU University Medical Center, Amsterdam, The Netherlands*

Background: Nasopharyngeal carcinoma (NPC) is the most prevalent head and neck cancer in Indonesia. WHO type III, representing the majority of NPC, is 100% related to Epstein-Barr (EBV) infection. The viral DNA load is elevated in nasopharynx (NP) of most patient at diagnosis. A NP brush was used for in-situ sampling, allowing simpler and less invasive NPC diagnosis. We have shown EBV-DNA load as promising new diagnostic method and use it to screen NPC cases in high risk population. A growing evidence demostrates that aberrant methylation in gene promoter is important in inactivating tumor suppressor gene (TSG) in NPC. This study aimed to quantify EBV-DNA load and determine methylation status of multiple TSGs in NPC, high risk individuals, and healthy EBV-carriers to evaluate wether methylation pattern may have additional value to identify early carcinogenic events.
Methods: NP brushing was taken from NPC, high risk patients presenting chronic problems in head and neck area, and normal EBV-carriers. Paraffin tissue of NPC patient was also included and subjected for DNA isolation in order to verify detection rate of methylation in brushing DNA. EBV-DNA load was measured using a quantitative real time PCR. DNA was modified using bisulfite treatment and amplified by methylation-specific PCR. Seven tumor suppressor genes were included (DAPK, CADM1, p16, RASSF1A, CHFR, RIZ1, and DLC1).
Results: All NPC patients showed elevated EBV-DNA and high frequency of methylated genes (DAPK 69.6%, CADM1 71.4%, p16 68.1%, RASSF1A 73.5%, CHFR 65.9%, RIZ1 41.7%, and DLC1 58.7%). Most of paraffin and brushing DNA revealed a concordance result of methylation status. The high risk individuals, who also demonstrated high EBV-DNA load, showed high frequency of methylated genes of DAPK (76.9%), CADM1 (61.5%), and DLC1 (61.5%), but low or undetected methylated genes of p16, RASSF1A, CHFR, and RIZ1. Healthy individuals showed low DNA load but similar methylation pattern as high risk population.
Conclusion: These result s suggest that EBV infection and promoter hypermethylation might serve as useful markers to screen early NPC. At the time a prospective analysis in high risk group using non-invasive brushing samples to identify early stage NPC is in progress. In Indonesian normals, much abnormal methylation on certain TSGs probably reflects exposure to co-carcinogens in environtment and food.

8529 POSTER

Pattern of locoregional failure after tomotherapy in head and neck cancer

A. Farrag[1], M. Voordeckers[2], K. Tournel[2], P. De Coninck[2], G. Storme[2]. *[1]Assiut University, Clinical Oncology, Assiout, Egypt; [2]UZ Brussel, Radiation Oncology, Brussels, Belgium*

Background: Helical tomotherapy is a new radiation device delivering a highly conformal dose from a rotational gantry resulting in a more uniform target dose and better avoidance of organs at risk. Treatment failure patterns of head and neck cancer treated with helical tomotherapy and the adequacy of the target volume definitions and delivery techniques currently used were analysed.
Materials and Methods: Between June 2005 and March 2008, 76 consecutive patients with biopsy proven head and neck cancer were treated with helical tomotherapy (Hi-Art TomoTherapy®, Madison, Wisconsin, USA) at the UZ Brussel. For patients with local or regional failure, the volume of failure (Vf) was determined on one or more diagnostic tools as computerized tomography (CT), magnetic resonance imaging or positron emission tomography obtained at the time of failure. The Vf is then contoured with Co-registration of the failure image (Vf) and the initial planning CT was performed. The failures were categorized as local or regional. The dose of radiation received by failure was calculated and analyzed using dose-volume histograms (DVHs) and accordingly it is classified as 1) In-field (InF): in which 95% or more of Vf was within the 95% isodose, 2) Marginal (MF), if 20% to 95% of Vf was within the 95% isodose, or 3) Outfield (OutF) if less than 20% of Vf was inside the 95% isodose. The mean, minimum and maximum doses received by each failure volume were displayed.
Results: Median follow up time was 14.8 months (3.5−38.8). Three-years overall survival, disease free survival and locoregional control were 69%, 47% and 59%, respectively. Twelve patients showed locoregional failure, 5 were local, 6 were regional and one showed both local and regional failure. With DVHs analysis, InF, MF and OutF were 9, 3 and 1, respectively. All MF had a history of surgey before radiotherapy.
Conclusions: Target defintion and coverage were adequate. The majority of locoregional failures were InF i.e. in the high dose regions. Future work on dose escalation to the highest risk regions is recommended. Special consideration for surgically manipulated patients must be taken in volume selections and coverage.

