

**M1****POSTOPERATIVE RADIOTHERAPY (PRT) FOR MALIGNANT PLEURAL MESOTHELIOMA (MPM): OUTCOME AND PATTERN OF FAILURE**

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*Objective:*

To examine the outcome and pattern of failure of multimodality therapy in patients with potentially resectable MPM and to examine the radiotherapy-technique in patients with MPM.

*Material and Methods:*

20 Patients with resectable MPM were evaluated for preoperative chemotherapy followed by extrapleural pneumonectomy (EPP) and (PRT) to the hemithorax and/or to areas at risk.

*Results:*

After 3 cycles of chemotherapy 9 patients had PR, 5 SD and 6 had progression. 17 patients were then considered resectable and underwent EPP. 13 patients were treated with PRT. 7 patients received hemithorax radiotherapy with an involved field boost. 6 of this 7 relapsed, 3 inside and 3 outside the field. 6 patients were irradiated involved field to the high risk area. 4 of this 6 relapsed, 3 inside and 1 outside the field. The median time to confirmation of recurrent disease was 19 month. The median survival was 23 month.

*Conclusion:*

Multimodality therapy in patients with resectable MPM is effective with acceptable toxicity. The role of radiotherapy in this trimodality regime is unclear. Whether an approach with higher doses to the hemithorax is superior to involved field radiotherapy to high risk areas remains to be investigated in further studies.

Protontherapy was successfully administered in children with tumours of bone and soft tissue at PSI. The results in these cases are promising. However, the advantage of protons has to be expected from reduction of late toxicity but not in higher cure rates. Thus, we need longer follow-up time and larger cohorts to investigate the incidence of secondary cancer and late effects.

**M2****CONCURRENT TWICE DAILY LOW-DOSE CHEST RADIOTHERAPY (IFRT) AND PROPHYLACTIC CRANIAL IRRADIATION (PCI) FOLLOWED BY CHEMOTHERAPY (CT) IN LIMITED-STAGE SMALL CELL LUNG CANCER (LD SCLC)**

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*Objective:*

To evaluate the outcome of low-dose bifractionated up-front IFRT and PCI before CT (4 cycles of cisplatin and etoposide) in LD SCLC.

*Material and Methods:*

Between 12/99 and 02/02, 17 pts with LD SCLC received IFRT of 20 Gy in 10 fractions (fx) and concomitant PCI of 18 Gy in 10 fx followed by chemotherapy (cisplatin 100 mg/m<sup>2</sup>, d8 and etoposide 100 mg/m<sup>2</sup>,d8-10 for 4-6 cycles).

*Results:*

Median FU was 36.3 months (20-44). All patients except one (death related to infection and bleeding after the first CT) completed treatment. No Grade 3-4 esophagitis or pneumonitis. Response rate (RR) was 88.2%, 41% (7/17) of the patients showing complete response and 47% (8/17) partial response. Median time to first event was 13 mths with first site of recurrence local in 47%, brain in 12% and distant in 18%. Median survival was 28 mths. Kaplan-Meier 1-, 2- and 3-y survival rates were 94%, 67% and 36%. Salvage was RT in 4 pts, and RT+CT in 7 pts.

*Conclusion:*

RR and OS are similar to those observed in combined modality studies of LD SCLC with higher doses of chest irradiation. Although the CR rate seems somewhat lower than those achieved with higher RT doses, the absence of severe toxicity is a striking advantage. Moreover, this program allows liberal use of salvage RT, perhaps explaining in part the favorable median survival observed.

## M3

### **RADIOTHERAPY IN MERKEL CELL CARCINOMA: A RARE CANCER NETWORK STUDY**

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*Objective:*

To evaluate the role of RT in treating Merkel cell carcinoma

*Material and Methods:*

A retrospective analysis with a standardised questionnaire of 122 patients from 17 centres with at least biopsy proven Merkel cell carcinoma was performed. Disease stage, type of primary treatment, single, total dose, and volume of RT, recurrent and/or meta-static disease and follow-up were evaluated

*Results:*

96 pts had a stage I, 23 stage II, 2 stage III (1 unknown). Radical surgery was performed in 113 pts, biopsy in 9, lymphatic drainage was operated in 16 pts. The PT was irradiated in 95 pts (median dose, 50 Gy, range 7-70), lymphatic drainage in 52 pts (median dose, 50, range 39.6-66), 12 pts received chemotherapy. For the PT 11/95 pts with RT vs. 16/27 with surgery only ( $p < 0.001$ ) suffered a recurrence, for the lymphatic drainage 7/52 pts with RT vs. 27/70 without RT ( $p < 0.002$ ). 46 pts developed metastatic disease with or without recurrence. Follow-up was median 510 days (range 16-3359). 51.6% of pts were alive without disease were, 24.6 % dead due to tumour, 4.9% alive with disease, 10.7% dead of other courses or unknown, survival was unknown in 8.2%.

*Conclusion:*

According to our data RT is the most important treatment modality in Merkel cell carcinoma, surgery alone is insufficient. The benefit of RT is independent of surgical margins and tumour stage. The role of chemotherapy is not known yet.

## M4

### **CONSOLIDATING RADIATION THERAPY OF NON-HODGKIN LYMPHOMA FOLLOWING AUTOLOGOUS BONE MARROW TRANSPLANTATION**

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*Objective:*

To investigate the role of external beam radiation therapy (RT) after autologous bone marrow transplantation (ABMT) for Non-Hodgkin Lymphoma (NHL) and assess the clinical outcome in a controlled setting.

*Material and Methods:*

A case-control study including thirty patients was performed. Patients were matched according to stage of disease, histology, undergoing ABMT as initial treatment or as part of the treatment of relapsing disease, and gender. Minimal follow-up time exceeded five years after diagnosis of NHL.

*Results:*

Five of 15 patients after ABMT and consolidating RT relapsed compared to 8 of 15 patients without consolidating RT (N.S.). External beam radiation therapy with doses varying between 36 and 45 Gy successfully avoided relapsing disease in treated regions in all the patients ( $p = 0.01$ ). RT was able to reduce local combined with loco-regional disease relapse, as well ( $p = 0.03$ ). There was no difference of disease progression outside the radiation fields. There was no evidence of disease-free survival, nor was there any evidence of a detrimental effect of radiation therapy.

*Conclusion:*

Radiation therapy of regions with voluminous NHL disease or subtotal response can avoid relapses without evidence of additional toxicity. A controlled prospective assessment of the role of RT after ABMT in the treatment of NHL is being encouraged.

## M5

### **EFFECT OF PROBUCOL AND EVBT: RESTENOSIS AFTER PTA OF FEMOROPOPLITEAL ARTERIES: A RANDOMIZED MULTICENTER TRIAL**

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#### *Objective:*

To evaluate the prevention effect of endovascular brachytherapy and the antioxidant probucol on the incidence of restenosis after PTA of femoro-popliteal arteries.

#### *Material and Methods:*

335 pts with claudicatio Rutherford 2/3 were randomized according to a 2x2 factorial design into 4 groups: EVBT, Probucol, EVBT+Probucol and placebo group. EVBT dose was 14 Gy applied from a non-centering endoluminal catheter at a depth of the radius of the dilated vessel plus 2mm. Probucol (1g/d) or placebo given according to a randomized, double-blinded protocol was started one month before up to 6 month after PTA; all pts received aspirin 100 mg/d) Primary endpoint was restenosis defined as >50% reduction of diameter as detected by Duplex ultrasound 6 months after PTA.

#### *Results:*

The actuarial restenosis rate at 6 months f-up was 17% in the group of patients undergoing EVBT, 20% in patients with EVBT + Probucol, 27% in those treated with Probucol and 42% in the control group ( $p < 0.01$  for both EVBT vs no EVBT and Probucol vs no Probucol). The rates of pts free of claudicatio at 6mo were 79% in the EVBT group, 74% in the EVBT+Probucol, 78% in the Probucol and 56% in the control group ( $p < 0.01$  for EVBT vs no EVBT). Late thrombotic occlusion occurred in 5%, exclusive. in pts. treated with EVBT after stent implantation.

#### *Conclusion:*

EVBT and Probucol after PTA reduce the restenosis rate by 50% and by 23%, respectively. EVBT also improves symptoms and reduces the need of reinterventions.

## M6

### **CORONARY VASOSPASM: A NEW INDICATION FOR INTRACORONARY BRACHYTHERAPY**

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#### *Objective:*

Intracoronary brachytherapy (ICBT) has proven effective to reduce restenosis of in-stent-stenosis. ICBT is frequently associated with immediate vasospasms. No experience exists so far in the therapeutic approach of ICBT in patients with highly symptomatic vasospasm.

