

salivary tissue. Radiation doses accumulated in submandibular glands much exceeded threshold doses of salivary tissue. This prospective study has been continued.

## 1043

## POSTER

**Role of Candida spp. in oral mucositis. Methods of correction**

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More aggressive treatment regimes improve local control and survival of patients with locally-advanced head and neck cancer, but are usually associated with higher acute mucosal toxicity. Pathogenesis of mucositis is complex and involves the interaction of cellular, tissue, and oral environmental factors. The purpose of the work was to study the influence of Candida species on severity and frequency of mucositis in patients with head and neck cancer and to propose methods of prophylaxis.

Since October 2002 to November 2004, 64 patients with stage III-IV head and neck cancer were randomized for standard correction of mucositis (arm A), standard correction + klotrimazol (Kandid-solution for oral cavity<sup>®</sup>) (arm B), standard correction + Immunal<sup>®</sup> (arm C), standard correction + klotrimazol + Immunal (arm D). Immunal is an immuno preparation made from Echinacea purple. All of them were performed concurrent chemoradiation therapy. Quantity of colony-forming unit (CFU) of Candida species in oral cavity was estimated before treatment and after total dose 40 Gy. Mucosal toxicity was scored according to RTOG/EORTC criteria. Standard correction consisted from antibacterials, fungicides, processing of oral cavity by broth of chamomile.

In arm A (18 patients), Candida was isolated in 17.7% of patients before treatment and in 88.2% after the dose of 40 Gy. Average quantity of CFU was 281 and 5721, respectively ( $p=0.004$ ). In arm B (17 patients), Candida species were isolated in 18% and 23.5% cases, respectively. CFU was 194 vs 4275 ( $p=0.08$ ). In arm C (14 patients), Candida species were observed in 21.4% and 78.6% of patients. Average CFU quantity was 228 vs 4681 ( $p=0.07$ ). In arm D (15 patients), C.albicans was detected in 26.7% patients before treatment. After the dose of 40 Gy, all the patients were free from Candida in oral cavity.

Changes of microflora in oral cavity correlated with severity and frequency of acute mucosal reactions. Arm A developed 75.3% grade 3+4 mucositis, arm B – 68.8%, arm C – 63.6%, arm D – 18.2%. Arm A and D demonstrated significant difference ( $p=0.004$ ), differences between A and B ( $p=0.09$ ) A and C ( $p=0.07$ ) were non-significant.

**Conclusion:** Candida spp. of oral cavity play a great role in acute mucosal toxicity. Local correction of oral micro flora combined with immunomodulation significantly decreases severity and frequency of mucositis.

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## POSTER

**Impact on radiation oncology department workload of daily IMRT treatments in patients with head and neck cancer: results from a comparative study**

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**Background:** Notwithstanding a possible improvement in dose distribution, the general impression of intensity modulated radiotherapy (IMRT) is that it is labor intensive, requiring long treatment and planning times. This study evaluates the impact of this technology on the workload of a radiation oncology department through the following end points: daily and overall treatment time and total treatment preparation time (contouring, treatment planning, quality assurance (QA), mould room).

**Materials & methods:** Ten patients undergoing treatment with IMRT for head and neck tumors were compared to ten similar patients treated with a conventional technique. IMRT treatment was delivered with five to seven gantry angles (five to fourteen fields) dynamic delivery with a single plan. Doses ranged from 50–70 Gy in 25–33 fractions. Conventional patients were treated with a standard multi-phase plan including lateral opposed fields for upper neck, off-cord block, posterior neck node electrons, and a half blocked (single isocenter) lower anterior neck field. Dose consisted of 70 Gy in 35 fractions. Treatment time per patient was recorded daily for 5 days. Treatment planning data was obtained from two radiation oncologists, two physicists, four dosimetrists and the mould room technologist.

**Results:** Average daily treatment time for IMRT was 18min±2min and 9min±1min for conventional technique. Average overall treatment time for IMRT was 7.5hrs and 11hrs for 25 and 33 fractions respectively. The conventional technique averaged 6.5hrs for 35 fractions. Physicists required 4hrs for planning IMRT (inverse planning system) and 2hrs for QA

leading to a total preparation time of 7.5hrs±1hr dependent on physician contouring time. Conventional technique required 10.2hrs to plan a typical 3-phase plan (2.75hrs±1.25hrs per plan depending on complexity of plan) (3D planning system) including 1hr mould room time needed to construct shielding for electron posterior neck fields. Weekly orthogonal check films were taken for all patients. All patients required aquaplast-orfit mask for immobilization.

