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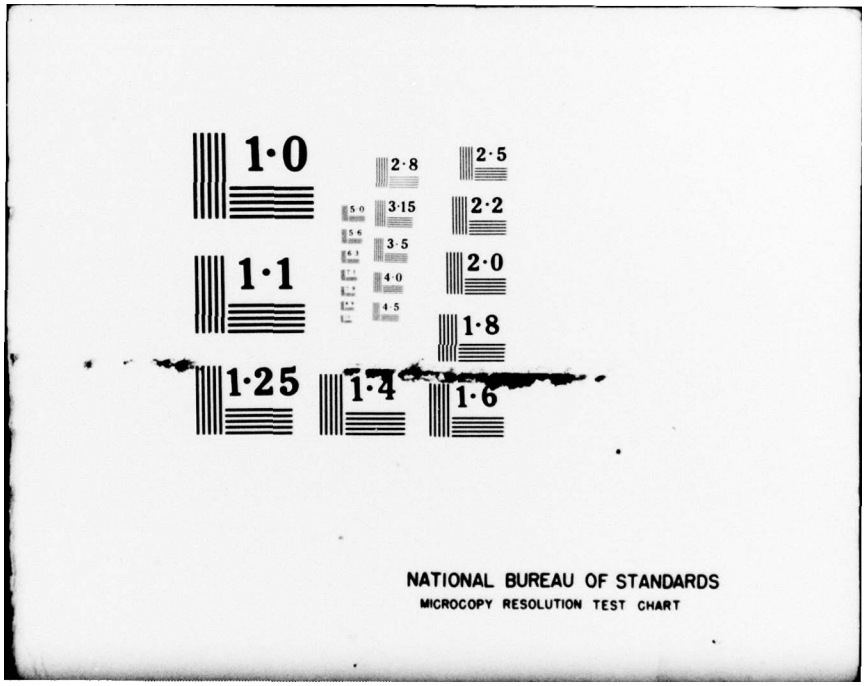
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Third Symposium on Neutron Dosimetry in Biology and Medicine, 1977

L.S. August*

19 September 1977

*Naval Research Laboratory, Washington, D.C.

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The major topics discussed at the Symposium are summarized, including depth-dose studies, dosimetry and monitoring, sources and facilities, spectrometry, radiation quality studies, ionization chambers, solid state detectors, novel dosimetry systems, and dosimetry intercomparisons. Post-symposium visits to two UK neutron cancer-therapy centers are also briefly discussed.

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THIRD SYMPOSIUM ON NEUTRON DOSIMETRY IN BIOLOGY AND MEDICINE, 1977

The international effort in neutron cancer-therapy has stimulated research in a number of the supporting areas of the clinical work—radiobiology, neutron physics, and dosimetry. Most of the work reported at this symposium was concerned with neutron dosimetry in the broadest sense. However, much neutron physics is involved, of necessity, in any discussion of neutron dosimetry because of the greater complexity of phenomena involved here as compared to photon dosimetry. Some attention was also given to radiobiology at the Symposium, but in a somewhat restricted sense. For example, cell systems were employed as relative biological dosimeters. This report is concerned primarily with some highlights of the Symposium. Also, visits to two UK neutron cancer-therapy centers are briefly discussed.

The Third Symposium on Neutron Dosimetry in Biology and Medicine, which lasted from 23 to 27 May 1977, was hosted by the Gesellschaft für Strahlen- (GSF) und Umweltforschung mbH, Neuherberg/München, Federal Republic of Germany. One hundred-forty participants from 18 countries attended the Symposium, the large number reflecting the increasing interest in neutron radiotherapy and its supportive research. There are 19 institutions throughout the world that are either currently performing neutron radiotherapy or planning to do so in the very near future. In addition, there are a number of research and standards laboratories that do neutron research directly related to medical work. The symposium was divided into 15 sessions extending over the 5 days and covered the following general topics in 71 papers: basic data; depth dose studies; dosimetry and monitoring; sources and facilities; spectrometry; radiation quality studies; ionization chambers; calorimetry; solid state detectors; and dosimetry intercomparisons. The following is a selective summary from these papers.

