treatment and monthly up until 3 months after finishing treatment. Treatment outcome at 3 and 6 months was retrieved in 131 patients. A two-tailed Fisher's Exact test was used to compare binary data between both arms. A Mann-Whitney U test was performed to compare continuous data.
Results: Data of 193 patients could be retrieved (experimental arm: n=96 , standard arm: n= 97). No significant differences between both arms were seen in social status, age, sex, tumor site, smoking and alcohol abuse, TNM stage, performance stage, total dose delivered, overall treatment time and pretreatment dysphagia. Dosimetrically, no significant difference was seen between both arms concerning PTV_{ther} coverage (for D_{95}: 67.5 Gy vs 67.3 Gy; p=0.9). As expected the median D_{95} of the PTV_{elect} was significantly lower in the experimental arm than in the standard arm (39.5 Gy vs 49.8 Gy; p<0.0001). Using this strategy we were able to significantly reduce the dose to swallowing structures (Table 1). There was no significant difference in acute mucositis, skin toxicity and weight loss between both groups. During treatment no difference was seen in severe dysphagia. Three months after radiotherapy however there was significantly less grade 3+ dysphagia in the experimental arm compared to the standard arm (2% vs 11%; p=0.03) (Figure 1). At 6 months, no significant difference was seen in locoregional control between both arms (88% vs 92%; p=0.6).
Conclusions: Using IMRT we were able to significantly reduce the dose to the elective nodal volumes and several organs at risk without compromising PTV_{ther} coverage. This resulted in a significant reduction of severe dysphagia 3 months after radiotherapy, without compromising locoregional control. Further follow-up is necessary to investigate whether these observations translate into a benefit on late treatment related dysphagia without affecting treatment outcome.

OC-0142
Conventional radiotherapy vs. chemoradiotherapy vs. accelerated radiotherapy in advanced head neck cancer
S. Ghosh Laskar[1], J.P. Agarwal[2], N. Kalyani[2], A. Budrukkar[2], T. Gupta[2], V. Murthy[2], M. Sengar[3], D.A. Chaukar[4], A.K. D' Cruz[4]
[1]*Tata Memorial Hospital, Radiation Oncology, Thane, India*
[2]*Tata Memorial Hospital, Radiation Oncology, Mumbai, India*
[3]*Tata Memorial Hospital, Medical Oncology, Mumbai, India*
[4]*Tata Memorial Hospital, Surgical Oncology, Mumbai, India*

Purpose/Objective: To compare conventional fractionation radiotherapy (RT, Arm A), conventional fractionation RT with concurrent chemotherapy (CTRT, Arm B) and accelerated radiotherapy (ART, Arm C), in terms of survival and toxicity for loco-regionally advanced, non-nasopharyngeal, Squamous Cell Carcinoma Head and Neck (HNSCC).
Materials and Methods: Between April 2000 and October 2007, 179 previously untreated, non metastatic, Stage III and IV HNSCC were randomised. There were 53, 64 and 62 patients in Arm A, B and C respectively. In arms A and B, all patients received conventional fractionation RT to a total dose of 66-70Gy in 6-7 weeks, five fractions per week. In Arm B, concurrent CT regimen consisted of Cisplatin 30 mg/m2/week. In Arm C, the total dose of radiotherapy was same, 6 fractions were administered per week, with concomitant boost being given on Saturday. Analysis was on an intention-to-treat basis.
Results: The median age of cohort was 49 years. The age, sex, primary sites, stage of disease were equally distributed in all three arms. Oropharynx was the most common primary site in all the three arms. The median treatment duration was 49, 51 and 40 days in 3 arms respectively. In arm B, the median number of chemotherapy cycles was 6. The mean and median follow up was 37.7 and 23 months respectively (Inter-quartile range 10-59 months). There was a significant difference in the Disease-Free Survival (DFS) and Overall survival (OS) for CT-RT arm compared with the others. The Median DFS in Arm A was 16 months compared to 34 months in Arm B and 10 months in Arm C (p=0.02). Median OS in Arm A was 32 months compared to 76 months in Arm B and 32 months in Arm C (p=0.05). In terms of acute toxicities patients of Arm A experienced fewer Grade 3 or more oral mucositis compared to Arms B & C (11 versus 22 versus 19 respectively). No incidence of G3 or more haematological toxicity was seen during the treatment in either of the arms. There was no difference in acute grade 3 skin toxicity or significant sequelae between the arms (14 versus 15 versus 10 respectively). In terms of late toxicities (RTOG Scale) G2-G3 xerostomia was similar in all the three arms (10 versus 14 versus 11 respectively). Similarly the late toxicity in terms of skin, mucosa and subcutaneous tissue was similar in the 3 arms. Salvage surgery was done in 19 patients (4 versus 6 versus 9 respectively in Arms A, B & C). Thirteen patients developed second primary cancer (3 versus 5 versus 5 respectively in Arms A, B & C).
Conclusions: Concurrent CTRT is associated with significant better OS and DFS as compared to RT alone (Conventional or Accelerated) without significant increase in late toxicities.

