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BIOLOGY AND MEDICINE QUARTERLY REPORT

July, August, September 1957

BERKELEY, CALIFORNIA

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BIOLOGY AND MEDICINE QUARTERLY REPORT

July, August, September 1957

BIOLOGICAL STUDIES OF RADIOACTIVITY AND IRRADIATION

Grocker Laboratory
University of California
Berkeley, California

BIOLOGICAL EFFECTS OF INTERNALLY DEPOSITED RADIOISOTOPES

Patricia W. Durbin and C. Willet Asling in charge

Muriel E. Johnston, Nylan Jeung, Marilyn H. Williams, Marshall W. Parrott, George Barr, and Ann Henderson

STUDIES OF AN OSTEOGENIC SARCOMA TRANSPLANTABLE IN RATS

The animals used and characteristics of the tumor have been reported previously.[1] It was hoped that the high specific uptake of rare earth isotopes (Tm^{170}, Tb^{160}, Ce^{144}) might lead to a possible therapeutic application. Ho^{166} was selected because of its high-energy radiations and short half life, and was administered to a large group of rats. A dose in the near-lethal range did not significantly affect the growth rate of the tumors.

The data on this experiment and on the Sr^{90} and Tm^{170} tracer experiments are being collected and will be reported in the near future.

The self-absorption curve for Ca^{45}, given by George Barr in Medical and Health Physics Quarterly Report, UCRL-2881, Feb. 1955, p. 16, should be corrected as follows:

Sample weight (mg/cm^2)		% activity
Reported	Corrected	
4.0	16	33
3.5	14	35
3.0	12	38
2.5	10	41
2.0	8	46
1.5	6	56
1.0	4	67
0.5	2	80
0.0	0	100

[1] Durbin, Asling, Barr, and Hessel, in Biology and Medicine Quarterly Report, UCRL-3758, Apr. 1957, p 1-12.

STRONTIUM-90 IN THE RHESUS MONKEY

In a preliminary report on the metabolism of Sr^{90} in the rhesus monkey, excretion curves were presented for four adult animals during the first 2 weeks after an intravenous injection.[2] More detailed information is now available for three additional monkeys for the first 5 months post-injection.

Two young adult female rhesus monkeys and one adult male Java monkey each received 35 μC Sr^{90} in isotonic sodium citrate by intraperitoneal injection. After the injection the animals were placed in metabolism cages for collection of excreta. Urine and feces were collected separately, daily for the first two weeks. Pooled excreta were collected for 1-week periods from the third until the nineteenth week. Weekly pooled samples are currently being collected once every 6 weeks.

Excretion samples were dried and ashed in a muffle furnace. After a 3-week storage period to assure attainment of radioactive equilibrium, the dry residue was re-ashed with conc. HNO_3 and diluted to 200 ml with 2N HNO_3, and 10-ml aliquots were dried in weighed porcelain ashing capsules. The dry aliquot samples were assayed for Sr^{90} content with a mica end-window G-M counter,* and appropriate corrections for self-absorption were applied.

The rate of urinary excretion for intraperitoneally injected Sr^{90} was the same as was previously determined for intravenously administered Sr^{90}. The data for the three animals of the present group and those previously reported for the other four animals have been combined in Fig. 1.[1] Each point on the curve represents seven monkeys, and indicates the standard deviation of the mean for the group.

The combined excretion-rate curve of three adult monkeys is shown in Fig. 2 for the first 165 days after injection. No analysis of these curves has been attempted because a constant slope has not emerged as yet.

In Fig. 3 the excretion data has been utilized to plot the bodily Sr^{90} retention. After the twelfth week the slope of this curve appears to be constant. Although future data may alter the equation for retention, a tentative equation may be put forth,

$$\% \text{ retention} = 55 \exp(-2.77\, t) + 45 \exp(-0.0107\, t),$$

where t is measured in weeks after injection. Qualitatively, these data augment our earlier report of the prompt excretion of 50% of the injected Sr^{90} by the adult monkey, followed by the elimination of the remaining 50% with a half time of 1.24 years. The 1.24-year half time is in surprisingly good agreement with the very rough estimate of 1.14 years reported previously for one adult male.[1]

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[2] Durbin, Parrott, Williams, Johnston, Asling, and Hamilton, "Metabolic Studies with Strontium-90 in the Rhesus Monkey" (preliminary report), UCRL-3634, Jan. 1957.