#### *Material and Methods:*

16 patients with frequent angina episodes despite intensive drug therapy, which showed no significant coronary lesion but inducible vasospasms by acetylcholine infusion, were included. Intracoronary brachytherapy was delivered by a beta-emitting source (32P, 20 Gy in 1 mm depth of vessel wall). Coronary flow of affected vessels, clinical improvement and Doppler flowmetry were monitored. Patients underwent invasive follow-up 145 and 80 days after ICBT.

#### *Results:*

ICBT of affected vessels resulted in a significant reduction of angina in patients with acetylcholine-induced coronary spasm (from 16.2 +/- 5.8 to 2.3 +/- 4.1 episodes per week,  $p < 0.001$ ). Antianginal therapy could be importantly reduced following ICBT.

#### *Conclusion:*

These are the first results on the effects of ICBT in highly symptomatic patients with coronary vasospasm. Invasive and clinical follow-up clearly demonstrate a major and sustained improvement of symptoms after intracoronary brachytherapy.

## M7

### RESULTS OF THERAPEUTIC SPLENIC IRRADIATION

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#### Objective:

To assess subjective and objective improvements after splenic irradiation.

#### Material and Methods:

Patients with myelo- or lymphoproliferative disorders and symptomatic splenomegaly were treated with low dose fractionated RT. Clinical, sonographic and radiological size of spleen was measured before/during and at the end of RT. Symptoms were recorded carefully. Hematological controls were mandatory always before the next RT-application.

#### Results:

Patient characteristics: Total: 45. Gender: 27 men, 18 women. Median age: 68 years (8 to 86 years). RT-regimen/course: dose of 0,3Gy 2-3x/week, TD: 1,2 – 3,6Gy, mean TD: 2,1Gy. 86 radiation courses were applied, e.g. almost 2 courses/patient (1 to max. 8). Time to next radiation course: average 10mts (1 – 81mts). Patients complained signs of upper left abdomen/symptoms in 82/86 courses at start of RT, at the end of RT only in 17/86. Reliefs: abdominal pressure 98%; nausea 97%; pain 93%. Improved situation at the end of RT in 80% of all series. Sonographic size of spleens: before RT: mean diameter 23,6cm (10 – 35cm), at the end of all courses applied: mean diameter 15,0cm (7 – 21cm). Hematological parameters: severe anemia (Hb <100g/l): before RT Hb 79g/l, at the end of RT Hb 87,6g/l, WBC: only moderate decrease (0,4 – 1,1G/l), thrombocytes remained stable. Leucocytosis (if hematological disease) improved distinctly: before RT 63,3G/l, at the end of RT 20,6G/l. 21 patients received chemotherapy before RT, 13 patients were treated with cytostatics after RT. In 31 out of 86 series blood transfusions were necessary during radiotherapy, after RT decrease of blood substitutions was noted in 6 cases. Survival after 1<sup>st</sup> radiation serie: average 21,5 mts (1 – 92mts), median 17mts. 20 patients died due to their hematological disease.

#### Conclusion:

Splenomegaly caused by hematological diseases can be treated easily with low dose radiotherapy with clinical improvement of almost 80%, hematologic parameters improve as well. Splenic irradiation is a true alternative specifically in those cases where medical treatments or splenectomy cannot be offered.

## M8

### HERPES ZOSTER (HZ) TREATED WITH RADIOTHERAPY(RT): RETROSPECTIVE STUDY WITH LONG TERM FOLLOW UP

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#### Objective:

Our goals were to determine the efficacy of radiotherapy to cure HZ and to reduce Postherpetic neuralgia PHN, identify risk predictors for the occurrence of PHN and the risk of tumor.

#### Material and Methods:

159 patients (pts) with HZ treated, between November 1975 – November 2003. Median age was 69 years. The treatment consisted in irradiation of the affected dorsal-root ganglion with a energy of 250 Kv. Between 1975-2000, the total dose was 1250-1500 cGy and the single dose 125 –150 cGy, and after 2000 respectively, 225-640 cGy and 30 cGy at 5-7 cm depth. Univariate, stratified, and multivariate analysis were implemented

#### Results:

For pts younger than 60 years, the risk of PHN three months after the end of RT was 21% After 6 months and more then one year they were respectively 18% and 14. In pts older than 60 years, the risks of PHN were 33% , 30%, 23 % after respectively 3 months, 6 months and more then one year. None of the pts less than 60 years for which RT was started in the acute phase develop PHN (100% pain relief). No tumor event was observed in relation to RT.

#### Conclusion:

RT is efficacious to reduce PHN. Age and delay from the acute phase of HZ, as well as start of RT more than 2 months are predictors of PHN

## M9

### PROSPECTIVE STUDY OF EXCLUSIVE STRONTIUM –90 IRRADIATION OF PRIMARY AND SECONDARY PTERYGIA

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#### Objective:

To demonstrate safety and efficacy of non-surgical, exclusive irradiation of non-operated pterygia.

#### Material and Methods:

We treated 21 primary pterygia out of 20 pat. and 6 secondary pterygia (recurrence after operation) of 6 pat. with an exclusive strontium-/yttrium-90 beta-irradiation with a total dose of 36Gy (6fx) and 48Gy (8fx) respectively between 11/99 and 3/02. These patients were referred from a single institution. The average f-up was 14+/-8 months (range: 3-27).

#### Results:

Prior to treatment the mean size of all pterygia was 2.6mm and shrinks to 1.6mm after treatment (p=0.001, student T-test). All 27 pterygia showed a reduction of size after therapy. The visual acuity of the eyes before treatment averaged on 0.73 and on 0.82 after treatment. This improvement is not significant (p=0.12). There was no eye with a decrease of the visual acuity and none of the 27 pterygia with a recurrence after the treatment either.

#### Conclusion:

The exclusive strontium-/yttrium-90 irradiation of the pterygium is a very efficient therapeutic method. As to the treatment management it is suggested to apply beta-irradiation before the development of an astigmatism-relevant pterygium, which makes excision necessary. It has to be assumed that a surgical excision may promote recurrence.

## M10

### BRACHYTHERAPY FOR EQUINE SARCOIDS

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#### Objective:

To realize local control in periocular equine sarcoids

#### Material and Methods:

The equine sarcoid is the most common skin tumor in horses. Its etiology is unclear and its incidence comes up to 0.5%. After surgical excision, cryotherapy or topical chemotherapy periocular tumors are presenting a nearly 100% local relapse rate frequently resulting in vision loss.

We treated 19 sarcoids by LDR interstitial brachytherapy (BT) using 192-Ir-wires with mean doses of 55 Gy.

#### Results:

After a median f-up of 30 months local control could be achieved in 16/18 (85%) lesions. The vision was normal in 14/15 lesions and the cosmetic result was stated as (very) good in 11/13 (85%) horses. Early reactions as edema and conjunctivitis were always observed, depigmentation and alopecia were seen as typical and common late changes.

#### Conclusion:

LDR-BT can promise a local control rate of ca. 90% in periocular equine sarcoids. It is associated with few side effects and very satisfying functional and cosmetic results.

In this tumor entity LDR-BT proved as highly superior to alternative treatment options, however, due to the necessary infrastructure this method will be feasible only in adequately equipped centers.

## M11

### EXTRACAPSULAR TUMOR SPREAD (ECS) IN PRE-MENOPAUSAL NODE-POSITIVE BREAST CANCER PATIENTS TREATED WITH CLASSICAL CMF: LONG-TERM RESULTS FROM IBCSG TRIAL VI

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#### Objective:

To evaluate if ECS is an independent prognostic parameter premenopausal node-positive breast cancer.

#### Material and Methods:

1475 eligible premenopausal patients were randomized to different schedules of 'classical' CMF (IBCSG Trial VI). After a review of pathology forms, 933 patients (63%) had information on the presence or absence of ECS.

#### Results:

The median f-up was 10 yrs. ECS was present in 49.5% .

Patients with ECS had a significantly worse outcome in terms of DFS, OS and local±regional failure (LRF)±distant failure (DF), which was no longer true after adjusting the models for log(nodes). For 382 patients with mastectomy, no radiotherapy, and 1-3 positive nodes the 10-yrs-DFS/OS was 50%(±4)/66%(±4) for ECS present vs 57%(±3)/ 76%(±3) for ECS absent [hazard ratio for ECS: 1.30 (95% CI: 0.95-1.78; p=0.10) and 1.37 (95% CI: 0.93-2.03; p=0.12) after adjusting for ER status, tumor size, VI and age group]. No significant differences in LRF or LRF±DF were found in patients with or without ECS [LRF: 13%(±3) vs 14%(±2); LRF±DF: 18%(±3) vs 17%(±3)].