8530 POSTER

Clinical results and prognostic factors in radiotherapy for early glottic squamous cell carcinoma

T. Nomiya[1], Y. Kuroda[1], M. Suzuki[1], M. Murakami[1], H. Wada[1], K. Nemoto[1]. *[1]Yamagata University, Radiation Oncology, Yamagata, Japan*

Background: The purpose of this study is to determine the prognostic factors for local control in T1a, T1b and T2N0M0 glottic squamous cell carcinomas.
Material and Methods: Data from 249 patients with T1−2N0M0 (T1a: 115, T1b: 48, T2: 86) Stage I-II glottic carcinomas, who were treated with definitive radiotherapy during 1976 to 2002 were analyzed retrospectively. Age, source, total dose, field size, overall treatment time, average fraction size, fractionation regimen, chemotherapy and etc. were set as variables in multivariate analysis.
Results: The 5-year local control rates (LCR) were 92%, 85% and 83% for patients with T1a, T1b and T2 glottic carcinomas, respectively. Only total radiation dose ($p = 0.048$) was a significant prognostic factor for local control in multivariate analysis of T1b glottic carcinoma. Local control in the higher total dose group was better than that in the lower total dose group (5-year LCRs were 100% and 76% for the group of >66 Gy and the group of $\leqslant$66 Gy, respectively. $p = 0.024$, logrank test). None of the treatment parameters were shown to be significant prognostic factors in multivariate analysis of T1a glottic carcinoma. In the analysis of T2 glottic carcinoma, OTT (overall treatment time of radiotherapy) ($P = 0.0003$) and Total dose ($P = 0.0036$) were the significant prognostic factors on local control in multivariate analysis. Higher total dose group ($\geqslant$67 Gy vs. <67 Gy) showed favorable prognosis (5-year LCR: 91% vs. 60%, respectively. $P = 0.0013$: logrank test). And the shorter OTT group ($\leqslant$54 days vs. >54 days) showed favorable prognosis (5-year LCR: 87% vs. 71%, respectively. $P = 0.023$).
Conclusions: Radiotherapy with a total dose of >66 Gy seemed to be required for local control in T1b glottic carcinoma. No significant benefit of total radiation dose >64 Gy was shown in the analysis of T1a glottic carcinoma. Radiotherapy total dose of $\geqslant$67 Gy delivered with shorter period is required for T2 glottic cancer. The fractionation regimens of accelerated hyperfractionation is more effective than conventional fractionation in terms of shortening OTT and delivering high total dose with acceptable toxicity.

8531 POSTER

Prediction of clinical radiation induced toxicity through study of radiation induced apoptosis in peripheral blood lymphocytes (PBLs)

A. Ruiz[1], P. Lara[2], M.A. Cabeza[1], E. Bordon[2], J.C. Rodriguez[2], J. Alcobe[1], B. Pinar[2], A. Castaño[1], E. Lanzos[1]. *[1]H 12 Octubre, Radiotherapy and Oncology, Madrid, Spain; [2]H U Gran Canaria Dr Negrín, Radiotherapy and Oncology, Las Palmas de GC, Spain*

Background: To analyze radiation induced apoptosis in PBLs of patients with head and neck (H&N) cancer, the application of a semilogarithmic model RID (Radiation Induced cell Death)= $\beta.\ln(Gy)+\alpha$, to assess the association among the defined constants of this model and its utility as a prediction model for toxicity in patients treated with radiation therapy.
Material and Methods: A total of 79 patients with H&N cancer treated with radiation therapy, with or without surgery and chemotherapy were included. PBLs were obtained from peripheral blood samples using density gradient centrifugation (Ficoll Hipaque). Apoptosis was assessed by Anexin V and Propidium Iodide (IP) staining. Triple analysis at doses of 0, 1, 2, and 8 Gy were performed in all patients after 24 hours. Clinical toxicity was assessed by the ROTG classification.
Results: RID was increased by the dose of radiation administered. α(initial value at x axis) and β (apoptosis increase due radiation dose–slope of the curve) constants, defined in the model, were statistically associated. β was associated with radiation induced toxicity, such as grade III or higher xerostomy bivariate ($p = 0.035$) and multivariate analysis ($p = 0.034$; EXP (B) 2,553, 95% CI (1,074−6,070).
Conclusions: Radiation sensitivity of peripheral blood lymphocytes can be estimated using the Anexin IP staining to assess radiation induced apoptosis. The later adjusts to the α/β semilogarithmic model and allows to

define individual variables for radio-sensitivity. Alpha and β values showed a pattern of individual sensitivity that correlates to the clinical toxicity observed in this study.

