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Hypoxic tumour characteristics evaluated by fluorine-18-labeled fluoromisonidazole positron emission tomography in head and neck cancer

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Background: Tumor hypoxia is an important determinant of locoregional control from radiation therapy. In this study, we demonstrate a way of defining hypoxic tumor volume (HTV) by using fluorine-18-labeled fluoromisonidazole positron emission tomography/computed tomography (^{18}F-FMISO PET/CT) in head and neck cancer patients and evaluate hypoxic tumor characteristics by comparing with other tumor characteristics and clinical outcome after treatment.
Materials and Methods: Twenty-six newly diagnosed head and neck cancer patients were enrolled prospectively. All patients had undergone CT or MRI of head and neck, fluorodeoxyglucose (FDG) PET/CT and ^{18}F-FMISO PET/CT before any treatment. From these imaging studies, sizes of primary tumors and metastatic lymph nodes, gross tumor volumes (GTV) and metabolic tumor volumes (MTV) were measured and obtained. The HTV was defined by using the tumor-to-cerebellum ratio (T/C) of 1.3 as a threshold from ^{18}F-FMISO PET/CT. Hypoxic tumor fraction (H/G) was calculated by defining as hypoxic-to-gross tumor volume fraction. These tumor volume characteristics were analyzed to find out whether they had correlations with each other and were evaluated with the clinical outcomes in patients who had received definitive radiation therapy.
Results: The mean hypoxic tumor fraction (H/G) was 18.3±23.4%. It was significantly correlated with the size of metastatic lymph nodes ($p = 0.020$), but not with the size of primary tumor or GTV. Patients with higher maximal standard uptake value (mSUV) in ^{18}F-FMISO PET or FDG PET, had significantly larger hypoxic tumor fraction. Although the number of patients was small, patients with pharynx origin cancer had significantly ($p = 0.003$) lower hypoxic tumor fraction than with paranasal sinus or larynx origin. Also, the hypoxic tumor fractions were significantly lower in patients who had gained complete response than had shown partial response after definitive radiation therapy ($p = 0.001$). However, no significance was found between the hypoxic tumor fraction and local failure.
Conclusions: We described a way of defining hypoxic tumor volume with ^{18}F-FMISO PET/CT. Although there may be limitation due to small number of patients, our result provides the understanding of hypoxic tumor characteristics in head and neck cancer patients and could be useful when concerning hypoxia-guided intensity modulated radiation therapy.

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Microinvasive access to the visceral autoflaps for microsurgical reconstruction in head and neck cancer patients

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Background: Microinvasive diagnostic and surgery is one of the most promising lines of up-to-date oncology. In the P.A. Hertzen Moscow Cancer Research Institute was developed a method of microinvasive abdominal access to form the visceral autoflaps in cancer patients.
Methods: We have an experience of treatment 44 patients aged from 16 to 55 years (male 17, female 26) with malignant local spreaded craniofacial (24) and oropharyngeal tumors (20).
In 14 cases it was the tumor of the scalp, 5 – maxilla, 5 – cellulae ethmoidales, 4 – oral cavity, 5 – tongue, 3 – oropharyngeal, 2 – laryngopharyngeal, 1 – face soft tissues sarcoma, 1 – mandible, 4 – parotid gland. For plastic closing the large postoperative defect were used the abdominal organs. We chose Para umbilical incision as the appropriate access to the abdominal cavity with minimal external trauma of the anterior abdominal wall. Using video assisted technique (video endoscopy system) aponevrosis was dissected along median centerline. Donor's organs (omentum, greater curve of the stomach, transverse colon) were delivered through the minilaparotomy wound on the anterior abdominal wall, then vessel's peduncle of free flap was exposed (right gastroomental vessels, vessels colicae media) and visceral autoflap was formed. Dissection away the transplant followed by the extracorporeal forming of the organs' anastomozis. In 3 cases was made an attempt to form the 1 gastroomental and 1 colon-omental autoflaps and in 1 case at adiposity during formation omental flap. After inspection the abdominal cavity usual upper median laparotomy was performed. The massive commissural process in the abdominal cavity caused the widening of the access. The plan of the operation among these 3 patients was fulfilled; the flaps were formed and transported on recipient's wound.
Results: In 41 cases the operation was completely made through the minimal access (4 patients had abdominal operative intervention before). It was formed and prepared for autotransplantation 23 omental free flaps, 4 gastroomental and 14 colon-omental flaps. There were no intra- and postoperative abdominal complications. Based on the results of clinical and morphological data comparison there were no reliable feature of any structural and functional changes of gastric and omental flap mucous. The follow up period was up to 1 year.
Conclusion: Microinvasive technology to form visceral autoflaps for head and neck reconstruction allows to minimize operative trauma and to shorten the period of post-surgical treatment. We recommend using this access when operating the weak cancer patients and young women to avoid additional undesirable scar on donor's site.