#### Conclusion:

Our results revealed no independent prognostic value of ECS, nor a general recommendation for irradiation in premenopausal patients with 1-3 positive nodes treated with classical CMF.

## M12

### CONCOMITANT USE OF TAMOXIFEN INCREASES RADIATION-INDUCED SUBCUTANEOUS FIBROSIS IN ADJUVANT BREAST CANCER TREATMENT

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#### Objective:

To assess whether concomitant tamoxifen (TAM) and adjuvant radiation therapy (RT) increases the risk of subcutaneous fibrosis after conservative or radical surgery in breast cancer patients.

#### Material and Methods:

We evaluated 147 women with breast cancer treated with adjuvant RT after conservative surgery or mastectomy who took part among 399 patients with miscellaneous cancers included in the KFS 00539-9-1997/SKL 00778-2-1999 prospective study evaluating the predictive value of CD4 and CD8 T-lymphocyte apoptosis on the development of radiation-induced late effects.

#### Results:

Median age was 57 years (range: 26–82). RT consisted of 50-Gy whole-breast or chest-wall irradiation in 2-Gy fractions using either Co60 (n = 95) or 6-MV (n = 52) photons completed with a localized external electron boost up to 66 Gy. Adjuvant TAM concomitant with RT was prescribed at a dose of 20 mg/day for a period of five years in 90 patients. All patients receiving TAM were hormonal receptor positive, and none of them received adjuvant chemotherapy. There were 11 pre- and 79 postmenopausal patients (median age: 59 years; range: 35–82). Acute and late toxicities were assessed according to the CTC v2.0 and the RTOG/EORTC grading systems, respectively. Breast volume and skin dose was assessed in all patients. In a median follow-up of 29 months (range: 23–73), 142 patients are alive with (n = 5) or without disease. Five patients died from breast cancer without any grade 3 side effects (1, 13, 33, 38, and 41 months). Acute skin toxicity was observed in all but 4 patients (3%). One hundred and four (71%), 34 (23%), and 5 (3%) patients experienced grade 1, 2, and 3 acute side effects, respectively. No statistically significant difference was observed between the TAM and no TAM groups in terms of acute toxicity (p = 0.61). There was no correlation between the early and late toxicity (R<sup>2</sup> = 0.05). Among the 143 patients evaluated at two years, 35 patients out of 87 (40%) in the TAM group and 15 out of 56 (27%) in the no TAM group experienced grade 2 or more late skin toxicity (p = 0.35). However, grade 2 or more subcutaneous fibrosis was significantly higher in patients treated with concomitant TAM (42 patients out of 87 [48%] in the TAM group vs. 10 out of 56 [18%] in the no TAM group; p = 0.002). Breast volume and skin dose did not interfere with subcutaneous fibrosis. However, grade 3 telangiectasia incidence was more frequent but not statistically significant in patients with high breast volume irradiated with Co60 compared to 6-MV photons. No grade 3 fibrosis was observed for patients with radiation-induced CD8 apoptosis >24%. A decreased percentage of grade 2 or more fibrosis was observed for increasing values of CD8 apoptosis. There was an inverse relationship between side effects and radiation-induced CD8 apoptosis, and patients with low CD8 apoptosis given TAM showed significantly more fibrosis than those given TAM but showing high CD8 apoptosis. The 3-year cumulative incidence for grade 2 or more fibrosis was 76%, 23%, and 8% for patients in the three categories of percent CD8 T-lymphocyte apoptosis <16, 16–24 and >24, respectively. Multivariate analysis revealed that the two independent factors influencing the grade 2 or more fibrosis-free survival were radiation-induced CD8 apoptosis (p < 0.001) and the use of TAM (p = 0.03).

#### Conclusion:

We conclude that the concomitant use of TAM with RT increases significantly subcutaneous fibrosis, especially for radiosensitive patients. In these patients, adjuvant hormonal treatment with TAM should be delayed until the completion of RT, or the use of aromatase inhibitors should be considered.

## M13

### CONCOMITANT BOOST RADIOTHERAPY AS A ROUTINE TREATMENT FOR H&N CANCERS: A 10-YEAR SINGLE INSTITUTION EXPERIENCE

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#### Objective:

To report the 10-year experience of a single institution in the routine use of concomitant boost radiotherapy (RT) as standard radical treatment in patients (pts) with advanced H&N cancers

#### Material and Methods:

From 1991 to 2001, 296 pts were treated with concomitant boost RT either alone (67%) or combined with cisplatin-based chemotherapy, with a median tumor dose of 69.9 Gy. Tumors were located in the oropharynx in 52%, and the other sublocation (hypopharynx, larynx, nasopharynx and oral cavity) in 48%. UICC stage III-IV disease represented 77% of tumors. Median follow-up for surviving pts was 55 months.

#### Results:

All patients but one patient completed the RT schedule to the prescribed dose. Twenty pts (7%) had a treatment interruption (median 5 days). Grade 3-4 RTOG acute toxicity was observed in 77% of pts and nutritional support was required in 110 pts (37%). For all pts, the 5-year actuarial locoregional control and disease free-survival rates were 72% and 61%, respectively. Grade 3-4 late toxicity occurred in 14%, mostly bone and cartilage necrosis.

#### Conclusion:

The present accelerated RT regimen is logistically feasible. It represents a good choice when considering implementation of an altered RT fractionation schedule as standard treatment for H&N cancers. Moreover, concomitant chemotherapy administration is feasible.

## M14

### RECOVERING OF SWALLOWING AFTER IRRADIATION IN H&N TUMOUR PATIENTS WITH PERCUTANEOUS ENDOSCOPIC GASTROSTOMIA

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#### Objective:

To evaluate the recovering from dysphagia following radical and postoperative external beam treatment (EBT).

#### Material and Methods:

In 2001 25 patients (median age 55 years, m:f 2,6:1) got a PEG to maintain enteral nutrition prior or during EBT. Total dose was 60 to 70 Gy given in 6 fractions per week (23/25 pts).

#### Results:

Median follow-up was 21 months (range 4-31). 14 pts were alive at last follow-up. 7 out of 25 pts (28%) failed at locoregional sites. Median time of PEG was 7 months (range 2-24, and more than 1 year in 7 pts (18%) respectively). PEG could not be removed in 11 pts (44%) due to persistent/progressive disease (n=6), functional disorder (n=4) and esophageal stenosis (n=1).

#### Conclusion:

Persistent impairment of the swallowing mechanism after declining of the acute side effects in patients with PEG might be caused by fibrosis of the striated muscles of the pharynx and larynx. To overcome this problem patients are supported by analgetics and narcotics and encouraged to continue swallowing even during irradiation for functional stimulation.

## M15

### INTERSTITIAL LOW DOSE RATE BRACHYTHERAPY (LDR-BT) IN PATIENTS WITH SQUAMOUS CELL CANCER OF THE LIP

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#### *Objective:*

To analyze the results of radical and postoperative treatment of squamous cell cancer (SCC) of the lip with LDR-BT in our clinic.

#### *Material and Methods:*

Between 1990 and 2002 we treated 67 patients with 70 tumours (62 lower lip, 8 upper lip). 43 times in a radical setting and 17 times postoperative with R1 or R2-resections. Median age was 71 (37-90). There were more male patients (6:1). In 11% we treated recurrent disease after surgery or former brachytherapy. Histologically we found in 93% SCC, 44% G1-, 24% G2-, 4% G3- and 20% GX-differentiated. According to TNM-classification there were 56% T1, 37% T2 and 7% T3 tumours. One patient was N+. We applied a median dose of 60 Gy (50-70) with a median reference dose of 70 cGy/h and with 2-8 (median 3) applicators.

#### *Results:*

90% of the patients were alive after a mean follow-up of 33 months. 1 patient died of the SCC, 3 intercurrent and 3 of 2<sup>nd</sup> malignoma. 2 patients (2,9%) suffered from local recurrence (<2 years) & 4 from loco-regional recurrence (<42 months). In all cases salvage therapy was successful. We had no severe side effects (f.e. osteonecrosis, etc.) with excellent functional and cosmetic results.

#### *Conclusion:*

LDR-BT is an attractive treatment option in patients with SCC of the lip with excellent functional and cosmetic results and a very low recurrent rate. In case of recurrence salvage therapy is normally successful.

## M16

### HEMOGLOBIN LEVEL DECREASE INFLUENCES THE OUTCOME IN HEAD AND NECK CANCER PATIENTS TREATED WITH POSTOPERATIVE RADIOTHERAPY

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#### *Objective:*

To assess the influence of preoperative and postoperative hemoglobin (Hb) levels, and the amount of its decrease in locally advanced head and neck cancer (LAHNC) patients treated with surgery and postoperative adjuvant radiotherapy (RT).

