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Conference on Dosimetry of Total-Body Irradiation by External Photon Beams

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Conference on Dosimetry of Total-Body Irradiation by External Photon Beams

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DOSIMETRY OF TOTAL-BODY IRRADIATION BY EXTERNAL PHOTON BEAMS

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Introduction

A conference on total-body dosimetry, attended by physicists, radiobiologists, and clinicians* was held at Oak Ridge Associated Universities (ORAU) on February 23 and 24, 1967, under the auspices of the National Aeronautics and Space Administration (NASA)† and ORAU.‡ Its purpose was to review work on total-body irradiation, and if possible to arrive at a consensus on a uniform way of reporting the doses delivered. Discussion was restricted to photon irradiation, with emphasis on the physical rather than on the biological aspects.

Although much of the work had appeared in the open literature, some of it first came to light during the conference. The meetings were informal and as much time was allotted to discussion as to presentation of papers. The authors of the present paper were the organizers and also served as rapporteurs. What follows is their view of what took place; it does not follow exactly the order in which the talks were given. Instead the topics are divided into two groups: I. Methods of irradiation; and II. Measurement and calculation of dose.

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* Appendix I gives the participants and the program.

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PART I: METHODS OF IRRADIATION

After a welcome by Andrews and introductory remarks by Cloutier, Lushbaugh stated that the aim of the ORAU survey, undertaken on behalf of NASA, is to establish a quantitative relation between radiation dose and a number of biological responses in man. Retrospective studies on the case histories of all known patients exposed to total-body irradiation, both in the United States and abroad, are under way and future studies are in prospect. Lushbaugh expressed the hope that some uniform method of reporting the dose received by irradiated patients would be agreed upon as a result of the present meeting, and that the method would be widely used in future studies. He described the methods used in seeking out information for the ORAU-NASA survey and stressed that considerable difficulty arose in interpreting records, particularly if the work reported on had been carried out many years ago. No two institutions used the same system of reporting, and many vital items in both dosimetric and medical histories, originally thought to be unimportant, were now irretrievably lost.

He reported that the average dose and the exposure at the midline in the absence of the subject were most frequently used to describe the patient's total-body irradiation. Several other radiation units were also used; the one Lushbaugh favored was what he called "epigastric dose"; that is, the number of rads delivered to the upper abdominal compartment. He pointed out that this quantity was the variable with which the severity of systemic symptoms seemed to be most readily correlated. In replying to a question by Focht, Lushbaugh stated that at ^{137}Cs energies the number of rads delivered to the epigastrium is, in persons of normal size, approximately 0.66 times the exposure (R) that would have existed at the position of the epigastrium if the patient's body were removed.

Another objective of the present study is to change the rather widely held concept that a specified dose level invariably brings about a certain physiological response. Thus, the statement that 200 R would invariably induce vomiting should be replaced by a statement of the probability that 200 R would cause vomiting. Lushbaugh then outlined the system of probit analysis used at ORAU to correlate "go, no-go" phenomena, such as vomiting or diarrhea, with the dose that would induce these effects with a certain probability.

From initial analyses of a limited number of cases, which give remarkably consistent results, it is possible to estimate for any effect E, the dose ED_x that causes the effect to occur with a probability of x percent.

Beck then summarized the material available for analysis. It now consists of about 1800 cases located at 38 institutions (Table I). For the NASA study any number of irradiations given on the same day were considered as one treatment. One or more irradiations given in a period of one week constitute an intermediate group. Multiple irradiations extending beyond one week are considered as a fractionated treatment, and irradiations separated by six weeks or more are considered as separate treatment series. The collaborating institutions, on the other hand, used quite different conventions.

Questions from Shonka and others brought out that most of the ORAU patients had suffered from leukemia or lymphomas but patients from other institutions generally had epithelial neoplasms. It also emerged that some patients had been exposed to more than 1000 R in a single day, although in the vast majority the exposure had been much less.

Typical Total-Body Irradiators

Beck then described the radiation equipment used at collaborating institutions. As a general rule, the older work was done with X-ray equipment not specifically designed for total-body irradiation, whereas the more recent equipment tended to be custom-built and relied predominantly on gamma rays. Only fragmentary dose data existed for patients treated in the 1930's, whereas dosimetric information for patients irradiated in recent years was generally in more detail.

