is due to the geometrical error in the diode positioning. The GRD results were in good agreement with those from the Gafchromic film for almost all the collimators.
Conclusions: For the GRD output factor measurements in water of CK system. It is found that GRD is a useful dosimeter for circular collimators smaller than 10 mm diameter, in good agreement with a Gafchromic film. Future study will be devoted to investigate for possibility of using GRD for quality assurance audit program of stereotactic radiosurgery units.

5512 POSTER

Expression of NHEJ genes in head and neck squamous cell carcinoma is associated with tumor response to 5-fluorouracil and cisplatin-based induction chemotherapy

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Expression of NHEJ genes in head and neck squamous cell carcinoma is associated with tumor response to 5-Fluorouracil and cisplatin-based induction chemotherapy.
Background: Concomitant chemoradiotherapy (CRT) or 5-Fluorouracil (5-FU) and cisplatin-based induction chemotherapy (IC), followed by CRT or radiotherapy (RT), are used to treat locally advanced head and neck squamous cell carcinoma (HNSCC). We studied the relationship between tumor expression of non-homologous end joining (NHEJ) repair genes (Ku80, Ku70 or DNA-PKcs) and their response to IC. The role of NHEJ in double-strand break (DSB) repair, genomic instability (HNSCC chromosomal rearrangements) and apoptosis suggests a possible role on tumor response to RT, 5-FU or cisplatin since all these agents induce DSBs.
Patients and Methods: In a Prospective Study, we evaluated the mRNA levels of Ku80, Ku70 and DNA-PKcs in 50 pre-treatment HNSCC biopsies by RT-PCR.
In a Retrospective Study, we evaluated Ku80 and Ku70 protein expression in pre-treatment HNSCC biopsies of an independent cohort of 52 patients by Immunohistochemistry (IHC) staining. Protein expression was assessed by morphometric image analysis, applying the HSI color model. This method makes it possible to measure the percentage of Ku80 and KU70 positive tumor cells present in a given tumor sample image.
To establish the relationship between Ku80, Ku70 and DNA-PKcs mRNA levels (or Ku70 and Ku80 protein expression) and response, we classified tumors in two groups according to response after IC. The responder group included patients with a reduction in tumor size higher than 50%, whereas the non-responder group included patients with an increase, stabilization or decrease in tumor size lower than 50%.
Results: Tumors included in the responder group had significantly higher mRNA levels for Ku80 ($p = 0.002$), Ku70 ($p = 0.005$) and DNA-PKcs ($p = 0.017$) than tumors in the non-responder group.
We also observed by IHC that the percentage of Ku80 and Ku70 positive tumor cells was significantly ($p = 0.021$, $p = 0.023$, respectively) higher in the responder group than in the non-responder group.
Conclusions: Ku80, Ku70 and DNA-PKcs expression in pre-treatment biopsies of patients with locally advanced head and neck squamous cell carcinoma is significantly associated with tumor response to 5-Fluorouracil (5-FU) and cisplatin-based induction chemotherapy.
In spite of these results additional independent studies will be necessary to validate the capacity of these genes to predict response to induction chemotherapy and to establish the best expression cut point.

5513 POSTER

Topical chemoprevention of skin cancer with dual inhibitors of 5-LOX and COX-2 via a microemulsion system

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Background: The cyclooxygenase (COX) and the 5-lipoxygenase (5-LOX) pathway have been suggested to play an important role in oral, colon, and other tissue carcinogenesis. However, it is unknown whether 5-LOX pathway contributes to skin carcinogenesis, and importantly whether combination of inhibitors of both pathways may have synergistic or additive effects of chemoprevention. In this study, we test topical combination application inhibitors of both pathways as a promising way for chemoprevention of skin cancer.
Material and Methods: Twenty four nude mice were intradermally inoculated with squamous cell carcinoma cells. Then these animals were divided into 3 groups (8 of each) to receive following treatments: (1) Celecoxib (a specific COX2 inhibitor); (2) combination of Zileuton (a specific 5-LOX inhibitor) and celecoxib; and (3) no treatment as a control. We investigated for the chemopreventive effects through topical application by a microemulsion system. Tumor growth continued to be measured for 15 days.
Results: The T50 (the time latency for the first 50% tumor to appear on all inoculated skin sites) were 3 days, 5days, and 6 days in control group, 6% celecoxib group, and 6% celecocib+6% zileuton group, respectively. Statistically, a significant difference of tumor growth was found between the control and two treatment groups. But the groups with the combined treatment had the best result, and showed an additive inhibitory effect on the incidence and growth of squamous cell carcinoma ($P < .001$).
Conclusions: The results clearly shows that both 5-LOX and COX2 play important roles in skin carcinogenesis, but a dual application of agents will significantly improve the results. We also found it would be a promising way to delivery celecoxib and zileuton through microemulsion system for topical inhibition of skin cancer. This is the first study for topical chemoprevention of skin cancer by combining inhibitors of 5-LOX and COX2.

