after treatment. A long term follow-up is necessary to conclude in term of LP rate, quality of live and functional larynx rate.

8509 POSTER

Development of a nomogram for prediction of survival and local control in larynx carcinoma treated with radiotherapy alone: a cohort study based on 994 patients

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Background: To advice a patient with a larynx carcinoma which treatment is best, a tool to predict survival and local control is needed. A number of prognostic factors for survival as well as local control have been identified. However, the exact importance of these factors in daily clinical practice and the treatment-decision making process needs to be determined. We therefore developed prediction models for survival and local control, for patients treated with radiotherapy alone, taking into account established prognostic factors.
Material and Methods: We performed a population based cohort study on 994 patients with a larynx carcinoma, treated with radiotherapy alone at the MAASTRO Clinic from 1977 until 2008. Prognostic factors that were investigated were: pretreatment hemoglobin level, age, sex, cT-status, cN-status, location of the tumor (glottic versus non-glottic), and eqd2T (total radiation dose corrected for fraction dose and overall treatment time). Performance of the models was expressed as the C-statistic. The maximum value of the C-statistic is 1.0; indicating a perfect prediction model. A value of 0.5 indicates that 50% of the patients are correctly classified, e.g. as good as chance. Hazard ratios (HR) were reported. The results of the multivariate analysis were used to develop a nomogram.
Results: Median follow-up was 140 months. Median 6-year survival for stage I and stage II disease was 72 months, for stage III disease 44 months, for stage IVA 17 months, and for stage IVB disease 5 months. In the multivariate analysis, independent unfavorable prognostic factors for overall survival were low hemoglobin level ($p < 0.0001$, HR 0.67), male sex ($p = 0.0002$, HR 2.30), high cT-status ($p < 0.0001$, HR 1.22 for T2 compared to T1, 2.22 for T3, and 4.29 for T4), presence of nodal involvement ($p = 0.034$, HR 1.46), higher age ($p < 0.0001$, HR 1.04), lower eqd2T ($p = 0.0037$, HR 0.97), and non-glottic tumor ($p = 0.0725$, HR 1.31). Prognostic factors for local control were hemoglobin level ($p < 0.0001$, HR 0.75), sex ($p < 0.0001$, HR 2.47), cT-status ($p < 0.0001$, HR 1.52 for T2 compared to T1, 2.48 for T3, 4.28 for T4), presence of nodal involvement ($p = 0.0059$, HR 1.51), age ($p = 0.0012$, HR 1.02), and eqd2T ($p = 0.0011$, HR 0.97). C-statistic of the models was 0.73 and 0.67, respectively.
Conclusions: We have built visual, ready to use nomograms for prediction of survival and local control with several easy assessable clinical factors, for patients with larynx carcinoma treated with radiotherapy alone.

8510 POSTER

'About Face' survey uncovers significant between-country variation across Europe in general public's awareness of head & neck cancer

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Background: In Europe, the reported incidence and mortality rates of head and neck (H&N) cancer are approximately 143,000 and 68,000 per year, albeit with significant differences between individual countries. Despite this, the general public's awareness of H&N cancer is thought to be very low across the continent. The pan-European 'About Face' survey was planned and conducted in collaboration with the European Head & Neck Society (EHNS) to gauge current awareness and understanding of H&N cancer, with a focus on whether there are significant differences between countries that need to be addressed.
Methods: A total of 7,520 Omnibus internet interviews were conducted in France, Germany, Italy, The Netherlands, Spain, Sweden and the UK in September 2008.
Results: Overall, 77% of respondents were unaware of the term H&N cancer (ranging from 89% in the UK to 61% in Italy), while 89% were not aware that they knew anyone who had been affected by the disease (96% UK, 75% Italy). Those countries where more respondents believed that they knew someone who had been affected by H&N cancer also showed an increased awareness of the term, and vice-versa. German and Swedish respondents were more likely to identify body parts affected by H&N cancer correctly, although 60% overall believed that 'H&N cancer' includes tumors of the brain. There was general consensus across all countries that certain lifestyle factors may increase the risk of developing the disease. Awareness that certain sexual habits may increase risk was low in all countries (mean: 5%, range: 4−9%). Respondents from both Italy and Spain had a lower level of knowledge of the symptoms of H&N cancer than other countries, especially Germany. Overall, consequences of surgery were seen as the most distressing potential symptom of H&N cancer, particularly in Sweden (33% of respondents) and the UK (32%).
Conclusions: The pan-European 'About Face' survey identified a lack of knowledge amongst the general public of the risk factors and symptoms of H&N cancer. Moreover, there were significant differences between individual countries which should be investigated further. In some countries (e.g. the UK), a simple increase in awareness of the disease in general is required, while educational activity in countries such as Italy and Spain may need to focus more on increasing awareness of symptoms of H&N cancer. Further education of the general public on H&N cancer is clearly warranted.