As typical arrangements, Beck chose to describe those at ORAU, Peter Bent Brigham, Mary Imogene Bassett, and City of Hope Hospitals. In the ORAU installation, the early work was done with a ^{60}Co source enclosed in a spherical shield. Most of the patients, however, have been treated in a later irradiator (*1*) with multiple ^{137}Cs sources, providing remarkably uniform exposure over the treatment area (*2*). Exposure rates available were between 0.7 and 2.0 R/min. Results were recorded as midline air exposure, average abdominal dose, or total-body average dose. The City of Hope Hospital in Duarte, California, also has a specially-built installation with eight ^{137}Cs sources. The exposure rates were between 0.02 and 4.7 R/min. Results were given

as "average midplane, midbody dose" (*3*). At the Peter Bent Brigham Hospital, in Boston, Massachusetts, multiple portals were used to cover the whole body. A 250-kV machine was used with an exposure rate of 5.5 R/min; the midbody depth dose was recorded (*4*). The irradiator at the Mary Imogene Bassett Hospital, Cooperstown, New York, consists of two ^{60}Co sources with the patient in between. Exposure rates ranged from 6 to 25 R/min. Both exposure and depth dose at the center of the body were given (*5*).

In the first invited paper, Shalek described the 250-kV X-ray facility used at the M. D. Anderson Hospital during the 1950's for the irradiation of 263 patients. The half-value thickness (HVT) was 3 mm Cu. The patients were placed 275 cm from the X-ray target and irradiated laterally while in a crouched position. The "edges" of the beam (taken to coincide with the 50% isoexposure line in air) enclosed an area of 1200 cm^2, which was large enough to accommodate the crouching patient. After one-half of the exposure had been given, the patient was turned and irradiated from the opposite side. The dose within the patient varied ±20% with the minimum dose at the patient's center. The exposure rate was 3.8 R/min. Both the exposure at midline and the average dose, calculated by one of Mayneord's formulas were reported for all patients (*6*).

At Baylor University in Dallas, West reported that the initial irradiations had been performed with a 220-kV X-ray machine while the patient lay on a stretcher. Half the exposure was given AP and the other half PA. The surface dose was taken as 100% (*7*). The exposure rate was 5 R/min. Later, X rays from a 2-MeV accelerator were used with the patient sitting up in a rotating chair. The dose at the center of the body was calculated to be 68 to 72% of the air exposure. Integral doses were also calculated by Mayneord's equations, correcting for nonuniformity of the beam (*8*).

Hayes presented details of dose measurements carried out at the ORAU irradiator with three anthropomorphic phantoms corresponding to three typical body sizes: a small child, an adolescent, and an adult. The complete isodose distribution (Fig. 1) within the phantom was determined with an ionization probe. In addition, chemical dosimetry was used to measure the average dose to the whole body and for separate body compartments. The integral dose calculated graphically from the isodose lines differed by less than 5% from the values obtained with the chemical dosimeter.

A comparison was also made, with the same phantoms and chemical system, of the average dose in various body

compartments when exposed to radiation from two temporary ^{60}Co irradiators used at ORAU during the early total-body irradiation studies. There was less variation in average dose from one compartment to the other with the eight ^{137}Cs-source facility than with the bilateral ^{60}Co radiation setup (*9*).

Kereiakes reported that the irradiator at the Cincinnati General Hospital consisted of a single ^{60}Co source housed in a teletherapy head. The patient was placed in a sitting position, the lower extremities were raised, and the head was tilted forward. In this way the patient was made to fit within the 50% isoexposure line of the beam. The distance from source to the patient's center was 282 cm. One-half the dose was administered from one side, the patient was rotated, and the remaining dose was given. The exposure rate was 3.5 to 6 R/min at the center of the body, in the absence of the patient. Skin doses were calculated and verified by means of ionization chambers and lithium fluoride dosimeters. Depth-dose measurements in a masonite phantom indicated that dose variation in the trunk of a typical patient was only ±8%. Dosage was expressed as rads at the patient's midline (*10*). More recently, integral doses have been calculated by Mayneord's method. For a given midline dose, the integral dose varies depending upon the patient's lateral dimensions.

Campbell reported that the total-body irradiator at the Manitoba Cancer Treatment and Research Foundation, Winnipeg, Canada, provides a uniform exposure rate (±2.4%) within a cylindrical treatment volume 6 feet high with a base diameter of 8 feet. The uniformity becomes ±4% if the base diameter is increased to 10 feet. The uniform field is produced by six ^{60}Co sources; four of them, positioned at the midplane of the irradiation volume, provide 99% of the exposure; two small sources one above and one below the treatment volume provide the remaining 1% of exposure. The exposure rate is about 0.5 R/min. The facility has not been placed in routine use for patients. Depth-dose measurements in phantoms have not been done (*11*).

