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BIOLOGICAL AND CLINICAL DOSIMETRY

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I. SUMMARY

Detailed studies of three cyclotron produced, ^9Be (x,n) neutron spectra have been conducted. These include:

1. The measurement of on-axis depth dose distributions at a number of SSD's. These data have been analyzed in a fashion which allows dose rates to be calculated as a function of SSD and depth.
2. The measurement of the contaminant gamma ray dose as a function of depth in water.
3. The measurement of LET spectra at three depths of water. The variation of RBE and OER with depth have been calculated from these data and compared with values, measured at this laboratory, using HeLa cells.

^{252}Cf medical neutron sources are being evaluated for application to implant radiotherapy. Preclinical studies include basic dosimetry measurements and, in support of preclinical radiobiology, apparatus designed to meet specific dosimetric requirements.

Construction and assembly of a tissue equivalent micro-calorimeter have been completed and initial measurements of the temperature stability are reported.

A small prototype ultra pure germanium gamma camera utilizing the orthogonal strip geometry has been under evaluation. Spatial resolution of within 4 mm has been obtained for images of extended isotopic sources. Initial application to small mammalian organs have been made. Representative images are presented along with data obtained from measurements of operational characteristics of the matrix array.

Pulsed electron sources such as 600 kV field emission generators can deliver doses in excess of 10^6 rads in single pulses having duration times of a few nanoseconds. When these sources are used to irradiate thin layers of cells, the measurement of absorbed dose is complicated by the associated high dose rates, the relatively low electron energy, and the thickness of the sample which may be only a few microns. In this laboratory the problem of measuring absorbed dose has been investigated by the use of thin disks of Pilot-B, a commercially available fast response plastic scintillator. A thin foil absorbed dose calorimeter was used to provide a calibration for the scintillator light output. Since the dynamic range of the scintillator system is quite large, it was possible to perform absorbed dose measurements over the large range of doses used for various radiobiological experiments.

II. NEUTRON DOSIMETRY AND ABSORBED DOSE MICROCALORIMETRY (T.R. Canada, J.C. McDonald, A. Mittleman, and J.S. Laughlin)

A series of measurements have been made to compare the radiation quality and quantity, as a function of depth in water, for the neutron spectra produced in ^9Be (x,n) reactions with proton, deuteron and ^3He beams from the Sloan-Kettering Institute cyclotron. These measurements were made at a SSD of 30 cm. with no collimation which is the general geometry used in present biophysics experiments at this laboratory. Dose rates and depth dose distributions have been measured with a tissue-equivalent ionization chamber. The gamma ray dose as a function of depth was determined using ^7LiF teflon thermoluminescent dosimeters. LET spectra have been measured in air and at three depths (0.5, 5. and 15 cm.) using a spherical proportional counter with an effective diameter of 1.0 μ . From these spectra, RBE and OER values are calculated and compared with some recently measured values. The results of these measurements and calculations are presented in section A below.

The construction and initial testing of the tissue equivalent absorbed dose microcalorimeter described in last years report (1) is discussed in section B. A number of preclinical dosimetry studies of ^{252}Cf , including some measurements made in support of specific radiobiological experiments, are described in section C.

A. A Comparison of Absorbed Dose Characteristics for Cyclotron Produced Neutrons

1. Depth Dose and Gamma Ray Contaminant-Measurement and Comparison.

A recent paper (2) reviewed some of the basic parameters of the fast neutron beams produced by the 30 inch isochronous cyclotron of the Sloan-Kettering Institute. The authors concluded that this cyclotron was a satisfactory source of fast neutrons for radiobiological and dosimetric research and has possible clinical study applications. Of the targets studied, ^9Be appeared to be the most satisfactory, on the basis of such criteria as dose rates, depth dose distributions and simplicity. The present work is a more detailed comparison of the radiation quality and quantity, as a function of depth in water, for the neutron spectra produced when 15 MeV protons, 8 MeV deuterons and 23 MeV ^3He beams are incident upon a thick ^9Be target. Such a comparison is necessary for further hardware and experiment design.

The neutron spectra from these three reactions are distinctively different. (3) The $^9\text{Be}(^3\text{He},n)$ reaction, for example,

gives a spectrum whose median neutron energy is approximately 8 MeV. The spectrum shows a broad peak at approximately 7 MeV (a full width at half maximum of ~9 MeV) with a long tail ending at approximately 26 MeV. The spectrum from the $^9\text{Be}(d,n)$ reaction, on the other hand, is rather strongly peaked at ~2.5 MeV with a FWHM of MeV and a tail extending to only 8 MeV. Unfortunately, the $^9\text{Be}(p,n)$ spectrum has only been determined for neutron energies >0.5 MeV. This spectrum peaks at 0.5 MeV, indicating that a major portion of the spectrum lies below this energy. The median energy for neutrons with $0.5 \text{ MeV} < E_n < 8 \text{ MeV}$ is ~2 MeV.

The depth-dose curves shown in Figure 1 reflect the difference of these neutron energy spectra. The data were collected at 30 cm SSD with no collimation using a tissue equivalent ionization chamber and a water phantom described in reference 2. These data reflect the dose dependence arising from all secondary radiations, including gamma rays. The solid lines are fits to the data of the function $Ae^{\mu d}/r^2$ where d is the depth in water, r is the distance from the target to the measuring point, and A and μ are variable parameters. The half-value depth and the fitted value of μ are indicated for each curve. As expected from considerations of the neutron energy spectra, the half-value depth is largest for the ^3He induced reaction.

