

The retreatment volume was confined to the site of recurrence in the nasopharynx. Treatment was delivered with 4-6 MV X-rays or Co-60 g rays. The re-irradiation dose ranged from 20 to 60 Gy, with a median of 50 Gy. Treatment was delivered at 1.8-2 Gy/ fraction/ day, 5-days/ week. Chemotherapy was used in 17 (41.5%) patients.

Results: Median follow-up was 23 months (range: 3 to 143 months). The 2-, 5-, and 10-year local progression-free rates were 39, 23, and 23% respectively. 14 (34.1%) were free of further local recurrence after retreatment. A total of 27 patients (65.9%) had local failures and 24 patients (58.5%) had neck failures with a median time to recurrence of 12 months and 13 months, respectively. The 2-, 5-, and 10-year actuarial overall survival following retreatment was 48, 28, and 11% respectively. On univariate analysis, age ($p=0.0467$), total re-irradiation dose ($p=0.0008$) were significant prognostic factors for local progression-free rate. For overall survival, age, total re-irradiation dose, stage, T stage were significant. On multivariate analysis only total dose ($p=0.005$) was significant for local-regional progression-free rate and total re-irradiation dose ($p=0.021$), interval to recurrence, stage were significant for overall survival.

Conclusion: Early diagnosis of local recurrence and adequate total dose by re-irradiation are crucial for improving the chance of local salvage and survival.

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POSTER

Long time treatment outcome of accelerated hyperfractionated radiotherapy for stage II laryngeal cancer

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Purpose/objective: Laryngeal preservation was a very important issue in the quality of life of patients with laryngeal cancer. However, it has been considered that conventional fractionation radiotherapy (CFR) is not good enough for cases with relatively large volume tumor. To improve the local control and laryngeal preservation rate in stage II laryngeal cancer, we conducted a Phase II trial of accelerated hyperfractionated radiotherapy (AHFR) since April 1986. In this study, we analyzed long time treatment outcome of these group to compare with our historical control of CFR group.

Materials & Methods: From April 1986 to December 2001, we treated 83 cases of stage II laryngeal cancer with AHFR. The AHFR group was irradiated with a fraction dose of 1.5 Gy twice a day at least 6 hours apart, 10 times a week to a total dose of 72 Gy within 6 weeks. The CFR group consisted of 89 cases treated from December 1966 to December 2001. Pathological type of all cases in both groups was squamous cell carcinoma. We divided glottic T2 into T2a (no impaired vocal cord mobility) and T2b (with impaired vocal cord mobility). In AHFR group, there were 63 glottic (T2a 51, T2b 12), 17 supraglottic and 3 subglottic tumors. In CFR group, there were 76 glottic (T2a 59, T2b 17), 9 supraglottic and 4 subglottic tumors. Patient characteristics of age, gender, pathological differentiation, field size, anterior commissure involvement, and hemoglobin concentration did not differ between the two groups.

Results: Five-year actuarial local control rate (LCR) was 73.0% for AHFR group and 70.0% for CFR group (n.s.). Five-year LCRs were 76.1% and 73.9% for glottic cancers (n.s.), 73.3% and 76.6% for glottic T2a cancers (n.s.) and 88.9% and 64.7% for glottic T2b cancers (p

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POSTER

Is the usefulness of routine triple endoscopy for head and neck cancer patients debatable?

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Background: The use of tobacco and/or alcohol is linked with the occurrence of head and neck squamous cell carcinoma, esophagus cancer and lung cancer. If this carcinogenic factor can induce the development of a cancer in one of these locations, it would seem reasonable that a second cancer could appear in another of those areas. The aim of the present study was to analyze the results obtained by the triple endoscopy during the initial evaluation of a primary carcinoma of the head and neck. Patients and methods: patients had no evidence of metastasis or of second primary cancer on the thoracic CT scan or chest X-ray. Second synchronous primaries were defined by a tumor located at a site distant from the margin of the first primary head and neck tumor, separated by normal mucosa. All pa-

tients had a triple endoscopy including nasopharyngoscopy, laryngoscopy, pharyngoscopy, bronchoscopy and esophagoscopy.