**Conclusion:** The results of this study show that the overall treatment time is slightly to moderately longer (1.0–4.5hours) with IMRT but with a significant decrease in treatment preparation time (30%) versus the conventional technique. Therefore, the impact of IMRT on the overall workload of the department is modest making it a reasonable option for treating head and neck cancer.

	IMRT (70Gy/33)	IMRT (60Gy/25)	Conventional (70Gy/35)
Total Plans	1	1	3
Contouring time* (average)	0.5–2.5 hrs (1.5 hrs)	0.5–2.5 hrs (1.5 hrs)	0.05–0.5 hrs (.275 hrs)
Planning Time* (average)	4 hrs	4 hrs	1.5–4 hrs/plan (2.75 hrs)
QA*	2 hr	2 hr	0
Mould Room Time*	0	0	1 hr
Average treatment preparation time	7.5 hrs	7.5 hrs	10.2 hrs
Average Daily treatment time	18 min	18 min	9 min
Average overall treatment time	11 hrs	7.5 hrs	6.5 hrs (including 10 posterior neck electron treatments)
Average overall workload time	18.5hrs	15 hrs	16.7hrs

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## POSTER

**Outcome and prognostic factors in olfactory neuroblastoma: a multicenter rare cancer network study**

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**Background:** To define prognostic factors and patterns of failure in olfactory neuroblastoma.

**Materials/Methods:** Fifty-six patients treated for non-metastatic olfactory neuroblastoma in 13 European and American centers between 1971 and 2004 were included in this study. Median age was 50 years (range: 15–79), and male-to-female ratio was 29/27. Diagnostic work-up included CT-scan in 51 (91%), and MRI in 28 (50%) patients. According to Kadish classification, there were 7 (12%) stage A, 24 (43%) stage B, and 25 (45%) stage C patients. Forty-eight patients presented with N0 (86%) disease. Most (n=46) benefited from surgery (S). Treatment consisted of a combination of S, radiation therapy (RT), and chemotherapy (CT) in 12 patients (21%), S+RT in 29 (52%), S alone in 5 (9%), RT+CT in 6 (11%), and RT alone in 4 (7%). Total excision was possible in 40/46 operated patients (28 R0, 12 R1, and 6 R2). All but 5 patients benefited from RT with a median dose of 60 Gy in median 2 Gy/fr (range: 1.6–2.5). RT was delivered using 2D-RT in 27 patients (48%), 3D-RT in 22 (39%), and intensity modulated RT (IMRT) in 2 (3%). PTV included the tumor bed in 44 (86%), and tumor bed and involved lymph nodes in 7 (14%) patients. Chemotherapy was given in 18 patients (32%). Median follow-up was 74 months (range: 7–314).

**Results:** Median time to locoregional progression was 27 months. Local progression was observed in 23 patients (41%), regional in 16 (29%), and distant metastases in 10 (18%). Causes of death included progression in 25, postoperative complications in 3, and intercurrent disease in 2 patients. The 5-year overall survival, disease-free survival (DFS), and locoregional control was 60%, 43%, and 53%, respectively. In univariate analyses, factors favorably influencing the DFS were T1-T3 disease vs.

T4 ( $p=0.06$ ), N0 ( $p=0.0007$ ), RT dose 54 Gy or more ( $p=0.006$ ), surgery ( $p=0.01$ ), and total resection ( $p=0.009$ ) or R0/R1 resection ( $p=0.01$ ) in operated patients. In multivariate analysis, best independent factors were T1-T3 ( $RR=0.69$ ;  $p=0.05$ ), N0 ( $RR=0.60$ ;  $p=0.05$ ), R0 or R1 resection ( $RR=0.33$ ;  $p=0.008$ ), and RT dose 54 Gy or more ( $RR=0.30$ ;  $p=0.007$ ). **Conclusions:** Olfactory neuroblastoma had the best outcome especially treated with R0/R1 surgical resection followed by at least 54-Gy postoperative RT. Novel therapies including concomitant chemotherapy and/or higher dose IMRT should be prospectively investigated in this rare disease.

