

for the critical structures were superimposable in all cases, reflecting the fact that they were not adjacent to an air cavity. A detailed analysis of the impact of the air/flooded cavities on the dose distributions will be presented.

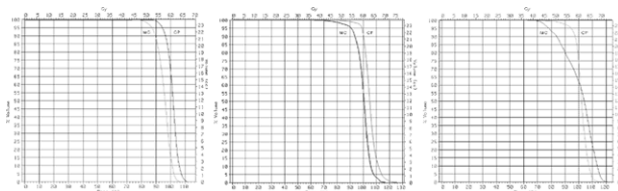


Fig. 1: MC vs. CP calculations for the effect of presence or absence of air cavities in the beam path for (a) anterior, (b) lateral and (c) posterior beam arrangements.

Conclusion: The use of multiple fields did not compensate for the effect of air cavities, as MC consistently demonstrated suboptimal PTV coverage. Of the three arrangements, the posterior one gave the most heterogeneity in PTV dose. This study emphasizes the importance of using MC as a verification tool for IMRT. The clinical consequences of the under dosage could be clinically important and merit further investigation.

1012 POSTER Oral cavity cancer treatment variations and survival comparisons in Ontario, Canada

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Medical practice may vary because of the paucity of randomized trial evidence for the treatment of oral cavity cancers. It is important to assess whether practice variations exist and whether variations are associated with differences in survival and control of the disease.

We used a cancer-registry based database that includes treatment and survival information for all 1809 patients in the province of Ontario, Canada diagnosed with carcinoma of the floor of mouth or anterior tongue between 1991 and 1998. The radiotherapy to surgery ratios, overall survival and cause-specific survival were compared across the nine geographic regions served by the regional cancer centres and among socioeconomic groups (determined using census income information).

The surgery to radiotherapy ratios varied from 1.6:1 and 1.7:1 in the two regions of eastern Ontario (where brachytherapy was available) to 8.6:1 in the Toronto area, where 43% of the patients live. Among socioeconomic quintiles, the poorest group was more likely to be treated with radiotherapy (surgery:radiotherapy ratio of 2.7:1) while the ratio in the other socioeconomic groups ranged from 4.2:1 to 5.2:1. Differences in 5-year overall survival and cause-specific survival were not statistically significantly different across the geographic regions (ranging by 13% and 9% respectively with logrank p-values of 0.47 and 0.98). Overall 5-year survival differed among the socioeconomic groups with 44% survival in the lowest quintile and 55% survival in the highest (logrank p < 0.001). Cause-specific survival varied marginally with rates of 67% in the lowest quintile to 72% in the highest (logrank p = 0.09).

Practice variations in oral cavity cancer may be leading to modifiable differences in the control of the disease. We are currently conducting a population-based retrospective cohort study of over 2500 patients in Ontario to further understand the care delivered to these patients and how it affects outcomes.

1013 POSTER Minimally invasive parathyroidectomy: even without the intraoperative use of quick parathormone measurement or gammaprobe a good operative procedure for primary hyperparathyroidism

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Background: minimally invasive parathyroidectomy is becoming a standard operative procedure for primary hyperparathyroidism. Apart from preoperative localising investigations, the intraoperative use of quick parathormone (PTH) measurement or gammaprobe is advocated. We evaluated the results of minimally invasive parathyroidectomy without the use of these intraoperative techniques.

Patients and Methods: Between May 2001 and May 2005, 65 patients with primary hyperparathyroidism in whom preoperative investigations had shown a solitary adenoma underwent minimally invasive surgery through a 3 cm (lateral) neck incision. Intraoperative PTH assessment and a gammaprobe were not part of the operative procedure.

Results: In 58 patients (89%) minimally invasive parathyroidectomy led to normocalcemia. In the remaining seven patients conventional neck exploration was necessary and resulted in normocalcemia as well. In three of these seven patients the adenoma had been "missed" by the surgeon, while in four patients preoperative investigations had predicted the localisation of the adenoma erroneously.

Conclusion: without the use of intraoperative PTH assessment or gammaprobe minimally invasive parathyroidectomy was successful in 89% of the patients.

1014 POSTER Economic aspects of amifostine (AM) as adjunctive treatment in during radical radio(RT) and radiochemo(RCT)therapy for head and neck cancer (HNC)

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Objectives: Several studies have shown that Amifostine protects against adverse effects of radical radiotherapy (RT) and radiochemotherapy (RCT) for head and neck cancer. The present study investigates the economic aspects of using amifostine during RT and RCT for patients with head and neck cancer compared to treatment without its use in Switzerland.

Materials and Methods: A meta-analysis of randomised trials was performed to compare the results of RT vs. RT+amifostine and RCT vs. RCT+amifostine on RT-and RCT-induced side effects and to quantify the radioprotective effects of amifostine. The incidence rates for adverse effects (mucositis, acute xerostomia, late xerostomia) were calculated and the resource use for the adverse effects assessed. Medical services and drugs utilised were priced using official tariffs. Resource use data for RCT vs. RCT+amifostine was derived from a randomised phase II study. Incidence rates and unit costs were combined to estimate total treatment costs of treating RT-induced side effects. The benefit of amifostine was then evaluated by comparing total costs of RT and RCT-treatment with/without adjunctive amifostine.