Results: A total of 487 patients with a squamous cell carcinoma of the head and neck was studied. A synchronous primary invasive carcinoma of the lung and the esophagus were diagnosed in 5 (1%) and 10 (2%) patients, respectively. In addition, 9 lesions were considered to be a regional extension of the primary tumor to the esophagus, and 9 in-situ carcinomas were observed. Interestingly, a significant relationship was found between the risk of second synchronous esophageal carcinoma and the initial location of the primary head and neck cancer (χ^2 test: $p = 0.002$). Esophageal cancer was observed in 1.3% of the patients with an oropharynx tumor, 2% of the patients with a larynx tumor, 0% of the patient with an oral cavity tumor and 9.2% of the patients with an hypopharynx tumor.

Conclusion: The role of bronchoscopy and esophagoscopy in the presence of a normal thoracic CT-scan is questioned because of the presence of a second esophageal and/or lung primary tumor is relatively low for the overall incidence. Nonetheless, based on the same incidence criterion, it seems reasonable to schedule a routine esophagoscopy for patient with hypopharynx squamous cell carcinoma.

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POSTER

Adjuvant chemo-radiotherapy in high risk head and neck elderly cancer patients (pts).

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Introduction: The loco-regional failure of pts with positive margins (+) and/or vascular/perineural invasion (VI/NI) and/or extracapsular spread (R+) is high and results in poor survival. Adjuvant chemo-radiotherapy (CT-RT), as recently shown, improves the treatment outcome but its applicability to elderly (EL) cancer pts is not established.

Patients and Methods: Forty EL pts (median age=73.5 yrs; range 70-78) were enrolled (35 m, 5 f; PS0 =26, PS1=12, PS2=2; site= oral c. 10, oropharynx 12, hypopharynx 8, larynx 10; pT N, 8 / pT N, 12 / pT N, 8 / pT N, 12) with the following poor-prognosis characteristics: (+)=6, VI=14, NI=16; R+=26. All pts were treated with CT (carboplatin 30 mg/m² d. 1⋄ 5 of the week 1,3,5) concomitant with RT (54 Gy + 10 Gy on high risk volumes; 1.8 Gy/d).

Results: No grade 4 toxicity was observed. Grade 3 toxicity: mucositis, 25%, neutropenia, 15%, dermatitis, 5%, thrombocytopenia, 2%. Median RT given dose = 52 Gy + 10. Thirty-two pts (80%) received 3 cycles of CT, 6 (15%) 2 cycles and 2 (5%) one cycle. Three-year estimates are as follows: disease-free survival = 58%, overall survival=64%, time to progression=64%, local control=79%.

Conclusions: The results confirm that adjuvant CT-RT can be performed successfully in EL pts who are physically healthy enough to receive such treatment. The results are better than those observed in a superimposable previous group treated with RT alone and are very similar to those reported in a younger group with the same poor prognosis characteristics treated with CT-RT.

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POSTER

Medullary thyroid carcinoma (MTC): genetic screening in Slovenia 1997-2002

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Background: MTC is a rare, endocrine tumor that occurs sporadically or is inherited. In hereditary MTC, germ line point mutations in RET proto-oncogene (RET gene) are responsible for the development of tumor and inheritance of settings MEN 2A, 2B and FMTC. Inherited MTC can be identified by genetic screening.

The aim of our study was to identify carriers of RET gene mutations in our patients with MTC and their kindred. The decision for therapeutic or prophylactic thyroid surgery was based on genetic testing results and clinical features.