5514 POSTER

Green tea extracts induce apopoptosis and inhibit in HGF-induced HNSCC progression in vitro

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Purpose: Activation of hepatocyte growth factor(HGF) and its receptor, c-Met, has been known to be involved in many human cancer development and progression. During the search for an effective molecule inhibitor of HGF/c-Met signaling, we have found that Epigallocatechin-3-gallate(EGCG), the major bioactive polyphenol present in green tea, might inhibit HGF/c-Met signaling. Studies were performed to address whether EGCG inhibit HGF-dependent tumor proliferation and invasion in HNSCC.
Method: We performed RT-PCR and Western blot of HNSCC cell line. Proliferation assay, dispersion assay, wound healing assay, and invasion assay were performed in HGF 0, 10, 30 ng/mL HGF10+EGCG 1 μM, HGF10+EGCG10 μM, HGF30+EGCG1 μM, HGF30+EGCG10 μM. RT-PCR and zymography were performed to examine the roles of MMP-2 and MMP-9, as well as the relationship between HGF and MMPs in FaDu invasiveness. In addition, we confirmed HGF-mediated plasmin activation. We performed Tunnel assay, DNA fragmentation analysis, Annexin V staining, and FACS analysis for apoptotic effect of EGCG in HNSCC.
Results: Exogenous HGF significantly enhanced the growth of HNSCC cell and this phenomenon was inhibited by EGCG in dose-dependant manner. ($p < 0.05$) EGCG inhibited HGF-induced scattering of HNSCC cell. EGCG inhibited HGF-mediated migration and invasion of HNSCC cell in dose-dependant.($p < 0.05$). EGCG inhibits the HGF-Met-uPA-Plasmin network and MMP2, 9. We confirmed EGCG induced apoptotic phenomenon in Tunnel assay, Annexin V staining, DNA fragmentation analysis and FACS.
Conclusions: Inhibition of HGF/Met signaling by EGCG leads to decrease of proliferation and invasion in vitro, suggesting the possible use of EGCG in HNSCC associated with downregulation of HGF/Met signaling and the HGF-Met-uPA-Plasmin network and MMP2, 9.

5515 POSTER

Comparison of the efficacy and safety of miconazole 50 mg mucoadhesive buccal tablets to those of miconazole 500 mg gel in the treatment of oropharyngeal candidiasis: a prospective, randomised, single blind, multicenter, comparative, phase III trial in patients treated with radiotherapy for head and neck cancer

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Background: Topical antifungal treatments are recommended as first line therapy for oropharyngeal candidiasis (OPC) in cancer patients. However, they are not used because of multiple daily dosing, bad taste and poor acceptance by patients. Miconazole 50 mg mucoadhesive buccal tablet (MBT) is a new delivery system that was reported to produce rapid and prolonged effective concentrations of miconazole in the mouth. Its pharmacokinetic profile is well suited to the treatment of OPC.
Patients and Methods: This prospective, single blind, randomised, comparative, multicenter trial was aimed at comparing the efficacy and safety of a 14-day treatment with MBT once daily to those of miconazole 500 mg oral gel (MOG) administered in 4 divided doses in head and neck cancer patients having undergone radiation therapy. Primary end point was clinical success at day 14. Secondary endpoints included clinical success at day 7, clinical cure, improvement in clinical symptoms, mycological cure, relapse rate and safety.
Results: A total of 282 were enrolled. Patients from both groups were not different at baseline, except for the extent of lesions and severely impaired

salivary secretions that were unevenly distributed. At day 14, the success rate was statistically not inferior ($p < 0.0001$). After adjustment on extent of lesions and salivary secretions, a strong trend towards superiority was observed in favour of MBT ($p = 0.13$).