*A 70 mg/cm^2 aluminum filter was interposed between the counter tube and the specimen to eliminate the necessity of correcting for K^{40} background, which becomes troublesome with 1- to 2-g samples of urine ash.
Durbin and Asling

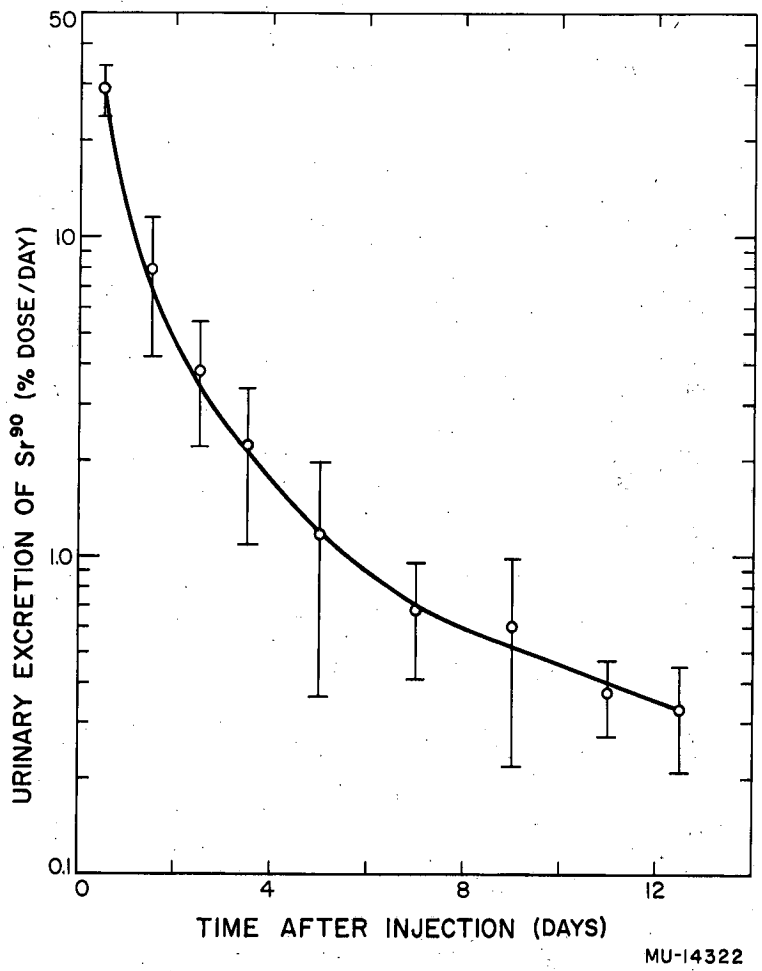

Fig. 1. Rate of change of urinary excretion of parenterally administered Sr^{90} in the adult rhesus monkey. Each point represents 7 animals (3 male, 4 female) who were sexually mature at the time of injection.