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Treatment of T2N0−1 laryngeal cancer (LC) with hyperfractionated radiotherapy (HRT) and cetuximab

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Background: Local control rates for T2 LC with HRT alone at the Instituto Angel H. Roffo are about 61%, increasing to 75−80% with salvage surgery. The addition of cetuximab to HRT significantly enhanced the local control and survival rates compared with HRT alone, with similar reported toxicities to locally advanced head and neck cancer. Cetuximab was added to HRT for the treatment of T2N0−1 LC with the primary objective of enhancing local control rates and the secondary objective of extending the time free of laryngectomy (TFL) for T2 LC.
Materials and Methods: Twenty patients (pts) (19 male;1 female; median age 64 years) with T2 LC were enrolled. Two pts (10%) had N1 tumors that were 65% glottic and 35% supraglottic. Pts received HRT to a total dose of 76.8 Gy over 6.5 weeks. Cetuximab was administered at 400 mg/m^2 one week before HRT followed by 7 weekly doses of 250 mg/m^2. Pretreatment evaluation consisted of a CT scan and fibrolaryngoscopy (FLC) and toxicity assessments were performed weekly. After treatment, pts were evaluated monthly during the first year and then every three months with FLC. All pts signed an informed consent and the trial was approved by the institutional review board and submitted to the country's medical authorities.
Results: Eighteen pts (90%) completed HRT, receiving a median HRT dose of 76.7 Gy over a median 7-week duration, and 17 pts (85%) received 8 doses of cetuximab. The median duration of treatment was 8 weeks. At end of treatment, a complete response (CR) was reported in 16 pts (80%), 3 pts (15%) had persistent disease and all 3 had surgery. Four pts with CR relapsed at a median time of 9 months and received surgery. To date, after a median follow-up of 15 (range 6.7−⩾29) months, 18 pts (90%) are disease-free; 12 (66%) of whom did not require a laryngectomy. Median TFL for all the pts was 17 (range 6.7−⩾29) months. Grade 3/4 toxicities were reported for stomatitis (6 pts), acne-like rash (4 pts), radiation dermatitis (5 pts) and dysphagia, diarrhea, vomiting, fatigue, skin infection and pneumonia (1 pt each). Six pts (30%) were admitted to hospital due to toxicity and 2 pts (10%) died; 1 with a sudden death not related to cetuximab and 1 due to progressive disease at 15 months.
Conclusions: Treatment according to protocol was administered to 85% of pts. CR, disease-free survival and TFL rates were higher than historical rates at the Instituto Ángel H. Roffo when pts with T2N0−1 LC received cetuximab in addition to HRT.