#### *Material and Methods:*

Between December 1997 and June 2002, 79 (male to female ratio 62/17; median age: 60 years [range: 36-81]) consecutive patients treated with curative surgery followed by adjuvant accelerated RT with pT1-pT4 and/or pN0-pN3 LAHNC were included in this study. Postoperative RT was indicated because of positive surgical margins (n = 18) or for pT4 tumors (n = 3) in 21 (27%) patients; or because of extranodal infiltration with (n = 29) or without (n = 25) positive surgical margins in 54 (68%) patients. Four patients (5%) with more than 3 positive nodes were also included. RT consisted of 66 Gy (2 Gy/fr) in 5 weeks and 3 days. Preoperative and postoperative Hb levels were collected in all patients. In this study, Hb cut-off was considered <120 g/l in women and <130 g/l in men. The influence of the amount of decreasing Hb between pre- and postoperative Hb values was analyzed as well. Median follow-up was 22 months (range: 12-61).

#### *Results:*

Median time to locoregional relapse (n = 11) was 11 months (range: 3.5-22). Two-year actuarial locoregional relapse rate (LRS) was 26±9% in those with low Hb levels compared to 12±6% in those with normal Hb levels but the difference did not reach statistical significance. However, when decreasing Hb values between pre- and postoperative Hb levels were taken into account, 2-year disease-free survival (DFS) was significantly higher (71±6%) in patients (n = 61) with Hb difference less than 38 g/l (quartile value) compared to those (n = 18; 41±13%) with higher than 38 g/l (p = 0.01).

#### *Conclusion:*

We conclude that decreasing Hb more than 38 g/l after surgery probably secondary to blood loss influences the outcome when postoperative RT is indicated. A new prospective study is warranted to evaluate the role of erythropoietin in this setting.

## M17

### SPOT-SCANNING PROTON RADIATION THERAPY FOR INTRACRANIAL MENINGIOMAS

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#### Objective:

To assess the safety and efficacy of spot scanning proton beam radiation therapy (PRT) in the treatment of intracranial meningiomas.

#### Material and Methods:

Sixteen patients with intracranial meningioma were treated with PRT between July 1997 and July 2002. Eight patients had skull base lesions. The median prescribed dose was 56 CGE at 1.8 – 2.0 CGE per fraction. The median follow-up time was 34.1 months (range, 6.5 – 67.8).

#### Results:

Cumulative 3-year local control, progression-free survival and overall survival were 91.7%, 91.7% and 92.7%, respectively. No patient died from recurrent meningioma. One patient progressed locally after PRT. No distant metastasis was observed. Cumulative 3-year toxicity free survival was 76.2%. No radiation-induced hypothalamic/pituitary dysfunction was observed.

#### Conclusion:

Spot-scanning PRT is an effective treatment for patient with untreated, recurrent or incompletely resected intracranial meningiomas. Observed ophthalmologic toxicity is dose-related. Protons offer highly conformal irradiation for complex-shaped intracranial meningiomas adjacent to organs at risk with the potential of dose escalation for atypical and malignant meningeal tumors.

## M18

### THE ADVANTAGE OF PROTON THERAPY FOR SOFT TISSUE AND BONE TUMOURS IN CHILDHOOD

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#### Objective:

In paediatric radiotherapy, the reduction of dose to all normal tissues is essential to reduce potential late side effects.

#### Material and Methods:

Twelve children were treated with protons at PSI for soft tissue tumours between 1997 and 2003. For each case, IMRT plans have been calculated and compared to the delivered proton dose distributions. Criteria for the comparison were integral dose to the non-target normal tissues, and mean doses to selected organs at risk (OARs).

#### Results:

Median age of 7 children was 12 years. Diagnoses included 3 chordomas, 2 chondrosarcomas, 2 rhabdomyosarcomas, a osteosarcoma, a synovial sarcoma, a MPNST, a desmoid tumour, and an aneurysmatic bone cyst. The total integral dose delivered to the patients by the IMRT plans was predicted to be between 1.5 to 6.1 (mean 3.5) times higher than that for the corresponding proton plans. For selected organs at risk the mean doses were between 2.7 to 14.3 (mean 6.4) times higher with IMRT.

#### Conclusion:

The use of protons has been found to reduce significantly the dose load to OARs and all non-target tissues compared to IMRT. In paediatric radiotherapy, the reduction of both low and medium dose level could be an important factor in minimizing the risk for secondary cancer and organ deficiencies in young children.

## M19

### PROTON RADIATION THERAPY (PT) FOR SPINAL AXIS-ASSOCIATED CHORDOMA (1997-2003)

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#### Objective:

To describe patient and tumor characteristics; technical problems and innovations; acute and late toxicity; tumor-related outcome.

#### Patients and Methods:

Between September 1997 and December 2003, 28 patients (pt) were treated for spinal axis-associated chordomas (C1 to sacrum). Every effort was made to reduce macroscopic tumor mass before PT. Pts were treated in a supine position (cervical region) or prone. The intended dose @ PSI is: 74 CGE (37x2; 4f/w) by protons only, if implant-associated hot-spots and large volumes: 72 (40x1.8). To restrict dose to the myelon, an "inverted horseshoe" approach was used initially in a 2<sup>nd</sup> series, compromising the PTV distal to the myelon/cauda. In 2002, we developed an intensity modulated PT (IMPT) based method delivering a donut-shaped high-dose conformation wrapping around myelon/cauda (7 pt treated to date).

#### Results:

Median follow-up was 36 months (0-72; mean: 29; 2 pt >60; 7 pt in 2003). PT was very well tolerated (no >G3 CTCAE). No clinically apparent nerve damage has been reported. Of the 28 pt, 27 are still alive, 2 of them with metastasis, 1 (horseshoe) also with a local failure; 1 pt died from local progression (huge sacral chordoma). All metastases and local failures (so far) occurred in female pt.

#### Conclusion:

These data demonstrate the safety and high clinical efficiency of conventional spot-scanning PT delivery; a longer follow-up period is required to assess potential clinical advantages of IMPT in the treatment of this very challenging tumor entity. In agreement with the literature, our limited data suggest enhanced risk in females.

## M20

### ESTIMATED EFFECT OF PATIENT NON-COMPLIANCE TO DOSE-TIME CONSTRAINTS IN FIVE RANDOMIZED CLINICAL TRIALS OF ALTERED FRACTIONATION IN RADIOTHERAPY FOR HEAD-AND-NECK CARCINOMAS

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#### Objective:

To investigate the effect on treatment outcome of non-compliance to the dose-fractionation prescription in five randomized controlled trials of altered fractionation in radiotherapy for head-and-neck carcinoma.

#### Material and Methods:

Individual data from 2566 patients participating in the European Organization for Research and Treatment of Cancer (EORTC) 22791, EORTC 22811, EORTC 22851, Princess Margaret Hospital (PMH), and continuous hyperfractionated accelerated radiotherapy (CHART) head-and-neck trials were merged in the fractionation IMPACT (Intergroup Merger of data from Altered or Conventional Treatment schedules) study database. The ideal treatment time was defined as the minimum time required to deliver a prescribed schedule. Compliance to the prescribed overall treatment time was quantified as the difference between the actual and the ideal overall time. An overall measure of compliance in an individual patient, the total dose lost (TDL), was calculated as the dose lost due to prolongation of therapy (assuming a D(prolif) of 0.64 Gy/day) plus the difference between the prescribed and the actual dose given

#### Results:

The time in excess of the ideal ranged up to 97 days (average 3.9 days), and 25 % of the patients had delays of 6 days or more. This quarter of the patients with long treatment protraction were estimated to loose at least 10 percentage points in tumor control probability. World Health Organization (WHO) performance status and nodal stage had a significant effect on TDL. TDL was significantly higher in the conventional than in the altered arm of the EORTC 22851 and CHART trials. In the PMH trial, TDL was significantly higher in the hyperfractionation than in the conventional arm. Centers participating in the three EORTC trials varied significantly in their compliance. There was a significant improvement in compliance in patients treated more recently

#### Conclusion:

Even in randomized controlled trials, compliance to the prescribed radiation therapy schedule may be relatively poor, especially after conventional fractionation. This affects treatment outcome and may potentially affect the interpretation of the outcome of these trials

## M21

### PREDICTON OF H&N CANCER PATIENTS OUTCOME USING THE PRE-TREATMENT FDG UPTAKE

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#### Objective:

To assess the predictive value of pre-treatment FDG uptake in patients (pts) with H&N cancer managed either by radiotherapy (RT) or surgery.