Methods and patients: From 1969-2002, 105 (44 M (16-93y), 61 F (12-78y)) patients with MTC were treated and/or diagnosed at the Institute of Oncology, Ljubljana. From 1997 onwards, genetic testing was performed in 72 (29 M (16-93y), 43 F (12-77y)) of 105 (71.4%) patients with MTC and

in 50 relatives of these patients. The tests were made by the Institute of Pathology, Medical Faculty, Ljubljana. Point mutations of RET gene were detected by single strand conformation polymorphism analysis, double strand conformation and heteroduplex analyses and were examined by direct sequencing of PCR product and restriction enzyme analyses. In case of positive result, genetic testing (including new blood sample) was performed again in order to exclude the possibility of interchanging the samples or documentation.

Results: Germline mutations of RET gene were found in 12 (2M (16y, 65y), 10F (23-55y)) of 72 index patients and in 14 (5M (18-57y), 9F (12-54y)) of 50 relatives. Mutations at codon 634 were detected in 5 families (12 pts) (46.1%) at codon 618 in 4 families (9pts) (34.6%) and at codon 790 in 3 families (5 pts) (19.2%).

Clinical features of MEN 2A were recognized at 4/5 families with codon 634 mutations and FMTC resulted in codon 618 and 790 mutations.

In spite of genetic screening, MTC was diagnosed in 23/26 RET mutations carriers and prophylactic thyroidectomy was performed only in 3 of our patients, aged 12, 20 and 51 years.

Conclusion: Since the introduction of genetic screening we registered less advanced MTC tumors than before. A higher proportion of codon 790 mutations were detected in our patients. Our three patients who underwent prophylactic thyroidectomy after detecting codon 618 mutations and twice 790 mutations had no evidence of MTC or C-cell hyperplasia on permanent histology.

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POSTER

High MMP-13 expression levels are associated with increased risk of recurrent tumor in squamous cell cancer of head and neck

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Background Matrix metalloproteinases (MMPs) are proteolytic enzymes, which can degrade all components of extracellular matrix. MMPs have a critical role in cancer invasion and metastasis, and some of them are increasingly expressed in squamous cell carcinomas (SCCs) of cervix and tongue and associated with poor prognosis. Inhibition of MMP function by synthetic inhibitor BB-2516 (marimastat) has lead to survival benefit in the treatment of advanced gastric cancer or glioma. MMP-13 is a potent collagenase, which is rarely expressed in normal tissues, but which expression is often upregulated in situations, where rapid matrix turnover is needed, as in local invasion and growth of a malignant tumor.

Materials and methods 41 patients with stage I-IV SCC of head and neck were operated and/or treated with radiotherapy and followed up 60 months. Pre-treatment tumor samples were studied for MMP-13 expression by immunohistochemistry using a specific anti-MMP-13 antibody. The tumor and stromal cells expressing MMP-13 were counted and the percentage of positive tumor cells in sample tissue and staining intensity were correlated to tumor size and stage, and survival parameters.

Results Increased expression levels and staining intensity of MMP-13 in tumor cells seems to have a tendency to associate with poor survival in SCC of head and neck. This finding is presently tested in a larger patient material.

Conclusion Our results reveal that MMP-13 expression in primary SCC tumors of head and neck might correlate to survival parameters, which should be amenable for novel treatment modalities.

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POSTER

Management of the clinically negative neck nodes in early stage mobile tongue carcinoma.

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Purpose: To determine the role of elective neck treatment and the risk of occult node metastases in early stage mobile tongue carcinoma.

Methods and Materials: Between 1967 and 1999, 170 out of 318 patients (pt) with histological diagnostic of squamous oral tongue carcinoma presented early stage (I and II) disease. Patient characteristic: 127 males / 43 females; median age: 57 years (range: 29-89); stage (TNM classification,

2002): I: 69 pt, II: 101 pt. Primary tumor was treated with brachytherapy (110 pt), external beam therapy alone (3 pt) or a combination of both (57 pt). The management of neck nodes was individualized according to patient characteristic: eleven pt were treated with elective neck dissection, 67 pt with elective neck irradiation (median dose: 50 Gy), whereas 92 pt were carefully followed up without elective treatment. Statistical analysis: Kaplan-Meier and Log-rank test for survival curves comparison.