The functional dependence of the depth dose curves is well described by the simple expression given above, which assumes that the dose at a given depth is due to radiation originating from a point source. If this assumption is satisfied, a single value of μ should represent the absorption of a given neutron spectrum independent of r . Table I lists the values of μ obtained by fitting depth-dose curves to a depth of 20 cm at a number of SSD's. Figure 2 shows three of these (at 70 cm SSD) with the fits extrapolated to 30 cm depth in water. These data show that over a 20 cm depth range μ is indeed constant. However, as the dose rate due to the primary neutron originating from the target is reduced, due to increased SSD or attenuation, the measurement becomes sensitive to additional sources. This is seen in Figure 2 where the dose decreases more slowly than the predicted curve at depths of 20-30 cm. This additional contribution arises from scattered radiation and may be largely reduced when the target is removed from the irradiating room and a well designed collimator is employed.

The percentage of the dose which arises from gamma radiation as a function of depth, and its dependence upon the beam particle is of immediate interest. To determine these parameters ^7LiF Teflon thermoluminescent dosimeters (shielded with aluminum) were exposed at a number of depths for each of the three beams. The dosimeters were individually calibrated by exposing them to a ^{60}Co gamma ray source of known dose rate.

Figure 1. Central axis, uncollimated neutron beam, depth dose distributions. The solid lines are fits to the data (see text). Half-value depths are shown.

Figure 2. Central axis, uncollimated neutron beam, depth dose distributions. The solid lines are fits to the data to a depth of 20 cm. Half-value depths are shown.

^9Be (x, n) REACTIONS

TOTAL ABSORPTION Coefficient μ

(for depths to 20 gm/cm² in water)

DOSE RATES (rad/ $\mu\text{a} \cdot \text{hr}$)

(measured at
0.7 gm/cm² depth in water)

SSD	^3He	d	P
30 cm	0.066 $\pm$.001	0.085 $\pm$.001	0.084 $\pm$.002
50	0.066 $\pm$.002		0.084 $\pm$.001
70	0.065 $\pm$.001	0.085 $\pm$.001	0.083 $\pm$.001
90		0.082 $\pm$.001	

^3He	d	P
30.5	83.6	105.0
10.9		42.7
6.1	17.3	22.3
	9.3	

Table 1.

The results of these measurements are shown in Figure 3 where the percentage of the total dose at a given depth due to gamma rays is plotted as a function of depth for a SSD of 30 cm. The solid curves are intended only as straight line approximations to the data. The percentage of gamma ray dose increases with depth for all incident beams. This variation is approximately the same for the deuteron and proton beams, where $10 \pm 2\%$ of the total dose at the surface is due to gamma radiation. This percentage doubles in the first 10 cm of water. The increase with depth is smaller for the ^3He beam (a 30% increase in 10 cm of water), but the absolute percentage at the surface is larger ($15 \pm 2\%$).

The fast neutron response of ^7LiF is strongly dependent upon the neutron energy. (4) If $R(E) = r(E_n)/r(^{60}\text{Co})$ is defined as the ratio of the response, $r(E_n)$, of a ^7LiF dosimeter when exposed to a given neutron dose (neutron energy = E_n) and its response $r(^{60}\text{Co})$ when exposed to an equal dose of ^{60}Co gamma rays, then $R(E_n)$ is found to vary from ~ 0.012 at $E_n = 1$ MeV to ~ 0.12 at $E_n = 10$ MeV. Because of this fast neutron sensitivity, the percentages of the total dose due to gamma radiation presented in Figure 3 are upperlimits. It is difficult to estimate in detail the contribution arising from the fast neutrons because of the complex spectra being considered. However, a rough estimate suggests that 20-30% of the observed response for the proton and deuteron beams is due to fast neutrons. The corresponding number for the ^3He beam would be 40-50% which accounts in part for the higher surface percentage and slower variation with depth of the ^9Be ($^3\text{He}, n$) curve shown in Figure 3.

2. Energy Deposition Produced by Fast Neutron Irradiation.

In many radiobiological experiments, Characterization of the energy deposition by absorbed dose is inadequate to describe the observed biological response. The relative biological effectiveness per unit dose is found to depend upon the local energy distribution in volumes comparable to those of the systems under study.

To determine the spectral distributions of LET for the secondary charged particles produced by the neutron sources described above, a 1.27 cm diameter, Rossi-type proportional counter (effective $d = 1.0$ micron) was used in conjunction with standard low-noise electronics, including a preamplifier, a linear amplifier and a 256 channel multichannel analyzer. Spectra were obtained in air, and at depths of 0.5 cm, 5 cm. and 15 cm. in water.

Figure 3. Percentage of the total dose arising from gamma radiation as a function of depth in water (30 cm SSD). The solid lines are straight-line approximations to the data.

Figure 4 shows the result of these measurements at three positions plotted as the weighted dose distribution, $Y \cdot D(Y)$ versus the event size, Y . This presentation of the data allows the structure of a given distribution to be clearly discerned and easily compared to other distributions. The area under a curve is proportional to the total dose, so that the fraction of the total dose arising from various regions of Y may be easily estimated.