#### Material and Methods:

Pretreatment tumor FDG uptake, as measured by the Standardized Uptake Value (SUV), was obtained in 120 pts studied prospectively using PET scanning. Treatment consisted of radical RT +/- chemotherapy (73 pts) or radical surgery +/- post-operative RT (47 pts). Median follow-up of the surviving pts was 48 months.

#### Results:

Patients with high FDG uptake tumors (SUV > median, 4.76) had poorer LC (p= 0.003) and DFS (p= 0.005) in mono-variate analysis. This difference was also observed when the RT and surgery groups were analyzed separately. In the multivariate analysis T-category (p= 0.005) and SUV (p= 0.046) were independent adverse factors for LC, whereas N-category (p= 0.004), T-category (p=0.02) and SUV (p= 0.05) were independent determinants of DFS.

#### Conclusion:

Pre-treatment tumor FDG uptake represents an independent prognostic factor in pts with H&N cancers, whatever the primary treatment modality. Tumors with high FDG uptake are at greater risk of failure and should be considered for more aggressive therapy.

## M22

### PROTON RADIATION THERAPY FOR SARCOMAS OF THE SOFT TISSUES AND BONES

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#### Objective:

Proton radiotherapy offers the possibility to deliver conformal high dose to lesions of challenging shape, large volume and/or in sensitive surroundings. Sarcomas often fulfill these characteristics. We present the outcome of proton therapy with respect to toxicity and local control of 12 soft tissues and bone sarcoma patients.

#### Material and Methods:

Between 1997 and 2002, 12 patients were treated for 11 soft tissue sarcomas and 1 bone sarcoma. 8 pats. were male, 4 female; age ranged from 7 to 66 (med. 33) years. Proton therapy was given as boost or as full course treatment. Dose ranged from 14 to 72 (med. 45) CGE, the number of fractions from 7 - 36 (med. 25). Treatments prior to proton therapy were: 3 incomplete surgical resections, 4 resections + chemotherapy, 3 resections + chemotherapy + photon irradiation, 2 biopsies + chemotherapy. 9/12 patients were treated with curative intent.

#### Results:

Ater med. follow up of 26 m. (range 12 - 64), 6/12 lesions were locally controlled. 8 out of 12 patients are alive at med. 36 m.. Of the six patients with LF, 4 died at 1 - 32 m., med. 9 m. Late toxicity >grade 2 RTOG was seen in 1 patient.

#### Conclusion:

Proton irradiation is a safe and effective treatment for sarcoma patients, also in combination with surgery and chemotherapy. Toxicity is rare. To improve outcome, interdisciplinary pre-treatment discussions and concepts should become routine.

## M23

### CONSERVATIVE TREATMENT OF ANAL CANAL CANCER: EXPERIENCE OF LAUSANNE AND MONTPELLIER

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#### Objective:

To assess the outcome and prognostic factors in the conservative treatment of squamous-cell carcinoma of the anal canal (SCCAC).

#### Material and Methods:

We retrospectively evaluated 160 consecutive patients with SCCAC treated with curative intent in Lausanne and Montpellier between November 1987 and April 2003. Male to female ratio was 31/129, and median age was 64 years (range: 30-94). T-classification according to UICC included 32 (20%) T1, 77 (48%) T2, 30 (19%) T3, and 21 (13%) T4 patients. There were 134 (84%) patients without nodal extension. Pathological grade included 61 (38%) grade 1, 31 (19%) grade 2, 47 (30%) grade 3 tumors, and grade could not be obtained in 21 (13%) patients. Treatment consisted of external radiation therapy (RT) alone in 21 (13%) patients, RT + chemotherapy (CT) in 38 (24%), RT + brachytherapy (BT) in 60 (38%), RT + BT + CT in 35 (22%), and BT alone in 6 (3%) patients. RT consisted of 10x3 Gy + BT boost in 35 (23%) patients, 25x1.8 Gy + BT boost in 50 (32%), and 33x1.8 Gy without BT in 69 (45%) patients. RT technique consisted of AP/PA irradiation 89 (58%) patients, direct electron beam in 38 (25%), and 3-field technique (1 PA + 2 lat) in 27 (17%) patients. Median BT boost dose was 25 Gy. Chemotherapy was administered in 46% (n = 74) of the patients (mitomycin + 5-FU in 50 [68%] and platin + 5-FU in 24 [32%]). Median follow-up was 69 months (range: 6-183).

#### Results:

Five-year overall survival, cancer-specific survival (CSS), disease-free survival, local control, colostomy/disease-free survival (CDFS) was 87±3%, 94±2%, 82±3%, 83±3%, and 80±3%, respectively. Grade 3 acute toxicity (CTC v2.0) consisted of erythema in 21 (13%), and diarrhea in 4 (3%) patients. Median time to locoregional relapse was 15 months (range: 4-41) in 25 patients (16%), and distant metastases without locoregional failure were observed in 9 (6%) patients. Salvage treatment consisted of abdominoperineal amputation in 21 patients, lymph node dissection in 2 nodal failures, and local excision for a small local failure in one patient. Palliative RT was given in one patient with massive locoregional progression. We observed grade 3 late toxicity (RTOG/EORTC) in 5 (3%) patients, and grade 4 in 12 (8%). Multivariate analysis (Cox model) revealed that independent factors with a better CSS were CT (RR = 13), grade 1 or 2 (RR = 10), BT (RR = 10), and limited circumferential extension (RR = 7). Standard-technique RT using AP/PA fields was the only independent predictor for a better CDFS.

#### Conclusion:

We confirm an excellent outcome using sphincter-sparing conservative treatment in patients with SCCAC. CT is an important part of the treatment. BT boost gives an excellent local control but seems to be related with increased sphincter toxicity. Prospective studies using 3D conformal and/or intensity modulated RT combined to concurrent CT are warranted.

## M24

### COMBINED MODALITY TREATMENT IN HIV-POSITIVE PATIENTS WITH ANAL CANCER.

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#### Objective:

To assess the efficacy and tolerance of standard fluorouracil/mitomycin-based chemoradiation in the treatment of anal cancer in HIV-positive patients.

#### Material and Methods:

We reviewed all consecutive patients with invasive anal cancer treated from 1988 until 2002 with curative intent at our institution. HIV-positive patients were compared to HIV-negative patients in respect of toxicity, disease control and survival.

#### Results:

Ten patients were HIV-positive and 78 HIV-negative. The HIV-positive patients were of younger age (median 40.5 vs. 60 years) and predominantly male gender (80% vs. 26%). Local control and sphincter preservation was achieved equally well in both patient populations. Cancer specific survival rate in the HIV-positive group was half of the survival rate of HIV-negative patients. Patients amenable to HDR-boost therapy seemed to benefit in respect of disease free survival, although only one HIV-positive patient was treated with HDR. Treatment related toxicity was seen more frequently in HIV-positive patients, however no treatment related death occurred.

#### Conclusion:

In the HIV-positive study population cancer specific survival seems to be reduced and toxicity more pronounced requiring more stringent clinical surveillance.

## M25

### FDG-PET BASED AUTOMATED TREATMENT PLANNING FOR PREOPERATIVE RADIATION THERAPY OF RECTAL CARCINOMA.

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#### *Objective:*

We have shown that radiation-treatment planning is potentially more performing and safer if imaging acquisition is performed on a PET/CT with a  $^{18}\text{F}$ -fluoro-deoxy-2-glucose-positron emission tomography (FDG-PET) integrated in a computer-assisted tomography (CT) (IJROBP 2003 57:853).

#### *Material and Methods:*

Here, we present an algorithm for the purpose of automated and immediate volume definition for preoperative RT of rectal cancer. RT planning is started with the isolated PET signal co-localising to the rectal structure of interest on the CT.

#### *Results:*

Three-dimensional segmentation in 26 various directions allows the software to reliably determine the tumor volume basing on the PET signal corresponding to the tumor. The specific automatically delineated structure can be used as GTV. In a second step, the automatically computed added safety margin results in the planning treatment volume (PTV).

#### *Conclusion:*

This approach leads to a highly reproducible and standardised treatment volume definition and allows immediate initiation of RT with a predefined beam geometry as available for intensity-modulated radiation therapy (IMRT).

## M26

### PHASE I-II TRIAL OF CONCOMITANT PRE-OPERATIVE RADIOTHERAPY (RT) AND GEMCITABINE FOR LOCALLY ADVANCED RECTAL CANCERS (LARC)

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#### *Objective:*

To assess the maximum tolerated dose (MTD) of gemcitabine when administered concomitantly with hyperfractionated RT preoperatively in patients (pts) with LARC and to investigate the mid-term efficacy of such a regime.

