Results. Median follow-up was 17.3 (0.5–65) months. The 1 and 2-year survival rates for all patients were 75 and 68%, with 45% loco-regional control. Median survival was 16.8 months (4.5 for palliative and 19 for curative). Eight patients died, all of them with locally progressive disease. Grade 3–4 radiation-related toxicities occurred in 55% of all cases, with 1 fatal carotid rupture. Nasopharynx localization, non surgical cases, systemic treatment and lower total RT doses were associated with worse survival. Recurrent tumors, surgical cases and higher total RT doses were associated with worse toxicity.
Conclusions. Re-RT results in encouraging rates of local control and survival, although severe toxicities are substantial. Investigations to identify patients who could benefit most from re-RT and the development of techniques to lower side-effects are warranted.

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Incidence and prognosis of human papilloma virus induced oropharyngeal cancer

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Introduction. Tobacco and alcohol consumption are the primary risks factors for development of head and neck squamous cell carcinoma. However, it has recently been recognized that the human papilloma virus (HPV) can play a role in the pathogenesis of a subset of these cancers, especially in those arising in the oropharynx.
Objectives. To analyze the incidence of oropharyngeal squamous-cell carcinomas induced by HPV in Spain, and to determine the prognostic significance of HPV status on overall survival, disease-free survival and loco-regional control among patients treated with conservative treatment.
Methods. A retrospective analysis was performed on 102 patients with oropharyngeal squamous-cell carcinoma, treated with curative radiation or concurrent chemoradiation therapy in four university hospitals from Madrid (Spain) between 2000 and 2010. Immunohistochemical expression of p16 was analyzed in matched pretreatment paraffin-embedded tumour blocks from these patients. The influence of p16 status on loco-regional control, disease-free survival and overall survival was analyzed using the Kaplan-Meier method (univariant analysis) and COX's regression analysis (multivariant analysis).
Results. p16 positivity by IHC was found in 27 tumours (26.7%). No statistical significant differences were observed between the HPV+ and HPV− groups regarding tumour stage, gender, age or smoking. The median follow-up period was 28 months. Overall survival was improved for HPV+ compared to HPV− patients: with an estimated 3-year overall survival of 67.4% vs 49.7% ($p = 0.095$). Three-year disease-free survival was also improved for HPV+ patients, although the difference was not statistically significant: 63.6% vs 54.6% ($p = 0.336$). Three-year loco-regional control was 52.7% vs 51.1% ($p = 0.47$).
Conclusions. The incidence of HPV-related oropharyngeal carcinomas in our group of patients, 26.7%, is similar to that reported in other European countries. HPV positivity, measured by p16 IHC expression, was associated with improved overall survival in oropharyngeal cancer patients treated with conservative treatment.

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Institutional experience in head and neck cancer treated with IMRT

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Purpose. Was evaluated IMRT (integrated boost) treatment in locally advanced head and neck tumors, 4 years follow up.
Material and methods. 179 patients treated from May 2007 to December 2011. Mean of age 59 years (25–88) – Stage ≥ T3: 56%, ≥N1: 72%. Primary tumor location: Oropharynx 21%, Hypopharynx 14%, Larynx 30%, Nasopharynx 16%, Oral cavity 17%, Multifocal 2%. 62% received radical treatment, 38% of them treated with neoadjuvant chemotherapy schema based platinum. 38% of all patients were treated with adjuvant protocol. Used planning CT scan with 5-mm slice thickness. A customized thermoplastic mask covering the head to shoulder region is made to in movilize the patient. A total dose of 69.96 Gy at 2.12 Gy/fraction was given to the PTV1 (gross volumen). While the CTV that included potential microscopic infiltration received 59.40 Gy (PTV2) at 1.80 Gy/fraction. And the neck with clinically negative findings received 54.12 Gy (PTV3) at 1.64 Gy/fraction. The postoperative dose in surgical bed was 66 Gy at 2 Gy/fraction.
Results. Acute toxicity: more than 80% of patients presented less or equal GII Mucositis and Dermatitis. 14% of patients suffered treatment interruption (4% secondary of acute toxicity). Evaluated Chronic Xerostomia: more or equal than GII 15%. The overall

survival of all cases of head and neck cancer at 3 years is above 60%. The complete response was 53%, persistence disease 3%, local progression 4.5%. Distance metastasis: 7%.
Conclusions. IMRT treatment is the technique of choice to provide a high level of coverage with a low threshold dose distribution in critical organs, allowing Radiotherapy with moderate toxicity and local control. Overall survival results are comparable to those published in the literature.