8511 POSTER

Long-term outcome and morbidity after treatment with accelerated radiotherapy and weekly cisplatin for locally advanced head and neck cancer

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Background: To evaluate the long-term outcome and morbidity after treatment with accelerated radiotherapy combined with weekly cisplatin for locally advanced head and neck cancer.
Methods and Material: Between May 2003 and December 2007, 77 patients (median age 53 years) with locally advanced (stage III-IV) squamous cell carcinoma of the oral cavity (n = 12), oropharynx (n = 41), hypopharynx (n = 23) and larynx (n = 1) were treated at our hospital. Treatment consisted of accelerated radiotherapy with concomitant boost up to a dose of 68 Gy over a total period of 5.5 weeks and concurrent intravenous cisplatin 40 mg/m^2 weekly. Long- term survivors were invited to a multidisciplinary outpatient clinic for assessment of late morbidity using the RTOG/EORTC scoring system. All patients had a radiologic evaluation of swallowing function.
Results: The median follow up for the whole group was 28 months (range 3−68). Three-year disease specific survival, disease free survival and overall survival rates were 69%, 51% and 57% respectively. Local recurrence free survival at three years was 66%. Radiotherapy was given as planned in all but one patient and 91% received at least 5 cycles of cisplatin. At time of evaluation 43 patients were still alive of whom 32 patients participated in the mulitdisciplinary late morbidity clinic. Five patients (16%) suffered grade 4 toxicity, 2 had a laryngeal necrosis and 3 osteoradionecrosis. The five year actuarial rate of grade 3 or 4 toxicity on all sites was 52% and 25% respectively. Of the 32 patients who participated, 5 patients (16%) were able to eat without any restrictions and 2 patients (6.3%) depended on a gastric feeding tube. Radiologic evaluation demonstrated impaired swallowing in 57% of the patients. In 7 patients (23%) there was silent aspiration on liquids or thickened fluids, 8 (27%) suffered from stasis above the epiglottis and 9 (28%) had problems with transporting the thickened fluids or solid food from the oral cavity to the oropharynx.
Conclusion: This regimen of accelerated radiotherapy with weekly cisplatin produces 3-year survival rates that compare favorable to regimes using only accelerated radiotherapy or conventionally fractionated radiotherapy plus chemotherapy for advanced head and neck cancer. Long-term morbidity however was not insignificant and swallowing was objectively impaired in the majority of the patients with more than 20% silent aspiration. This has important consequences for supportive care and rehabilitation.