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POSTER

#### Dose escalation of daily carboplatin concurrent with accelerated radiation by delayed concomitant boost for locally advanced head and neck cancer

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**Background:** Accelerated radiation by delayed concomitant boost (AFX-CB) and concurrent chemoradiation represent two major advances in head and neck cancer treatment; however, the optimal regimen integrating these advances has yet to be defined.

**Methods:** We investigated escalating small daily doses of carboplatin prior to each fraction of AFX-CB to maximize radiosensitization and avoid severe hematologic toxicity. Thirty five patients (27M;8F) with 2002 AJCC Stage II-IVB [12 resectable cancers requiring total laryngectomy and 23 unresectable cases (T4b: 20 or N3: 3)] were treated with AFX-CB to 70 Gy/6weeks (BID RT last 2 weeks) with daily doses of carboplatin escalating from 10 to 17.5 mg/m<sup>2</sup>/d and given within 1 hour prior to radiation. Treatment sites were primarily oropharynx  $n=16$  or larynx  $n=12$ . Dose limiting toxicity (DLT) was defined as NCI common toxicity grade 2 hematologic toxicity or grade Gr 4 mucositis. Erythropoietin (EPO) was initiated if hemoglobin (Hgb) fell below 12 g/dl.

**Results:** 94% (33/35) completed a full course of chemoradiation. Median radiation dose: 70 Gy (53–71.6 Gy). Ten patients were treated at 10 mg/day; 12 at 12.5 mg, 9 at 15 mg and 4 at 17.5 mg. The maximum tolerated dose was 15 mg/m<sup>2</sup>. 9 patients required a treatment break with a median duration of 3 days (1–5d). Grade 2 or 3 hematologic toxicities were as follows: anemia 0%/3%, leukopenia 15%/3% and thrombocytopenia 0%/0%. One patient had a Gr 4 mucositis. Acute Gr 3 toxicities were as follow: 1) mucositis:58%, 2) pharyngitis 58% and 3) dermatitis:12%. Median weight loss was 4.6% (0–14.4%). EPO raised Hgb levels by a median increment of 1.5 g/dl (0.2–3.0 g/dl) and above 12 g/dl in 13 of 15 pts. 3 patients are PEG dependent.

At a median followup of 15 mos, actuarial estimates of 1-year locoregional control are 72% among unresectable cancers and 89% for organ preservation patients. One year overall survival are 77% and 89%, respectively. Distant metastases at 1 year are 24% and 11%, respectively.

**Conclusion:** The addition of carboplatin to AFX-CB is well tolerated and the MTD is 15 mg/m<sup>2</sup>. Organ preservation rates with daily carboplatin are comparable to high-dose cisplatin but without associated severe hematologic toxicity. Daily carboplatin with AFX-CB for unresectable patients yields excellent locoregional control and allows for further intensification of therapy due to its relatively low toxicity profile. EPO can effectively correct mild anemia during chemoradiation.

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POSTER

#### Factors affecting immediate postoperative outcome in surgically treated patients of oral cancers

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**Introduction:** Due to the tobacco chewing habit, oral cancer is the most common cancer in our country. Most of the patients with these cancers are treated with major ablative surgery with or without flap reconstruction. The goal of this study is to determine the risk factors for post-operative complications and overall morbidity for patients of oral cancers who underwent surgical excision with or without flap reconstruction.

**Material and Methods:** A prospective study of 185 surgically treated patients of oral cancers was conducted in a tertiary cancer hospital over a period of eight months. These patients were evaluated after various surgical and reconstructive procedures during perioperative and postoperative period. The outcomes were classified into major and minor complications and morbidity was calculated in terms of prolonged hospital stay. Multiple

variables were recorded and cross tabulated against major and minor complications. The statistical analysis was done with SPSS 11.5 software using Chi square test and Fisher's exact test.

