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POSTER

Nasopharyngeal carcinoma: retrospective analysis of 629 patients treated with radiotherapy

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Purpose: To analyze the treatment results achieved at the Istituto del Radio di Brescia for the patients with nasopharyngeal carcinoma (NPC), to point out the prognostic factors and the different results in function of the period of recruiting, the clinical presentation, the histology and the factors related with the treatment.

Methods and Materials: The results of 629 patients (194 female, 435 males) with NPC T1-4, N0-3, M0 treated during 1977-2000 have been retrospectively analyzed. The end-points examined have been the Overall Survival (OS), the Disease Specific Survival (DSS), the Disease Free Survival (DFS) and the Local Control Free Survival (LRFS).

Results: The survival results in the whole series are as follows.

	5 yrs	10 yrs
DSS	60±2%	56±2%
OS	53±2%	41±2%
LRFS	63±2%	56±3%
DFS	46±2%	41±3%

The performance status (Karnofski index), the histology (better prognosis for undifferentiated carcinoma), the T and N classes, the fixity of the nodes, the nodal level involved (worse prognosis when the supraclavicular region is involved), were statistically significant at univariate analysis for all the end points.

The prognosis for female sex was significantly better for the DSS and the OS. An higher total dose was significantly better for the local control but had no impact on survival. The prognostic impact of the addition of chemotherapy to radiotherapy has not been analyzed owing to the small number of cases treated with chemotherapy.

On the whole, there has been a better outcome for the patients treated in the last period (DSS 48±4% before 1985, 63±5% after 1990). Even if the use of CT and MRI in T staging gave an improvement in the results, the correlation between the methodology of study of the local extent of the tumor and the prognosis seems difficult to clarify. The study with CT/MRI/US of the nodes gave a statistical significant advantage in locoregional control of disease, but non in survival (OS, DSS and DFS).

Conclusions: this analysis confirms the data of different other retrospective series of cases. The better outcome in the cohorts of patients treated more recently, pointed out by other authors, will be analyzed in detail, also with the use of multivariate analysis.

References

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POSTER

Nasopharyngeal carcinoma in adolescence and young adults: a single institute experience

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Introduction: Nasopharyngeal carcinoma (NPC) is a very distinct type of head and neck cancer, in terms of epidemiological, clinical presentation, outcome of disease, and treatment strategies. NPC represents only one third of the primary malignant tumors of the nasopharynx in patients 30 years old or younger. Recently published series on nasopharyngeal carcinoma reporting children and young adult patients in the same category. In this study, we evaluated our experience in the treatment and outcome of adolescent and young adult NPC patients.

Patients and Methods: Between January 1990 and December 2001, 294 patients diagnosed with NPC were treated at the Istanbul University

Institute of Oncology. After excluding patients presenting with distant metastases and second line therapy for recurrent disease, 279 patients were identified as having only primary locoregional disease and they serve as the study population. Fifty-nine patients were aged between 15-30 years old (21.5%) in our NPC patient group. There were 29 males (49.1%) and 30 females (50.9%). Their median age was 22 years. Histopathologically, 2 pts (3.4%) had World Health Organization (WHO) type I, five pts (8.5%) had WHO type II, and 52 pts (88.1%) had WHO type III carcinomas.

Because a variety of staging systems had been used over the years, all cases were restaged according to the American Joint Committee for Cancer Staging (AJCC) 1997 classification. There were one patient stage II, 26 pts stage III, 32 pts stage IV. Five pts (8.4%) had T1, 15 pts (25.4%) had T2, 13 pts (22%) had T3, 26 pts (44.1%) had T4 tumors. Nodal staging at presentation was as follows; No two pts (3.4%), N1 two pts (3.4%), N2 42 pts (72.3%), N3 13 pts (22%). The skull base invasion was present at 16 pts (27.1%) and cranial nervus infiltration was present at five pts (8.5%). Fifty-one patients (86.4%) received neoadjuvant cisplatin-based chemotherapy. Twenty-nine pts (49.2%) had PE (cisplatinium, etoposide), 18 pts (30.5%) had BEP (bleomycine, etoposide, cisplatinium), and 4 pts (6.8%) had PF(cisplatinium, fluorouracil) chemotherapy regimen. Median 3 cycles (2-6 cycles) chemotherapy had given. All patients treated with external beam radiotherapy by using cobalt machine and linear accelerator with customized blocking. Two lateral treatment portals covered entire nasopharynx, base of skull, posterior portion of orbit and maxillary sinus, posterior half of nasal cavity and upper neck. Lower neck and supraclavicular region were treated with a anterior field. Daily fraction size was 1.8-2 Gy, median total radiation dose for tumor and metastatic cervical lymph nodes was 70 Gy (range 44-76 Gy), and for non-metastatic and supraclavicular lymph nodes was 50 Gy (range 30-50 Gy).