8512 POSTER

Swallowing complaints strongly correlate with salivary gland function, 1 year after radiotherapy for head and neck cancer

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Background: Swallowing complaints and xerostomia after radiotherapy (RT) for head and neck cancer negatively influence quality of live of

the patient. Improvement of salivary function after radiotherapy may lead to better swallowing function. In this study we focus on the correlation between prospectively measured parotid salivary output and quality of life items concerning xerostomia and swallowing based on the EORTC H&N questionnaire.
Materials and Methods: Since 1996 we prospectively perform measurements of stimulated parotid salivary output, using Lashley-cups, before and 6 weeks, 6 months and 1 year after radiotherapy. For 167 patients the relative parotid salivary output is correlated with the mean parotid dose and quality of life measurements using the EORTC H&N quality of life questionnaires. The tumour was located in the larynx, pharynx, oral cavity and other locations in 22%, 56%, 10% and 12%, resp. Advanced T-stage and positive nodes were noted in 31% and 50%, resp. Conventional RT, IMRT and Chemo (IMRT) RT was used in 91, 55 and 21 patients, resp. The mean dose of the parotid glands was 34 Gy. A parotid flow complication was defined as <25% of pre-RT flow. For analysis three groups were defined: both (A), one (B), or no parotid glands (C) with a flow complication.
Results: One year after radiotherapy the distribution of group A, B, and C was 27%, 34% and 39%, resp. At one year, on a scale of 1 (not at all) to 4 (severe) the distribution for complaints of dry mouth was 21%, 27%, 33% and 19%, and of sticky saliva 37%, 29%, 25% and 9%, respect. For the same scale, difficulty in swallowing solid food was seen in 50%, 27%, 13% and 11%, resp. Tube feeding was given in 5%, namely after chemoRT (18%). In univariate analysis, the grade of difficulty in swallowing solid food significantly correlated with therapy, tumor localization (grade 4 20% oropharynx, 0% larynx), N-stage, dry mouth and sticky saliva. After logistic regression three independent variables remained: treatment ($p = 0.006$), dry mouth symptom ($p = 0.001$), and, marginally, the number of parotid glands with a complication ($p = 0.04$).
Conclusion: One year after RT swallowing complaints strongly correlated with complaints of a dry mouth, however not with complaints of sticky saliva. Sparing one or both parotid glands was marginally related to swallowing complaints. Sparing one submandibular gland may further decrease dry mouth complaints, and is subject of on-going research.

8513 POSTER

Image guidance with bone matching alone is insufficient for conformal radiation of early glottic cancers − an analysis of laryngeal positional uncertainty based on daily cone beam CT

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Background: Highly conformal radiation therapy for early glottic cancers will require accurate daily image guidance to be safe and maximally spare voice and swallowing function. This study uses daily cone beam CT (CBCT) imaging to investigate the daily positional uncertainties of the glottis during a course of treatment and its relationship to the skeletal anatomy.
Methods: 160 CBCT image-sets of 8 patients with T1aN0M0 glottic cancer treated with intensity modulated radiation therapy (IMRT) with daily kilovoltage CBCT were used in this offline study. Daily setup variations were measured with the Elekta Synergy XVI 4 ® platform using an automatic bone match and a manual match of laryngeal soft-tissues by a radiation oncologist. Discrepancies between these matches were calculated to evaluate the extent of laryngeal displacement in relation to vertebral bodies. An internal target volume (ITV) was generated using the formula suggested by van Herk (2000).

Table 1: Setup errors with different image match protocols

Axis	Manually verified soft-tissue match	Automatic Bone Match	Setup disparity between manual and bone match
ML			
Mean	0.7 mm	0.8 mm	0.7 mm
Range	0.0−2.3 mm	0.1−2.9 mm	−0.1 to +0.7 mm
SE	0.9 mm	1.0 mm	0.4 mm
SI			
Mean	1.1 mm	0.0 mm	2.5 mm
Range	0.1−3.9 mm	0.3−2.9 mm	−1.0 to +5.9 mm
SE	2.0 mm	1.7 mm	2.6 mm
AP			
Mean	0.3 mm	0.7 mm	1.0 mm
Range	0.1−2.0 mm	0.1−1.7 mm	−0.6 to +1.4 mm
SE	0.9 mm	0.9 mm	0.3 mm