Events in the various regions of Y may be characterized according to the properties of the secondary particle spectrum. Gamma ray events appear as counts with $Y < 4 \text{ KeV}/\mu$. Protons contributed to spectrum at values of Y less than $91 \text{ KeV}/\mu$. The upper part of this region ($20 \text{ KeV}/\mu < Y < 91 \text{ KeV}/\mu$) corresponds to low energy protons ($0.1 \text{ MeV} < E < 1 \text{ MeV}$) and the lower portion ($Y < 20 \text{ KeV}/\mu$) to higher energy protons. Alpha particles fall in the $91 \text{ KeV}/\mu < Y < 220 \text{ KeV}/\mu$ region and heavy ions (C, N, O) in the $Y > 220 \text{ KeV}/\mu$ region. These divisions are approximations but they allow, none the less, some qualitative discussion of the observed $Y \cdot D(Y)$ vs Y structure. The data presented in Figure 5 cover a range in Y between 4 and $230 \text{ KeV}/\mu$ (i.e. the secondary proton and alpha particle regions).

The distributions measured in air for the three incident particles reflect the differences in the neutron energy spectra discussed above. Specifically:

- (A) The ${}^9\text{Be}({}^3\text{He}, n)$ neutron spectrum is characterized by a broad "high energy" peak resulting in a broad peak in the $Y \cdot D(Y)$ distribution centered at approximately $Y = 15 \text{ KeV}/\mu$.
- (B) The broad "low energy" neutron spectrum of the ${}^9\text{Be}(p, n)$ reaction gives a broad peak centered at a much larger Y ($30 \text{ KeV}/\mu < Y < 70 \text{ MeV}/\mu$).
- (C) The more sharply peaked ${}^9\text{Be}(d, n)$ neutron spectrum gives a sharper peak in the $Y \cdot D(Y)$ distribution, centered between those of the ${}^3\text{He}$ and proton induced distributions. And finally
- (D) The higher energy ${}^3\text{He}$ induced neutrons generate a larger number of secondary alphas than either the deuteron or proton beams.

The characteristic differences in these three distributions becomes noticeably less distinct as the depth in water is increased. This is especially true for the proton and deuteron generated neutron distributions which show very little difference after 5 cm of water.

Figure 4. Weighted dose distributions $Y \cdot D(Y)$ vs Y , for neutron spectra produced by three $^9\text{Be}(x,n)$ reactions, measured in air and two depths of water.

To show the change of an individual spectrum as a function of depth, it is useful to plot the function $R(Y) = D(Y)_d / D(Y)_{0.5}$ versus Y where $D(Y)_d$ and $D(Y)_{0.5}$ are the dose distribution at depths of d and 0.5cm respectively. Such a plot is shown in Figure 5 for each of the neutron spectra considered here.

The variation of $R(Y)$ with Y and depth is least for the "high" energy ^3He induced neutrons and greatest for the "low" energy proton spectrum. It is interesting, however, that the type of variation seen for both is the same, i.e. dose is removed from the region $10 < Y < 100 \text{ KeV}/\mu$ and added to the $Y < 10 \text{ KeV}/\mu$ and $Y > 100 \text{ KeV}/\mu$ regions. This corresponds to an increase in the average energy of the recoil protons and a relative increase in the number of secondary alpha particles. This in turn, implies that the average energy of the neutron is increasing as a function of depth. A similar variation is observed in the case of the deuteron induced neutrons at low and intermediate values of Y . There is a difference, however, at values of Y corresponding to very low energy recoil protons where the dose increases. Such effect require a broadening of the rather sharply peaked neutron energy spectrum as a function of depth.

Finally these data are shown in Figure 6-9 as dose distributions in LET [$D(L)$ vs L] as a function of depth and incident beam at 5 cm. depth (Figure 9). These distributions offer another means of viewing the differences and variations discussed above.

Barendsen et al. (5) have measured the relative biological effect and oxygen enhancement ratio for T-1 human kidney cells as a function of LET. Their results are shown in figure 10. If it is assumed that the response of a given biological system is identical to that shown in this figure, effective RBE and OER values may be calculated for the three neutron spectra considered above. For example, the effective RBE is given by

$$\text{RBE} = \frac{\int_{L_1}^{L_f} \text{RBE}(L) \cdot D(L) dL}{\int_{L_1}^{L_f} D(L) dL}$$

This integration was performed using the $D(L)$ and the $\text{RBE}(L)$ shown in Figures 6-9 and Figure 10 respectively, for $4 < L < 230 \text{ KeV}/\mu$. The gamma ray contaminant shown in Figure 3 was corrected for the fast neutron response of the TLD's and included with an RBE of 1.0. The portion of the dose with $L > 230 \text{ KeV}/\mu$ is very small and is ignored in the present calculation. The results are shown in Table II and Figure 11 for each of the three depths and neutron spectra considered. The uncertainty in the absolute magnitude of these values is modestly estimated to be 5-10%. The uncertainties in the variations as a function of spectrum and of depth, are, however, smaller (perhaps ~5%).

Figure 5. Ratio curves, $R(Y)$ vs Y , (see text) for three neutron spectra.

Figure 6. Dose distributions $D(L)$ vs L at several depths for the neutron spectrum produced in the ${}^9\text{Be}({}^3\text{He},n)$ reaction.

Figure 7. Dose distributions $D(L)$ vs L at several depths for the neutron spectrum produced in the $^{9}\text{Be}(d,n)$ reaction.

Figure 8. Dose distributions $D(L)$ vs L at several depths for the neutron spectrum produced in the $^{9}\text{Be}(p,n)$ reaction.

Figure 9. Dose distributions $D(L)$ vs L measured at a depth of 5 cm. in water.