Clinical Response adjusted on:	MBT 50 mg	MOG 500 mg	Variation in %	P*
Lesions				
unique localised	28/49 (57.1%)	33/57 (57.9%)	−1.4%	0.94
multiple localised	44/75 (58.7%)	24/64 (37.5%)	56.6%	0.013
spread or confluent	7/17 (41.2%)	11/19 (57.9%)	−28.8%	0.32
Saliva				
normal	6/6, (100%)	2/5 (40%)	150%	0.034
partial	59/105 (56.2%)	60/116 (51.7%)	8.7%	0.50
absent	14/30 (46.7%)	6/19 (31.6%)	47.8%	0.30

*After adjustment on extent of lesions and saliva secretion.

Likewise, MBT was numerically superior to MOG on almost all secondary endpoints. Compliance with MBT was excellent, with >80% of patients completing treatment. Both drugs were safe.

Conclusions: MBT is significantly not inferior to MOG in the treatment of cancer patients with OPC. After adjusting for prognostic variables, a strong trend towards superiority was observed in favour of MBT, in particular in patients with multiple lesions. MBT is well accepted and tolerated by patients with critical oral conditions and therefore can be used as first line treatment in cancer patients with OPC as an alternative to systemic antifungal agents.

5516 POSTER

Thyroid cancer. No siempre senor buena genta

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Background: The incidence of thyroid cancer is increasing. For the majority treatment with surgery and radioactive Iodine results in high cure rates and a normal survival experience. A minority however die from their disease or suffer considerable morbidity. This paper discusses those who do badly and attempts to provide indications for the use of external beam radiotherapy.

Materials and Methods: Patients presenting to a single institution Thyroid Cancer Clinic from 1974 to 2004 were reviewed. 2307 patients were seen and 171 (7.4%) died of thyroid cancer. Good prognosis tumours included well differentiated papillary and follicular histology and T-Stage 1, 2 and 3.

Results: On multivariant analysis the factors predicting a poor disease specific survival are, Sex M:F hazard ratio 1.33 ($p = 0.05$), Age hazard ratio 1.06 ($p = 0$). With regard to T-Stage only T4 makes any significant difference with a hazard ratio of 1.88 ($p = 0.01$), N Stage hazard ratio is 1.61 ($p = 0.01$), M Stage M0 or M1 has a hazard ratio of 2.36 ($p = 0.0001$). Histology indicates that papillary, follicular and Hurtle have the same outcome with a hazard ratio of 1.30 ($p = 0.27$). However medullary tumours have a hazard ratio of 2.11 ($p = 0.01$) and anaplastic tumours have a hazard ratio of 7.12 ($p = 0$). The use of external beam radiation is associated with a poor prognosis but this is due to selection bias. Inoperability is associated with a poor prognosis.

Conclusions: External beam radiotherapy needs to be high dose in the order of 60 Gy and the late effects particularly in young people may be quite considerable and therefore management with radioactive Iodine and surgery is preferred even for those with extensive nodal disease. The groups benefiting from external beam radiation are those with poorly differentiated or anaplastic histology, widespread invasion of vital structures such as trachea and oesophagus, medullary cancers and patients with well differentiated histology who have failed to take up radioactive Iodine. There is an urgent need for systemic therapies for tumours which no longer take up I-131, medullary cancers and anaplastic cancers.

5517 POSTER

Regional control of melanoma neck node metastasis after (selective) neck dissection +/− adjuvant radiotherapy

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Purpose: To examine the effect of adjuvant radiotherapy and type of neck dissection on regional control in patients with melanoma neck node metastasis

Materials and Methods: A retrospective study was carried out in 64 patients treated between 1989 and 2004 for neck node metastasis from melanoma. Twenty-four patients were treated with surgery (S) only; of these patients fifthteen underwent a (modified) radical neck dissection [(M)RND] and nine a selective neck dissection (SND). Forty patients underwent surgery [28 (M)RND and 12 SND] and adjuvant radiotherapy (RT) of the whole ipsilateral neck Criteria for adjuvant radiotherapy were $\geqslant$2 positive nodes (before 1992: $\geqslant$3 positive nodes), extra capsular rupture (ECR), nodes larger than 3 cm or recurrence. Radiotherapy dose was 4−6 times 6 Gray, delivered once a week.