Results: Pooled results of 6 studies showed an overall relative risk reduction (RR) in mucositis of 0.702 (95% CI, 0.492 to 1.001, p=0.050). Five studies showed a significant reduction in favour of patients treated with amifostine with respect to acute xerostomia (RR=0.506, 95% CI, 0.361 to 0.709, p=0.000) and three studies a statistically significant benefit of amifostine on late xerostomia (RR=0.368, 95% CI, 0.132 to 0.868 p=0.024). Economic analysis estimated total treatment costs of side effects at CHF 7,516 vs. CHF 13,439 (RT vs RT+amifostine) and CHF 9,364 vs. CHF 10,759 (RCT vs. RCT+amifostine). Total complications costs per patient were CHF 7,516 vs. CHF 4,670 and CHF 9,364 vs. CHF 2,966 respectively. Higher costs with amifostine treatment of CHF 5,923 (RT) and CHF 1,395 (RCT) represent 44% and 13% of total treatment costs of adverse events. Late xerostomia followed by mucositis was the major cost driver in both treatment modalities. The acquisition cost of amifostine was partially offset by reduced costs (CHF 2,769 and CHF 6,306 respectively) from RT-induced side effects.

Conclusions: Amifostine protects against RT-induced side effects. Preliminary results from this study suggest a cost-saving potential of amifostine as an adjunctive treatment for head and neck cancer patients in Switzerland under both treatment modalities examined, RT and RCT.

1015 POSTER Imatinib with cisplatin in recurrent and/or metastatic adenoidcystic carcinoma – preliminary results of a phase II study of 18 patients with response assessed by morphological and functional imaging

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Background: Adenoidcystic carcinoma (ACC) of salivary glands may be characterised by slow growth, systemic metastases and poor response to conventional chemotherapy. 80 – 90% of ACC demonstrate c-kit positivity such that treatment with imatinib is conceptually attractive. 3-dimensional synergy analysis has been performed at this centre for both ACC primary

cultures and squamous carcinoma cell lines; mild synergy between cisplatin and imatinib was found in two of three cell lines as well as in ACC culture. Consequently we chose imatinib with cisplatin for a phase II study in patients with recurrent and/or metastatic ACC.

Material and methods: 18 patients (aged 29–77) with advanced ACC have entered the study. Imatinib was used alone in an initial dose of 800 mg daily for two months with response assessed using both FDG-PET and conventional imaging. Patients then received a combination of imatinib at a reduced dose with cisplatin 80 mg/m² at monthly intervals. Depending on responses and toxicity, patients then continued on maintenance imatinib.

Results: of 17 evaluable patients, two developed progressive disease on imatinib alone and left the study. 3 patients have shown a partial response with imatinib and cisplatin with 1 of these 3 on maintenance imatinib, without progression 27 months after commencement. 12 patients had stable disease on cisplatin plus imatinib but 9 of these have progressed since discontinuation of cisplatin and have stopped imatinib. Toxicity from the imatinib-cisplatin combination (median 5 cycles) included one grade 4 thrombocytopenia, one grade 3 anaemia and three grade 3 neutropenia. Non-haematological toxicities included one grade 3 hyponatraemia, four grade 3 fatigue and one grade 3 oedema. After a median follow-up period of 18 months for the 17 patients, 4 have died with progressive disease.

Conclusion: The combination of imatinib (400 mg daily) and cisplatin (80 mg/m²) appears to be effective in stabilising the disease but this response is maintained in only a minority of patients. FDG-PET proved useful in assessing early response.

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POSTER

A new model for concurrent chemoradiation in advanced oropharyngeal cancer: an Indian experience

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Accelerated repopulation (Acc.rep) of tumour cells and repair of sub lethal and potentially lethal damage are the major cause of treatment failure in head & neck cancers. Most successful attempt so far to overcome this problem is concomitant chemoradiation. In spite of impressive gain in local control and disease free survival (DFS), unfortunately this benefit is enjoyed at the cost of increased acute toxicity. The objective of the present model was to utilize the differential between the onset of Acc. rep of tumour clonogens and that of early reacting normal tissue (4 weeks vs. 2 weeks) and thus to minimize acute toxicity. It incorporates concom. chemotherapy only after Acc.rep of early reacting normal tissue is already set in (i.e. 3rd week of radiation) to avoid mucositis. At the same time radiotherapy schedule was so designed that Acc.rep of tumour cells is taken care of by sequencing conventional fractionation (till 3rd week) with twice daily fractionation from 4th week onwards (i.e. Late Hyper fractionation).

Material and Methods: It is a prospective randomized 2-arm study. Control arm received conven. radiotherapy (64 Gy/32 F: BED 15 = 57.7) with weekly cisplatin (30 mg/sq. M) from week 1 to week 6.

Study arm includes late hyperfractionated radiotherapy (30 Gy/15 F/3weeks followed without split by 120 cGy/F X 2 F daily, 6 hours apart, 5 days a week for another 40.8 Gy (TD=70.8 Gy: BED 15 = 63.26) combined with weekly cisplatin (30 mg/sq. M) from week 3 to week 6.