Figure 10. RBE and OER values, for human kidney cells, measured as a function of LET by Barendsen et al. (5)

Depth (cm)	RBE $(4 < L < 230 \text{ KeV}/\mu)$			RBE _T		
	³ He	d	p	³ He	d	p
0.5	2.14	2.38	2.50	2.06	2.30	2.32
5	2.25	2.43	2.51	2.12	2.24	2.28
15	2.23	2.36	2.26	2.07	2.13	2.00

TABLE II.

Calculated values of RBE for three ⁹Be (x,n) produced neutron spectra.

Depth (cm)	OER $(4 < L < 230 \text{ KeV}/\mu)$			OER _T		
	³ He	d	p	³ He	d	p
0.5	2.18	2.02	2.12	2.21	2.06	2.21
5	2.21	2.12	2.14	2.26	2.26	2.22
15	2.22	2.16	2.18	2.28	2.25	2.28

TABLE III.

Calculated values of OER for three ⁹Be (x,n) produced neutron spectra.

Figure 11. HeLa cell RBE values (20% survival level) vs depth in water. The lines are smooth curves drawn through the calculated points. In the top portion calculated and measured values are compared. In the bottom portion calculated values are compared for three neutron spectra.

The average RBE for that portion of the dose arising from the secondary protons and alpha particles ($4 < L < 230$ KeV/ μ) is approximately constant as a function of depth (See Table II). (The proton induced spectrum shows a 10% reduction at 15 cm.) With the inclusion of the gamma ray contaminant, however, the average RBE (RBE_T) decreases slightly for the proton and deuteron induced spectra, but remains constant for the ^3He cases.

The latter case is compared in the top portion of Figure 11 with some recent RBE measurements made at this laboratory by Dr. Djordjevic et al. (6) using HeLa cells. The calculated and measured values are in reasonable agreement, i.e. variation with depth is not demonstrated outside the experimental uncertainty in either case and the absolute values are within the uncertainties of one another.

Oxygen enhancement ratios were calculated in a similar manner. The results (Table III) show no variation of OER with depth or neutron spectrum. Again, this is in agreement with Djordjevic et al. (6) who has measured the OER for the $^9\text{Be} (^3\text{He}, n)$ neutron spectrum with HeLa cells at 2.5 cm. (OER = 1.48 ± 0.35) and 16 cm. (OER = $1.68 \pm .44$) depths and finds no variation outside the experimental uncertainty. His measured value is, however, somewhat smaller than the calculated value of 2.2 ± 0.2 . This value was obtained assuming the OER(L) function to be the same for all mammalian cell systems. That this is in fact not the case has been demonstrated for human kidney-derived T-1 cells and P-88 tumor cells. Therefore, a difference of this magnitude is perhaps not surprising in the present case.

B. Construction and Testing of a Tissue Equivalent Absorbed Dose Calorimeter

A tissue equivalent absorbed dose calorimeter has been constructed to serve as a primary standard for the evaluation of the response of various dosimetry systems to fast neutrons. The design is described in detail in reference 1. Briefly, (Figure 12) the calorimeter consists of a 0.8 gm. wafer core which is enclosed in an adiabatic shield. These elements are enclosed in three buffer shields and a temperature control shield. The entire structure is suspended in a vacuum chamber. All elements, except the lids of the vacuum chamber, are constructed of Shonka A-150 tissue equivalent conducting plastic. The Shonka plastic lids used in the initial design were found to suffer structural fatigue when repeatedly flexed in going from air to vacuum conditions. There were replaced by lids of the same thickness constructed of Dupont Nylon 6/6 which has properties very similar to that of the Shonka plastic.

TISSUE EQUIVALENT CALORIMETER WITH COVER PLATES REMOVED

Figure 12.

All of the interior plane parallel surfaces are coated with an evaporated layer of gold to provide low emissivity and good electrical contact for the wires to the central core, the adiabatic shield, and the control shield. These electrical leads allow each of the three elements to be heated independently using the ohmic resistance of the conducting plastic.

A calibration circuit similar to that described in reference (7) has been constructed. This circuit will heat the central core and adiabatic shield at equal rates and allow measurement of the electrical energy input corresponding to a temperature change to within $\pm 0.1\%$.

The Shonk plastic has been found to have very poor vacuum properties. Extensive outgassing requires extended pumping times (i.e. days). The recently built pumping system, maintains a vacuum of 0.06 microns at a monitoring point near the end of the calorimeter pumping stem. This suggests that the vacuum at the core is < 1 micron which is adequate for the required thermal isolation.

The calorimeter's overall sensitivity depends upon the temperature stability of the environment in which it is placed. To measure accurately the dose rates of 10-50 rads/min, equilibrium temperature variations of the order of 10^{-6} °C/min. are required. In this design the temperature stability at the core is determined by the regulation shield. This shield is heated to 5°C above room temperature and is regulated using an Artronix temperature stabilizer. The initial design criterion for temperature stability at the regulator shield was of the order of 10^{-3} °C/hr. Measurements, however, showed that only 10^{-1} °C/hr. was being obtained. By redesigning the temperature sensing components at the regulating shield and improving some components of the Artronix unit, an improvement by a factor of 5-10 was achieved. It is now possible to obtain temperature variations at the core of 5×10^{-5} °C/min. for periods of approximately 30 minutes. Further improvements, which will increase the sensitivity by the require factor of 10, are in progress.

