Table: Spearman's correlation between dosimetric parameters and esophagitis

Parameter	Correlation coefficient	P
Dmax (Gy)	0.226	0.080
Dmean (Gy)	0.342	0.007
V10 (%)	0.297	0.020
V15 (%)	0.301	0.018
V20 (%)	0.309	0.016
V25 (%)	0.304	0.017
V30 (%)	0.370	0.003
V35 (%)	0.419	0.001*
V40 (%)	0.405	0.001
V45 (%)	0.357	0.005
V50 (%)	0.333	0.009
V55 (%)	0.259	0.044
V60 (%)	0.134	0.304
V65 (%)	-0.047	0.718

Abbreviations: Dmax = maximal esophageal dose; Dmean = mean esophageal dose; V10-V65 = percentage of esophageal volume receiving > 10 to 65 Gy; *Greatest statistical significance

1379 POSTER

High-dose rate brachytherapy in uterine cervix cancer: local control, survival and complications of a 10-year Brazilian protocol

S. Aisen, M. Gorayeb, H. Carvalho, J. Petitto, W. Nadalin. *Hospital das Clínicas – University of São Paulo, Oncology – Radiotherapy/InRad, São Paulo, Brazil*

Objectives: Evaluate survival, local control and complications of irradiation alone in the treatment of uterine cervix cancer.
Methods: 874 women treated from January 1991 to December 2001, with squamous cell carcinoma, adenocarcinoma and adenosquamous cell carcinoma of the uterine cervix with no prior treatment. Patients' median age was 53 years (24–85) with a 52 months (6 – 71) median follow-up. The pelvis received 39.6 Gy in a four-field box technique, 1.8 Gy daily, 5 times a week. High-dose rate brachytherapy (HDR) was delivered in 4 weekly fractions of 7 Gy, concomitantly with external radiation (ER). The parametria received a boost of 10–20 Gy, according to clinical stage. The disease free survival and overall survival were calculated by Kaplan Meier actuarial method.
Results: Disease free and overall survival were 67.3% and 65.3% respectively. For clinical stage IB, disease free survival was 90.9%, 84.2% for IIA, 73.2% for IIB, 50% for IIIA, 51.5% for IIIB and 40% for IVA. Karnofsky performance status, clinical stage, tumor volume, and bilateral parametria involvement, negatively influenced local control ($p < 0.001$). The 5-year actuarial survival rates were better for patients with lower clinical stage, no bilateral parametria involvement and tumors <4 cm ($p = 0.05$). Rectal complications were observed in 61 (6.9%) patients, only 14 (1.6%) presented grade 3 and 4, and minor bladder complications in 30 (3.4%).
Conclusion: The results suggest that the association of HDR and ER is a practical, reliable and feasible method of treatment of uterine cervix carcinoma. The results are similar to the worldwide literature and complication rates are low and comparable to conventional techniques.

1380 POSTER

Three-dimensional conformal radiation therapy (3D-CRT) in the treatment of locally advanced non-small cell lung cancer (LAD-NSCLC): Influence of clinical and dosimetric parameters on patterns of failure and survival

M. Moreno Jiménez[1], J. Aristu[1], L. Arbea[1], C. Garrán[1], M. Cambeiro[1], J.M. López-Picazo[2], G. Nagore[1], R. Martçinez-Monge[1]. [1]*Clínica Universitaria, Division of Radiation Oncology, Pamplona, Navarra, Spain;* [2]*Clínica Universitaria, Division of Clinical Oncology, Pamplona, Navarra, Spain*