The first three sessions were concerned with basic data and included reports on: kerma calculations based on existing cross-section data, stopping-power ratios, and W values, i.e., the energy required to produce an ion pair, for various materials, particles, and energies. R.S. Caswell and J.J. Coyne (National Bureau of Standards, Washington, D.C.), in reporting on the NBS kerma calculations, stressed the need for good neutron-reaction cross-section data on tissue elements, especially O, C and N, for neutron energies greater than 20 MeV. D.I. Thwaites and D.E. Watt (Dundee Univ., UK) made the interesting point that the stopping power of a material depends to some extent on its phase. For example, 5% differences can occur for the same material depending upon whether it is in the solid or gaseous phase. In commenting on the uncertainty in absolute dose, H. Bichsel and A. Rubach (Univ. of Washington, Seattle) stated that neither "W" nor the stopping power for materials used in neutron

dosimetry are particularly well known. As an example, they attempted to place limits on the stopping-power ratio of wall to gas for an ionization chamber consisting of a graphite wall and filled with CO_2 gas. Depending upon how the calculations were made and the data employed, this ratio could vary by as much as 12%.

While relatively low-yield neutron sources can be used in obtaining basic data, intense neutron sources are required for therapeutic purposes in order to achieve treatment times that are tolerable to the patient. Such sources are also necessary to treat a relatively large number of patients per day in order to gather sufficient clinical statistics, so that the efficacy of neutrons relative to x-rays can be determined in a finite number of years for each tumor type being treated and compared. One entire poster and reporting session was devoted to the subject of neutron sources. Of the present 19 worldwide neutron therapy centers, 9 are cyclotron-based, 9 employ D-T generators, and one uses a linear accelerator. No attempt will be made here to address the question as to which type of source is "best," since such a judgment depends on the exact requirements of an institution, the available funding, and the state-of-the-art of neutron-source technology at any given time. It is clear that adequate neutron sources are available today to do meaningful clinical trials. What the future holds for neutron therapy appears to be mostly dependent upon the results of the current worldwide clinical trials. If neutrons prove clearly superior to x-rays in a significant number of cases, it seems clear, from the source development work going on, that intense, efficient neutron sources suitable for hospital installation will be available. Some of the more interesting source developments discussed at the Symposium will now be recounted.

At one time it was thought by some that D-T neutron sources give less skin sparing than do cyclotron-based neutron sources of roughly comparable average neutron energy. Results discussed at the Symposium [J.J. Broerse *et al*, Netherlands Central Organization for Scientific Research (TNO), Rijswijk, the Netherlands and W. Grant *et al*, M.D. Anderson Hospital, Houston, Texas] show that the two types of sources are either intrinsically comparable or else can be made so with respect to skin sparing. Also, the newest D-T generators can now provide dose rates of about 20 rads per minute or perhaps a bit more. Additionally, tube life is being extended. These machines are usually fabricated in an isocentric mount, thus providing greater flexibility in treating patients than most cyclotron-based sources, which have either a fixed horizontal or vertical beam. However, cyclotron facilities at Essen and Edinburgh have isocentric treatment facilities. These are the first cyclotron-based isocentric facilities in the world. The cyclotrons are installed in a shielded vault and their median planes are horizontal. A deuteron-ion beam of approximately 100 μA and 15.5-MeV energy is extracted from the commercially available accelerator. The d + Be reaction is employed, and the resulting neutron spectrum is quite similar to the one at Hammersmith

Hospital, London (deuteron energy = 16 MeV). The deuteron beam passes through a flexible vacuum-coupling and then is deflected by a 45° bending magnet that is rotatable with the isocentric head. The deflected ion-beam travels through evacuated tubing into and through another 45° bending magnet in the head of the isocentric unit. Various magnet currents are adjusted so that the focused ion-beam strikes the center of the thick Be target. A large amount of hydrogeneous material is used in the isocentric head for neutron shielding. Many slow neutrons are produced in the head as a result of the slowing down of the fast neutrons by this hydrogeneous material. Immediately after a simulated treatment, there has been an uncomfortably large amount of beta and gamma activity produced, primarily as a result of neutron capture by aluminum which leads to the 2.3-minute activity from ^{28}Al. The aluminum parts are being interchanged with other materials that will significantly reduce the short-term activation. Until the interchange of parts is completed, the fixed-horizontal beam treatment room is being used for all neutron therapy.