#### *Material and Methods:*

37 pts with stages II-III tumors were enrolled. RT consisted in 50 Gy given in 2 daily fractions of 1.25 Gy in 4 weeks. The starting dose of gemcitabine was 10 mg/m<sup>2</sup>/day twice weekly with planned escalation steps of 5 mg/m<sup>2</sup>/day. Median follow-up was 32 months.

#### *Results:*

2/4 pts presented with dose-limiting rectal toxicities at the level of 45 mg/m<sup>2</sup>. Thus, the gemcitabine biweekly dose of 40 mg/m<sup>2</sup> was considered as the MTD. 17 pts (47%) had a marked pathological response (complete in 6 and microscopically residual carcinoma of less than 1 cm in 11 pts). All pts had a clear surgical margins. At 3 years actuarial locoregional control was 94.5%.

#### *Conclusion:*

In pre-operative treatment of LARC, the recommended dose of gemcitabine is 40 mg/m<sup>2</sup> when administered biweekly concurrently with 50 Gy hyperfractionated RT. The encouraging pathological response rate and the very low locoregional recurrence rate suggest that this innovative approach merit further investigation.

## M27

### **PATHOLOGICAL DOWNSTAGING AFTER NEOADJUVANT RADIO-CHEMOTHERAPY FOR RECTAL CANCER**

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#### *Objective:*

To analyse the impact of preoperative chemoradiotherapy on pathological downstaging, resectability, acute toxicity, sphincter sparing and local control.

#### *Material and Methods:*

Between March 1998 and December 2002 34 patients were entered into the protocol (20 m, 14 f, median age 61 y). UICC Tumorstages 2 and 3 with 15 and 19 patients respectively. The whole pelvis was irradiated with 45 Gy (5x1.8 Gy per week). Simultaneous chemotherapy was applied via continuous infusion with 5-FU (240 mg/m<sup>2</sup>/d for 5 weeks) or as bolus (500mg/m<sup>2</sup>/d for d 1-3 resp. 29-31). Restaging after 4 weeks, surgery after 6 weeks.

#### *Results:*

A sphincter sparing resection was possible in 21/34 patients. Surgical morbidity was low with 11.7% (4/34): 2 leakages, 1 stenosis, 1 local infection). The postoperative mortality after 30 days was 0%. Pathological downstaging was achieved in 44.1% (15/34), in 5/34 patients (14%) no residual tumour was found. The local control after a minimum follow up of 12 months is 97.1 % (1/34 local recurrence).

#### *Conclusion:*

Combined preoperative radiochemotherapy for locally advanced rectal cancer is well tolerated, results in an excellent even complete downstaging allowing often a sphincter sparing surgical procedure with a high local tumour control.

## M28

### **PROSPECTIVE ASSESSMENT OF QUALITY OF LIFE (QOL) IN PATIENTS WITH RECTAL CANCERS TREATED BY PREOPERATIVE RADIOTHERAPY (RT)**

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#### *Objective:*

To study changes over time of QoL parameters in patients treated by preoperative RT for locally advanced rectal cancers (LARC).

#### *Material and Methods:*

53 patients (pts) treated by a bifractionated RT (50 Gy in 40 fractions/4 weeks) and surgery were studied. QoL was assessed by using 2 validated EORTC questionnaires. Pts were asked to complete the questionnaires before and 1-year after treatment.

#### *Results:*

At 1-year post-treatment, pts reported significant improvement in their emotional state (p<0.0001), their perspective for the future (p=0.0004) and their global QoL (p=0.0008). However, the sexual dysfunction score increased significantly in males (17 vs 83, p=0.0045). Pts with colostomies reported similar or significantly improved symptom scores compared to pts without colostomies.

#### *Conclusion:*

1-year post-treatment for LARC, pts exhibit significant improvement in some important QoL outcomes. Moreover, QoL considerations do not justify sphincter-conserving approaches if loco-regional tumor control would be compromised thereby.

## M29

### COMBINED USE OF GOLDMARKERS FOR SETUP IN FRACTIONATED HDR BRACHYTHERAPY (BT) AND ORGANTRACKING DURING EBRT OF PROSTATE CANCER

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*Objective:*

To analyse the use of gold markers in combined radiotherapy of advanced prostate cancer.

*Material and Methods:*

21 pts. with advanced prostate cancer underwent combined HDR BT (3 x 7 Gy) and EBRT (50 Gy). During anesthesia for the BT implant, 3 gold markers were inserted into the prostate, serving as intraprostatic reference to readjust the length position of the applicators prior to each BT fraction and as reference for organ tracking during EBRT. We measured the deviation of a applicator length positions on radiographs. During EBRT, the position of markers was monitored by use of an EPID.

*Results:*

The length position of applicators varied substantially between BT fractions (average -4mm [range -16 mm to 3 mm] at fraction 2; average 1 mm [range -10 to 7 mm] at fraction 3. However, the original position of the applicators could be easily readjusted prior to each fraction. The marker positions were stable during BT and EBRT, one marker got lost during EBRT, without compromising the online setup procedure for patient repositioning. In one patient, organ tracking was impossible due to excessive intra-fraction prostate movement.

*Conclusion:*

Gold markers represent a reliable tool to improve quality of combined radiotherapy in prostate cancer.

## M30

### PROSTATE CANCER RADIOTHERAPY: INFLUENCE OF RECTAL VOLUME ON PTV MARGINS

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*Objective:*

Random rectal volume changes during radiotherapy are the main factor for prostate motion in the anteroposterior (Y) axis. We tested the hypothesis that small rectal volumes at simulation are stable during treatment allowing for a significant reduction of PTV margins (in the Y axis) without jeopardizing precision.

*Material and Methods:*

Forty patients with prostate cancer were simulated and treated in the supine position with an empty bladder, without immobilization. All underwent sequential weekly CT scans of the pelvis under identical conditions to those at simulation. After each CT scan, the CTV (prostate and seminal vesicles) was redefined and a new isocenter was obtained. Isocenter shifts (mean, systematic error, and random error) in the Y axis were obtained for each patient and PTV margins were estimated (according to McKenzie et al).

*Results:*

For large (> 80cc) and small (<80 cc) rectal volumes at simulation, estimated PTV field margins (covering 90% of cases with 95% of the prescribed dose) were 12 and 7 mm, respectively.

*Conclusion:*

Target motion in the Y axis is dependent on rectal volume changes and appear to be most marked for large rectal volumes at simulation. Thus, PTV margins should be larger for the latter patients but can be significantly reduced for patients with small rectal volumes at simulation.

**M31****PALLIATIVE INTERSTITIAL HDR BRACHYTHERAPY (BT) FOR PELVIC TUMORS**

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*Objective:*

RT is often the most effective treatment for palliation of cancer symptoms associated with local disease. We describe CT-guided implantation techniques to perform BT in the pelvic area.

*Material and Methods:*

CT-guided implantation of BT catheters was performed in 156 pts with local recurrences or metastatic disease in the pelvic area. The site of the primary was colorectal in 86/156 pts, sarcoma 11/156, kidney 12/156, NSCLC 13/156, breast 12/156, cervix/uterus 16/156 and prostate in 6/156. 59 pts were implanted using metallic needles and 97 using plastic tubes. Post-implant CT scans were used for 3D conformal BT planning. Pts with metallic needles were given a single fraction of 10-15 Gy using HDR <sup>192</sup>Ir and those who received implants of plastic catheters were given fractionated BT, twice daily 4-5 Gy to a total dose 28-40 Gy.

*Results:*

Follow-up is available in the range 6-60 months. The treatment was well tolerated and no acute complications were observed. One patient developed a fistula after 8 months. The mean tumour volume was 293 cm<sup>3</sup> with a range of 30-2103 cm<sup>3</sup>. The median post-brachytherapy survival was 16 months. Tumour response was as follows: 118/156 stable disease, 19/156 partial remission and 19/156 local progression. Significant pain relief was recorded in 143 pts and the mean duration of this palliative effect was 8 months with a range of 1-19 months.

*Conclusion:*

The CT-guided HDR BT can be performed safely and can provide effective palliation for pts with locally unresectable recurrences and distant metastases in the pelvic region.

**M32****SQUAMOUS-CELL CARCINOMA OF THE PENIS: RADIATION THERAPY ALONE OR COMBINED SURGERY AND RADIATION THERAPY?**

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*Objective:*

To assess the prognostic factors and the outcome in patients with squamous-cell carcinoma of the penis.

