Although it is easily seen that a non-uniform exposure to penetrating radiation requires a higher dose of radiation to at least some portion of the body to produce a similar or equal degree of a given effect, then is necessary with uniform whole body exposure, the full quantitative characterizations of dose and dose effect relationships are necessarily more complex for non-uniform than for uniform doses. For uniform whole body exposure, all tissues receive essentially the same dose, and thus the dose delivered to any tissue is satisfactory in characterizing "the dose" received by the animal. The absorbed dose at the midline is commonly used for convenience, with no implications that a particularly sensitive organ or region lies in that location. With non-uniform exposure, however, it has been shown clearly that, for depth from the bone marrow syndrome, either the entrance dose, the absorbed dose at the midline of the animal, the exit dose, the integral dose nor the average dose will normalize and allow dose effect perdictions for the full spectrum of different dose distributions. Thus additional factors must be taken into account and a weighted, dose averaging procedure, must be used to perdict dose effect relationships, as will be mentioned later.

Before pursuing this concept of dose distribution and some possible characterization for the non-uniform exposure, let me indicate briefly our personal interests in this problem in the University of Cincinnati College of Medicine. We have a program for total body exposure and

for partial body exposure (either upper half or lower half) of patients for the treatment of cancer. The radiation is delivered by Cobalt-60 teletherapy unit under the following exposure conditions:

The radiation beam is directed _____ at a wall 338 centimeters away with the patient midline at 282 centimeters from the source. The beam area for the 50% isodose curve at the patient midline distance is a square approximately 70 centimeters x 70 centimeters. The patient is placed in the sitting position with legs raised and head tilted slightly forward. The radiation is given by delivering half the specified exposure laterally through one side of the patient; the patient is then turned and the other half exposure delivered laterally through the other side. The variation of air exposure with distance from the source is determined with a Victoreen 25R Chamber. The results indicated no departure from the inverse relationship for distances used in the study. Therefore no correction was required for a possible dose contribution to the patient due to the backscatter from the wall. Preliminary measurements were made in a masonite phantom using dosimeters placed on lateral surfaces at the midline of the head, trunk and knee portions of the phantom. These results are shown on the next slide. It is seen that if midline doses to the trunk, head and knees are compared, the maximum variations in these doses is about 16%. The exposure to the patient was determined as follows. Percentage depth dose at different depths for 400 square centimeter field area and source skin distance of 80 cms. is given by A.G. Johns. Depth dose at the greater source skin distances used for the patient were postulated found by multiplying the depth doses at 80 cm by the F factor by Maynard & Lamberton. By using the corrected depth dose at patient midline (1/2 lateral dimension of the trunk) and a conversion

factor of .979 rads per roentgen for Cobalt gamma radiation, the surface dose and midline air exposure required to give a desired midline absorbed dose in rads was calculated. A direct comparison was calculated and measured (phantom) doses was made for one patient who had the same lateral trunk dimensions as the phantom. A larger depth dose for each lateral exposure to this patient is given in the next slide. The dose is indicated by crosses or measurements made in the phantom and compared quite well with the calculated doses. The combined doses of the two radiation fields is also given in this figure. It shows a good homogeneous dose distribution through this patient. Maximum variation in lateral dose distribution with plus or minus 13% for one patient having a lateral trunk dimension of 36 centimeters.

Air exposure rates were 3R per minutes to 6R per minute.

In the individuals receiving partial body radiation, the teletherapy collimator is used to restrict the beam. ~~The isodose curves for this latter case is shown in~~ The spatial dose distribution for this latter case is shown on the next slide. The relative dose distribution for upper body radiation is shown in the next slide: that for the lower body in the following slide. The phantom measurements were determined with thermoluminescent dosimeters. For partial body radiation, the ~~xyphoid~~ xiphoid was used as a boundary.

We were then confronted with some approach to allow comparison between the so-called uniform and non-uniform exposure as presented by our specific study. That is total body exposure versus either upper half or lower half body exposure. Vick Bond and the group at Brookhaven have provided a basis dealing with ~~non~~ uniform exposure.