OC-0143
Managing mucositis with humidification during radiotherapy for head and neck cancer: TROG 07.03 RadioHUM results
A. Macann[1], S. Porceddu[2], C. Milross[3], M. Penniment[4], T. Fua[5], C. Fraser-Browne[6], V. Thomson[7], H. Hockey[8], M. Bell[9], M. King[9]
[1]*Auckland City Hospital, Radiation Oncology, Auckland, New Zealand*
[2]*Princess Alexandra Hospital, Radiation Oncology, Brisbane, Australia*
[3]*Royal Prince Alfred Hospital, Radiation Oncology, Sydney, Australia*
[4]*Royal Adelaide Hospital, Radiation Oncology, Adelaide, Australia*
[5]*Peter MacCallum Hospital, Radiation Oncology, Melbourne, Australia*
[6]*Auckland City Hospital, Oncology Research, Auckland, New Zealand*
[7]*Auckland City Hospital, Head and Neck Service, Auckland, New Zealand*
[8]*Biometrics Matters Ltd, Biometrics, Hamilton, New Zealand*
[9]*University of Sydney, PoCOG, Sydney, Australia*

Purpose/Objective: To assess the role of domiciliary based humidification (HUM) on the natural history of mucositis during radiotherapy (RT) for head and neck cancer. To evaluate the impact of HUM on patient reported outcomes (PRO).
Materials and Methods: In this phase III multi-site trial, patients with SCC of the oral cavity, oropharynx, larynx, hypopharynx, nasopharynx receiving definitive or adjuvant RT ± chemotherapy were randomised to either institutional standard of care (control) or HUM using the Fisher and Paykel Healthcare MR880 humidifier. HUM commenced day 1 of RT and continued until CTCAE version 3.0 mucositis clinical exam score (CMuc) was ≤1. Compliance was recorded electronically. HUM Compliance ratio (HCR) was calculated using the formula: total days compliance ≥ 4 hours from RT start to CMuc ≤ grade 1 / total days from RT start to CMuc ≤grade 1. HCR of > 0.33 was set as the cutoff for the per protocol population analysis (PPA). CMuc was assessed weekly until week 12 or resolution of CMuc score ≤ 1. The primary endpoint was the area under the curve (AUC) of CMuc grade >1. A credentialing programme promoted CMuc scoring consistency among investigators. The secondary endpoint CTCAE v 3.0 mucositis functional score (FSMuc) was analysed with similar methodology. PRO assessments included McMaster University Head and Neck Questionnaire (HRNQ) at baseline, 4, 7,12 and 20 weeks. Symptom cluster questions within HRNQ associated with mucositis analysed in addition to the normal HNRQ domains included severe cluster (difficulty tasting food, clearing secretions, swallowing or chewing) and moderate cluster (low energy, fatigue, dryness mouth, reduced appetite, pain mouth, pain throat, difficulty sleeping). The primary PRO comparison was the difference in means between the 2 arms at each timepoint.
Results: 210 patients were randomised (control 105; HUM 105). There was no difference in AUC CMuc means for the intention to treat population (ITT): control 9.0 (95% CI; 8.1 – 10.0); HUM 8.9 (95% CI; 8.0 -9.8); p 0.97. When patients with HCR < 0.33 were excluded for the PPA (60HUM patients; 58%), there was again no difference: control 9.0 (8.1 – 10.0) HUM 7.8 (6.3 – 9.2) p 0.25. There was no difference in AUC FSMuc for ITT: control 9.6 (8.7 – 10.4) HUM 8.8 (8.0 – 9.5); p 0.22, but a significant difference for PPA: control 9.6 (8.7 – 10.4) HUM 7.7 (6.7 – 8.7); p 0.009. For HNRQ ITT analysis, there was no difference in outcomes at any timepoint. The HNRQ PPA showed few significant differences but estimates were in the direction that favoured HUM with less symptom severity.
Conclusions: There was no difference in the primary endpoint of AUC CMuc with HUM. There is a trend in the HNRQ PPA suggestive of efficacy with HUM which is reflected in the AUC FSMuc PPA as well but the major difficulties in achieving consistent patient compliance suggests this is not an effective therapy for mucositis in its current format.