Focht described the irradiator that Heublein and Craver used in the 1930's at Memorial Hospital, New York. Since dosimetry was not then very advanced, accurate dose estimates could not be made. Dosage was given at that time in erythema units. On the basis of available information about the X-ray machines (kilovoltage, milliamperage, etc.), Focht has estimated the doses in rads that the patients had received. Although it is difficult to assess the accuracy of the estimates, the data are unique in that they represent

observations for low exposure rates and low-energy radiation, whereas most other work was carried out at higher exposure rates and at higher energies.

Comments

The preceding presentations, together with data from other institutions that were not represented at the meeting, may allow a few generalizations.

1. Several techniques of total-body irradiation have been used. The most common one has been to irradiate the patient with a single beam of X rays generated at about 250 kV. The patient was usually two or three meters from the X-ray tube. The exposure was given AP-PA or from each lateral side of the patient. Dose uniformity within the body was from ±15 to ±30%.

2. Several investigators used the same technique but with ^{60}Co gamma rays or 2000-kV X rays. Dose uniformity within the body was between ±8 and ±15%.

3. Special facilities using eight ^{137}Cs sources gave a dose uniformity within the body comparable to that obtained with opposing beams at about 1-MeV.

4. The exposure rates were generally between 1 and 6 R/min.

5. Dose has been reported in a variety of ways, and many institutions use more than one expression. Exposure (usually at the patient's midline) is by far the most common figure given. Dose estimates in use are (a) midtrunk dose; (b) integral dose; (c) average dose; (d) midplane, midbody dose; (e) skin dose; and (f) epigastric dose.

Evaluation of Reported Dose

Comas, Beck, and Cloutier explained how they attempted to unify the dosimetry of all patients treated with total-body irradiation in the 38 institutions of Table I. The first step was to select dose expressions that would be common to all patients.

Of the available choices, the average total-body dose appeared to be open to the fewest objections and was calculated when sufficient data were available from the

patients' records. Lushbaugh is using this dose expression in current attempts to correlate dose and response.

The midbody dose was also calculated but has the objection that it represents the dose to only a small fraction of the body tissues (see Fig. 1).

Target-organ dose, although an appealing concept, has the drawback that the identity of the organ responsible for a specific biological effect is generally not known and, if known, the organ's dose is difficult to calculate. On the assumption that the prodomal syndrome is related to the dose absorbed in the upper abdomen, "epigastric doses" were computed for those patients on whom enough information was available. Lushbaugh used this dose estimate in his early attempt to correlate dose and response.

Exposure and integral doses were also calculated if data were available. Objections to these dose expressions had been well explained in the report of Sinclair and Cole (*6*): "It is evident that we cannot accurately compare the effects produced in animals and humans, or even in different human beings, by means of either the air dose or the integral dose . . . We would not, for instance, consider that a very large man, placed at the point where 200 R might be measured in air, experiences a much greater effect because the integral dose to his body is much greater than that of a man only half his weight."

In this connection Robinson argued that the average total-body dose could also be misleading. For example, suppose that several kilorads were given to only the foot. Here the average total-body dose might still be hundreds of rads; however, the systemic response would clearly not correlate with the average total-body dose. Others pointed out that concepts applicable in partial-body irradiation were not necessarily transferable to total-body irradiation. O'Foghludha indicated that it would not avoid the issue to give a complete description of the doses at different parts of the body. He said that the phantom studies of Hayes, Oddie, and Brucer (*9*) were as complete as one might wish, yet the information contained in the isodose plots was not readily usable for the purpose of relating biological response to radiation dose; for this, one needed a single dose value.

The ORAU speakers went on to describe how they converted the doses, as given by the participating institutions, to average total-body dose. They indicated that this study was still in progress and that data from only 21 of the 38

reporting institutions had been analyzed. Of the 757 treatments reviewed, exposures have been calculated for 724 and average doses have been calculated (or measured in phantoms) in 504. Table II gives the distribution of patients according to exposure and total-body average dose. About 5% of the patients could not be given any kind of dose estimate for lack of sufficient data.

Beck explained that the average total-body dose for ORAU patients was obtained by multiplying the patient's exposure by a conversion factor (Table III) derived from the phantom measurements of Hayes *et al.* (*9*). This factor is the ratio of the average number of rads per roentgen of exposure and is sensitive to patient size and weight. For the ^{60}Co opposing-field technique, the average dose changes more rapidly with patient weight than for the 8-source ^{137}Cs facility.