C. ²⁵²Cf Dosimetry (L.L. Anderson, J.S. Laughlin)

²⁵²Cf medical neutron sources are being evaluated at Memorial Hospital and Sloan-Kettering Institute for application to implant radiotherapy. Preclinical studies during the year have included basic dosimetry measurements and, in support of preclinical radiobiology, apparatus designed to meet specific dosimetric requirements. Neutron and gamma-ray absorbed dose rates have been measured in a nylon phantom along the transverse axis of a ²⁵²Cf applicator tube (active length 1.5 cm). An ion chamber having tissue equivalent walls and filling gas was used to measure the total absorbed dose rate from neutrons and gamma-rays, and the gamma-ray absorbed dose rate was determined separately with an aluminum chamber using argon filling gas. The collecting volume in each chamber was about 0.05 cm³. For distances of 1-5 cm. from the source the absorbed dose rate from neutrons ranged from 1.89 to 0.056 rad/ μg -hr, that from gamma rays from 0.83 to 0.052

rad/ μ g-hr. The gamma ray results agree closely with measurements in other laboratories, while the neutron data are intermediate among values obtained elsewhere.

HeLa cell irradiations with ^{252}Cf and radium sources have been performed by Dr. Dhordjevic (8) using the irradiation apparatus shown in Figure 12a. These studies were performed to measure relative biological effect (RBE) and oxygen enhancement ratios (OER). Cells in suspension are contained in the central 10 cm portion of 1 ml polystyrene pipettes for irradiation at a distance of 2.2 cm. from sources contained in thin-wall stainless steel tubing located on the axis of the cylindrical array. The ^{252}Cf absorbed dose rate was 13 rad/h from neutrons and 7 rad/h from gamma rays whereas the radium dose rate was 64 rad/h source. Calculations indicate a total absorbed dose rate of about 20 rad/h, uniform within $\pm 3\%$ over the central 10 cm portion of each pipette, i.e., the cell-containing region of the pipettes. Hypoxia is achieved by surrounding the cells with an excess of metabolizing but non-cloneforming cells which have been pre-dosed with 3000 rads of x-rays. The cell holder portion of the apparatus is withdrawn from the bath for individual pipette removal at irradiation times appropriate for the intended dose levels. The design allows accurate repositioning of the cells with minimal exposure of the operator.

A rabbit restraining mold used in testis irradiations with other radiation sources has been specially modified and outfitted for ^{252}Cf irradiation. A nylon phantom has been provided to assure sufficient uniformity and accuracy in neutron dosimetry, and source-positioning devices have been fabricated to permit irradiations to be carried out with minimal personnel exposure. The single-plane irradiation geometry calls for two applicator tube sources in each of three nylon tubes positioned between and on either side of the testes. Computer-calculated dose distributions show neutron and gamma absorbed dose uniformity within about $\pm 10\%$ through the treatment volume. Reduced sperm production in the post-irradiation period as carried out by Dr. E. Hahn, Radiotherapy Research serves to indicate radiation injury as a function of dose to the spermatogonial cell system.

Figure 12a. HeLa Cell irradiation apparatus

III. GERMANIUM GAMMA CAMERA

The solid state detector program is currently concentrated on the construction of a semiconductor gamma camera from an array of ultra pure germanium diodes and biological applications of the initial prototype. Ultra pure germanium diodes have been found preferable to lithium drifted diodes in this work because of their superior bulk and surface stability and because they do not involve the troublesome lithium drift process in their production. Also in a "clean" vacuum system they do not require cooling except during operation. The germanium camera being constructed employs the orthogonal strip geometry originally developed in this program and demonstrated for such use with a silicon lithium drifted diode (9). For convenience of reference, the orthogonal strip geometry and the mode of signal address with its use are shown in Figure 13 (a,b), respectively.

A. Prototype Germanium Camera

1. Assembly

A small prototype camera has been under evaluation during the period covered by this report. The detector in this unit is a square, $(2 \times 2) \text{ cm}^2$ orthogonal strip matrix, 5 mm. thick with 36 detection regions (cells) on the single substrate. The electronic monitoring system employed for the 6×6 matrix consists of twelve data channels each of which contains a charge sensitive preamplifier, main amplifier, and single channel analyser. The requirement is currently being filled by PASCA 817 double width nuclear instrumentation modules produced by a commercial firm.* Processing of signals from the gamma camera employs both a multi-channel analyser (M.C.A.) and our 1800 computer. Specifically, the data from a particular measurement with the camera are recorded with the M.C.A. on punched paper tape in terms of the total counts accumulated in each matrix cell. This is accomplished by uniquely weighting the electronically summed signals from the row and column corresponding to each matrix cell. A coincidence requirement is used before the summing operation. Image data are obtained from the digital data on the punched paper tape through a suitable computer program which remaps the linear data of the analyser back into the plane and presents it both digitally and in analog form on a storage scope. Examples of the latter display are given in Figures 24, 25 and 26 and will be discussed below. Since this prototype orthogonal strip gamma camera comprises an array of discrete matrix cells, the coordinates of each gamma-ray absorption which takes place in an individual matrix cell are determined to the precision of the cell dimensions. Therefore, the total accumulation of counts for each matrix cell are randomly distributed over

*Canberra Industries

Figure 14. Electronic system used with prototype germanium camera

the area of the cell in the computer generated dot images from the camera. A functional schematic for the camera readout is shown in Figure 14.