*Material and Methods:*

A retrospective review of 60 consecutive patients with non-metastatic invasive carcinoma of the penis, treated between 1962 and 2003, was performed. The median age was 61 years (range: 35-85). Eight (13%) patients were circumcised, 48 (80%) were married, and only 3 (5%) had a history of venereal disease. Existence of a penile mass was the first symptom in 49 (82%) patients. The anatomic site was distributed as follows: glans in 24 (40%), prepuce in 16 (27%), shaft in 13 (22%), coronary localization in 4 (7%), prepuce and glans in 2 (3%), and shaft and prepuce in 1 (1%). According to UICC staging, there were 22 (37%) T1, 32 (53%) T2, 5 (8%) T3, and 1 TX (2%) tumors. The N-stage was distributed as follows: 42 (70%) patients with N0, 13 (22%) with N1, 3 (5%) with N2, and 2 (3%) with N3. Eighteen patients had grade 1, 17 grade 2, and 14 grade 3 tumors (grade was not determined in 11). Forty-five percent (n = 27) of the patients underwent a curative surgery: partial penectomy (n = 23) with (n = 8) or without (n = 15) lymph node dissection, or total penectomy (n = 4) with (n = 3) or without (n = 1) lymph node dissection. All but 5 patients (operated) underwent definitive (n = 33) or postoperative (n = 22) radiotherapy (RT) to the penis and inguinal lymph nodes (n = 23), penis alone with (n = 4) or without (n = 11) brachytherapy, inguinal lymph nodes alone (n = 12), or brachytherapy alone (n = 1). The median and mean follow-up period was 62 months (range: 6-454).

*Results:*

Median time to locoregional relapse was 14 months (range: 5-139). There were local relapse in 22, regional relapse in 9, and 10 distant metastases (local and regional relapse were observed together in 3 patients). Local failure was observed in 3 out of 27 (11%) patients treated with penile surgery ± postoperative RT vs. in 19 out of 33 (56%) treated with definitive RT (p = 0.0001). Sixteen (73%) out of 22 local failures were successfully salvaged with surgery. At the time of analysis, among the 33 patients treated with definitive RT, local control was obtained with organ preservation in 13 (39%) patients. In the remaining 20, 15 out of 19 local failures were salvaged by partial (n = 8) or total penectomy (n = 7), and 4 out of 19 local failures could be salvaged conservatively resulting in an ultimate penis preservation rate of 17 out of 33 (52%) patients treated with definitive RT. In all patients, 5- and 10-year overall and cancer-specific survival rates were 43% and 25%, and 61% and 55%, respectively. The 5- and 10-year local and locoregional control rates were 63% and 48%, and 50% and 39%, respectively. In patients treated with definitive radiotherapy, 5- and 10-year probability of surviving with penis was 43% and 26%, respectively. There was no difference in terms of 10-year cancer-specific survival between the patients treated with definitive RT ± salvage surgery and primary surgery ± postoperative RT (56% vs. 53%; p = 0.16). In multivariate analyses (Cox model), independent factors influencing the survival were the N-classification (p = 0.01) and the pathological grade (p = 0.03). Surgery was the only independent factor predicting the local control.

*Conclusion:*

We conclude that, in patients with squamous cell carcinoma of the penis, local control is definitively superior with surgery. However, there is no difference in terms of survival between patients treated with surgery and those treated with definitive RT ± salvage surgery, with 52% organ preservation.

## MP1

### FIRST RESULTS OF RADIOTHERAPY FOR BONE AND SOFT TISSUE TUMOURS IN CHILDHOOD WITH PROTONS AT PSI

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#### *Objective:*

Protontherapy provides high conformity of dose for the target volume with steep fall off to the surrounding tissue. Thus it can help to reduce the risk for late effects after radiotherapy.

#### *Material and Methods:*

12 children were treated at PSI for bone and soft tissue tumours with total doses of 45.0 to 74.0 CGE (median 63.2 CGE). Median age was 12.0 years (range 7.5-16.1). Histopathological diagnoses were chordoma (n=3), chondrosarcoma (n=2), rhabdomyosarcoma (n=2), osteosarcoma, synovial sarcoma, desmoid tumour, malignant peripheral nerve sheath tumour and aneurysmatic bone cyst (n=1). In 9 patients protontherapy was administered after surgery. Chemotherapy was applied in 4 children, in 2 children following surgery. One child received definite radiotherapy only.

#### *Results:*

Two children died 2 and 12 months after therapy because of progressive disease. In one other child with a synovial sarcoma of the cervical spine local failure occurred, but it was still alive at last follow up.

#### *Conclusion:*

Protontherapy was successfully administered in children with tumours of bone and soft tissue at PSI. The results in these cases are promising. However, the advantage of protons has to be expected from reduction of late toxicity but not in higher cure rates. Thus, we need longer follow-up time and larger cohorts to investigate the incidence of secondary cancer and late effects.

## MP2

### RISK FACTORS FOR DEVELOPING A SECOND AERODIGESTIVE CANCER AFTER RADIOTHERAPY WITH OR WITHOUT CHEMOTHERAPY FOR HEAD AND NECK CANCER: AN EXPLORATORY OUTCOME ANALYSIS

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#### *Objective:*

To assess whether the administration of chemotherapy simultaneously with altered fractionation radiotherapy influences the risk of developing a second aerodigestive cancer in locoregionally advanced non-metastatic carcinomas of the head and neck (H&N).

#### *Material and Methods:*

The data of 518 patients with a minimum follow up of 1 year were pooled: 223 patients from the SAKK 10/94 trial, treated with 1.2 Gy BID to 74.4 Gy, with or without simultaneous Cisplatin (nasopharyngeal and maxillary sinus carcinoma were excluded), and 295 patients from Geneva, all treated with accelerated radiotherapy with concomitant boost to 69.9 Gy (nasopharyngeal carcinoma were included), 33% with concomitant chemotherapy. The data of 452 patients was analyzed. In an exploratory analysis including competing risk methodology it was investigated whether the addition of chemotherapy or other factors at diagnosis of the initial H&N cancer influences the risk of developing a second carcinoma after completion of therapy.

#### *Results:*

A total of 65 second carcinoma were observed after a median observation of 4.8 years. There was no second carcinoma after treatment for nasopharyngeal carcinoma, pointing to a difference in the pathogenesis of this cancer. There was no difference in time until occurrence of second carcinoma in cumulative incidences between the treatment with and without chemotherapy (p=0.99). The differences stratified by patient characteristics were not significant, either. However, graphical indication of a lower risk (not significant) was found for women. Up to 64 months the cumulative incidence was the same for patients with and without nodal involvement at diagnosis of primary tumor; thereafter the incidence was higher in patients without nodal involvement.

#### *Conclusion:*

Our data do not suggest that addition of chemotherapy to radiotherapy influences the incidence of second cancers in patients with H&N cancer.

## MP3

### SQUAMOUS CELL CARCINOMA OF THE BREAST

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#### Objective:

Pure squamous cell carcinoma (SCC) of the breast is a rare tumour included in metaplastic breast carcinomas with an incidence < 0.1%-2% of all breast carcinomas. Prognosis seems to be similar to others breast carcinomas. We report our experience of two patients (pts) treated in our service between January and March 2003.

#### Material and Methods:

Two women of 49 and 45 years presented with a 3 cm solid mass and a 7 cm cyst respectively in both mammography and ecography.

The cytology showed SCC. Primary treatment consisted in mastectomy and axillary dissection. Only one patient showed lymph node involvement. Hormonal status (progesterone and estrogen receptors) was negative. Chemotherapy was administrated in the patient with lymph nod involvement (4 EC). Local radiotherapy was performed for the two pts with 60 Gy (50 Gy chestwall and 10 Gy scare).

#### Results:

The two pts are still alive without evidence of disease with a follow-up of 5 and 11 months.

#### Conclusion:

Little is known about the long-term outcome and no definite recommendations exist to handle this entity. The role of adjuvant radiotherapy has not been studied but may have an important role in the treatment of these patients.

## MP4

### WELL-KNOWN AND NEW PARAMETERS IN BREAST RT-TREATMENT PLANNING: THEIR CORRELATION WITH IRRADIATED HEART VOLUME

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#### Objective:

To evaluate therapy-planning related parameters in left-sided breast cancer (lsBC) patients after breast conserving surgery. To evaluate if 'heart diameter' (HD) resp. the 'heart/chest quotient' (HCQ) and the distance of the inferior field border to diaphragma (DFD) in the scoutview correlates with irradiated heart volume.

#### Material and Methods:

Tangential treatment plans of 27 consecutively irradiated lsBC patients (median age: 55yrs) were reviewed for several parameters: eg. Central lung distance (CLD), maximum heart distance (MHD), dose volume histograms (DVH including V10, V20, V40), HD, HCQ and DFD. Beside the original RT plan (RToriginal) we also standardized the CLD to 10, 20 or 30mm (RTstandard) for all patients for better comparison.