Low-energy cyclotrons (deuteron energy < 15 MeV) present several problems when the attempt is made to use such accelerators in neutron cancer-therapy. Because of the low energy, the dose rate per μA of ion-beam current is quite low, and the penetrability of the neutrons produced also tends to be low. A possibility that showed promise for low-energy machines was the D-D reaction using a high-pressure deuterium gas target. In the low-MeV deuteron-energy range, both the dose rate per μA and the penetrability show an increase with increasing deuteron energy. F.T. Kuchnir, F.M. Waterman and L.S. Skaggs (Univ. of Chicago, Illinois) have developed a cryogenically cooled deuterium-gas target, and have measured dose rate in air per μA and penetration in tissue over an energy range from 6.8 to 11.1 MeV. Neutron time-of-flight spectra have also been obtained in order to see how the neutron spectrum changes with energy for the D-D reactions. Whereas the dose rate in air per μA increases by a factor of five from 6.8 to 11.1 MeV, the penetration of the neutrons in tissue is essentially constant over this energy range. The time-of-flight spectra show the reasons for this set of conditions. At the lower energies, the D(d,n)^{3}He reaction is the dominant one, and the relatively high-average neutron energy (and penetration in tissue) increases with increasing energy. However, as the deuteron energy increases, the D(d,np)D reaction becomes increasingly more important. The average energy of the break-up reaction is much lower than that of the D(d,n)^{3}He reaction, and there is a compensation which keeps the average energy constant over the energy range studied. However, the half-dose depth in unit density tissue is about 10 cm, and this penetration is adequate for treating many types of tumors. At an ion-beam current of 180 μA, a dose rate in air of 30 rads per minute can be obtained at a treatment distance of 126 cm. The liquid nitrogen consumed by the target for cooling is 4 liters for a 5-minute treatment period, and the cost of the nitrogen will be about $2 per patient treatment.

Many papers were concerned with various details of neutron dose measurement, including the theory of operation of various ion chambers, calculations of dose in phantom, dose measurements in and out of phantom, and neutron-gamma dose separation. As physicists probe more and more deeply into the details of various dosimetric questions, the path leads inevitably to neutron physics. Relevant neutron physics research permeated many talks, and several papers were explicitly concerned with the neutron physics that illuminated some specific dosimetric problems. Approximately 60% of the papers were devoted to the broad topics outlined above, and in the following comments some that may be of general interest are discussed.

A number of presentations were concerned with achieving a better understanding of the basic mechanisms involved in ionization-chamber response. In discussing some results obtained with a very widely used, commercially available ionization chamber, C.J. Parnell (Hammersmith Hospital, London) made two important points. When using tissue-equivalent (TE) gas flowing through the TE chamber at flow rates below 0.50 cc/min, problems can arise due to air diffusion into the chamber, thereby causing a lower ionization-current reading than when the chamber contains only TE gas. He recommends flow rates >0.50 cc/min if this diffusion problem is to be avoided. The radiation source used in the work was a long-half-life gamma source (^{137}Cs) which simulates a constant strength source very well over the times involved in the measurements. Another problem was encountered in making saturation curve measurements to correct ion-recombination effects. When the ion-chamber voltage was changed, especially at lower voltages (<50 V), the ion current took a rather long time (about 10 minutes) to reach a constant value. When going from 500 V to 0 V, the chamber did not reach a constant value even after 1 hour. This time-delay difficulty was ascribed to static charge build-up on insulators in the chamber. Parnell recommends voltages greater than 100 V for routine dosimetric use of this type of chamber. The higher voltages greatly reduce the time delay before equilibrium is reached.

A.G. Sherwin [National Radiological Protection Board (NRPB), Harwell, UK] presented two papers, one of his own and one submitted by A.A. Edwards (NRPB), that were concerned with the calculation of absolute dose as measured by ion chambers in which (1) the counter size was taken into account, and (2) the ion distributions within the ionization chambers were considered in detail, since gamma rays and neutrons can give quite different ion distributions. These two papers emphasized the subtleties involved in neutron dosimetry, as well as the problems encountered in attempting to make highly accurate absolute dose measurements with ion chambers.

H. Bichsel (Univ. of Washington, Seattle) commented on one possible explanation for the difficulties encountered in using the C + CO_2 system (a graphite chamber with CO_2 gas) in a paired-chamber experiment designed to determine gamma dose in a mixed neutron-plus-gamma field. He pointed

out that the neutron/gamma sensitivity ratio can vary by a factor of three over the range of neutron energies encountered in neutron therapy. Not properly accounting for such variations may explain why paired chamber measurements using TE and C + CO_2 systems sometimes yield negative gamma doses.