Results: Prognostic factors were worse in the S+RT group than in the S group ($\geqslant$2 positive nodes 85% versus 38%, ECR 35% versus 8%). With a median follow up of 2.1 years, regional recurrence inside the treated volume was not significantly different between the groups (S+RT: five year recurrence rate 25%; S: 35%). Five year loco-regional recurrence outside the treated volume was 15% in the S+RT group (3 contralateral neck, 2 local, no ipsilateral neck) and 44% in the S group (2 contralateral neck, 3 local and 3 ipsilateral neck outside the treated volume) ($p = 0.12$). Univariate analysis revealed that patients who underwent SND, instead of (M)RND, had a higher risk of loco-regional recurrence outside the treated volume. Ipsilateral recurrence outside the treated volume was found in 33% of patients who underwent SND without RT, in contrast tot 0% of patients who underwent SND followed by RT. All patients with an ipsilateral recurrence had a single positive node for which they underwent SND of a limited number of levels (2 $\times$ level I-III, 1 $\times$ level IV-V). Five year survival was 19% in the S+RT group and 40% in the S group ($p = 0.08$).

Conclusions: Selective neck dissection without radiotherapy leads to a substantial risk (33%) of ipsilateral recurrence outside the operated volume. Even in patients with low risk neck disease it is indicated to perform a (modified) radical neck dissection or selective neck dissection combined with radiotherapy to improve ipsilateral regional control.

5518 POSTER

Neo-adjuvant chemotherapy followed by radical chemo-radiation in treatment of advanced head and neck cancer

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Background: A study designed to test the efficacy and toxicity of neo-adjuvant chemotherapy followed by radical chemo-radiation in treatment of advanced Head and Neck cancer.

Methods: Patients treated with 2 cycles of neo-adjuvant chemotherapy followed by definitive chemo-radiation for squamous cell carcinoma of the head and neck region, from 2001–2006 at the Royal Marsden Hospital, formed the basis of this study. Cisplatin (100 mg/m^2) on day 1 and 5-FU (100 mg/m^2) day 1−5 was the standard regimen used for neo-adjuvant treatment. Cisplatin (100 mg/m^2) on day 1 and day 29 was used for concomitant treatment. The radiation was delivered using conformal technique. The macroscopic and the microscopic disease were treated to a dose of 65 Grays (Gy) in 30 fractions (6 weeks) and 50 Gy in 25 fractions respectively. Data on patterns of relapse and acute (NCICTCv.3.0) were collected.

Results: 129 patients were included, median age was 58 (range 27−78). The site of tumour was: oropharynx 70 (54%), larynx/hypopharynx 54 (42%), and other 5 (4%). The median follow-up was 19 months (range 4−58). Local control, disease specific survival and overall survival at 2 years were 71%, 68% and 63%, respectively. The distant recurrence rate at 2 years was 9%.

10 patients required dose reduction during neo-adjuvant chemotherapy due to toxicity. The dose of 5-FU was reduced in 6 patients and that of cisplatin in 4 patients. The incidence of grade 3/4 toxicity was: neutropenia 5%, thrombocytopenia 1%, nausea and vomiting 3%.

One cycle of concurrent cisplatin was omitted in 23 patients due to toxicity. All patients completed the full dose of radiation. The incidence of grade 3/4 toxicity was: skin 20%, dyaspagia 65%, mucositis 60%, neutropenia 3%, anaemia 1%, nausea and vomiting 4%, nephrotoxicity 1%.

Conclusions: Neo-adjuvant chemotherapy followed by radical chemo-radiation is a safe and tolerable regimen in the treatment of advanced Head and Neck cancer. Distant recurrence rates are lower with equivalent local control and survival compared to chemo-radiation alone (historical controls).