SYMPOSIUM: MANAGEMENT OF BRAIN OLIGO-METASTATIC DISEASE

SP-0144
Management of Brain Oligo-Metastastic Disease: The Dose Issue Perspective
S.E. Combs[1]
[1]*Univ. Klinikum Heidelberg, Radiation Oncology, Heidelberg, Germany*

Treatment of patients with oligo-metastasic disease has moved into focus since it has been shown that limited disease volume and sites contribute favorably to outcome. This is also relevant in metastastic lesions to the brain. However, due to the dose-response relationship

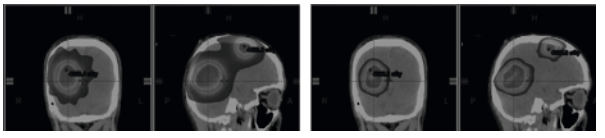
known for the treatment of brain metastases and due to the sensitive organ at risk, i.e. the brain and its eloquent regions, dose and volume have to be selected cauteously when treating such patients.
With highly precise techniques such as radiosurgery or hypofractionated treatments, the dose required is dependent on several factors, including volume of the lesion, vicinity to normal tissue structures, pre-existing clinical symptoms, overall performance status of the patient including prognosis, as well as underlying disease. All factors must be taken into account in clinical decision making, reflecting dose and volume recommendations from published clinical studies. The main limiting factor is the development of unwanted effects after treatment, also including neurocognitive functioning and preservation of quality of life (QOL).

SP-0145
The volume perspective - whole brain vs no whole brain
D. Vordermark[1]
[1]Martin Luther University Halle-Wittenberg, Radiation Oncology, Halle / Saale, Germany

The use of whole-brain radiotherapy remains a topic of great controversy. Historically, whole-brain radiotherapy has been the standard treatment for all patients with brain metastases. Randomized trials confirmed that in selected patients with limited, especially solitary brain metasteses, the addition of local treatment (surgery, radiosurgery) improves overall survival.
Conversely, other trials have asked whether in such patients with limited brain metastases, "upfront" whole-brain radiotherapy is necessary or can be delayed after local therapy only. The randomized EORTC trial 22952-26001 confirmed that adding whole-brain radiotherapy to local treatment of brain metastases improves local control, distant brain control but not overall survival [Kocher et al., J Clin Oncol 2011].
Whole-brain radiotherapy does have adverse effects on neurocognitive function and quality of life as has been demonstrated by meticulous studies of its prophylactic use in small-cell lung cancer [Le Pechoux et al., Ann Oncol 2011]. Assuming that intracranial tumor control is a prerequisite for maintaining neurocognitive function and performance status, the benefit of whole-brain radiotherapy in individual patients will depend on the "net effect" (beneficial regression of metastases vs. toxicity). The most recent quality-of-life analysis of the above EORTC trial indicates that patients in the arm with whole-brain radiotherapy had worse scores in some areas than patients in whom this treatment was initially withheld [Soffietti et al., J Clin Oncol 2013].
In patients with oligometastatic brain disease who are not candidates for local treatment, whole-brain radiotherapy may also have limitations. Recent data from a large prospective quality-of-life study show that many functions and symptoms deteriorate within three months after radiotherapy [Steinmann et al., BMC Cancer 2012]. It is under discussion if patients in poor performance status (RPA class 3) should receive whole-brain radiotherapy or best supportive care alone.

SP-0146
The new technique perspective - Arcs and Tomotherapy for brain metastases?
F.J. Lagerwaard[1], B.J. Slotman[1]
[1]VU University Medical Center, Radiation Oncology, Amsterdam, The Netherlands