Average doses for the Cincinnati General Hospital patients were estimated by using the ORAU conversion factors for the temporary ^{60}Co unit in the third column, Table III. This was justifiable because the irradiation techniques at both institutions were almost identical (bilateral ^{60}Co radiation in both cases; treatment distances of 282 cm at Cincinnati, 275 to 285 cm at ORAU). Furthermore, a comparison of measured central-axis depth-dose data showed that the radiation distribution inside a phantom was the same at both facilities (Fig. 2). The data from Mary Imogene Bassett Hospital were treated in the same way although a comparison of central-axis depth-dose curves could not be made.

The City of Hope Hospital reported their doses as "average midplane, midbody dose" (*3*). This dose is the arithmetic mean of point values in the midcoronal plane of the trunk. For the NASA study, the reported values were converted to average total-body doses by means of the conversion factors of Table III. Justification for using the factors in Table III, which were determined for the 8-source ORAU irradiator, was the similarity of the ORAU and City of Hope facilities. A comparison of the radiation distribution measured in phantoms at ORAU and City of Hope showed that the dose at similar points was almost identical.

Whereas in gamma-irradiated patients dosimetry had been based on experimentally determined data, the same approach could not be followed for the far greater number of patients treated with X rays. The irradiation conditions varied so that phantom studies designed to reproduce all combinations of radiation energy, distance, and HVT would have been

impractical. Instead, Cloutier explained, average doses were calculated by means of Mayneord's equations (*12, 13, 14*), which give average dose as the product of the mean skin dose and certain tabulated factors. The skin dose usually had to be calculated from the midline air exposure; this was straightforward except for some uncertainty about the proper choice of backscatter factors.

Mayneord's calculations require a knowledge of the radiation quality and the trunk dimensions. In those cases where the HVT of the beam was not recorded, no estimate of average dose could be obtained; when the trunk dimensions were unknown, it was assumed that the correct AP trunk thickness was given by the expression (*15*):

$$\text{AP (cm)} = \sqrt{\frac{\text{weight (g)}}{\text{height (cm)}}}$$

It was also assumed that the lateral dimension was 1.5 times the AP thickness.

As a check on the validity of Mayneord's method of calculation, three phantoms were irradiated with 250-kV X rays (HVT 1.8 mm Cu) and average doses were measured with a ferrous sulfate dosimeter. The agreement between measured values and those obtained by Mayneord's method is good for the adolescent phantom, only fair for the adult, and poor for the child (Table IV). This may be a result of the failure of the theory when applied to conditions very different from those assumed in deriving it, incorrect choice of constants, or a combination of both factors.

The measured average total-body dose, for one roentgen exposure in air at the midbody position, is higher for this radiation quality than for a similar opposing-beam treatment using ^{60}Co radiation. The radiation distribution inside the phantom, however, is presumably less uniform, although this was not investigated.

[Excerpt continues on p.17]

with 350 rads delivered nonuniformly. The equivalence arises because 350 rads delivered unilaterally spares the same number of stem cells as 270 rads delivered bilaterally.

CONCLUSIONS

How should Dose be Reported?

All participants agreed that specification of the radiation field alone was insufficient to describe the irradiation completely. For example, a statement of the exposure in roentgens, although forming an essential part of the record, is not enough. An attempt should always be made to specify the energy deposition or dose. If details of the method and results of dose measurements as well as the exposure are quoted, later recalculation is possible and intercomparison with the results of others is simplified.

In specifying the dose a choice must be made between the maximum, minimum, modal, integral, or average doses (*31*). The physical arguments for and against the various specifications have already been given. The choice depends to some extent on the response that is clinically interesting or important. Langham cited the possibility of erythema in an astronaut exposed to low-energy radiation. In this circumstance the skin dose is of critical importance. On the other hand if lethality is the response under study, the dose to the bone marrow is most important since the marrow appears to be the target organ, at least when the dose is of the same order of magnitude as the $ED_{50/60}$. In some situations, of course, the target organ is unknown as in the prodromal syndrome where the means by which anorexia, nausea, and vomiting are induced remain obscure. Since the onset of these symptoms is unlikely to be related to irradiation of the extremities, a specification of the average dose to the trunk - or possibly the upper abdomen alone - is of value. Where the physiologically important organ cannot be localized even to this degree of accuracy, the average dose to the whole body is the most appropriate value to quote.