2. Performance Measurements With Collimation.

Originally, when the camera's orthogonal strip matrix was constructed, it was inserted into its special cryostat without a collimator, along with a 1 mm beam ^{57}Co test source. A vacuum feed-through which was mounted in a glass window at the top of the cryostat permitted external positioning of the source. Figure 15 is a computer generated isometric display showing the response of the matrix to this source at two different positions above the matrix separated by less than 4 mm. The plane represents matrix spatial coordinates while the vertical height represents the number of counts at each position of the source above the matrix. It can be seen that the peaks are clearly separated in the image. Spectral measurements made while the ^{57}Co source was still within the cryostat were presented in the previous report and will not be repeated here.

Interelectrode strip measurements were made for both sides of the orthogonal strip matrix. These data are important for several reasons. Unless the electrical resistance of the grooves between the electrode strips is high enough, excessive noise injection between electrode strips will seriously impair the spatial resolution of the camera. Also, groove resistance has a bearing on the electrical field distribution at the boundaries of the separate electrode strips of the array and is expected to have a significant influence on ultimate spatial resolution through its effect on charge collection at the edges of the electrode strips. Finally the high groove resistance may make possible the application of a simpler electronic monitoring system in operating the camera. This would involve the use of suitable external divider networks. N-side groove resistance measurements for a number of reverse biases on the matrix are presented in Figures 16, 17, and 18. The asymmetry in the voltage-current curves is expected since the voltage across each groove opposes the bias voltage across the matrix for one polarity while adding to it for the other. The indicated polarity on the graphs is to be understood only as relative to the electrode strips bounding each groove and not to the bias voltage across the matrix. It can be seen from these data that the inferred resistance, $\frac{\Delta V}{\Delta I}$, exceeds 10^{12} ohms over the linear portions of the curves for all grooves on the n-side. For groove number 3, the slope corresponds to a resistance value of greater than 10^{14} ohms for all bias voltages. Figure 19 is a plot of groove resistance data for a representative n-side groove for a range of bias voltages and shows that even at low bias voltages, n-side groove resistance values remain high over the linear portion of the curves. The only effect of lowering the reverse bias

Figure 15. Isometric display of response of germanium camera to ^{57}Co (122kev) point source at two positions above the matrix separated by less than 4 m.m.

ORTHOGONAL STRIP MATRIX- ULTRA PURE GERMANIUM

n-side groove resistance 150 volts bias

Figure 16.

ORTHOGONAL STRIP MATRIX- ULTRA PURE GERMANIUM

n-side groove resistance 200 volts bias

Figure 17

ORTHOGONAL STRIP MATRIX
ULTRA PURE GERMANIUM
n-side groove resistance 250 volts bias

Figure 18

ORTHOGONAL STRIP MATRIX- ULTRA PURE GERMANIUM

n-side groove resistance of
representative groove for a
number of reverse biases

Figure 19

voltage across the matrix is to reduce the voltage threshold at which the curves depart sharply from a linear relation between voltage and current across each groove.

The situation on the p-side is different since in ultra-pure germanium the depletion layer of the diode matrix moves from the n-side toward the p-side with increasing reverse bias until the entire region between p and n sides is depleted. The character of the voltage-current curves of the p-side, appears in Figures 20, 21 and 22. As was found for the n-side, the p-side resistance values derived from the slope of the linear portions of the curves are well in excess of 10^{12} ohms at all bias voltages.

Figure 23 shows the voltage-current characteristic of a representative p-side groove for a number of different reverse biases on the matrix. It can be seen from the linear sections of the curves that for matrix bias voltages as low as 180 volts, there is a linear, high resistance portion of the voltage current curve. However, at 177 volts reverse bias the resistance across the groove drops by orders of magnitude, becoming insignificant relative to its values at higher reverse biases. Calculation shows that this is consistent with the depletion layer not reaching the bottom of the groove on the p-side for voltages not greater than 177 volts. This behavior of the current-voltage curve provides a rough check of the impurity concentration maximum in the germanium along each groove. By comparing depletion voltages for each groove and using the known groove depth, the coarse variations in the maximum impurity concentration in the germanium along the grooves on the p-side can be calculated. This calculated value agrees within a few percent of the impurity concentration value of $1.6 \times 10^{10}/\text{cm}^3$ provided by the supplier for the groove data given in Figure 23. The spread in the depletion voltage for the other grooves implies a value of $1.6 - 2.0 \times 10^{10}/\text{cm}^3$ from one edge groove on the p-side to the other edge groove.

3. Camera Images with Collimation

To evaluate the capabilities of the prototype camera in imaging distributed radionuclide sources in phantoms and in-vivo, a one inch thick, straight bore collimator was installed within the matrix cryostat, taking the place of the copper infra-red shield that was over the matrix in the initial test arrangement. A glove bag was used to minimize dust and to maintain a partial atmosphere of dry argon during the insertion of the collimator into the matrix cryostat. In the entire process, the matrix was exposed to room temperature for around ten consecutive hours. Electrical characteristics, measured shortly following cool-down, indicated no observable change had occurred in this time. Following gain adjustments in the monitoring electronics (see Figure 14) the collimator alignment with respect to the matrix cells was checked

ORTHOGONAL STRIP MATRIX-ULTRA PURE GERMANIUM

*P-side groove resistance
200 volts bias*

Figure 20

**ORTHOGONAL STRIP
MATRIX-ULTRA PURE
GERMANIUM**

*P-side groove resistance
250 volts bias*

Figure 21

ORTHOGONAL STRIP
MATRIX-ULTRA PURE
GERMANIUM

P-side groove resistance
300 volts bias

Figure 22

ORTHOGONAL STRIP MATRIX-ULTRA PURE GERMANIUM

*P-side groove resistance of
representative groove for
a number of reverse biases*

Figure 23

using a collimated 1 m.m ^{57}Co beam source. These measurements showed that the matrix was slightly misaligned with respect to the collimator but not seriously enough to warrant reopening the cryostat to correct it.