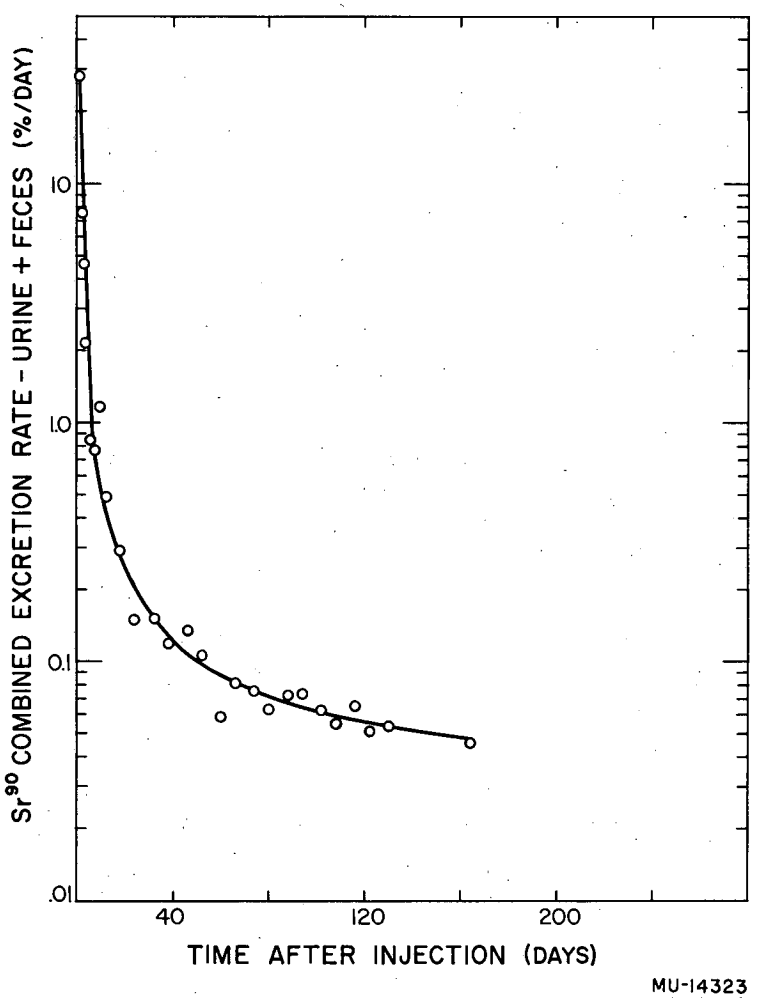

Fig. 2. Combined daily excretion rate (urine plus feces) of Sr^{90} in adult monkeys (1 male Java, 2 female rhesus).

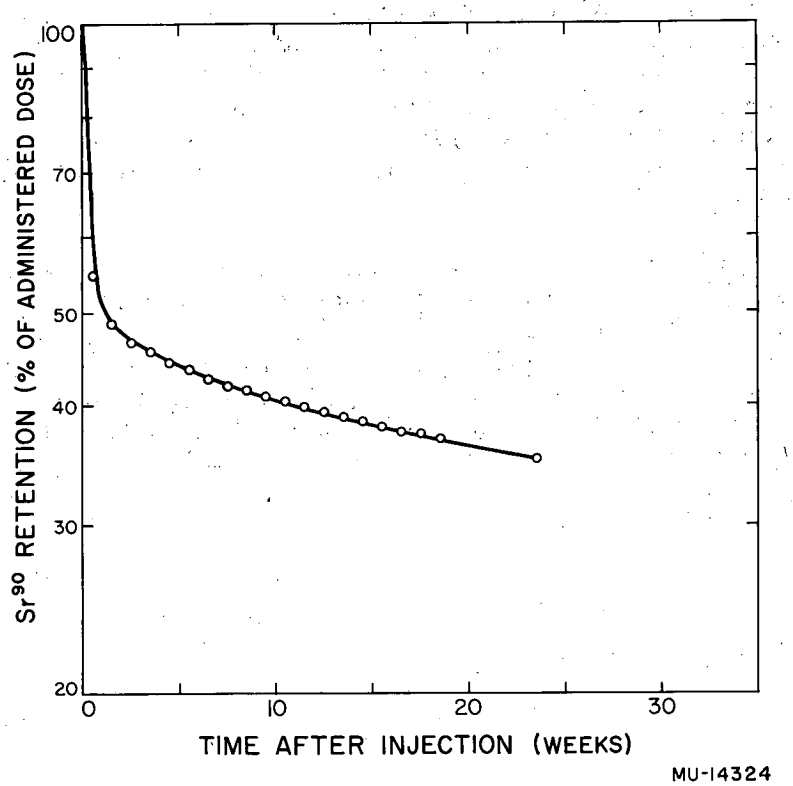

Fig. 3. Retention of parenterally administered Sr^{90} by three adult monkeys, determined from assay of collected excreta.

LOCALIZATION OF CERIUM-144 IN FETAL SKELETAL TISSUE

(A study by C. Willet Asling, Muriel A. Johnston, Patricia W. Durbin, and Joseph G. Hamilton has been reported in "Localization of Cerium-144 in the Skeletal Tissues of Fetal Rats" and issued as UCRL-8024, October 18, 1957. The abstract is included here.)