Background: 3D-CRT selects optimal treatment to increase tumor dose and reduce normal tissue dose, potentially representing an enhancement of the therapeutic ratio of radiation therapy for LAD-NSCLC. The purpose of this study was to assess failure patterns and survival.
Material and methods: Between April 1995 and March 2001, 80 pts (72 males and 8 females; median age: 58 years, range: 32–78) with stage IIIA (20%) and IIIB (80%) NSCLC were treated with cisplatin-based induction chemotherapy (ICT) followed by concurrent chemotherapy (CCT) and hyperfractioned 3D-CRT (1.2 Gy b.i.d.; median dose: 72.41 Gy, range: 54.13–85.89). Potential predictive factors evaluated included clinical parameters (sex, age, performance status, stage, histology, weight loss >5%, tumor site, pre-existing lung disease), therapeutic factors (IQT schedule, 3D-CRT dose, treatment response), and dosimetric factors according to the ICRU definitions (volume and dose of GTV, PTV-2, CTV y PTV-1). Local recurrences were dosimetrically analyzed using dose-volume histograms after definition of the recurrent tumor volumes with the pretreatment CT dataset. Recurrences were divided into four categories, in terms of percentage of recurrent tumor volume located within the high-dose region (95% of the prescription dose): recurrences with more than 95% of their volume within the high dose region were considered "central"; those within 80% to 95%, 20% to 80%, and less than 20% were considered "in-field", "marginal", and "extreme", respectively. The overall survival (OS) and local/distant failure free survival (LFF/DFF) were obtained using the Kaplan-Meier method. Univariate and multivariate analyses were performed.
Results: All patients complete IQT and 3D-CRT. Fifty five pts (82%) received the prescribed CCT. Analysis of the 77 evaluable pts showed that the patterns of failure were loco-regional in 12%, distant metastases in 42% and both in 13%. Loco-regional recurrences were classified as central in 31%, in-field in 16%, marginal in 42%, and extreme in 10%. With a median of follow-up of 4.5 years (range: 13–98 months), the median OS and LFF were 20 months and not reached yet, respectively. The 2 and 5 year OS and LFF were 47% and 9%, and 71% and 54%, respectively. Multivariate analysis showed that age $\geqslant 60$ years, ($HR = 2.47$, $p = 0.01$), GTV >270 cc ($HR = 2.87$, $p = 0.03$), and mean lung dose >25 Gy ($HR = 1.8$, $p = 0.04$), were independently associated with worse OS; PTV-1 >1146 cc ($HR = 3.54$, $p = 0.007$) was the only factor independently associated with worse LFF; and female gender ($HR = 3.7$, $p = 0.003$), nodal stage N3 ($HR = 3.77$, $p = 0.02$) and GTV >270 cc ($HR = 1.1$, $p = 0.02$) were associated with worse DFF.
Conclusions: This study shows that local control was acceptable and was independently related with the PTV-1 size. The great majority of loco-regional recurrences were centrally located (into the high-dose region). Age, GTV and mean lung dose were independent prognostic factors of overall survival. Dosimetric and clinical parameters may contribute to improve radiation therapy results n multidisciplinary protocols of patients with LAD-NSCLC.

1381 POSTER

Prostate and pelvis radiotherapy using IMRT and ultra small superparamagnetic nano-particles to optimise dose to involved lymph nodes

N. van As[1], A. Jackson[2], S. Sohaib[3], C. South[4], E. Charles-Edwards[4], S. Reinsberg[4], M. Leach[4], D. Dearnaley[2]. [1]*Royal Marden Hospital and Institute of Cancer Research, Academic Department of Radiotherapy and Oncology, London, United Kingdom;* [2]*Royal Marden Hospital and Institute of Cancer Research, Department of Radiology, London, United Kingdom;* [3]*Royal Marden Hospital, Joint Department of Radiotherapy Physics, London, United Kingdom;* [4]*Royal Marden Hospital and Institute of Cancer Research, CRUK Clinical MR Research Group, London, United Kingdom*

Purpose: To demonstrate how ferumoxtran (Sinerem) enhanced MRI may help to define the clinical target volume for a lymph node boost with intensity modulated radiotherapy (IMRT) in patients with prostate cancer and pelvic nodal involvement.
Patients and methods: As part of an ongoing phase I dose escalation trial, patients with prostate cancer and either a high risk of, or with overt pelvic nodal involvement are treated with 3 years of androgen deprivation and radiotherapy to the prostate (70 Gy) and pelvic lymph nodes (60 Gy) using an IMRT technique. Overtly involved lymph nodes are boosted with a further 5 Gy. Two patients with prior suggestion of pelvic nodal involvement radiologically, underwent MRI before and after administration of the ultrasmall superparamagnetic iron oxide (USPIO) contrast agent ferumoxtran (Sinerem®, Guerbet, Paris, France). A novel flat top couch insert was used for MRI scanning to give better comparability with the planning CT scan. The MR images were used in conjunction with the planning CT to define the nodal boost volume.
Results: Pre-treatment imaging had demonstrated suspicious lymph node enlargement in both obturator regions in one patient and the pre-sacral region in the other. At the time of planning CT and ferumoxtran contrasted MRI, each patient had received androgen deprivation for 12 months. For the first patient, the radiotherapy planning CT scan showed probable lymph nodes at the previously noted sites, with the left obturator node measuring 8 mm in its short axis diameter. MRI following ferumoxtran showed signal retention typical of malignant infiltration at the sites of previously suspected lymphadenopathy, whereas there was the expected signal loss due to uptake of USPIO contrast in other nodal areas. Fig 1a and 1b show the pre and post ferumoxtran MR images respectively for the first patient. A suspicious lymph node in the left obturator region is arrowed. The MR images facilitated segmentation of the suspicious lymph nodes using co-

registration with the radiotherapy planning CT in the first patient, and with reference to bony anatomical landmarks in the second. A radiotherapy boost dose was then delivered to the sites of lymphatic involvement using an IMRT technique. Fig 1c shows the radiotherapy dose distribution for the first patient at the level of the involved lymph node in the left obturator region.