Results: Five-year actuarial cause-specific survival and local control were 71.6% and 73.3%, respectively. Whole 5-year regional disease-free survival was 75.2%. Nodal relapse-rate according to treatment modality were 0%, 20% (12% in field) and 29% for elective neck dissection, elective irradiation and observation, respectively. The corresponding 5-year regional disease-free survival were 100%, 82.8% (excluding relapses outside the field) and 69.5% (p=NS). To evaluate the risk of occult nodal metastases, we analyze the prognostic variables in the subset of patients without any elective neck therapy. The tumoral thickness was identified as prognostic factor to regional relapse in multivariate analysis (5-year regional disease-free survival was 86.7% vs. 16.8%, for thickness >1cm vs. < 1cm, p=0.0003). The 5-year disease-free survival was 35.1% for nodal-relapsed patients compared with 92.7% for non-relapsed patients (p<0.0001).

Conclusions: Due to the high relapse rate in the neck and poor survival of relapsed patients, we recommended elective neck treatment in all patients with early stage oral tongue carcinoma.

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POSTER

Comparison between 2D-conventional, 3D-CRT and IMRT techniques for irradiation of parotid gland carcinoma. Clinical Experience in IMRT.

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Background: For most patients, adjuvant radiotherapy is recommended, and literature studies suggest that this combined modality treatment is associated with reduction of local recurrence rate to 5-40%. In this paper we compare external beam techniques using conventional 2D radiotherapy (2D), three dimensional conformal radiotherapy (3D-CRT) and intensity modulated radiotherapy (IMRT) for our patient treated with 3D-CRT and IMRT.

Material and methods: Since march 2002 we have been treated with adjuvant radiotherapy for parotid gland carcinoma, combining 3D-CRT and IMRT as a boost. The planning target volume (PTV) and the organs at risk (contra-lateral parotid gland, eyes, brain stem, cochlea, PRV spinal cord and spinal cord) were outlined, according to ICRU Report n.50 and 62, on CT images acquired with a 3 mm step. Conventional and optimised 3D-CRT plans were created with forward Treatment Planning System (CadPlan, Varian Dosetek v.6.3.5) and compared with inverse-planned (Helios, Varian Dosetek) IMRT dose distribution using dose volume histograms. Clinical target volume (CTV) is defined as parotid gland surgical bed radiographically visible. A 5 mm margin was added in three dimension in order to accounting for uncertainties in target definition and patient movement to produce PTV. The planning goal was treat the PTV to a dose of 60 Gy in 2 Gy fractions at the ICRU point. All treatments were performed with 6 MV beams produced by a LINAC (600 CD Varian, *MLC-120 leaves).

– 2D planning procedure (2D): Two wedged rectangular ipsilateral beams with 6 mm margin between the PTV and field edge.

– 3D-CRT planning procedure: Three ipsilateral wedged fields with MLC.

– IMRT planning procedure: Four field (345°-320°-220°-190°) as class solution. Constraints for maximum doses were: 6 Gy contra-lateral parotid, 20 Gy oral cavity, 45 Gy brain stem maximum dose, 40 Gy cochlea. IMRT plan was delivered with a dynamic sliding windows MLC technique.

Results and Conclusions: All techniques produce an equivalent PTV mean dose irradiation (ranging from 58.8 and 59.8 Gy) but a larger dishomogeneity is observed in 2D and 3DCRT vs. IMRT technique (2.8% and 3% vs. 1.6%). The IMRT class solution keeps the dose to contra-lateral parotid gland at level acceptable (0.4 Gy vs. 2 Gy with 3DCRT) and also reduces the maximum dose to cochlea (17.3 Gy vs. 25.6 Gy and 20.7 with 2D and 3DCRT respectively). This our experience of parotid carcinoma treated with IMRT reflects the philosophy of our centre of the employment of IMRT not only for dose escalation programs but in particular for sparing organs at risk in young peoples.