The majority of patients with brain metastases (BM) from solid tumors have a prognosis of only a few months, based on unfavorable factors such as extensive extracranial tumor activity, and will be candidate for a short course of palliative whole brain radiotherapy (WBRT). Classification systems using independent prognostic factors such as performance status, primary tumor control, activity of extracranial metastases and age enable identifying subsets of patients that may have long-term survival, provided that the BM can be treated aggressively. For the these selected groups of patients with 'oligometastatic' disease, several more aggressive techniques for treatment of BM are available, including neurosurgery, radiosurgery or a combination of WBRT and radiosurgery.
Radiosurgery, a well-established treatment modality for a limited number of BM, involves the high-precision delivery of usually a single fraction of approximately 18-20 Gy directed to the lesion(s), resulting in local control rates of 60-90%, dependent on the size and aspect of the lesion (poorer control for necrotic lesions). Although radiosurgery has been available in the clinic for decades, recent years have seen major advances in treatment planning and delivery. In particular, the introduction of 'frameless' radiosurgery techniques with dedicated mask systems replacing invasive frames, has greatly facilitated logistics and lowered the threshold for accepting patients for radiosurgery. Several radiation delivery techniques are available ranging from multiple fixed beams, multiple non-coplanar arcs using cones or high-definition multileaf collimation, and recently also intensity modulated arcs or Tomotherapy.
The question whether WBRT should be added to RS has been a long-standing unresolved issue with proponents highlighting the improved intracranial control, and opponents pointing out the neurocognitive toxicity of WBRT and available salvage options.The recently completed EORTC study 22952-26001 has not been able to resolve the controversy, as it again showed that adjuvant WBRT after radiosurgery (or surgery) in a limited number of BM reduces intracranial relapses and neurologic deaths, but failed to improve the duration of functional independence and overall survival. As the risk of developing new BM following RS alone is not only dependent on extracranial tumor activity (reseeding) but also on the number of initially treated BM, a more differentiated approach towards adjuvant WBRT may be better suited, with for instance radiosurgery used as a single modality for 1 or 2 brain lesions, and a combination of WBRT and radiosurgery for multiple lesions.
A well selected patient group with multiple BM in good performance status and absent progressive extracranial disease may be candidates for radiation delivery integrating WBRT and stereotactic (fractionated) radiosurgery. Techniques such as volumetric intensity-modulated arc therapy (VMAT, RapidArc) or Tomotherapy have enabled fast and accurate delivery of fractionated stereotactic integrated boosts to multiple BM in combination with WBRT. The integrated approach of this planning technique allows steep dose gradients to be generated outside the boosts to the BM, much steeper than with a conventional summation of WBRT and radiosurgery (Figure; conventional left panel, VMAT right panel). This could theoretically decrease toxicity that has been observed in previous combined modality studies. Another advantage of this volumetric arc approach is that even complex treatment plans can be delivered within just minutes, although the use of a single isocentre instead of multiple isocentres necessitates dedicated patient setup including correction of rotational errors. Early experience with this technique have reported relatively high intracranial control, but it remains important to identify appropriate 'oligometastatic' patients in order to justify this advanced treatment delivery. At the time of the meeting, some planning considerations and preliminary clinical results will be presented.



PROFFERED PAPERS: PHYSICS 3: DEVELOPMENTS IN FUNCTIONAL IMAGING

OC-0147
Diffusion weighted MRI and corresponding histological characteristics
J. Driessen[1], J. Caldas-Magalhaes[2], F.A. Pameijer[3], C.H. Terhaard[2], L.M. Janssen[1], W. Grolman[1], M.E. Philippens[2]
[1]UMC Utrecht, Otorhinolaryngology, Utrecht, The Netherlands
[2]UMC Utrecht, Radiotherapy, Utrecht, The Netherlands
[3]UMC Utrecht, Radiology, Utrecht, The Netherlands

Purpose/Objective: Diffusion weighted MRI (DWI) is increasingly being used in head and neck cancer, where response prediction might become an important application for treatment personalization. DWI and the derived apparent diffusion coefficient (ADC) reflect microstructural features of tissues, as water diffusion can be restricted by cell membranes and tortuosity in the extracellular matrix. In head and neck squamous cell carcinomas (HNSCC), a correlation has been found between local failure after (chemo)radiotherapy and pre-treatment apparent diffusion coefficient (ADC) [1]. However, the pathohistological basis of this correlation is not clear. The aim of this study was to investigate how histological characteristics of HNSCC are related to ADC.
Materials and Methods: Sixteen patients with laryngeal or hypopharyngeal squamous cell carcinomas were enrolled (median age 60 years, range 49-78 years). Before having a total laryngectomy (TLE), patients underwent 1.5 Tesla MRI including diffusion weighted single shot spin echo echo planar imaging (DWI) with STIR fat suppression, TR/TE 5872/70ms, TI 180ms, nsa 4, FOV25x20cm^2, slice thickness 4mm, matrix 121x101mm^2. ADC maps were created with a linear fit of the signal intensity of the DWI with b 150 and 800 s/m^2. After resection, whole-mount heamatoxylin-eosin-stained sections