#### Results:

The median heart and left lung volumes were 499ccm (299 to 768) and 1160ccm (790 to 1744); median HD: 12cm (11.6 to 16.3); median HCQ: 0.54 (0.44 to 0.67); median DFD: 1.2cm (-2.2 to 5.3). RToriginal: HCQ (p=0.01), CLD (p=0.02), DFD (p=0.05) was significantly correlated with MHD, HCQ and DFD also with irradiated heart volume measured by V10, V20 and V40. RTstandard: We found similar results for CLD10, 20 and 30mm: eg. 20mm: Significant correlation of HCQ and DFD with eg. V20.

#### Conclusion:

New parameters like HCQ and DFD showed a significant correlation to irradiated heart volume. Appropriate patient positioning and a close inferior field border selection are likely to reduce DFD and also the irradiated heart volume.

## MP5

### PALLIATION OF PAINFUL BONE METASTASIS OF HORMONE REFRACTORY PROSTATE CANCER BY 186-RHENIUM (186-RE)

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#### Objective:

To assess the clinical outcome following 186-Rhenium treatment in patients (pts.) with bone metastasis of prostate cancer.

#### Material and Methods:

From 10.1999 to 09.2002, 17 pts. (median age: 68,7) were treated by 186-Re for painful bone metastasis with an intravenous injection and for an average dose of 34 mCi (1,26 GBq). The main indication was multiple painful sites not responding to other modalities (i.e. palliative hormone or chemotherapy, biphosphonates, opioïdes). Pts. have been evaluated concerning the response and the outcome.

#### Results:

Mean time from diagnostic to bone metastasis was 30 months (5 pt. diagnosed with bone metastasis) and 17,8 months from metastasis to 186-Re treatment. 2 (11,7%) pts. had 2 administrations. Other treatments were: biphosphonates in 12 pts. (70,6%), surgical castration in 13 pts. (76,4%), chemical castration in 4 pts. (23,5%), palliative hormone therapy in 13 pts. (76,4%), palliative chemotherapy in 7 pts. (41,1%). Flare up phenomenon was observed in 5 (29,4%) pts. Opioids were used in 11 (64,7%) pts. before and in 12 pts. (70,5%) after 186-Re administration. Following the treatment, 11 pts. (64,7%) had decrease of pain in the first month, 7 (41,1%) pts. needed more, 4 pts. (23,5%) needed less analgesics and for 4 pts. (23,5%) the dose was unchanged; 8 pts. (47%) needed external radiotherapy for pain relief. Mean survival following the 186- Retreatment was 8,1 months. There was no death due to treatment complication.

#### Conclusion:

186-Rhenium may be efficient in around 2/3 of patients but the evaluation of the pain relief may be complexe with co-existing treatments in this group of patients with a poor outcome.

## MP6

### MODIFIED 3-D CONFORMAL RADIOTHERAPY (RT) TECHNIQUES FOR PROSTATE CANCER IN PATIENTS WITH METALLIC HIP PROSTHESIS: INFLUENCE ON THE RECTAL DOSE.

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#### Objective:

To compare the rectal dose between the usual and modified prostate RT techniques in patients with metallic hip prosthesis.

#### Material and Methods:

From 01.2001 to 12.2003, 8 prostate cancer patients with metallic hip prosthesis underwent curative RT by using modified techniques avoiding the prosthesis. In dosimetry without inhomogeneity correction, we observed that these patients had a greater mean (26%) and median (38%) rectal dose by 5- field technique compared to 6- field technique. Then we decided to perform a comparative dosimetric study for 5- and 6-field prostate techniques with a HELAX-TMS 6.1A (Theranostics, Freiburg) in patients without metallic hip prosthesis to take into account the inhomogeneities of patient. All patients had 5 mm CT scan slices. The evaluation of dosimetry was done by using collapsed cone algorithm.

#### Results:

Preliminary results for 8 patients show that the modification of a 6-field technique to a 5-field is associated with an average 12,6% and 23,6% (respectively mean and median) more dose in the rectum. Updated statistical results with a greater number of patients will be reported.

#### Conclusion:

Modification of prostate RT techniques by using less fields in order to avoid the metallic hip prosthesis may increase the rectal dose. The choice of the optimal modified technique should be made at an individual basis.

**MP7****FEASIBILITY AND EFFICACY OF SUBCUTANEOUS AMIFOSTINE IN HEAD AND NECK CANCER TREATED WITH CURATIVE RADIATION THERAPY**

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**Objective:**

To assess the feasibility and efficacy of subcutaneous amifostine in head and neck cancer patients treated with curative radiotherapy (RT).

**Material and Methods:**

Between November 2000 and January 2003, 33 (male to female ratio 27/6; median age: 54 years [range: 39-76]) consecutive patients treated with curative exclusive (n = 19) or postoperative (n = 14) radiation therapy with (n = 26) or without (n = 7) chemotherapy. The T-classification included 10 patients with T1-T2 tumors and 23 with T3-T4. The N-classification included 15 patients with N0-N1 and 18 with N2N3. Postoperative RT was indicated because of positive surgical margins or for pT4 tumors. All but one of the patients treated with exclusive RT received concomitant chemotherapy (cisplatin and 5-fluorouracil), and 8 of 14 patients treated with postoperative RT received EORTC-type adjuvant concomitant cisplatin chemotherapy. All patients received 3D conformal RT evaluating dose-volume histograms not only for GTV/CTV/PTV but also for parotid glands. RT consisted of 70 Gy (2 Gy/fr) in 6 weeks in exclusive RT patients, and 66 Gy (2 Gy/fr) in 5 weeks and 3 days in the postoperative setting. Parotid glands received at least 50 Gy in all patients. Amifostine (Ethyol<sup>®</sup>) was administered at total dose of 500 mg subcutaneously (sc) 15-30 min before every RT session with daily blood pressure monitoring. All patients receiving amifostine were given daily 200 mg dolasetron (Anzemet<sup>®</sup>) prophylactically. Acute and late toxicity was scored according to the CTC v2.0 and RTOG/EORTC system, respectively.

**Results:**

The 2-year overall survival was 74±9%. One patient died of chemotherapy toxicity during RT. Seven patients relapsed: nodal progression in 4 patients (one with local relapse and another with distant metastases) and systemic progression alone in 3 patients). All patients received their planned treatment (including chemotherapy). Four patients received the full schedule of amifostine, 15 received 20-29 doses, 4 received 10-19 doses, 5 received 5-9 doses, and 5 patients received less than 5 injections. Fifteen patients (45%) did not show any intolerance related to amifostine. Amifostine was discontinued because of nausea in 11 (33%) patients, hypotension in 6 (18%), and patient refusal in one. No grade 3 amifostine-related cutaneous toxicity was observed. Grade 3 acute toxicity included mucositis in 14 (42%) patients, erythema in 14, and dysphagia in 13 (39%) patients. Weight loss ranged between 0 and 13 kg (median: 4.5 kg). Late toxicity included grade 2 or more xerostomia in 17 (51%) and fibrosis in 3 (9%) patients. Grade 2 or more xerostomia was observed in 8 (42%) of 19 patients receiving 20 injections or more vs. 9 (64%) of 14 patients receiving less than 20 injections (p = 0.15).

**Conclusion:**

We conclude that subcutaneous amifostine administration is feasible. Compared to intravenous use of amifostine, the major side-effect of subcutaneous administration was nausea despite prophylactic antiemetic medication, and hypotension was observed only in 18% of the patients.

**MP8****THE VALUE OF PERITONEAL CYTOLOGY IN EARLY STAGE ENDOMETRIAL CANCER**

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**Objective:**

To assess the prognostic importance of positive peritoneal cytology

**Material and Methods:**

All 278 stage I and 53 stage IIIa endometrial cancer patients recorded between 1980-1996 at the Geneva Cancer Registry, were included. Stage IIIa cancers were re-categorised into cytological stage IIIa (positive peritoneal cytology alone, n=33) and histological stage IIIa (serosal / adnexal infiltration, n=20). Survival according to stage was analysed by Kaplan Meier method. Prognostic importance of cytology was analysed by Cox model adjusting for, amongst others, radiotherapy.

**Results:**

Five year disease specific survival rates of stage I, cytological stage IIIa and histological stage IIIa were 92%, 91% and 50% respectively (p<0.001). After adjustment for other prognostic variables, cytological stage IIIa patients were at similar risk to die from endometrial cancer as stage I patients (HR 0.7, 95%CI:0.18-2.3), while histological stage IIIa patients were at a fourfold increased risk to die (HR 4.2, 95%CI:1.7-10.3)

**Conclusion:**

Positive peritoneal cytology seems to have no impact on localised endometrial cancer survival.