A small phantom was constructed of Lucite to test the resolution of the camera with $^{99\text{m}}\text{Tc}$. Figure 24 (a) is a storage scope dot image of the response of the camera to two $^{99\text{m}}\text{Tc}$ "hot" spots of 3 and 4 m.m diameter in the phantom and separated by 9 m.m. In (b) of the same figure, are shown the same "hot" spots with a 5 m.m spot introduced between them. The three spots are resolved although the edge separation between the 5 m.m. spot and the other two is less than 4 m.m.

4. Initial Biological Applications.

A number of images were made of small mammalian organs in-vivo to test the operational characteristics of the camera under more realistic conditions than obtained from phantom measurements.

Figure 25 shows a dot image of a mouse liver obtained after the animal was injected with $^{99\text{m}}\text{Tc}$ (140KeV) sulfur colloid. Part (b) of the same figure is an image of the excised spleen of the same animal. The depth and position of this organ under the liver made it undetectable in the presence of the technetium in the liver.

For thyroid function imaging, ^{123}I , which has a gamma-ray of 159KeV and a 13 hour half-life, is well suited to use with the germanium gamma camera. An isotonic solution of ^{123}I was supplied for this use by Section 5501 after its production with the cyclotron.

The material was injected in the tail-vein of a rat. Initially, no image of the thyroid was obtained due to slight traces of carrier iodine in the solution, which caused saturation of the small iodine uptake capacity of the rat thyroid, and most of the isotope proved to be concentrated in the abdominal region. The problem was eliminated by preparing several rats with an iodine-free diet. Almost all of the radionuclide then concentrated in the thyroid a short while after injection. The dot image obtained with the germanium camera is shown at the bottom of Figure 26. The thyroid was later excised and an anterior and posterior photograph of the organ, still attached to a section of trachea, is shown in the upper part of the same figure. The two lobes of the thyroid are clearly resolved in the gamma camera image although the maximum dimensions of the organ are less than 1 cm.

Figure 24. A. Image of mouse liver following injection of animal with ^{99m}Tc (140keV) sulfur colloid. B. Image of excised spleen. The position of this organ made it undetectable in the presence of the technetium in the liver.

Figure 25.

- (A) Image of ^{99m}Tc (140KeV) phantom containing 3 and 4mm "hot"spots separated by 9 m.m.
- (B) 5 m.m. hot spot introduced between other two. Although the edge to edge separation between the center spot and the others is less than 4 m.m., all three are resolved.

Dot image of thyroid of rat injected with ^{123}I .

Figure 26.

Lower part is a gamma camera image of a rat thyroid following injection of the animal with ^{123}I (159KeV). Upper section is a photograph of the thyroid taken after its excision. The two thyroid lobes are resolved by the gamma camera although the maximum dimension of the organ is less than 1 cm.

5. Camera Operational Stability.

Spectral resolution of the matrix elements has been checked periodically to determine whether any degeneration was occurring with time in the operating characteristics of the matrix. Extensive groove resistance measurements were also made. No loss of spectral resolution has occurred within the past year. For all matrix cells, resolution of 4KeV (FWHM) or less is typical at ^{57}Co gamma-ray energies.

Although some change took place in the groove resistances since the time of earliest measurements around nine months ago, these changes have only resulted in a lowering of the groove voltage threshold at which the curves become non-linear on the p-side. The extent of this can be seen by comparison of a representative measurement at 300 volts reverse bias in Figure 27 with the earlier data of Figure 22. The latest groove resistance measurements still show the p-side groove resistances to exceed 10^{12} ohms. On the n-side the surface changes that slightly degraded the p-side caused a significant improvement in the n-side groove resistance. These trends in groove resistance values are reminiscent of the relative trends observed in the p and n side grooves resistance levels of the previously described lithium drifted silicon matrix (9).

It can be seen from the previously mentioned image of Figure 26 which was made shortly before the last groove resistance measurements, that the later levels are compatible with good image resolution.

B. Larger Area Orthogonal Strip Matrices

1. Construction

Since ultra pure germanium ingots of 5 cm. diameter are now being produced commercially, it is possible to produce orthogonal strip matrices with around 200 detection cells on the single substrate. The larger the size of the single substrate matrix arrays, the fewer will be needed in assembling a larger area gamma camera. A nearly square piece of large diameter (over 4x4 cm.) has been provided by the supplier* as a research specimen, prior to receipt of another being purchased. This wafer is in the diode production phase. An initial attempt to utilize the recently reported Palladium p^+ contact (10) was not successful. At present, it appears that this contact type may be too fragile for practical use with the orthogonal strip matrix. However, these results are preliminary and further tests are planned.

Facilities have recently been completed for construction of Boron p^+ contacts on ultra pure germanium using the Boron trifluoride gas discharge technique developed at General Electric. The suitability of this type of p^+ contact on large area matrices will also be determined in future work. The system constructed is modelled, in principle, after the one used by General Electric. However, instead of constructing a self-contained glass vacuum system, a vacuum evaporator already on hand is being employed to

*General Electric, Schenectady, N.Y.

