November 2, 1971

Active Bone Marrow Dose Related to Hematological Changes in Whole Body and Partial Body Exposures

We have been interested in finding an approach to allow the prediction of hematologic changes to be expected following uniform and non uniform exposures (whole body, upper body, lower body, & trunk) used in this program in the treatment of cancer patients. A quantitative approach to evaluating the effects of non-uniform exposure has been proposed in the literature. In applying this approach to our specific project, one has to know the distribution of bone marrow (assumed to parallel that of stem cell) and the radiation dose distribution throughout the bone marrow. The detailed distribution of active bone marrow for standard man at age 40 was adapted from the literature. A tissue equivalent phantom containing a human skeleton and simulated lung cavities was used to experimentally determine the active bone marrow dose under simulated whole body and partial body (upper, lower, and complete trunk) bilateral cobalt-60 exposure conditions. Capsules filled with lithium fluoride were placed in bone cavities. The xiphoid served as the boundary field for upper and lower body exposures. The doses for each section were averaged and multiplied by total grams of active marrow in that section. The active bone marrow integral doses for upper body, lower body and complete trunk are 48%, 61%, and 75% respectively, of that determined for whole body exposures.

Using the measured radiation dose distribution to active bone marrow, we then proceeded to calculate the weighted stem cell sur-

vival for the various exposure conditions. For mortality in the LD_{50} range, the normalized mouse bone marrow stem cell survival data was obtained from the literature. The sum of the products of the fraction of total marrow irradiated and relative stem cell survival for that radiation dose yields the weighted relative stem cell survival. Thus, for any of the given non-uniform exposures, one can determine the dose of uniform whole body radiation that would result in the same cell mortality rate. The corresponding "doses" thus derived for uniform whole body exposures can be thought of as being "dose equivalent." This approach is extended to the circulating fractions of the peripheral blood elements at the nadir point for the patients treated in this study. It is assumed in the extension of this approach that circulating fraction for a given blood element at the nadir is equal to the surviving fraction of marrow stem cells by the given exposure. The validity of this extension was tested by comparing the predicted and measured nadir of circulating fractions of white blood cells and platelets for several groups of patients. Peripheral blood counts of the patients were obtained prior to irradiation and were followed for as long as practical following exposure. The data reported here were obtained from patients shown to have normal blood counts prior to exposure. The patients were grouped as to type of exposure and the midline dose received. A comparison was made for three groups of patients who received

whole body exposures of 100, 150 and 200 rad midline absorbed dose respectively; and two groups of patients who received lower body exposures of 200 and 300 rads midline absorbed doses, respectively. In view of the assumptions made in the study, there appeared to be fair agreement between the proposed model and the average clinical findings in terms of the nadir of circulating fractions of white blood cells and platelets.