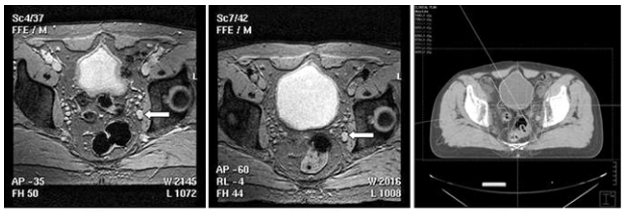

Fig 1a Fig 1b Fig 1c

Fig. 1

Discussion: MR scanning pre and post ferumoxtran at the time of the radiotherapy planning scan can provide clarification of pelvic lymph node status in patients with suspicious radiological findings at presentation. Such MRI images can be co-registered with the planning CT in order to achieve more precise target definition.

1382 POSTER

Validation of perfusion computed tomography (CT) parameters as surrogate markers of hypoxia in squamous cell carcinoma of the head and neck

K. Newbold[1], A. Sohaib[1], I. Castellano[2], D. Mears[2], R. A'Hern[1], P. Rhys-Evans[1], C. Fisher[1], K. Harrington[1], C. Nutting[1]. [1]*The Royal Marsden NHS Trust, Head and Neck Unit, London, United Kingdom;* [2]*The Royal Marsden NHS Trust, Sutton, United Kingdom*

Background: Hypoxia is a determinant of radiation responsiveness and correlates with outcome in squamous cell carcinoma of the head and neck (HNSCC). A non-invasive method for identifying areas of reduced oxygenation within tumours may enable radiotherapy planning and delivery to be individually optimised.
Aim: To validate perfusion CT parameters as surrogate markers of hypoxia in HNSCC. These parameters were compared to pimonidazole hydrochloride, an extrinsic marker of hypoxia.
Methods: 48 measurements of perfusion CT parameters from 12 regions of interest (ROIs) were made in 5 patients with HNSCC prior to surgical resection. All scans were performed on a GE Lightspeed 16® scanner. The CT protocol includes a cine perfusion sequence with a rotation time of 1 sec, total acquisition time of 50 secs, using 80 kV and 100 mAs. Intravenous contrast agent, iohexol 300 was injected at a dose of 0.5 ml/kg at 4 ml/sec. Perfusion CT parameters are analyzed using GE CT Perfusion 3® software which yields parameter maps of tissue blood volume, BV(ml/100 g); blood flow, BF (ml.100 $g^{-1}min^{-1}$); mean transit time, MTT(s) and microvascular permeability surface area product, PS (ml.100 $g^{-1}min^{-1}$). 0.5 g/m^2 pimonidazole hydrochloride was administered intravenously 16–20 hours before surgery. At resection the tumour was orientated such that the pathological specimen was sectioned in the image plane. The pimonidazole uptake was identified by immunohistochemistry. A histological section within the tumour was matched to the corresponding image slice and corresponding ROIs drawn on both the image slice and the section. The percentage of pimonidazole staining within the ROIs defined the hypoxic fraction. Correlations between the perfusion CT parameters and the hypoxic fraction were assessed using the Spearman rank correlation coefficient (Rs).
Results: see table 1

	BF		BV		MTT		PS	
Min	Mean	Min	Mean	Max	Mean	Max	Mean	
Rs	0.726	0.389	0.583	0.483	−0.431	−0.431	−0.536	0.35
95%CI	0.242 to 0.92	−0.256 to 0.794	−0.005 to 0.872	−0.144 to 0.834	−0.812 to 0.209	−0.812 to 0.209	−0.854 to 0.075	−0.298 to 0.777
P	**0.01**	0.23	**0.05**	0.12	0.18	0.18	0.08	0.29

Conclusion: These preliminary results suggest that selective parameters derived from perfusion CT may be of use as surrogate markers of hypoxia in HNSCC. Such a non-invasive, spatial mapping of intratumoural hypoxia may enable targeted radiation dose escalation to radioresistant clonogens with the potential for improved local control and survival in this group of patients.