If one knows the dose distribution, and the distribution of the bone marrow (assumed to parallel that of stem cells). Bone marrow distribution for standard man is given in the next slide. This is the data of Ellis obtained in the original work of Mechanic but corrected for percentage _____ factors as provided by Custard. These are correction for cranium, mandible, vertebral column and pelvis by _____ factor values obtained by Custard for the vertebra. Further work by Atkinson allowed also an assessment on the bone marrow distribution with age as a parameter. In the absence of any large scale study of the distribution of active marrow in man, the above is considered to be the best data that can be obtained at the present. ~~We are interested in obtaining--~~

We were then interested in obtaining dose distribution data for a given exposure; namely, whole body versus upper half and lower half body exposure. Each unit of bone marrow appears to act independently of the other sub units, as regard to response to radiation of stem cells in that sub unit. Given the dose to a number of sub units in marrows and percent of bone marrow stem cells in that subunit, one can determine the relative number of surviving stem cells for each subunit using the data given by Bond. Summing over the entire marrow we use the total ~~number of relative stem cells~~--- relative number of stem cells in the body that would survive the exposure. Mortality level to be expected from this stem cell survival can be read from the left hand ~~coordinate~~ coordinate of the data provided by Bond. Thus for any given non-uniform dose distribution, a dose of uniform whole body radiation will result in the same mortality rate can be determined. To obtain the dose distribution data the following procedure was used. The purpose of the study was to determine experiemtnally "active" bone marrow dose

under simulated whole body and partial body cobalt-60 exposure conditions for humans. A tissue equivalent phantom (Randall) containing a human skeleton and simulated lung cavities was used. Capsules filled with lithium fluoride were judiciously placed in bone cavities as demonstrated by radiographs of each phantom section. ~~By these cavities were selected~~ The cavity selected were based on locations of active bone marrow spaces as indicated by the work mentioned above by Ellis. The next series of slides indicates to some extent the placement of these thermoluminescent capsules in the phantom. The slides included are the following: radiograph of head section; line drawing of the same section without outline of bone structure in placement of capsules; dosimetry displacement in the ribs; dosimeter placement in the spine; and dosimeter placement in the pelvis and femoral ~~necks and heads~~ heads, necks.

The next series of slides indicate exposure of the Alderson phantom to Cobalt beam to simulate the actual whole body and upper half and lower half expsoure in humans. Show next three slides. ~~From the~~

From the average rad dose and "active bone marrow weight, the integral dose to active bone marrow was calculated. As seen in the next slide, active bone marrow integral doses for lower half body and upper half body (~~are simulated both~~ under our simulated exposure conditions) are 68.9% and 37%, respectively, of that determined for whole body exposure under the radiation exposure conditons given above.

We then proceeded to determine that for a given nonuniform dose distribtuion, the dose of uniform whole body irradiation would result in the same mortality rate, as determined using the data for relative stem cell survival as given by Bond. The corresponding "doses" thus derived for the uniform whole body exposure can be thought of as being dose equivalent, rather than absorbed dose. This is because

in the averaging process for non-uniform exposure, each increment of dose was weighted by the amount of bone marrow irradiated at that dose level, and by the relative effectiveness of that dose increment to destroy the stem cells. The dose survival curve for bone marrow stem cells is known most accurately for the mouse. The model presented by Bond to handle non-uniform exposure has been shown to apply to the rat as well as the mouse, using the same curve for stem cells. It was thus assumed by Bond and also assumed in this paper that this curve also applies to man. The model also assumes the following: that the number of mature cells is proportionate to the total number of surviving stem cells, whatever their distribution in the body; and that the requirement for mature cells following any non-uniform exposure is the same as that following the uniform exposure equivalent to it with respect to total stem cell survival. It also assumes a moderate degree of non-uniformity - extremes of local doses to any part of the body not exceeding a value of approximately 1,000 or 1200 rads. The reason for this is that the higher doses may cause local blood vessel damage to become a significant factor, leading to increased requirements for both _____ and platelets. In addition, high doses locally to the bowel can produce death in the absence of significant marrow damage.