The developing fetal skeleton of the rat was used to study the microscopic localization of the rare earth Ce^{144} in bone. Nineteen-day-old rat fetuses were injected with Ce^{144} in isotonic sodium citrate via the umbilical vein. They were sacrificed one-half hour after the injection by immersion in 80% alcohol fixative. The fetuses were embedded in paraffin and sectioned at 10 to 12μ. Semiserial sections were treated with periodic acid–Schiff stain for mucopolysaccharides, and by the von Kossa technique for calcium. Contact x-ray-film autoradiographs and NTB stripping-film autoradiographs were prepared.

Photographs of representative sections and their respective autoradiographs are presented for various bones. This material strongly suggests that the initial binding site of Ce^{144} in the skeleton is in the organic matrix of cartilage and bone, especially where this matrix is just entering the calcifiable state. This conclusion is highly dependent upon the specificity of the von Kossa stain for calcium. Further studies are under way to correlate this histochemical test with the autoradiographic demonstration of tracer Ca^{45}.

Durbin and Asling

RADIATION CHEMISTRY

Warren M. Garrison in charge

Boyd Weeks, Michael Jayko, Winifred Bennett,
Sibyl Cole, and Margery A. Andrews

The major effort of the radiation chemistry group during the past quarter has been largely directed to the further application of techniques recently developed in this laboratory for the study of radiation-induced reactions of protein in aqueous solution. These techniques, which have gradually evolved during the past several years from our studies of simpler organic compounds containing chemical bonds and groups common to protein, now appear to make possible the detailed study of the precise locus of the indirect (and possibly also the direct) action of radiation on complex structures of immediate biological interest.

OXYGEN-AERATED PROTEIN SOLUTIONS

The observation that the carbonyl group represents the principal product of the reactions induced by OH attack on protein in oxygenated solutions[1] has provided a general method for the radiation-chemical study of protein oxidation. The conclusion that oxidation at the peptide link is involved in the formation of part of the carbonyl groups has been substantiated. The process is represented by the reactions

$$\sim\!CO\text{-}NH\text{-}CHR\!\sim + OH \longrightarrow \sim\!CO\text{-}NH\text{-}CR\!\sim + H_2O,$$

$$\sim\!CO\text{-}NH\text{-}CR\!\sim + O_2 \longrightarrow \sim\!CO\text{-}N{=}CR\!\sim + H_2O_2,$$

$$\sim\!CO\text{-}N{=}CR\!\sim + H_2O \longrightarrow \sim\!C(=O)\text{-}OH + RC(=O)\!\sim + NH_3.$$

Samples of irradiated gelatin solutions after dialysis and hydrolysis have been found to contain a mixture of a α-keto acids. Corresponding studies with aqueous pepsin also show a multiplicity of keto acid products. The nature and relative yields of the keto acids from each protein reflect the differences in amino acid content of the original material.

A detailed report of the earlier phases of this work is in preparation. Studies now in progress indicate that specific information on the various sites of radical attack, both on main and side-chain linkages, can be obtained; these data are now being evaluated and will be described fully in the next Quarterly Report.

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[1] Michael E. Jayko and Warren M. Garrison, Formation of >C=O Bonds in the Radiation-Induced Oxidation of Protein in Aqueous Systems, UCRL-3872, July 1957.

OXYGEN-FREE SYSTEMS

In a previous Quarterly Report (UCRL-3880), we outlined an alternate method for studying the locus of OH attack on aqueous protein. The proposed technique involves the irradiation of an oxygen-free protein solution containing an added C^{14}-labeled solute. The latter is a simple organic species which gives a known radical on OH attack. By the choosing of the appropriate concentration of protein (pepsin) and C^{14}-labeled acetic acid, it has been possible to bring about the following radiation-induced reactions:

$$P + OH \longrightarrow P' + H_2O,$$

$$CH_3C^{14}OOH + OH \longrightarrow CH_2C^{14}OOH + H_2O$$

$$P' + CH_2C^{14}OOH \longrightarrow P\text{-}CH_2C^{14}OOH.$$

The data obtained to date show that sufficiently large amounts of C^{14} activity can be incorporated into protein by this process. Control experiments have established that the C^{14} activity is not introduced via non-radiation-induced processes. Identification studies of the C^{14}-containing products obtained on hydrolysis of the new protein derivative $P\text{-}CH_2C^{14}OOH$ are in progress. These data will provide basic information on the nature of P'.