M. Zielczynski (Institute of Nuclear Research, Swierk, Poland) described an interesting development which appears to greatly reduce the difficulties encountered with the C + CO_2 system in determining gamma dose in a mixed field. The CO_2 pressure employed is 15 atm, and the voltage applied to the chamber is 300 V. Under these conditions the neutron sensitivity is 1% of the gamma sensitivity for a neutron energy of 10 MeV. For all neutron energies below 20 MeV, the neutron sensitivity is less than 3% of the gamma sensitivity. The explanation for the greatly reduced neutron sensitivity of the C + CO_2 system lies in the ion recombination that occurs. The alpha particles produced in the chamber by the incident neutrons give densely ionizing tracks, and, because of the high pressure, ion recombination eliminates most of the ion current from this source. On the other hand, the gamma-produced ion pairs, having a far less dense distribution, are detected with about a 75% efficiency.

As to be noted in the comments above, as well as in numerous other papers presented at the Symposium, the problem of separating the total dose into the neutron and gamma components is a topic of continuing interest. Over the past several years, values of the percent gamma dose relative to the total dose have varied by an order of magnitude for essentially the same kinds of mixed fields, with values ranging from negative ones to 30% or 40% even along the neutron beam axis. While such wide variations were not reported at this Symposium, it was still evident that substantial disagreement (a factor of two or somewhat more) among various investigators still exists. In an attempt to place realistic limits on the gamma dose in phantom along the beam axis, L.S. August *et al* (Naval Research Laboratory, Washington, D.C.) utilized TE spherical proportional counter data and neutron activation employing the reaction $^{27}Al(n,\alpha)^{24}Na$. The proportional counter work showed that along the beam axis, even though attenuation occurs, the fast neutron-spectrum shape does not change in a measurable way. The constancy of the neutron-spectrum shape along the beam axis in phantom was corroborated by other workers at the Symposium. Since the spectrum is constant with depth, a high threshold ($\sim$5 MeV) reaction such as $^{27}Al(n,\alpha)^{24}Na$ should give activation values proportional to the fast-neutron-only doses. By making an air calibration of the activation dosimeter and reasonable assumptions to account for the changes in the neutron spectrum in air and in phantom, upper and lower limits could be placed on the neutron-only doses in phantom. By subtracting these values from the total doses measured with a TE ionization chamber, gamma-dose limits were obtained as a function of depth in the phantom.

H.G. Menzel *et al* (Universität des Saarlandes, Homburg, Germany) reported on some interesting work that bears directly on the question of separating the neutron and gamma doses in phantom. By enhancing the signal-to-noise ratio for the system, a Rossi counter (i.e., spherical proportional counter) is used down to an event size of 0.06 keV/μm, and the event-size distribution is extended down to 0.01 keV/μm by using an extrapolation method employing a ^{24}Na spectrum. Spectrum stripping must be invoked in order to separate the gamma and neutron components, and an error of about 20% is assigned to the final gamma-dose values. For moderate-size fields a gamma-ray dose of about 10% is assigned at a depth of 8 cm. This value falls midway between the limits given by August *et al* at 8 cm depth. The two sources employed in the work presented by August and Menzel have the same average energy, but different neutron spectra [d + Be (E_d = 35 MeV) versus D-T]. What effect this difference might have, if any, on the gamma dose in phantom requires further investigation.

The question of spectral quality as measured by a Rossi counter was also addressed by G.H. Harrison *et al* (Univ. of Maryland Hospital, Baltimore), but they were concerned with the high-LET (linear energy transfer) events produced by neutrons interacting with TE material. Neutron beams of average energy 32 and 50 MeV, produced by the reactions d + Be (E_d = 80 MeV) and p + Be (E_p = 100 MeV), respectively, were employed in the measurements. For the deuteron reaction, 1/3 of the neutron dose is caused by the high-LET events (LET > 100 keV/μm). Of this fraction, 1/3 (or about 10% of the total dose) is caused by events with LET > 300 keV/μm. Harrison *et al* raised the question as to whether multifragment events, involving alpha particles or other light ions, might be temporally but not spatially coincident and cause distortions in the high-LET region of the LET distribution. Elastic n-^{16}O measurements plus kerma calculations on the recoiling ^{12}C and ^{16}O ions compel Harrison *et al* to conclude that the broad peak centered at about 400 keV/μm is not due primarily to recoiling heavy ions, but rather the coincidence of lighter spallation fragments. They can account for only a few percent of the 10% dose in this LET region by the recoiling heavy ions.

A number of innovative and potentially promising dosimetric techniques were discussed. One such development was the use of lyoluminescence to measure dose. In this type of dosimeter the light emitted on dissolving the material in water is related to the dose received. K.J. Puite and J. Zoetelief (Associate Euratom-ITAL, Wageningen, the Netherlands) reported on the use of the monosaccharide mannose ($C_6H_{12}O_6$). In the 100-rad range, the reproducibility was ±7%, but efforts are being made to improve on these results. The fading of the signal with time is reported to be small, being only 6% during the first week after irradiation. The interest in materials of this type stems from their similarity to tissue in elemental composition.