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Lymph node control with RT/QT in tumors of head and neck N0, staged by CT and PET. Is necessary to dose level used currently for subclinical disease?

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Background. High levels of local and regional control obtained with RT-QT not excessive volumes of disease, the accuracy of the staging with CT and PET and accuracy in the delivery of the dose in the volumes to radiate with IMRT techniques they do that you might have the possibility of reducing the dose in regions effectively irradiated with the consequent advantage in acute and late toxicity.
Methods and materials. Retrospective analysis of 26 patients (6 women and 20 men) with mean age: 61 years and diagnosed with head and Neck Cancer: nasofaringe: 4 oropharynx: 1, paranasal sinuses: 4, oral: 2, supraglottis: 9, glottis: 6 (T2, T3 and T4) treated in HUPH between January 1, 2009 and February 30, 2013 in N0 after CT and PET situation and treated with concomitant RT/QT.
Results. 24 were irradiated by IMRT and 2 with conformal 3D. Dose happens of RT: 68.4 Gy. Dose happens of fractionations on the GTV1: 2.1 Gy/day. Minimum dose in elective volumes 54–66 Gy with subdivisions of 1.6–1.8 Gy/day. Median of follow-up: 17.8 months (min 24–max 45). A patient lost in the follow-up. The local control of the disease was achieved in 24 patients (92.3%). Overall survival a year: 91%, 2 years: 82% at 3 years: 71% disease-free survival and survival free of local relapse 2 years: 92%. Free survival of lymph node recurrence and within distance 2 years: 91%. The date of completion of the study, 4 (15.3%) had died, only one due to the tumor.
Conclusions. With the limitations of this study by the small number of analyzed patients and follow-up can venture that the excellent control of the lymph node disease in these patients at stage N0 CT and PET would justify an investigation of greater importance directed to reduce the dose of RT in elective areas.

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Molecular basis of the radiotherapy-induced mucositis. Beneficial effects of melatonin

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Aims. Radiotherapy-induced oral mucositis is one of the main side-effects of this therapy in patients with cancer. The molecular mechanisms of the oral mucositis are currently unknown, thus difficulting the treatment. It was reported that during cell stress, the free radicals produced by the mitochondria are responsible for the NLRP3 inflammasome activation, which in turn yield intracellular changes conducting to pro-inflammatory cytokines activation. During these responses, the NF-kB pathway is also activated, increasing the pro-inflammatory response. The objectives of this study were to analyze the molecular pathways involved in the development of oral mucositis, and to evaluate whether melatonin can prevent this pathology.
Materials and methods. Male Wistar rats were subjected to irradiation with a X-ray YXLON Y.Tu 320-D03 irradiator, and the animals received a dose of 7.5 Gy/day for 5 days in their tongues. Rats were treated with 45 mg/day melatonin or vehicle during 21 days post-irradiation, either by local application into their mouths (melatonin gel) or by sc injection. After treatments, rat tongues were obtained for the subsequent determinations. Pharmaceutical preparation of melatonin in gel is currently under patent.
Results. We observe an amelioration of the acute mucosal effects of radiotherapy with topical gel melatonin. Melatonin decreases the expression of NF-kB, iNOS/i-mtNOS, NLRP3, ASC, caspase-1, and proinflammatory cytokines. Melatonin restored mitochondrial function increasing the activity of the mitochondrial antioxidant enzymes and respiratory chain activity. Electron microscopy also showed tongue's mitochondria significantly damaged and broken after radiotherapy, which was also prevented by local melatonin gel administration, and we observe a decrease of fibrosis with melatonin.
Conclusions. Considering the low toxicity of melatonin even during long term, which makes possible its clinical use, our results provide evidence for the therapeutic value of melatonin to prevent mucositis in cancer patients. Supported in part by grant no. SAF2009-14037

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