(37–58). Dose per fraction was 2 Gy in the majority of the patients (n = 70). Prior to RT, all patients were tested using a rapid (48 h) apoptosis assay where fresh blood samples were irradiated with 8 Gy X-rays. Lymphocytes were collected and prepared for flow cytometric analysis. Apoptosis was assessed by gradual degradation of DNA (sub-G1 peak on the DNA histogram). Acute (CTC v2.0) and late (RTOG/EORTC) toxicities were graded in all patients. Median follow-up period was 31 months (23–43).
Results: Following in vitro 8 Gy irradiation, median radiation-induced CD8 apoptosis was 20.88% (5.69–57.00%). Radiation-induced CD8 apoptosis significantly predicted grade 2 and 3 late effects. The area under the curve of the receiver-operated characteristic curve (sensitivity versus 1-specificity) of CD8 apoptosis was 0.83. Median time to locoregional relapse was 30 months (1–43 months). There were 13 locoregional relapses among the 37 patients showing CD8 apoptosis below the median compared to 5 of 38 who were above (p = 0.02). Two-year estimated locoregional relapse rate was 31% (95% CI: 17–45%) versus 14% (95% CI: 3–25%), respectively (p = 0.03).
Conclusions: In patients with head and neck cancer treated with definitive or postoperative RT, in vivo apoptotic response of CD8 lymphocytes depends on genetic radiosensitivity, and the tumor follows the same genetic radiosensitivity of normal tissues. However, these findings should be confirmed prospectively, and future dose escalation studies could be stratified using the apoptosis assay.

1392 POSTER

Tolerance and efficacy of high-dose 3D-Conformal Radiation Therapy (CRT) in cirrhotic patients with small hepatocellular carcinomas (HCC) not suitable for curative therapies

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Background: Patients (pts) presenting with small size hepatocellular carcinoma (HCC) benefit from curative therapies (liver transplantation, surgical resection or percutaneous destruction) when others are only candidates for palliative options. Although conventional external radiotherapy is regarded as little efficient and potentially toxic in cirrhotic pts, 3D-conformal RT (CRT) for single HCC nodules demonstrated promising results.
Methods: Prospective phase 2 trial was conducted in 26 pts with small HCC (1 nodule $\leqslant$5 cm, or 2 nodules $\leqslant$3 cm), Child-Pugh A (15), B (8), 19 males, 7 females, mean age 70 (range 57–88 years), TNM stage I-II, mean tumor size 3.2 cm. The endpoints were the rate of complete tumor response, assessed by contrast-enhanced spiral computed tomography showing disappearance of the arterial contrast enhancement observed on 2 successive examinations at 3 mo interval, and assessment of toxicity, using NCI then RTOG-EORTC scales.66 Gy (2 Gy/fx, 5 D/W) was delivered with CRT, respiratory gating was used for recently enrolled pts. Liver dose-volume histograms (DVH) and normal tissue complication probability (NTCP) values were used to evaluate tolerance of 66 Gy.
Results: Out of the 23 currently evaluable pts, 18 (78%) achieved a complete tumor response, maintained with time (local control), and 5/23 demonstrated no response, after 6 months. 2 pts relapsed on the irradiated tumor bed at 12 and 30 months respectively. No G4 toxicity was observed in 16 Child-Pugh A pts, G3 asymptomatic biochemical toxicity was observed in 2 pts. G4 biochemical toxicity was observed in 2/9 pts, Child-Pugh B (thrombocytopenia, hyperbilirubinemia). Biochemical toxicity G3 was observed in 4 pts. 1 a G3 clinical toxicity (portal hypertensive bleeding), 1 jaundice with edema and ascites at 1 mo.
Conclusion: This phase II trial demonstrate that high Dose 3D-Conformal RT can induce complete tumor response, maintained with time (local control) in 78% of pts, with a good tolerance in cirrhotic pts, especially in Child-Pugh A pts. Nine percent of local relapse have been observed with a 17 months follow-up. This non invasive technique is highly suitable for some central or superior tumor locations, unreachable by percutaneous destruction. The future study will compare percutaneous destruction to 3D-CRT using an accelerated fractionation, in pts presenting with small size HCC. Updated results will be presented at the meeting.