8532 POSTER

Prognostic impact of comorbidity in elderly patients with head and neck squamous cell carcinoma (HNSCC)

M.A. Moreno Jimenez[1], I. Gonzalez Cebrian[1], R. Collado Martin[1], B. Medina Magan[2], A.L. Ortega Granados[1], M.J. Mateos Salido[1], R. Alonso Calderon[3], Y. Plata[1]. *[1]Hospital Medico-Quirurgico Ciudad de Jaen, Oncologia Medica, Jaen, Spain; [2]Hospital Torrecardenas de Almeria, Oncologia Medica, Almeria, Spain; [3]Hospital General San Pedro de Alcantara, Oncologia Medica, Caceres, Spain*

Background: there is no standard treatment for elderly HNSCC patients and comorbidity is known to be an independent predictor for mortality in head and neck cancer patients. We analyse the influence of comorbidity in survival and toxicity in elderly HNSCC patients.
Materials and Methods: A retrospective review was conducted in all patients with HNSCC over the age of 70 seen in a single cancer hospital from January 2004 till April 2009. Adult Comorbidity Evaluation 27 (ACE27) was used and compared with ECOG to calculated adjusted hazard ratio. All high-grade toxicity events per patient was summarise according to the National Cancer Institute Common Toxicity Criteria across the entire treatment period in a sequence form in those elderly HNSCC patients not intended for best supportive care (BSC)
Results: 77 patients were included. Median age was 76 (range 70−99) with a male/female ratio 4:1. Cancer subsite more commonly are larynx (32.5%) and oral cavity (29.9%). Stage IV was in 59.8%. ECOG 0 was in 23.4%, 1 in 49.4%, 2 in 22.1% and 3 in 5.2%. Comorbidity was severe in 29.9%, moderate in 27.3% and mild in 32.5%. 51.9% was qualify for chemotherapy as induction, concurrent or palliative treatment. BSC was intended for 23.4%. Grade 3−4 toxicity happened in 65% of patients qualify for chemotherapy including two toxic deaths. There were no differences according to age, gender, ECOG or ACE. 7 patients (10.7%) were excluded from analysis survival due to missing data. Compared with patients with mild or moderate comorbidity Kaplan Meier survival curves for patients with severe comorbidity was signifincantly worse in the whole population (median overall survival from diagnosis 36 weeks, 95% CI 25−46, $p < 0.05$, one year survival 28.4%) as well as in patients scheduled to undergo treatment (median overall survival from diagnosis 39 weeks, 95% CI 32−46 $p < 0.05$). In patients qualify for treatment cox regression model shows that adjusted hazard ratio was significantly in ECOG 0 patients (HR = 0.24; $p < 0.005$) and severe comorbidity patients (HR=1.43; $p < 0.05$).
Conclusions: Data from this retrospective review suggested that elderly HNSCC patients ECOG 0 could be worthy for treatment irrespective of ACE, and that elderly HNSCC patients ECOG 1−2 with severe comorbidity should be ruled out from treatments. Elderly HNSCC patients ECOG 2 shouldn't deserve exclusion from treatments solely due to moderate or mild comorbidity

8533 POSTER

The role of postoperative external beam radiotherapy in differentiated thyroid cancer with focal anaplastic change

W.I. Jang[1], H.G. Wu[1], C.I. Park[2], Y.K. Youn[1], K.H. Kim[1], B.Y. Cho[1], D.J. Park[1], J.K. Chung[1], K.W. Kang[1], K.C. Jung[1]. *[1]Seoul National University Hospital, Department of Radiation Oncology, Seoul, South Korea; [2]Korea Institute of Radiological & Medical Sciences, Department of Radiation Oncology, Seoul, South Korea*

Background: Anaplastic thyroid cancer is rare disease and has a very low cure rate with the very best treatments. The major problem with anaplastic thyroid cancer, is that it is usually too aggressive and invasive when it is diagnosed. We examine to determine the role of postoperative external-beam radiotherapy (EBRT) in the patients with differentiated thyroid cancer with focal anaplastic change.
Materials and Methods: Of the 6,345 patients diagnosed as thyroid cancer at our institution between January 1980 and June 2008, 115 had anaplastic thyroid carcinoma. Of these patients, 33 had focal anaplastic change. The median patient age was 53 years (range, 22−75 years). The majority of patients were female (75.8%) and had extrathyroidal tumors (72.7%). Two patients (6.1%) had distant metastasis at diagnosis. Total thyroidectomy was achieved in 25 patients (75.8%). Twenty patients (60.6%) received postoperative EBRT (EBRT group) to a median total dose of 61.2 Gy (range, 54.0−70.0 Gy) and 11 (33.3%) received radioactive iodine (no-EBRT group). The median follow-up duration was 19 months (range, 2−130 months).
Results: The 5-year overall and disease-free survival rates were 96.2% and 57.2%, respectively. The 5-year local failure-free survival rates were significantly different (100% in the EBRT and 52.5% in the no-EBRT $p = 0.024$). There were no significant difference in overall, disease-free, regional failure-free, and distant metastasis-free survival rates between the EBRT group and no-EBRT group. Thyroglobulin, palpable lymph node, anaplastic transformation from previous differentiated thyroid cancer, and multiple foci were significant prognostic factors.
Conclusions: Postoperative EBRT significantly improved local failure-free survival in patients with differentiated thyroid cancer with focal anaplastic change