The average dose has the advantage that it can be calculated with fair accuracy in most cases if the properties of the radiation field are known. Whether D_{av} is required for a single organ or for the entire body, its determination involves measurement or calculation of the integral dose Σ,

either explicity or conceptually. For this reason it may be advantageous to state D_{av} not in rads but in the dimensionally equivalent form "gram-rad per gram"; such a statement, though clumsy, draws attention to the way in which D_{av} was actually obtained.

The extremes between which values of the local dose vary should be reported as an indication of the degree of nonuniformity. If the frequency distribution about the mean were normal, the standard deviation could be used; but it is usually most appropriate to indicate the spread by quoting the highest and lowest doses in the region of interest.

National and international organizations have recommended standards for dose recording in portal therapy. Until similar standards are set up for total-body irradiation, it is suggested that:

1.) The characteristics of the radiation field used should be stated.

2.) The average dose D_{av} in the target organ and the method of calculation or measurement should be given. If the target organ is unknown, D_{av} for the entire body should be stated.

3.) The maximum and minimum doses in the region of interest or some other indication of the degree of nonuniformity should be reported.

Whatever method of dose specification is used, a single number is unlikely to provide a firm basis for the prediction of biological response. The more data one quotes, the more complete is the information, though the additional data may appear irrelevant or even confusing. Past experience proves that information once thought to be unimportant is later vital. Therefore, as much information as possible should be recorded to permit later evaluation in the light of new identification of target organs.

At the present time Mayneord's analytical technique and Snyder's computer study of individual photon histories offer powerful tools for the calculation of radiation dose. However, additional experimental corroboration of these theoretical methods is urgently needed for various phantoms and for a range of photon energies. The participants at this meeting expressed the hope that the next few years would see a rapid advance in the science of whole-body dosimetry.

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TABLE I

JANUARY 1967 AUDIT OF RETROSPECTIVE AEC/NASA STUDY OF HUMAN TOTAL-BODY IRRADIATION

Hospital or Institution	Anticipated Treatments	Retrieved Treatments	Treatment Types <Day	>Day but <8 Days	>8 Days	No. of Treatments Reviewed for Dose Estimation
Albert Einstein Medical Center	1	1	1			1
Baylor University	113	111	67	15	29	74
Bowman Gray	7					
Burge Protestant Hospital	5	5	1	2	2	
Cincinnati General	32	32	29	1	2	30
City of Hope Medical Center	53	58	36	8	14	43
Charity Hospital	80	98	3	18	77	
Colorado General	1	1			1	
Ellis Fischel State Cancer Center	77	84	2	9	73	
Franklin Hospital	85	85			85	
Jefferson Medical College	10	11	11			4
Long Beach Community Hospital	1	1	1			1
Los Alamos Hospital	9	9	9			1
Mary Imogene Bassett	22	27	15	11	1	19
Massachusetts General (McGovern)	6	7	7			7
Massachusetts General (Robbins, L.)	200					
M. D. Anderson Hospital & Tumor Institute	293	292	286	1	5	287
Medical College of Virginia	5	5	5			5
New York Memorial (Craver--Heublein)	144	188		112	76	108
New York Memorial (Nickson)	46	48	35	6	7	23
Oak Ridge Associated Universities-ORINS	138	138	134	1	3	123
Penrose Cancer Clinic	54	68			68	
Peter Bent Brigham	10	11	2	8	1	10
Philadelphia Children's	3					
Providence Hospital	45	288	236	3	49	
Rhode Island Accident	1	1	1			
Temple University	26	29	15	5	9	7
Thomas M. Fitzgerald Mercy	4	4	4			4
U. S. Naval Hospital	11	11	7		4	7
U. of Calif. Medical School, S. F.	163					
University of Michigan	128	128			128	
University of Pennsylvania	10					
V. A. Hospital at Denver	12	25	2		23	
V. A. Hospital at Long Beach	10	2	2			2
V. A. Hospital at New Orleans	24	57	5	16	36	
V. A. Hospital at Wood, Wisconsin	1					
Winnipeg General	7					
White Memorial Medical Center	2	2	2			2
Totals 38 Institutions	1839	1814	904	216	648	757