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Dosimetric changes of intensity modulated radiotherapy (IMRT) plan on the follow-up CT acquired during treatment in the patients with nasopharynx cancer

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Background: To evaluate the dosimetric changes of intensity modulated radiotherapy (IMRT) plan on the follow-up CT scan acquired during treatment in the patients with nasopharynx cancer.
Methods and Materials: Sixteen patients with nasopharyngeal cancer underwent follow-up CT scan during the treatment according to their treatment response after they received 30−50 Gy of RT. Seven port IMRT

plan using simultaneous integrated boost (SIB) technique was generated on the basis of initial CT scan. The prescribed doses were 70 Gy to the planning target volume (Gross tumor volume(GTV) with a 5 mm margin), 59.4 Gy to the high-risk subclinical volume (CTV59.4), and 50.4 Gy to the low-risk subclinical volume (CTV50.4). The initial IMRT plan was projected onto the follow-up CT scan. Target volumes and organs at risk (OAR) were delineated on the follow-up CT scan and dosimetric changes of target volumes and OAR were analyzed.
Results: The average reductions of GTV and CTV59.4 were 37% (SD = 22%) and 9% (SD = 7%). The parotid volume was also reduced. The average volume reduction of thirty two parotids was 34% (SD = 19%). The initial average mean dose irradiated to parotid glands was 2613 cGy (SD = 242 cGy) but the average mean dose irradiated to parotid glands on the follow-up CT scan was 3162 cGy (SD = 683 cGy). The average maximal spinal cord dose and maximal brain stem dose were changed from 4279 cGy (SD = 95 cGy) to 4496 cGy (SD = 268 cGy) and from 2199 cGy (SD = 211 cGy) to 5339 cGy (SD = 520 cGy), respectively. However dose coverage of GTV and CTV59.4 was not change significantly.
Conclusions: IMRT may give rise to he significant overdose to OAR, especially parotid gland if adaptation to the volume changes of OAR is not performed. To prevent this problem, adaptive RT or modification of IMRT plan during treatment are needed.

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Sentinel node mapping in patients with differentiated thyroid carcinoma: our institution's experience

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Background: The aim of this study was to evaluate sentinel lymph node mapping in patients with differentiated thyroid carcinoma (DTC).
Methods: From the year 2001 to 2008. we have performed SLNb in 40 with DTC. Before mobilization of the thyroid gland, approximately 0.2 ml of 1% solution of methylen blue dye was injected peritumorally. After approximately 10 minutes the dissection was continued above and beyond the omohyoid muscle, towards the internal jugular vein and common carotid artery until the blue stained lymph nodes were found and recognized and sent for frozen section examination. If any of the nodes was positive on frozen section, Modified radical neck dissection was performed after total thyroidectomy and routine dissection of central neck compartment.
Results: Twenty three patients had papillary thyroid carcinoma, eleven follicular carcinoma and six benign tumors. Identification of blue stained SLN was successful in 93.5% of case. Negative and positive predictive values were 94.7% and 100%, while overall accuracy of the methods was 95.6%. In the one patient with follicular carcinoma, SLN detection failed. Four patients had one radioactive node, one had three and one had four.
Conclusion: Our results imply that SLN biopsy in the jugulo-carotid chain using methylen blue dye mapping, is a feasible and accurate method for estimating lymph node status in the lateral neck compartment. The method could be helpful in detection of true positive but non-palpable lymph nodes and may support in patients with DTC.

8562 POSTER

Phase II study of docetaxel and carboplatin with concurrent radiation therapy for locally advanced head and neck cancer

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Background: Concurrent chemoradiotherapy with cisplatin has been a standard treatment of locally advanced head and neck cancer. The present study used docetaxel plus carboplatin concurrent with radiotherapy in stead of cisplatin. We sought to evaluate the clinical response rate at the tumor and safety profile of this treatment.
Materials and Methods: Thirty-eight patients were enrolled; 14 had oral cavity cancer (oral tongue 10, buccal mucosa 2, alveolar ridge 1, floor of mouth1), 10 had oropharyngeal cancer (base of tongue 5, tonsil 5), 13 had laryngeal cancer, and 1 had maxillary sinus cancer. Twenty- nine patients had stage IVA disease, and 9 patients had stage III disease. All patients received concurrent docetaxel 15 mg/m^2 one -hour infusion plus carboplatin AUC 2 30 minutes infusion on day 1, 8, 15, 22, 29, and 36. Radiotherapy began on day 1 of concurrent chemotherapy with 2 Gy per fraction, 5 fractions per week to total dose of 66−70 Gy. Tumor assessment was performed by CT scan after 3 months completion of concurrent chemoradiotherapy.
Results: Thirty-five patients were evaluated for response, two patients refused to receive all treatments, another one patient had serious adverse event from the first dose of docetaxel (rash, wheezing both lungs). Of 35 evaluable patients, 26 patients (74.3%) achieved a clinical response rate. Six patients (17.1%) had stable disease, and 3 patients (8.6%) had progression of disease. The 2 year disease free survival was 62.9%, The 2 year overall was 64.1%. The most common toxicity is radiation induced toxicity in every aspect with grade 2−3 mucositis in 85.7%, grade 2−3 skin dermatitis 51.4%, and grade 2−3 dysphagia 51.4%.
Conclusion: Administration of docetaxel plus carboplatin concurrent with radiotherapy results in high response activity and well tolerated in locally advanced head and neck cancer. The most common toxicity is radiation induced toxicity in every aspect.