Results: The median follow-up time was 69.4 months (range 8-179 months). The 5-year overall and relapse-free survival rate of whole nasopharyngeal carcinoma patients were 59.9%, 57.7% respectively. The 5 year overall and relapse-free survival rate of adolescent and young adult group were 70.41%, 65.6%, respectively. The young patients had statistically better survival rate (59.9% vs 70.41%) (p=0.03). Locoregional relapse was observed in 13 patients (22%). Systemic failure was observed in 13 patients (22%). Two patients (3.4%) had liver metastasis, and 13 patients (18.6%) had bone metastasis.

Sex, age, histopathology, T-stage, N-stage, radiation dose, and the addition of chemotherapy were evaluated as prognostic factors in univariate analysis.

Discussion: Nasopharyngeal carcinoma in young patients is distinguishable from the older patient form by its higher rate of undifferentiated histology, and a greater incidence of advanced locoregional disease. At diagnosis, the impact of age on prognosis remains controversial, but in this series young patients have better prognosis than elders.

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POSTER

Monte Carlo evaluation of air cavity effects in IMRT dose distributions for recurrent nasopharyngeal cancer

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Background: Significant discrepancies have been reported between commercial and Monte Carlo (MC) planning systems in targets adjacent to air cavities. These differences have been attributed to the inability of conventional inhomogeneity algorithms to model electronic disequilibrium. In this study we use MC to verify IMRT dose distributions calculated by CadPlan® (CP) for locally recurrent nasopharynx.

Materials & Methods: A submucosal PTV at the air-tissue interface was contoured with a target dose of 60Gy. Three beam arrangements, each consisting of 7 sliding window portals, were designed. The first was predominantly anterior, the second was unilateral, while the third one was posterior, thereby varying the amount of air traversed by the incident beams. To emphasize the inadequacy of the CP inhomogeneity algorithm, we developed a tool that allows flooding of the air cavities with water. We were able to quantitatively evaluate the effect of the presence or absence of air cavities in the beam path. All IMRT plans were optimized with Helios, and dose distributions calculated in CP using Batho inhomogeneity correction. The plans were recalculated using the BEAMnrc Monte Carlo algorithm and evaluated by dose-volume histograms (DVH) as well as slice by slice isodose comparisons.

Results: As expected, the MC calculations revealed lower mean doses in the PTV in the anterior and lateral beam arrangements, of 57.13Gy compared to 60.58Gy, and 59.84Gy compared to 63.05, respectively. The minimum/maximum doses exhibited a similar reduction resulting in the DVH shifts shown in Figure 1a/b. In contrast, the mean, minimum and maximum doses were much closer for the third beam arrangement but the PTV coverage was not as homogeneous (Figure 1c). Remarkably, the DVH's

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.

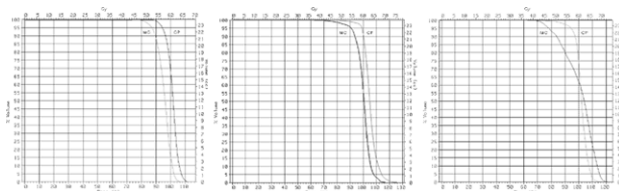


Fig. 1: MC vs. CP calculations for the effect of presence or absence of air cavities in the beam path for (a) anterior, (b) lateral and (c) posterior beam arrangements.

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.

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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.

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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