TABLE II

DISTRIBUTION OF PATIENTS
ACCORDING TO EXPOSURE AND TOTAL-BODY AVERAGE DOSE

Exposure (R)	Number of Patients	Total-Body Average Dose (rads)	Number of Patients
0-25	155	0-25	149
26-50	152	26-50	108
51-75	51	51-75	90
76-100	127	76-100	19
101-125	47	101-125	17
126-150	37	126-150	36
151-200	60	151-200	19
201-250	16	201-250	26
251-300	22	251-300	4
301-400	16	301-400	15
401-500	11	401-500	7
501-700	13	501-700	7
701-900	5	701-900	2
901-1100	6	901-1100	3
1101-1300	3	1101-1300	2
1301-1600	3	1301-1600	0
	724		504

January, 1967

TABLE III

ORAU WEIGHT-CORRECTED
CONVERSION FACTORS

Patient's Weight (Pounds)	AVERAGE TOTAL-BODY RAD/R	
	^{137}Cs TBI Facility	Temporary ^{60}Co Unit
35-45	0.75	0.77
45-55	0.75	0.74
55-65	0.75	0.71
65-75	0.75	0.69
75-85	0.74	0.67
85-95	0.74	0.65
95-105	0.74	0.64
105-115	0.73	0.63
115-125	0.72	0.62
125-135	0.72	0.61
135-145	0.71	0.61
145-155	0.70	0.61
155-165	0.70	0.61
165-175	0.69	0.61
175-185	0.69	0.60
185-195	0.68	0.60
195-205	0.68	0.60

TABLE IV

COMPARISON OF MEASURED AND CALCULATED AVERAGE DOSES

Phantom	Thickness	SSD	Average dose/R exposure		% Difference
			Measured	Calculated	
Adult	29 cm	285 cm	0.67	0.73	9
Adolescent	23 cm	200 cm	0.78	0.80	3
Child	16 cm	200 cm	0.79	0.93	18

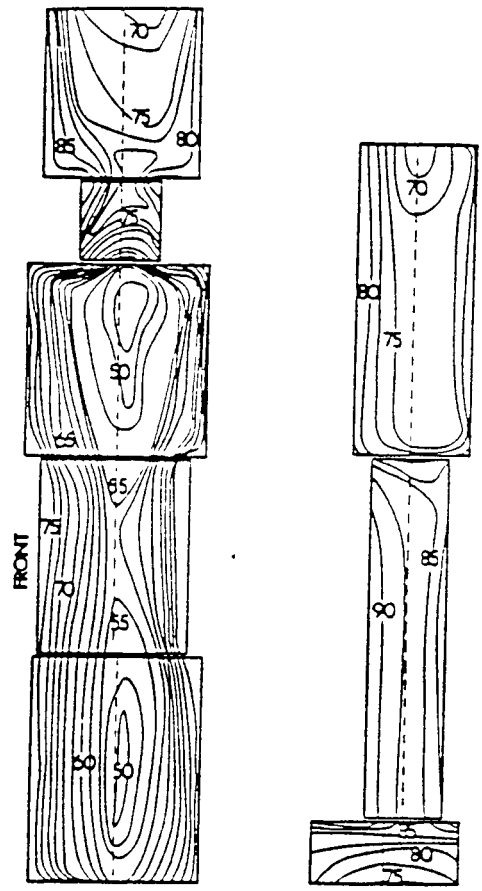

Figure 1. Isodose lines in an "adult" phantom, irradiated with eight converging ^{137}Cs radiation beams. ORAU total-body irradiation facility. Isodose lines normalized to 100-R exposure at the center of the phantom.

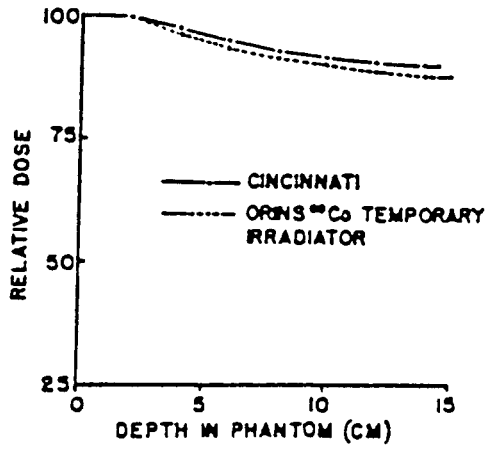

Figure 2. Central-axis depth-dose curves in the "trunk" of phantoms irradiated with opposing ^{60}Co radiation beams. Depth doses normalized to 100 at the phantom's surface.

Appendix I

WORK CONFERENCE

List of Participants
Program

WORK CONFERENCE

DOSIMETRY IN TOTAL BODY PHOTON IRRADIATION OF MAN

February 23-24, 1967

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