in vivo has been determined by plating *in vitro* for two types of tumour. Results obtained for growth delay and cell reproductive death indicate that, for different tumour types, the influence of the factors mentioned varies and that interpretation of tumour responses is only possible if all factors are adequately evaluated. For instance, a rat sarcoma, R-1, shows a short growth delay of 15 days after 2000 rad of X-rays because hypoxic surviving cells respond by an increased rate of cell proliferation, whereas a rat squamous cell carcinoma, RUC-2, experiences a delay of only 10 days after 2000 rad of X-rays because it consists of cells which exhibit a high intrinsic resistance to radiation.

Tumour regression and radiation response

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The rate of tumour regression after irradiation is a poor indicator of the number of tumour cells that have been killed. It may, however, be a useful prognostic indicator of the extent of re-oxygenation during fractionated radiotherapy, which would affect the tumour radiosensitivity.

Tumours of different histological types regress at different rates after irradiation. Carcinomas often regress quickly; sarcomas often regress very slowly or not at all. This relates to the proliferation characteristics in that carcinomas have a high cell-loss factor and a constant balance between cell production and cell loss. If cell production is halted by irradiation, rapid shrinkage could result from the normal cell-loss processes. Re-oxygenation is much more effective in the three rapidly shrinking carcinomas that have been studied than in the three slowly shrinking sarcomas.

Within one histological type of tumour, the C3H mammary carcinoma, regression during fractionated treatments has been analysed in relation to the local control of each tumour at 150 days. A significant correlation was seen between shrinkage and cure rates for 3F/4 days, 9F/10 days and 15F/18 days. A weaker correlation was seen for 9F/18 days and within one week after single doses. Thus, even within one tumour type, a high rate of shrinkage may lead to an increase in the radiosensitivity of the tumour.

Importance of recruitment of non-proliferating Q into proliferating P cells for the growth of an experimental rhabdomyosarcoma before and after irradiation with X-rays

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To improve radiation and chemotherapy regimens by enhancement of the selective destruction of the clonogenic tumour cells, it is important to obtain information on the variation in the fractions of clonogenic P and Q cells in tumours before and after therapy. The cell kinetic factors involved are: the net rates of production and loss of clonogenic and non-clonogenic P and Q cells, their life-span and the rate of recruitment of Q into P cells. This latter factor and the significance of hypoxia with respect to the P or Q status of the cells have been studied for the R-1 rhabdomyosarcoma by employing the semicontinuous labelling technique and autoradiography. Animals were injected with up to seven repeated doses of ^{3}HTdR within 30 hours. Half of the labelled tumours received an acute dose of 800 rad of 300 kV X-rays 15 min before the animals were killed, in order to induce reproductive death in more than 99 per cent of the well-oxygenated cells. A slice of each tumour was fixed and used for measuring the fraction of labelled tumour cells, LI_{tumour}; from the remaining tissue of each tumour a single cell suspension was prepared for plating *in vitro*. From cultures incubated for periods of 12, 24, 48, and up to 120 h the fractions of labelled cell foci, LI_{fo}, per culture were measured.

Analysis of the variation in LI_{tumour} as a function of time and of the number of injections indicates that the rate of recruitment of Q into P cells is less than 1 per cent per hour in unirradiated tumours.

Comparison of data on LI_{fo} measured for irradiated and unirradiated tumours indicated that clonogenic Q cells were more abundant among the fraction of clonogenic cells which survived 800 rad of X-rays. These results may also be important in explaining the delay of the rapid repopulation by clonogenic cells observed in R-1 tumours after acute irradiation with 2000 rad of X-rays, namely by assuming that this repopulation results from surviving hypoxic clonogenic Q cells.

Comparison of DNA histograms of cultured cells and corresponding solid tumours and their relation to data from autoradiographic analysis

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In the studies presented, a comparison is made between G_1, S, G_2+M fractions of a R-1 cell population in culture as derived from DNA histograms and from pulse-labelled mitosis curves. The same comparison is made for R-1 cells grown in solid sarcomas, which develop on injection of these cells into rats. In addition to fractions of cells in the various phases of the cell-cycle, fractions of cycling (P) and non-cycling (Q) cells are determined by both methods and compared.

A good correlation cannot always be shown between cell proliferation parameters of the solid tumour as determined by autoradiography and flow cytofluorimetry. Comparison with *in vitro* measurements does not satisfactorily clarify these discrepancies. The use of drugs, e.g. vinblastine, offers perspectives for the analysis of cell proliferation kinetics.

Tumour cell survival *in vivo* and *in vitro*; implications of recovery from potentially lethal damage

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The response of a transplantable mouse tumour to radiation has been measured in terms of the probability of local tumour control and of tumour cell survival *in vitro* after irradiation *in vivo*. The two methods of assay lead to apparently contradictory conclusions as regards the hypoxic proportion of cells in the tumour and the TCD_{50}, the dose of radiation to cure 50 per cent of a population of mice of their tumours. The hypoxic fraction and TCD_{50} measured using tumour control probability as the end-point were approximately 100 per cent and 78 Gy, respectively, whereas the values deduced from the (*in vitro*) cell survival curves were 5 per cent and approximately 50 Gy. The naturally hypoxic cells of this tumour are capable of recovery from potentially lethal damage (p.l.d.). This recovery reaches a maximum by about four hours after irradiation, the effect being to increase the D_0 of the survival curve for the hypoxic cells by a factor of 1·3 to 1·4. This recovery from p.l.d. can, in part, explain the discrepancies in the estimates of the hypoxic fraction and TCD_{50}.

The implications of recovery from p.l.d. on *in situ* assays of tumour cell response to radiation were discussed, with particular reference to measurements of re-oxygenation.

Measurement of cell surviving fraction following chemotherapy of the EMT6 mouse tumour—the problem of 'potentially lethal damage'

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The response of the EMT6 mouse tumour to a range of cytotoxic drugs has been determined using both serial measurements of tumour volume and *in vitro* assay for surviving fraction. For cyclophosphamide and BCNU, the cell survival measured 2 hours