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Treatment outcomes for squamous cell carcinoma of the external auditory canal and middle ear

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Background: Squamous cell carcinoma (SCC) of the external auditory canal (EAC) and middle ear is extremely rare, with a yearly incidence of around one per one million people. The purpose of this study is to evaluate treatment outcomes for SCC of the EAC and middle ear.
Materials and Methods: Between 1990 and 2008, 38 patients treated at our institute for SCC of the EAC and middle ear were retrospectively investigated. Twenty-nine (76%) patients had primary EAC cancer and 9 (24%) had primary middle-ear cancer. There were 15 (39%) males and 23 (61%) females. Fourteen (37%) patients had T1−2 disease and 24 (63%) had T3−4 disease according to the Pittsburgh classification. Lymph node involvement was found in 7 (18%) patients. Thirteen (34%) patients received surgery (S), 12 (32%) received radiotherapy (RT), and 13 (34%) received surgery combined with radiotherapy (S + RT). All 14 patients with T1−2 disease received S, with or without RT. All 12 patients in the RT group had T3−4 disease, and 9 of them received concurrent chemoradiotherapy. The median total radiation dose of the 25 patients treated by RT was 60 Gy (range: 24−70 Gy). The median overall treatment time for RT was 41 days (range: 15−54 days).
Results: The median follow-up period was 32 months (range: 1−122 months). Ten patients experienced recurrence: six locally, three locally and in regional lymph nodes, and one only in regional lymph nodes. Twelve patients died during the period of this study. Ten died of primary disease (including postoperative epidural hematoma). The five-year overall survival (OS), disease-specific survival (DSS), and locoregional control (LRC) rates for all patients by the Kaplan-Meier method were 66%, 72%, and 69%, respectively. The five-year OS, DSS, and LRC rates according to treatment modality (S/RT/S+RT) were 77%/53%/63% ($p = 0.49$ by log rank test), 84%/53%/63% ($p = 0.51$), and 83% /53%/66% ($p = 0.56$), respectively. The five-year OS, DSS, and LRC rates according to T stage (T1−2/T3−4) were 92%/50% ($p = 0.03$), 92% /52% ($p = 0.02$), and 85%/57% ($p = 0.11$), respectively. One patient in the S+RT group experienced late radiation toxicity in the form of Grade 4 osteonecrosis.
Conclusions: Our treatment outcomes for T1−2 disease were excellent, and our outcomes for T3−4 disease were comparable with those of several previous reports. Although the standard treatment modalities for SCC of the EAC and middle ear are still unclear, our results indicate that S with or without RT is an appropriate therapy for T1−2 disease and that concurrent chemoradiotherapy may be a useful modality for T3−4 disease.

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A Phase II study of docetaxel, cisplatin, and 5 FU induction chemotherapy followed by chemoradiotherapy in advanced nasopharyngeal cancer

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Background: The current standard treatment for locoregionally advanced nasopharyngeal cancer (NPC) is concurrent chemoradiotherapy (CCRT) with or without adjuvant chemotherapy. Several randomized trials of CCRT have demonstrated a progression-free survival (PFS) or overall survival (OS) benefit over radiation therapy (RT) alone. However, the