1383 POSTER

Dosimetric parameters on the development of radiation pneumonitis – the significance of topographic dose distribution

S.S. Kim, H. Bae, H.C. Park, B.C. Cho. *Hallym University Sacred Heart Hospital, Radiation Oncology, Anyang-Si, Korea*

Background: A variety of different dose-volume histogram (DVH) parameters have been reported to be correlated to the incidence of radiation pneumonitis (RP). But these DVH parameters do not take topographic dose distribution of lung into account. We tried to reveal the correlation of incidence of RP and the topographic dose distribution of lung including other known several DVH and clinical parameters.
Material and methods: From July 2000 to October 2004, of patients irradiated for small and non-small cell lung cancer, 63 patients who received more than 50 Gy and were followed-up for more than 6 months were analyzed for RP according to National Cancer Institute Common Toxicity Criteria. There were 46 males and 17 females and median age was 70 years (35~91 years). ECOG performance score was PS 0–1 in 29 and 2 or more in 34 patients. Most patients were stage III (I-II 4, IIIa 13 and IIIb 46). Prior to radiation therapy, five patiens received open thoracotomy without lung resection and 25 patients received induction chemotherapy. Concurrent chemotherapy was given to 23 patients during the radiation therapy. After acquisition of planning CT, 3D planning and dosimetric calculations were done with Pinnacle[3]® (Philips, USA). Total dose ranged from 50.0–70.2 Gy (median 63.0) with conventional fraction size (1.8–2.0 Gy). Analyzed parameters included clinical (age, gender, performance status, Stage, FEV1, open thoracotomy and induction or concurrent chemotherapy) and DVH (mean lung dose (MLD), V20 and V30) parameters. After dividing the normal lung volume into total (TL), involved lateral (IL), upper (UL) and lower (LL) (with equal volume), topographic distribution of DVH parameters were also analyzed.
Result: Median follow-up period was 13 months (6–52 months). Grade 2 or higher RP developed in 17 patients (27%). Median time to development of Grade 2 or higher RP was 3 months (2~14 months). Induction chemotherapy reduced the incidence of RP ($p = 0.0258$). Other clinical parameters did not influence on the incidence of RP. Total prescribed dose did not influence on the RP incidence ($p = 0.3852$). DVH parameters of upper half lung (MLD_UL, V20_UL and V30_UL) were not significant. On the other hand, although the mean value of MLD_LL was lower than that of MLD_UL (7.3 Gy vs 21.1 Gy, $p = 0.000$), parameters of lower half lung were all significant ($p = 0.0166$ for MLD_LL, 0.0027 for V20_LL and 0.0164 for V30_LL). MLD_TL also showed statistical significance ($p = 0.0206$), but other parameters of involved lateral and both lung did not show consistency.
Conclusions: Lower half lung seemed to be more sensitive to radiation pneumonitis. This topographic difference of the vulnerability to radiation pnuemonitis should be taken into account at the time of radiation therapy planning and biological response modeling.

1384 POSTER

Interclinican variability in delineation of tumour volumes for glioblastomas with the assistance of MRI fusion

S. David, M. Back, R. Mukherje, K. Lim, J. Liade. *National University Hospital, Singapore, Radiotherapy Centre, Singapore, Singapore*

Background: The aim of this study is to assess the intra- and interclinician variability in contouring target volumes of glioblastomas in the post-operative setting with and without the assistance of pre-operative MRI fusion.
Methods and materials: 8 clinicians participated in the study (including a radiologist) and were asked to contour tumour volumes on 2 randomly selected patients with typical glioblastomas. Both patients underwent pre-operative imaging with an MRI, followed by debulking surgery. Planning CTs were then performed post-operatively. Clinicians were asked to contour gross tumour volumes (GTVs) on the planning CT (GTV-CT), using the pre-operative MRI films as a guide to the tumour bed. This process was then repeated with on a fused CT-MRI image. Clinicians expanded the fused GTV (GTV-MRI) a planning target volume (PTV) using the EORTC guidelines (2–3cm margin). Variability was analysed in terms of total volume and position (by comparing the centre of the volumes (COV) in the x, y and z planes and by the amount of non-overlap (residual volumes) between the volumes).
Results: There was a significantly lower inter-clinician variability in the GTV-MRI volumes compared with the GTV-CT in cubic centimetres (standard deviation of 35 and 14 respectively, $p = 0.002$). Expansion to a PTV from the GTV-MRI resulted in an increase in the variability of the volumes (standard deviation = 22). The location of the COV of the GTV-MRI was less variable than the COV of the GTV-CT in 3 planes. The average spread of the COV in the x-, y-, and z-planes for both patients in cm was 0.93, 1, and 1.2 for the GTV-CT and 0.36, 0.25 and 0.6 for the GTV-MRI. The residual volumes in comparing the GTV-CT and GTV-MRI expressed