1. Plating efficiency depends on the total number of surviving cells after treatment.

2. Linearity of plating efficiency should be tested first within a range before drawing conclusions from clonogenic assays.

835 POSTER

MODIFICATION OF THE SPARING EFFECT OF USING LOW DOSE RATE TOTAL BODY IRRADIATION ON MURINE PULMONARY TOXICITY BY CYCLOPHOSPHAMIDE

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We have thus tested the effect of radiation dose rate and combining cyclophosphamide (CTX) with single fraction TBI on lung damage in a mouse model for BMT. Total body irradiation (TBI) was given as a single fraction at high dose rate (HDR, 0.71 Gy/min) or at low dose rate (LDR, 0.08 Gy/min). CTX (250 mg/kg) was given 24 hours before TBI. Bone marrow transplantation (BMT) was performed 4–6 h after the last treatment. Lung damage was assessed using ventilation rate (VR) and lethality between 28 and 180 days ($LD_{50/28-180}$). The LD_{50} for lung damage increased from 12.0 Gy (± 0.2) using single fraction HDR to 15.8 Gy (±0.6) using LDR. The LD_{50} values for the combined treatment were 5.3 Gy (±0.2) and 3.5 Gy (±0.2) for HDR and LDR, respectively. This indicates that the combined effect of LDR and CTX was more toxic than that of combined CTX and HDR. Lung damage evaluated by VR demonstrated two waves of VR increase within the first 180 days after treatment. We conclude that lung damage following TBI could be spared using LDR, however, CTX markedly enhance TBI-induced lung damage. The combination of CTX and LDR is more toxic to the lungs than combining CTX and HDR.

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836 POSTER

P16 AND P53 LEVELS AFTER DIFFERENT TREATMENTS IN HUMAN TUMOR CELLS

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It has been suggested that the product of p53 gene inhibits cellular growth by stimulating the production of p16 protein. We have examined by ELISA the protein levels of pl6 (ranged 0.80–3.44 O.D. unit per 10^6 cells) and p53 (ranged 2.20–4.65 O.D. unit per 10^6 cells) in human tumour cell lines. We have not found a quantitative relationship between these protein levels: neither in standard growth conditions nor after 6 Gy of radiation. The p53 product function has been surveyed by flow cytometry studying G0/G1 cell cycle arrest after irradiation of the cells at 6 Gy. Taking into account that concept we have divided our cell lines in two groups (A) cells with functional p53 protein and (B) cells with functional inactivation of the p53 gene product. Higher constitutive levels of p16 product were found in group A cells. Intracellular p16 levels change after 6 Gy but not a defined time course profile has been found. We have identified that p16 levels change markedly with growth conditions, ie, age of culture, growth rate modified by use of differents serum levels or after hormonal synchronization of human breast cancer cell lines. The implications of this for the radiation response and cellular proliferation of human tumour cell lines remains to be determined.

837 POSTER

COMPARISON OF RADIATION-INDUCED TRANSLOCATIONS IN EARLY AND LATE PASSAGE TUMOR CELLS BY FISH

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Chromosomes No 1, 2, 3, 4, 9 and 12 in early (1–3rd) and late (25–30th) passage cells derived from a *squamous cell carcinoma of the gingival mucosa* were analyzed. Translocations in unirradiated as well as in irradiated (D = 4 Gy) cells were determined by painting whole chromosomes with fluorescent hybridization probes (FISH). A radiation-induced polyploidization of all chromosomes analyzed was observed with the only exception of chromosome No. 4 in late passage cells. The frequency of radiation-induced translocations as well as the clonogenic cell survival was similar in early and late passage cells but translocation frequencies were not always proportional to the length of the corresponding chromosomes. The rate of spontaneous translocations was different for individual chromosomes and was not correlated with their radio-sensitivity.

When compared with the more radioresistant fibroblasts HSF-2 and the more radiosensitive breast cancer cells MCF-7, the investigated tumor cells showed a medium radiosensitivity with respect to both, translocation frequencies and clonogenic cell survival.

838 POSTER

S PHASE DURATION IN RELATION TO S PHASE FRACTION AS SIMULATED BY A COMPUTERIZED MODEL

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For several tumour types it has been found that there is a correlation between clinical outcome and the relative number of tumour cells in S phase as measured with DNA flow cytometry (FCM). From data showing that a high S phase fraction is associated with poor prognosis it has been concluded that these tumours have a high proliferative activity and therefore grow faster. Moreover, the size of the S phase fraction has also been used as an equivalent of labelling index to determine tumour growth fraction in experimental cell kinetic studies. In the present study the relationship between DNA distribution and the duration of cell cycle phases in tumours was investigated with the aid of a computerized mathematical model. In our study we found poor correlation between the size of the S phase fraction and the proliferative activity when tumour growth fraction was taken into account. A shortening of the duration of the S phase ie, increased cell production per time unit, led to a decrease in the relative number of S phase cells as measured by FCM.

839 PUBLICATION

CLINICAL RADIOBIOLOGY OF HDR CF-252 BRACHYTHERAPY FOR CERVIX UTERINE CARCINOMA

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45 pts (I) with cervix uterine carcinoma received combined radiation therapy; external Co-60 gamma therapy (37.3 Gy) for pelvis and HDR Cf-252 brachytherapy (point A—35, Gy-eq). The treatment results were compared with historical similar group—64 pts (II) treated by external Co-60 gamma therapy (39.7 Gy) and HDR Co-60 brachytherapy (point A—47.4 Gy).

There were no significant difference in 4 yr survival: 73.3% (I) vs 79.7% (II). Local failure was observed in 22.2% (I) and 10.9% (II) cases. The rate of late radiation complications was similar—4.4% (I) vs 1.6% (II). Acute reactions were brachytherapy dose dependent with ED50:80, 1 Gy-eq and 74.5 Gy in I and II groups, respectively.

Radiobiology analysis of obtained data show some possibilities to improve treatment results in HDR Cf-252 brachytherapy group.

840 PUBLICATION

A RADIORESISTANT LINE OF RAT GUERIN'S CARCINOMA: ITS OBTENTION, PROPERTIES AND A REGIMEN OF RADIOTHERMOTHERAPY

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We obtained a radioresistant line of rat Guerin's carcinoma through repeated courses radiotherapy (5 sessions of 10 Gy each). We followed 14 subsequent passages of the line, revealed a complex of signs testifying to radioresistance of tumor cells: an increase in their morphologic heterogeneity, nuclear and cellular area, number and size of nucleolus and number of binuclear cells. We proved alterations in the subpopulation composition of Guerin's carcinoma cells with an increase in the proportion of slowly proliferating but more radioresistant cells. A radioresistant line also features increased antioxidative activity of tumor cells, levels of non-protein thyol groups, induction of stress proteins with 140–150 kDa, whose levels are the same between the courses of radiotherapy, as well. It is experimentally shown that hyperthermia before radiotherapy effective