1393 POSTER

Comparison of setup accuracy of two commercially available immobilization systems for the treatment of head and neck tumors using simulation CT imaging

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Objective: To compare the setup accuracy, comfort level, and ease of use of two immobilization systems used in head and neck (H&N) radiotherapy.
Methods: 21 patients undergoing radiation therapy for H&N tumors were consecutively assigned to one of two immobilization devices: a standard thermoplastic head-and-shoulder mask fixed to a carbon fiber base (Type S) or a thermoplastic head mask fixed to the Accufix™ cantilever board equipped with the shoulder depression system. All patients underwent planning CT imaging followed by repeated control CT imaging under simulation conditions during the course of therapy. CT images were subsequently fused and Setup accuracy was examined by recording displacement in the 3 Cartesian planes at 6 anatomical landmarks and calculating 3-D vector errors. In addition, the time required for setup and the comfort of the two systems was surveyed.
Results: A total of 64 CT datasets were analyzed. There was no difference in the Cartesian total displacement errors between the two populations at any landmark considered. Total vector displacement in the Type S arm reached a SD of 1.77, 1.78, 2.25, 4.77, 6.87, and 3.38mm at the odontoid, right styloid, left styloid, C7 spinous process, right and left acromial extremities, respectively. The Accufix™ system respective displacements are 1.26, 1.16, 1.08, 7.54, 5.36, and 2.78mm. Nonetheless, there was a trend towards a smaller population mean systemic error for the upper landmarks as a single group favoring the Accufix™ system. There was no difference in the setup time required and comfort level between the two systems.

Mean Systematic 3D errors in 21 patients treated for head and neck tumors [a]

Immobilization Device	Systematic 3D error (mean ± 1SD, mm)							
	Odontoid	Styloid		C7 Spinous process	Clavicle		Landmarks	
		Right	Left		Right	Left	Upper[b]	Lower[c]
Type S	2.88 ±1.21	2.91 ±1.44	3.57 ±2.06	8.83±3.13	10.04 ±6.07	5.08 ±2.08	3.12 ±1.59	7.98 ±4.52
Accufix™ System	3.00 ±0.96	2.60 ±0.91	2.71 ±0.91	10.21±7.24	8.03 ±5.13	5.65 ±2.37	2.77 ±0.92	7.96 ±5.47

[a] Setup errors were assessed for each anatomical landmark according to the type of device (10 patients for Type S and 11 patients for the Accufix™ System).
[b] Odontoid, right and left styloid.
[c] C7 spinous process, right and left clavicles (acromial extremities).

Conclusions: No significant difference in 3D setup accuracy was identified between the standard thermoplastic head-and-should mask system and the thermoplastic head mask fixed to the Accufix™ system. The study reassures us that our technique provides accurate patient immobilization, allowing us to limit our PTV to <4 mm when treating H&N and base of skull tumors.

1394 POSTER

The impact of half-body irradiation on quality of life of patients with multiple bone metastases

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Background: Half-body irradiation (HBI) is palliative treatment of cancer patients with painful, skeletal dissemination. Using HBI, we obtain pain relief and decrease of analgesics intake. The aim of this study was an evaluation of HBI impact on quality of life (QL).
Material and methods: Material comprised of 80 patients (38 W, 42 M), aged from 31 to 83 (mean 61) treated by one fraction HBI because of multiple skeletal metastases. The most frequent diagnoses were breast (26) and prostate (24) cancers. The most numerous histopathological diagnosis was adenocarcinoma (53). 29 patients had upper (UHBI), 47 lower (LHBI) and 4 middle (MHBI) HBI. The dose of 6 Gy was delivered for UHBI and 8 Gy for L and MHBI. All patients were examined in HBI day, 2 weeks later, and next every month. The pain intensity in 11 degree scale (0–10), performance status (PS) and QL in 7 degree scale (1 - very bad, 7-excellent), and pain frequency in 4 degree scale (1 - never, 4- very often) were evaluated using EORTC QLQ-C30 form. Means of particular variables