SE: systematic error

Results: The mean translational setup errors in the mediolateral (ML), supero-inferior (SI) and antero-posterior (AP) directions for each type of match and the anatomical discrepancies are summarized in Table 1. Errors were most pronounced in the SI axis. There was an anatomical disparity in the bone-match compared to the manual soft-tissue match that was most pronounced in the SI axis (mean 2.5 mm, range −1.0 to +5.9 mm, SD = 2.6 mm) suggesting an independent daily positional variation of the laryngeal soft-tissues relative to the vertebral bodies. The calculated ITV margins for the larynx in relation to the bone match were 2, 8 and 2 mm in the ML, SI and AP axes.
Conclusions: There is a considerable daily variation in laryngeal position in relation to the vertebral anatomy. Image matching based on skeletal anatomy alone is inadequate and should not be regarded as a surrogate for laryngeal position. Image guidance and manual verification of soft-tissue setup errors is essential in order to proceed with highly conformal radiation therapy of early larynx cancer.

8514 POSTER

SPECTRUM, a phase III trial for patients with recurrent and/or metastatic squamous cell carcinoma of the head and neck (SCCHN) receiving chemotherapy with or without panitumumab: interim pooled safety analysis

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Background: Panitumumab (pmab) is a fully human monoclonal antibody against the epidermal growth factor receptor (EGFR), a therapeutic target in patients (pts) with SCCHN. SPECTRUM is assessing the safety and efficacy of pmab + standard platinum-based chemotherapy (CT) in pts with recurrent and/or metastatic (R/M) disease (ClinicalTrials.gov ID: NCT00460265; sponsor: Amgen Inc).
Methods: This is a global, phase III, open-label study. As of March 2009, the trial has completed enrollment of 658 pts. Pts with R/M SCCHN were randomized (1:1) to receive cisplatin (100 mg/m^2) IV on day 1+5 FU (1000 mg/m^2) continuous IV daily on days 1−4 Q3W for up to 6 cycles ± pmab (9 mg/kg). Pts receiving pmab without disease progression after 6 cycles may continue pmab monotherapy until disease progression. Substitution of carboplatin (AUC 5) is allowed for specific toxicities. Primary endpoint is overall survival. Key secondary endpoints include progression-free survival, response rate, and safety. This trial is overseen by an independent Data Monitoring Committee (DMC).

AEs of Interest[a] (N = 446[b])

AE (MedDRA terms)	Any grade, n (%)	Grade 3/4, n (%)
Nausea	248 (56)	24 (5)
Skin and subcutaneous tissue SOC[c]	207 (46)	31 (7)
Neutropenia	206 (46)	141 (32)
Vomiting	177 (40)	23 (5)
Stomatitis/mucosal inflammation	172 (39)	40 (9)
Anemia	166 (37)	64 (14)
Diarrhea	143 (32)	15 (3)
Hypomagnesemia	122 (27)	27 (6)
Fatigue	111 (25)	18 (4)
Anorexia	110 (25)	16 (4)
Thrombocytopenia	91 (20)	29 (7)
Weight decreased	91 (20)	5 (1)
Leukopenia	65 (15)	34 (8)
Febrile neutropenia	29 (7)	27 (6)

[a]Treatment-related (CT ± pmab) grade 5 AEs included cardiac/vascular disorders (n = 8), febrile neutropenia/neutropenia-related complications (n = 4), multi-organ/hepatic or renal failure (n = 3), and 1 each of hemorrhagic diarrhea, tumor hemorrhage and aspiration pneumonia; [b]Excludes 5 pts who did not receive any protocol treatment; [c]SOC, System organ class

Results: Pooled data from this interim safety analysis includes the first 451 pts of 650 planned pts; 99% received any study treatment; 86% are male; median age is 58 years (range 26−84); ECOG PS 0/1 = 33%/67%. Median follow-up time is 17.1 weeks; 85% have ended CT. 18 pts (4%) had