W. Porschen *et al* (Institut für Medizin der Kernforschungsanlage, Jülich, Germany) discussed an interesting *in vivo* dosimetry study using an *in vitro* analysis technique. Irradiation disturbs cell proliferation and alters the DNA-synthesis mechanism. The DNA-synthesis rate can be studied by incorporating a suitable radioactive precursor into the DNA. The precursor employed in this work is ^{125}I-deoxyuridine (^{125}IUdR). The incorporation rate of ^{125}IUdR into mouse bone-marrow cells is analyzed under *in vitro* conditions following irradiation with three different sources. These were: ^{137}Cs gammas; 15-MeV neutrons from a D-T generator; and cyclotron-produced neutrons of 7-MeV average energy. The data show the feasibility of biological dosimetry using as the dosimetric parameter the incorporation rate of ^{125}IUdR into the DNA. The maximum effect for each dose value occurs about four hours after irradiation. The effect could be observed even at a dose level of 5 rad. Porschen pointed out that in these studies 100,000 mice were used, i.e., two tons of mice!

The last session of the conference was devoted to the European Neutron Dosimetry Intercomparison Project (ENDIP). Twenty groups from eight countries participated in the series of measurements which were carried out during 1975 at GSF, Neuherberg/München and TNO, Rijswijk. H. Schraube *et al* (GSF, Neuherberg/München) reported on the facilities available for the intercomparison. At GSF measurements were performed with nearly monoenergetic neutrons in a minimum scatter configuration. The dose rate was 0.33 rad/min. At TNO the experimental arrangement was designed to simulate a therapy environment. Collimated beams of D-T and D-D neutrons were employed in free-air and water-phantom measurements. The dose rate at TNO was 1.5 rad/min.

J.J. Broerse *et al* (TNO, Rijswijk) discussed the results obtained during ENDIP. When the ENDIP results were first compared, a good deal of scatter was noted in the values obtained for total dose when the same neutron beam and experimental geometry was used. It was thought that the use of different dosimetric constants by various groups could account for some of the discrepancies, and the data were reanalyzed using the same constants for all groups. However, in spite of analyzing the data in this way, there was still a good deal of scatter in the results. Most of the values for the total dose are within ±5% of the mean, but to include all results a range of ±15% must be used. The reasons for these variations are not known, and further work is underway in an attempt to resolve the questions raised by this intercomparison.

The Proceedings of the Symposium are to be published in the fall of 1977 by the Commission of the European Communities, Center for Information and Documentation, Luxembourg.

Following the Symposium, one-day visits were made to both the Western General Hospital, Edinburgh, Scotland, and the Hammersmith Hospital, London, England. Neutron cancer-therapy clinical trials for head and

neck lesions began in the first part of June, 1977 at Edinburgh. This clinical research is an extension of the work that has been going on at Hammersmith for the past several years. There is considerable cooperation between the two facilities, since they are both under the administrative control of the British Medical Research Council (MRC).

At Edinburgh patients are treated five times per week in order to mimic exactly the fractionation schedule used in x-ray cancer therapy. At Hammersmith the patients are treated three times per week. Both hospitals have well-equipped shops staffed by highly competent machinists who fabricate the unique and often complex devices required in both the clinical and research programs. The Edinburgh group has developed a quite sophisticated computer program for complete treatment planning. There is an interactive scope display unit which can show very quickly the consequences that result from modifications of the plan being displayed. The Hammersmith facility also supports quite active programs in radiobiology, neutron physics, dosimetry and radioisotope development, utilization, and production for medical purposes. The radioisotope effort at Hammersmith is quite impressive with respect to both the excellent equipment available and the amount of cyclotron time the work requires. It is interesting to note that the MRC cyclotron unit at Hammersmith supplies radioisotopes for medical purposes to the US. The many projects going on at this unit require the services of about 140 staff members.

In summary, the visits to the UK cancer-therapy centers were useful for exchanging ideas and to compare the concepts and methods used with those in the US, especially the one at NRL. The large participation in the Symposium showed the considerable interest in neutron cancer-therapy on a worldwide scale. The exchange of ideas at the Symposium was quite brisk and most profitable for all who participated. The problems pointed out and the new methods and concepts introduced will probably serve as a basis for much of the material to be presented at the next symposium.