were calculated. Differences between analyzed data were checked by t tests. Analysis regarded only to 4.5 months after HBI because poor data in the later period.
Results: Pain level decreased during 2 weeks (from 6.2 to 3.3) and left on similar level (3.8 4 months later). Pain frequency decreased from 3.2 to 2.8 within two weeks, and next to 2.1 during 4 months. PS and QL did not increase during analyzed period (3.3 at the beginning, 3.4 at the end in both cases). Significant differences between pain intensity in HBI day and 0.5, 1, 2 months later ($p = 0.00007$, $p = 0.0006$, $p = 0.02$ respectively), between pain intensity 2 and 3 months after HBI ($p = 0.04$) and between pain frequency in HBI day and 0.5 and 1 later ($p = 0.04$, $p = 0.02$) were found. No significant differences between PS and QL in particular controls were found. Pain intensities were similar for U and LHBI (6.4, 6.2 in treatment day) and did not differ significantly during follow up. There was found one significant difference for pain frequency two weeks after HBI (2.4 UHBI, 3.1 LHBI, $p = 0.03$). There were no differences between U and LHBI regarding PS and QL.
Conclusion: Obtained results allow to form conclusion that HBI is good method of palliative, analgetic treatment of disseminated cancer patients not influencing significantly quality of their life.

1395 POSTER

Chemoradiation with concomitant boost followed by radical surgery in locally advanced cervical cancer: a dose-escalation study

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Seventeen patients were enrolled into a phase I study performed to determine the maximum tolerated dose of external radiotherapy in a scheme of neo-adjuvant chemo-radiation, followed by radical surgery, for locally advanced cervical cancer (FIGO stages IIb-IIIb).
Patients were submitted to a radiochemotherapeutic schedule of 3960 cGy in 22 fractions on pelvic lymph-nodal stations. During the first and the last week of treatment a combination of cisplatin (20 mg/mq/die, i.v., days 1–4) and 5-fluorouracil (1 g/mq/die, continuous venous infusion, days 1–4, no more than 1.5 g/die) was administered. The dose-escalation of external radiotherapy was delivered on the primary tumor, through the concomitant boost technique (90cGy per fraction), administering 3 different dose levels: 1) one weekly boost for a total dose of 4320 cGy; 2) two weekly boosts, total dose 4680 cGy; 3) three weekly boosts, total dose 5040 cGy. The MTD was not reached yet, being the only toxicities observed, represented by neutropenia G3 (3 cases), thrombocytopenia G3 (one case) and diarrhoea G2 (two cases) easily managed. Epoetin was given to 2 patients, Granulocyte-colony stimulating factor (G-CSF) was administered to 3 patients. Thirteen patients underwent so far radical surgery, and are therefore evaluable for pathological response. Among them 11 complete remissions (84.6%; 95% CI: 43.7–98.4, including one microscopical partial response), one partial response (7.7%; 95% CI: 0–40.2) and 1 progression (7.7%; 95% CI: 0–40.2) have been registered.
These data are preliminary, final results will be available by the time of the meeting, but the high percentage of pathological complete remissions in the absence of any major acute toxicity warrants the start-up of a phase II study.

1396 POSTER

Dynamic versus static ventilation derived from radiotherapy planning CT images

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Purpose: We propose to evaluate differences in regional lung ventilation between static and dynamic respiration using radiotherapy planning CT images. A difference in regional ventilation would suggest a discrepancy between the functional lung planned for treatment and the lung actually receiving radiation.
Methods: Regional lung ventilation was examined with paired exhalation (eBH-CT) and inhalation (iBH-CT) CT images registered to corresponding 4D-CT data sets. All CT sets were acquired in the same session with the patient in the identical position during routine clinical treatment planning for tumor motion evaluation. Contoured lung volumes were constructed for the BH-CT images and for peak inhalation and exhalation from the 4D-CT images. The peak expiratory and inspiratory 4D-CT image pairs and the eBH-CT and iBH-CT image pairs for each lung were mapped voxel by voxel using deformable image registration. The CT values for each corresponding tissue element were used to calculate the change in fraction of air per voxel (regional ventilation). Ventilation images were calculated for each CT pair. The regional differences between the 4D CT and the BH-CT derived ventilation were compared.
Results: Radiation planning CT images from 23 patients were obtained. Preliminary analysis of the first ten patients was performed. Tidal volumes (TV) between 4D- and BH-CT showed no correlation (mean of 921.4 cm^3 and 430.3 cm^3, respectively.) Regional lung ventilation comparison between right and left lungs, adjusted for CT number calculated lung mass, showed wide variability for 4D-CT and no correlation between BH- and 4D-CT sets (see figure 1).