ORTHOGONAL STRIP MATRIX
ULTRA PURE GERMANIUM
P-side groove resistance
300 volts bias

Figure 27

ORTHOGONAL STRIP MATRIX WITH CHARGE DIVISION READOUT

Figure 28

obviate the need to assemble another pumping system with associated metering and vacuum feed-throughs. The glass vessel which is used to hold the germanium and confine the BF_3 during the discharge can be opened and closed within the bell jar of the evaporator through the use of a translation-rotation vacuum feed-through. The apparatus is readily removed when the evaporator system is required for other purposes.

2. External Divider Network for Germanium Camera Read-out

The high groove resistance values obtainable from the ultra pure germanium matrix of the prototype gamma camera allow the possibility of employing a simpler electronic read-out system for the orthogonal strip gamma camera. This would employ a suitable resistive divider network on each side of the matrix. Ideally only three data channels would be required to monitor any size orthogonal strip array whether constructed from a single substrate matrix or an assembly of them with corresponding rows and columns electrically connected. A schematic of this approach is shown in Figure 28. This figure illustrates the use of charge division, although this is not the only mode of signal address being considered. Various type of impedance networks for monitoring position sensitive detectors already have been used widely with charged particle measurements and have yielded submillimeter spatial resolution (11, 12, 13, 14, 15, 16). Generally, high sheet resistance diode electrodes on single diodes have been employed to implement this technique of position sensing for semiconductor detectors. The use of such a method with a gamma-ray camera cannot yield such spatial resolution because of Compton scatter within the detector but it can be shown by calculation that the loss of spatial resolution from this effect is well under 3 m.m. (17) for gamma-rays under 200 KeV. Obviously, this approach to signal monitoring of an orthogonal strip matrix is applicable to charged particle measurements over large areas where submillimeter spatial resolution is not required. Both silicon and germanium arrays would be applicable in such instances. A resistive divider has been designed and built into the monitoring circuitry of the p-side of the prototype germanium camera. It is so constructed that the original circuit configuration can be quickly restored through the use of "jumper" pins. In this way the two methods can be readily compared. Preliminary measurements indicate that a major problem confronting the use of this type of monitor with a germanium camera is the level of Johnson noise in the resistive divider network relative to the signal levels that can be obtained over the camera's working gamma-ray energy range.

IV. DOSIMETRY OF ULTRA HIGH INTENSITY ELECTRON BEAMS

A. Introduction

The dosimetric studies at this laboratory in the high dose rate region include the determination of the absorbed dose in very thin layers of tissue equivalent and other materials, the characterization of electron beam parameters and the investigation of the dose rate response of various secondary dosimeters. Our previous progress report (1) described a method for determining the dose delivered to a thin sample by using an extrapolation technique. This method along with calorimetric and TLD measurements were applied to the problem of determining the dose delivered to HeLa cell layers, whose radiosensitivity was studied as a function of absorbed dose when cells were irradiated in air and nitrogen.

B. Dosimetric Measurements

A series of measurements were made to determine the dose as a function of distance from the field emission electron source. Since the pulsed electron generators have a fixed output per pulse, the dose is varied by using different length evacuated aluminum drift tubes. The range of dose necessary for these studies was from a few hundred to a few thousand rads. In order to achieve these relatively low doses without using extremely long drift tubes it was necessary to use an aperture plate which was placed in direct contact with the electron tube face. This aperture plate was made of aluminum and had a 1/4" hole through which the electron beam emerged.

Dose was measured with a beryllium calorimeter 1" in diameter and 0.001" thick which was placed at the irradiation position. The temperature rise was measured and the dose computed from a knowledge of the specific heat of beryllium. These measure values were then converted to absorbed dose in water by calculating the stopping power ratio for beryllium of water. This ratio if found to be constant to within $\pm 1\%$ over the range of electron energies up to 1 MeV.

Another method was also employed since the calorimeter sensitivity was low for such low values of absorbed dose. $\text{CaF}_2\text{:Mn}$ thermoluminescent dosimeters were placed on a petri dish and irradiated in the experimental geometry. When the dose as a function of source to detector distance was plotted (Figure 29) it was found that both calorimetric and TLD measurements fell on the same line indicating consistency between the two methods. Thus a dose axis was established for the HeLa cell irradiations at various distances from the electron tube.

Figure 29. Calorimeter and TDL Distance Function

There exists a possibility for dose build up in a sample so that a gradient might exist through the depth of the irradiated sample. If this were true then measurements made with the calorimeter or TLD which are thicker than the cell layer can be significantly different from the dose delivered to the HeLa cells. Measurements of the depth dose in polystyrene (Figures 30 and 31) using thin plastic scintillators show that build up, if it is present at all, is a small effect (less than 5%). The experimental geometry accounts for the lack of build up since there are two vacuum windows between the source and the experiment each of which is 0.002" thick Mylar. This intervening material puts the measuring point at a depth which seems sufficient to build up the dose to a plateau region. Since there is very little build up, these measurements indicate that the dose measured by the calorimeter is (when corrected for stopping power) the dose delivered to the thin cell layer.

For convenience of measurement a set of data was collected using a Faraday cup detector at the experimental position (Figure 32). Since the Faraday cup is directly read with an electrometer it is desirable to know the dose in terms of charge measured. Therefore, a distance function was measured using the Faraday cup and this information was used to determine the vacuum drift tube length necessary for a cell irradiation of a desired number of rads.

Figure 30. Depth Dose in Polystyrene

Figure 31. Depth Dose in Polystyrene

Figure 32. Faraday Cup Distance Function

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