PAPERS AND REPORTS ISSUED

M. E. Jayko and W. M. Garrison, Formation of the >C=O Bond in the Radiation-Induced Oxidation of Protein in Aqueous Solution, UCRL-3872, July 1957.

W. M. Garrison, Radiation Chemistry: A Review, Ann. Rev. Phys. Chem. 8, 1957.

W. M. Garrison, B. M. Weeks, J. O. Ward, and W. Bennett, Water Decomposition Yields in the Radiolysis of Aqueous Formic Acid Solution by Cyclotron-Produced Radiations, J. Chem. Phys., in press.

BIOLOGICAL STUDIES OF RADIATION EFFECTS

John H. Lawrence, M.D., in charge

Donner Laboratory of Biophysics and Medical Physics
University of California, Berkeley, California

Material for this report had not been received at the time of publication, but may be expected in a subsequent report.

RADIATION DETECTION AND PROTECTION

Radiation Laboratory
University of California
Berkeley, California

HEALTH CHEMISTRY

Nelson B. Garden in charge
Reported by Rosemary J. Barrett

APPARATUS AND EQUIPMENT

A list of items furnished by the Health Chemistry group during the third quarter of 1957 to researchers using radioactive materials is given below--items in addition to routine maintenance and replacement parts continuously afforded by Health Chemistry's services.

Unloading shield for 60-inch cyclotron: this shield is for use in disassembling target material from the collimator assembly of the cyclotron; as the collimator block gets the brunt of the beam, its resultant radiation fields present quite a problem during the process of disconnecting the helium, air, and water leads to the target; the shield, with its auxiliary equipment, is so arranged that the target may be loosened from the block with minimal exposure to the operators, and the block is removed remotely to storage for cooling until next use.

Processing equipment for MTR-irradiated transcurium sample: the 6-in. cave, 2-in. cave, and auxiliary gloved boxes are being readied in Bldg. 70 for an irradiated transcurium sample, to be received early in October.

Electrically heated ion-exchange column: an improved column has been designed and fabricated for use in transcurium chemistry.

Probe for deflector channel of 60-in. cyclotron: Health Chemistry collaborated with the 60-in. crew in designing and fabricating a probe that will reduce exposure to personnel.

Gloved boxes and enclosures, plus auxiliary equipment:

Individual boxes, specially fited, for chemistry on research involving each of the following: Cm^{244}, Am^{241}, Np^{239} (preparation for atomic beam); Ho^{166} chemistry, rat injections with Ho^{166}, Br^{82} (including 2-in. shield, used in preparing material for atomic beam), transcurium-rare-earth separation, Ni-Co work, Bi-Po work, preparation of special radioactive sources, (two boxes), and astatine chemistry (three boxes), including a shielded manipulator box and an enclosure for preparation of astatine spectrographic samples);

Box for protecting personnel from high-voltage (30-kv) transformer, used with an electrostatic device for source preparation (an old No. 2 centrifuge box was converted for this purpose);

One piano box, plus two inert-atmosphere boxes for use therein;
Boxes and enclosures for use in heavy ion linear accelerator (hilac) work involving 10^{11} cpm Cm^{244}; two enclosures for use in electrodepositon of target material; enclosure for loading the prepared target foils into target assembly; carrying box for transportation of foils from target area to chemistry counting area; other hilac equipment including vacuum supply to target, close-capture air-cleaning devices for the catcher-foil target assembly, and a pressure-sensitive, quick-closing gate to protect the post-stripper tank from contamination.

Specially fabricated radioactive sources, provided on request: 22 Sr^{90}, 3 Cs^{137}, 1 normal uranium, 4 enriched uranium, 1 Po, 6 Pu. The problem of fabrication of Cs^{137} sources for use in intracavity insertion in the treatment of cancer in humans (see also preceding two Quarterly Reports) continues to receive attention, for the present sources are not considered absolutely leakproof, as demonstrated in soaking tests. A present approach includes the use of platinum tubes containing the activity; study of ceramic carriers continues.