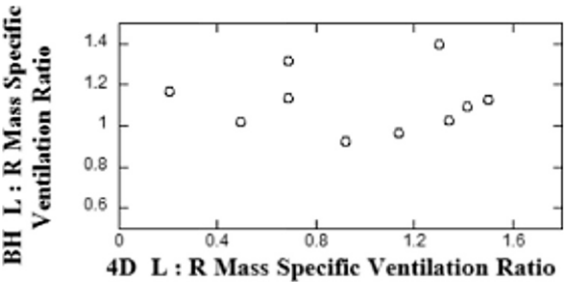

Fig. 1

Conclusions: Significant differences in regional ventilation exist between static BH-CT and dynamic 4D-CT derived ventilation. The use of dynamic CT data sets for radiation treatment planning may more accurately reflect tumor motion and underlying regional pulmonary function.

1397 POSTER

Optimal dose and fractionation for combination external beam radiotherapy and high-dose-rate intracavitary brachytherapy for uterine cervical cancer

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Background: To find optimal practice guideline about an optimal dose and fractionation for definitive radiotherapy for uterine cervical cancer.
Materials and methods: The subjects were 743 patients (Stage IB 198, IIA 77, IIB 364, IIIA 7, IIIB 89, IVA 8) with cervical cancer treated by radiotherapy alone from 1990 to 1996. A total dose of 23.4~59.4 Gy (Mo 45.0) of external beam radiotherapy (EBRT) was delivered to the whole pelvis. High-dose-rate intracavitary brachytherapy (HDR-ICBT) was also performed by various fractionation schemes. A Midline block (MLB) was begun after the delivery of 14.4~43.2 Gy (Mo 36.0) of EBRT for 495 patients while it couldn't be used for the other 248 patients due to slow tumor regression or huge initial bulk of tumor. The point A, actual bladder & rectal doses were assessed individually for all the patients. The biologically effective dose (BED) was calculated to the tumor ($\alpha/\beta = 10$) and late-responding tissues ($\alpha/\beta = 3$) for both EBRT and HDR-ICBT. The total BED values to point A, actual bladder and rectal reference points were the summation of those of EBRT and HDR-ICBT.
Results: The overall complication rate was 33.1% for RTOG Grade 1–4 toxicities. The 5-year actuarial pelvic control rate was 83% for all 743 patients. Median cumulative values of point A BED for tumor (A-BED Gy_{10}) was 93.0 Gy_{10} (range: 62.0~121.9), and for late responding tissue (A-BED Gy_3) was 137.6 Gy_3 (range: 93.6~187.3). Median cumulative values of actual rectal (R-BED Gy_3) and bladder point BED (B-BED Gy_3) were 118.7 Gy_3 (range 48.8~265.2) and 126.1 Gy_3 (range: 54.9~267.5) respectively. A-BED Gy_3 showed good correlation with rectal complications ($p = 0.003$), but not with bladder complications ($p = 0.095$). R-BED Gy_3 had very strong association ($p \leqslant 0.0001$), which is more predictive for rectal complications than A-BED Gy3. B-BED Gy_3 also showed significance in prediction for bladder complications in trend test ($p = 0.0298$). Any dose-response relationship for pelvic control was not observed.
Conclusions: This study demonstrated the strong predictive value of actual rectal and bladder reference dosing in radical radiotherapy for uterine cervical cancer. Present results suggested that R-BED Gy_3 should be kept below 125 Gy_3 to confer an acceptable late complication rate. To keep the total delivered dose less than threshold for the complication, early midline shielding, HDR-ICBT total dose and fractional dose reduction can be considered.