From April 2001 to Feb 2003 total 228 patients with stage III/IV oropharyngeal sq. cell cancer were enrolled (after taking informed consent) – 113 in control and 115 in study arm.

Study end points were acute effect, late effect, tumour control and DFS. Median F.U was 28 months till August, 2004.

Summary of Result: Overall response rate at 6 months and DFS at 2 year were 66% & 48% in control arm vs. 70% & 50.6% in study arm (p > 0.05). Acute toxicity of skin and mucosa are furnished in the table.

	Grade I	Grade II	Grade III	Grade IV	P value (III+IV)
Acute Mucositis					
Control arm (N = 113)	Nil	87	21	5	<0.001
Study arm (N = 115)	10	101	4	Nil	
Acute Skin Toxicity					
	Grade I	Grade II	Grade III	Grade IV	P value (III+IV)
Control arm (N = 113)	Nil	98	14	1	<0.001
Study arm (N = 115)	8	107	Nil	Nil	

Apart from significantly less mucositis and skin toxicity in study arm, onset of mucositis was also delayed: median onset of grade 2 mucositis was 22 days in control group vs. 34 days in study group.

Late toxicity (evaluated as per LENT SOMA score) of both skin and mucosa were comparable in both arms – none had Grade 3 or 4 toxicity in either arm.

Conclusion: This novel concomitant chemoradiation model, theoretically based on our present radio- and chemo-biological knowledge, was found to be able to retain the results of conventional concomitant chemoradiation so far as tumour response and DFS are concerned, with significantly less acute toxicity (both skin & mucosa), comparable late toxicity and so likely to have better patient compliance.

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POSTER

Neoadjuvant chemotherapy and concomitant chemo-radiotherapy with accelerated fractionation schedule in advanced carcinoma of the head and neck

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Background: Locoregionally advanced head and neck cancer is a challenging condition to confront with for oncologists. Treatment results with conventional approach (surgery and radiotherapy) are suboptimal. Combined chemo-radiotherapy or accelerated hyperfractionated radiotherapy have been proposed as treatment alternatives. We analyze toxicity, locoregional control rates and survival for advanced head and neck cancer, treated with neoadjuvant chemotherapy (CT) and concomitant chemo-radiotherapy with accelerated fractionation schedule.

Methods and Materials: In a prospective study, from 1999 to 2004, combined chemo-radiotherapy treatment was used in 68 pts (males 62, mean age 55.4 yrs old). Sites of origin were oropharynx 18 (26.5%), larynx 16 (23.5%), hypopharynx 15 (22.1%), oral cavity 14 (20.6%), unknown 3 (4.4%), paranasal sinus 1, and nasopharynx 1. Tumors were classified as UICC TNM stage IV 54 (79.4%), stage III 12 (17.6%), stage I-II 2 (3%). Neoadjuvant CT consisted of two cycles of cisplatin and 5-fluorouracil (CDDP 100 mg/sqm, day 1; 5-FU 1,000 mg/sqm iv, days 1–5 every 28 days). Concomitant CT consisted of weekly cisplatin (25 mg/sqm iv). 72 Gy in 42 fractions, 5 days a week, BID in the last 12 days of irradiation, were intended to be administered in 6 weeks. The mean RT treatment time was 45 days. Surgery as part of the primary treatment was attempted for biopsy-proven residual tumor at the primary site or clinical/radiological residual lymph nodes in the neck. Surgical rescue after tumor recurrence was attempted in 11 pts.

Results: Grade ≥3 mucositis was recorded in 53 pts (84.2%). Enteral nutrition through nasogastric-feeding tube or percutaneous gastrostomy tube was required in 21 pts (30.9%). Mortality rate attributable to treatment was 7.7% (3.8% acute and 3.8% chronic). The 5-year locoregional control rate was 77.1% (CI 65.0%–89.2%). The 5-year disease-free survival was 49.4% (CI 36.0%–62.8%). The 5-year overall survival was 43.5% (CI 29.3%–57.7%). In multivariate analysis, complete response after primary treatment was the only independent factor for survival.

Conclusions: In our study, the tumor response after combined treatment was the only independent factor for survival. The benefit in tumor control and survival rates has been obtained at the expense of severe acute and late toxicity. This approach could be offered under intensive supportive care to a selected population of patients.

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POSTER

A phase II dose escalation study by differential dose allocation to variable target sub-volumes of head and neck (H/N) squamous cell carcinoma (SCCa), using Intensity-Modulated Radiotherapy (IMRT)

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Purpose: We prospectively studied the potential impact of nominal and/or biological effective dose escalation to the tumor by differential dose allocation to different target subvolumes (dose painting) using IMRT. Main endpoints were local control and normal tissue toxicity.

Materials and Methods: Between Dec/2000 and Oct/2003, 33 patients with H/N SCCa (except nasopharynx) were treated by dose painting using IMRT. The GTV plus 5 mm was treated to 67.5 Gy/30 fractions. CTV was divided into CTV1 (GTV plus 1.5 cm margin and the first