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 possibilty 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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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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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 multivariante 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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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 leafs).

– 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.