**Results:** The major complication rate was 8.1% (15 out of 185 cases) and the minor complication rate was 43.2% (80 out of 185 cases). The total morbidity was 37.5% (69 patients). The univariate analysis showed that requirement of flap reconstruction was the most important prognostic factor for major complications ( $p<0.001$ ). The factors responsible for minor complications were advanced disease ( $P<0.001$ ), Blood loss  $>500$  cc ( $P<0.001$ ), Intra-operative tracheostomy ( $P<0.001$ ).

**Conclusions:** The incidence of complications in postoperative setting of advanced oral cancer (T3, T4) is high so also is the morbidity. Various factors which influence the outcome are highlighted and taking adequate precaution would help in progressing towards decreasing the morbidity, complications and hospital burden thus decreasing the hospital stay and improving quality of life.

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POSTER

#### Adjuvant IMRT for esthesioneuroblastoma – the early MD Anderson experience

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**Background:** Esthesioneuroblastoma is a rare cancer of the sinonasal tract that presents in an anatomically challenging region. Intensity-modulated radiation therapy (IMRT) promises to improve local control without increasing the risk for radiation morbidity. We examined our initial results with the use of IMRT for adjuvant treatment of this disease.

**Material and methods:** Eight patients presenting with esthesioneuroblastoma were treated from 2001 through 2004 with resection and adjuvant IMRT for local management. Stage was Kadish B in 4 patients, and Kadish C in 4. All patients had clear surgical margins, except for one Kadish C patient with microscopically positive margins. Treatment planning goals included delivery of 60 Gy in 30 fractions to a clinical tumor volume (CTV1) encompassing the surgical resection bed, and 54 Gy in 30 fractions to a CTV2 encompassing adjacent at-risk tissues and nodal levels. Average follow-up duration was 25 months (range: 12–42).

**Results:** Mean IMRT doses delivered to CTV1 and CTV2 were  $62.2\pm0.8$  Gy and  $58.6\pm1.1$  Gy, respectively. Mean total CTV coverage with target doses was  $96.3\pm1.7$ . Mean optic chiasm, optic nerve, eye, lens, and temporal lobe doses were  $38.6\pm6.1$  Gy,  $48\pm5.5$  Gy,  $23\pm4.4$  Gy,  $10.5\pm3.6$  Gy, and  $21.1\pm6.6$  Gy, respectively. Mean number of beams used was  $9.1\pm1.2$ . All patients remain free of disease progression and have no severe late radiation morbidity.

**Conclusion:** Our early results suggest that adjuvant IMRT for esthesioneuroblastoma permits conformal delivery of high dose radiation with excellent tumor control and tolerance

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POSTER

#### Photodynamic therapy and fluorescent diagnostics with different second-generation photosensitizers in head and neck cancer patients

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**Aim:** Photodynamic Therapy (PDT) and fluorescent diagnostics (FD) using Photosense 've been provided in 50 patients with head and neck cancer (HNC) T1–3 stage and in 89 patients with skin cancer, using Radaclorin (RC) – in 42 patients with T1–4 stage basal cell carcinoma (BCC), in 6 patients with oral cancer, FD with Alasense (5-aminolevulinic acid, ALA) in 127 patients with T1–3 BCC, squamous cell carcinoma (SCC).

**Materials:** FD with detecting the borders of tumor growth, accumulation in tumor, normal tissues 've been done by Spectral-fluorescent Complex (He-Ne-laser). Using light sources (380–440 nm) we've got 2-dimensional pictures of fluorescence. We used semiconductive lasers for PDT: Milon –  $660\pm2$  nm, light dose was  $200\text{--}300$  J/cm<sup>2</sup> and Biospec ( $672\pm2$  nm), multiple laser surface and interstitial irradiation was performed 24 hours after PS injection with total light dose till  $400\text{--}600$  J/cm<sup>2</sup> and single light irradiation with light dose  $200\text{--}300$  J/cm<sup>2</sup> using RC.

**Results:** We've got fluorescence of all tumors using AS: in 52% of patients it exceeded the borders of clinically detected sites. The intensity of fluorescence in SCC was positively higher than in BCC. In 35.7% patients with BCC additional fluorescence zones were found, cytological verification in 93.3%. We've got fluorescence of all tumors using PS and RC, additional fluorescence zones were found, cytological verification was got in most of cases. 2 months after PDT with PS in 50 patients with HNC we've had