Sample shaker for use in processing samples from Livermore's water boiler neutron source; the sources consist of radioactive sodium and potassium.
A new model of a large-area probe for use in alpha monitoring of floors, lab coats, and--eventually--Filter Queen papers.

Machinery for Bldg. 70 Berkeley Box exhaust system: a complete inspection and overhaul took place during this period. After 2 1/2 years' use, the 100% polyvinylchloride components were in good condition, but metal corrosion was evident. The first modified Scully-Rowell circuit was installed after a one-year laboratory test; a component failure occurred in 40 days and a protective improvement was worked out.

Sealed-bag equipment is becoming more acceptable to researchers, with its demonstrated elimination of air contamination otherwise resulting occasionally from box transfers of high-level alpha emitters.

The routine checking of the improved Sr^{90} sources showed no evidence of leakage (old Sr^{90} sources were all recalled for repackaging and reissuing at the discovery of premature corrosion of the aluminum foil window in one of the sources--see preceding two Quarterly Reports).

Emanation capture and gaseous decontamination problems: Br_2^{82} and like I_2^{131} have appreciable vapor pressures, and cause a gaseous decontamination problem, and as large amounts of these isotopes are being used, it has been necessary to undertake special studies regarding them.

MISCELLANEOUS

The 184-in. cyclotron, after having been shut down for over a year for improvements, was started up again during this period, and increasing numbers of targets of increased activity are now being carried by Health Chemistry's Transportation group from the cyclotron to the laboratories.

The 60-in. accelerator operators were persuaded to substitute methylene dichloride for petroleum ether when cleaning deflector and other cyclotron parts, thus reducing explosion hazards.

More than 5,000 radioactivity determinations were made on air samples during the quarter; some of these were for the Atomic Energy Commission's interest in connection with fall-out studies.

Garden

HEALTH PHYSICS

Burton J. Moyer in charge

STATISTICAL SUMMARY OF MONITORING PROGRAM

Survey Instruments Maintained

Beta-gamma meters	22
I D L meters	21
Juno ion chamber	20
Abacus logarithmic ion chamber	30
Recording-intensity meters	8
Victoreen proteximeter	3
Slow-neutron proportional counters	15
Fast-neutron proportional counters (portable)	11
Slow-neutron portable unit	4
Balanced chamber-fastneutron-portable	3
Special tissue wall survey instrument	1

Survey Instruments in Storage

Beta-gamma meters	7

Personnel Meters in Use - Berkeley Only

Total personnel covered with film badges	2000
Total man-days' coverage with electroscopes	5600
Total man-days' coverage with dosimeters	2880
Total man-days' coverage with slow-neutron chambers	2880

	Man-days	Number per day (approximate) for 3 months
Bevatron		
Electroscopes	1360	15
Bldgs. 10, 53, 80, and 7		
Slow-neutron chambers	1980	22
Dosimeters	1980	22
Electroscopes	1980	22
Crocker		
Slow-neutron chambers	900	10
Dosimeters	900	10
Electroscopes	900	10
Bldg. 70		
Electroscopes	1360	15

Cases of Weekly Exposure Above 0.3r*

Weekly film expos. above	184-inch area	60-inch area	Linac	Chem	Other	Total
0.3	0	9	0	2	0	11
0.5	0	1	0	0	0	1
1.0	0	0	0	0	0	0
1.5	0	0	0	0	0	0
2.0	0	0	0	0	0	0
2.5	0	0	0	0	0	0
3.0	0	0	0	0	0	0
4.0	0	0	0	0	0	0
5.0	0	0	0	0	0	0
6.0	0	0	0	0	0	0
6.5	0	0	0	0	0	0

*Excluding Livermore

RADIATION SURVEY AT THE 184-INCH CYCLOTRON

Lloyd D. Stephens

A comprehensive neutron survey was begun on August 24 this year at the 184-inch cyclotron. The entire building was rapidly surveyed to determine if any areas of hazardous radiation existed. Several areas were found, which under certain operating conditions could be considered to have too high a neutron flux for continuous occupancy.

Several beam conditions have been investigated. All have been at maximum energy of approximately 980 Mev. The beams that have been investigated so far are

1. Internal proton beam
2. Proton beam deflected into deuteron cave
3. Proton beam deflected into medical cave
4. South proton beam hitting meson target
5. North proton beam hitting meson target
6. Alpha beam deflected into medical cave.