8534 POSTER

Hyperfractionated radiotherapy with concurrent docetaxel in locally-advanced head and neck cancer

K. Karasawa[1], H. Izawa[1], H. Hirowatari[1], K. Ito[1], T. Furuya[2], S. Ozawa[2], F. Matsumoto[3], S. Ito[3], S. Oba[3], K. Ikeda[3]. *[1]Juntendo University, Radiation Oncology, Tokyo, Japan; [2]Juntendo University, Medical Physics, Tokyo, Japan; [3]Juntendo University, Otolaryngology, Tokyo, Japan*

Purpose/Objective(s): Altered fractionated radiotherapy and/or radiotherapy combined with chemotherapy have been used in locally advanced head and neck cancers to increase local control. Concurrent chemo-radiotherapy is now considered to be a standard treatment option for these cases. This study was designed to evaluate hyperfractionated radiotherapy with concurrent use of low dose docetaxel in locally advanced head and neck cancer.
Materials/Methods: Patients eligible for this study had stage III to IVB squamous cell carcinoma of the head and neck or stage II carcinoma with large tumor volume. Tumor volumes were calculated by a tool in the radiotherapy treatment planning computer. The hyperfractionated radiotherapy was delivered 5 days per week with a 4-MV photon beam at 1.2 Gy per fraction with more than 6 hours apart to a total dose of 72.0 Gy. Docetaxel at 10 mg/m^2 was administered every week during radiotherapy. Toxicities were assessed weekly and graded according to NCI-CTCAE ver.3.0. Treatment response was assessed at 1 month after treatment completion. Statistical analysis of survival was calculated using the Kaplan-Meier method.
Results: From March 2003 to October 2008, 70 patients were treated according to this regimen. Median age was 66 years and sixty-three patients were male. Primary sites were the oropharynx in 25, hypopharynx in 24, larynx in 18, oral cavity in 1 and primary unknown in 2. Eleven of the patients were stage II, 16 were stage III, 33 were stage IVA and 9 were stage IVB. The grade 3−4 hematological toxicities were lymphocytopenia in 29 (42%) and neutropenia in 2. The grade 3 non-hematologic toxicities were mucositis in 42 (60%), treatment related pain in 12 (19%) and dermatitis in 2 (2%). Fifty-five patients (79%) reached complete response (CR) and 13 (19%) reached partial response (PR). The median follow-up period was 18 months (ranging from 2 to 38 months). Seventeen patients developed a relapse or recurrence. Infield recurrence was observed in 11 and metastasis in 6. The two year overall survival rate was 71.7% and three year was 67.9% in entire group, respectively. Significant prognostic factors in two year relapse-free survival rates were primary site (51.5% in hypopharynx, 68.6% in oropharynx and 100% in larynx), clinical stage (100% in stage II-III, 64.8% in stage IVA and 0% in stage IVB) and tumor volume (less than 100 cm^3 in 75% and more than 100 cm^3 in 0%).
Conclusion: Although the follow up period was short, we can conclude that docetaxel combined with hyperfractionated radiotherapy may become a useful approach for the management of stage II to IVA head and neck cancer provided that appropriate measures are taken to reduce mucosal toxicities.

8535 POSTER

Induction chemotherapy within a multimodality treatment of nasal cavity and ethmoid sinus malignant epithelial tumours: report of an homogeneous series of patients

P. Bossi[1], R. Calderone[1], G. Cantù[2], P. Olmi[3], P. Quattrone[4], L. Locati[1], C. Bergamini[1], R. Granata[1], P. Potepan[5], L. Licitra[1]. *[1]Fondazione IRCCS Istituto Nazionale Tumori, Head and Neck Cancer Medical Oncology Unit, Milano, Italy; [2]Fondazione IRCCS Istituto Nazionale Tumori, Maxillo Facial Unit, Milano, Italy; [3]Fondazione IRCCS Istituto Nazionale Tumori, Radiotherapy, Milano, Italy; [4]Fondazione IRCCS Istituto Nazionale Tumori, Pathology Unit, Milano, Italy; [5]Fondazione IRCCS Istituto Nazionale Tumori, Radiology Unit, Milano, Italy*

Background: Ethmoid sinus and nasal cavity cancers are rare diseases, whose prognosis mainly stays upon histology and stage. Optimal treatment can hardly be stated, due to heterogeneity of tumour site, histotype, treatment and within limited series.