No deuteron beam has as yet been investigated.

Notably high neutron levels were found to exist outside the shielding of the medical cave when the proton beam was deflected into the cave, and outside the shielding of the deuteron cave when the proton beam was deflected into it, also outside the shielding in the general area of the entrance door to the cyclotron during the operation of a north proton beam hitting the meson target.

Recommendations have been made regarding additional shielding for the entrance area to the medical cave, and roof blocks to completely cover both the deuteron and medical caves, as well as thick steel beam stoppers in both caves. An additional 5 feet of concrete shielding placed in the region of highest neutron flux, Bays 11 and 12, decreased the neutron intensity by a factor of ~10 as measured in the roadway near Building 9.

Additional shielding will be placed inside the vacuum tank as well as in the passageway leading to the cyclotron. As this work is completed additional surveys will be made.

Recommendations made at the present time are that there be no prolonged reverse beam operation undertaken during any hours when the shops across the roadway are occupied.

Moyer

CARBON-ACTIVATION STUDY OF BEVATRON BACKGROUND RADIATION

Joseph B. McCaslin

In an attempt to investigate the Bevatron background radiation it has been decided to add to existing Health Physics instrumentation facilities for detecting high-energy neutrons via the reaction $C^{14}(n, 2n)C^{11}$. C^{12} has a 30-mb cross section above the reaction threshold of 20 Mev. C^{11} decays with a 20-minute half life by the emission of a 0.98-Mev positron. Plastic scintillators (5 in. long and 5 in. in diameter) are activated and subsequently counted. The background counting rate is about 2700 cpm looking at a 0.1- to 2-Mev window. Plans for further decreasing background are in progress. It is expected that a flux of 20 $n/cm^2/sec$ will produce a counting rate of about 3000 cpm above background for a scintillator counted 5 minutes after it has reached saturation activity.

Initially this system will be used to study the radiation from the tangent tanks under various operating conditions. Also, an attempt will be made to gather some information on the attenuation of these neutrons.

FAST-NEUTRON SURVEYS BY ACTIVATION OF INDIUM FOILS

Alan R. Smith

The process of thermal-neutron-induced activation of indium foils has been adapted to the measurement of fast neutrons. Foils are placed at the centers of 3-inch-radius paraffin spheres, which are in turn placed within cadmium boxes. Cadmium absorbs the thermal component of the neutron flux, while the paraffin acts as a moderator of the fast neutrons, to produce a thermal neutron flux at the sphere center, where foil activation takes place. The thermal flux at the foil is proportional to the incident fast flux, and as a result of the choice of moderator thickness, is relatively independent of neutron energy for the range 0.2 - 20 Mev. Foil activation is therefore a measure of the number of fast neutrons in the energy interval of greatest interest to Health Physics work.

The foil counting system, which was originally based on a Geiger-Mueller counter, has recently been improved in both stability and sensitivity by conversion to a methane-flow proportional counter and standard UCRL electronic equipment. A typical foil (0.4 gram indium) when activated to saturation would produce an initial count rate of 4 cpm for a neutron flux of 1 n/cm^2-sec. At the normal counter background of 10 cpm, the system is easily capable of detecting a flux of 3 n/cm^2-sec, a level considerably below the current tolerance level. There is no practical upper limit to the measurable flux.

The foil technique is particularly suited to neutron measurements where high instantaneous count rates are encountered, and where many simultaneous measurements are required.

Both conditions prevail at the Bevatron, especially inside the shield close to the machine itself. Thus the foils are being used extensively to study fast-neutron flux levels along magnet quadrants and on tangent tanks. Results obtained to date show that neutron levels at tangent tanks can be expected to be 10 times as high as along the magnet quadrants, and that tangent-tank levels correlate well with the presence or absence of a nearby target.

Foil data have contributed greatly to the understanding of the pattern of fast-neutron leakage from the Bevatron, and are expected to provide much additional information of this sort. Foil measurements are planned as a major part of the forthcoming study of neutron attenuation in several shield materials, to be done at a target location on one of the tangent tanks.

Moyer

Information Division
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