DOE/ER/60389--T2

U. S. DEPARTMENT OF COMMERCE
National Institute of Standards and Technology
Gaithersburg, Maryland 20899

Final Report
to
Office of Biological and Environmental Research
U. S. Department of Energy
DOE Contract No. DE-AI-05-86ER60389
February 17, 1998

Neutron Interactions with Biological Tissue

This program was aimed at creating a quantitative physical description, at the micrometer and nanometer levels, of the physical interactions of neutrons with tissue through the ejected secondary charged particles. We used theoretical calculations whose input includes neutron cross section data; range, stopping power, ion yield, and straggling information; and geometrical properties. Outputs are "initial" and "slowing-down" spectra of charged particles, kerma factors, average values of quality factors, microdosimetric spectra, and integral microdosimetric parameters such as $\bar{y}_F$, $\bar{y}_D$, y^* . Since it has become apparent that nanometer site sizes are also relevant to radiobiological effects, the calculations of event size spectra and their parameters were extended to these smaller diameters. This information is basic to radiological physics, radiation biology, radiation protection of workers, and standards for neutron dose measurement.

Principal Investigator

Dr. Randall S. Caswell, Chief (retired), Ionizing Radiation Division (846), Physics Laboratory, National Institute of Standards and Technology (NIST).

Participating Scientific Investigators

Dr. J. Joseph Coyne, Theoretical Physicist, Ionizing Radiation Division (846), Physics Laboratory, NIST (now retired).

Mr. Stephen M. Seltzer, Leader (current position), Radiation Interactions and Dosimetry Group, Ionizing Radiation Division (846), Physics Laboratory, NIST.

Dr. Lisa R. Karam, Leader (current position), Radioactivity Group, Ionizing Radiation Division (846), Physics Laboratory, NIST.

DISTRIBUTION OF THIS DOCUMENT IS UNLIMITED

MASTER

DISCLAIMER

This report was prepared as an account of work sponsored by an agency of the United States Government. Neither the United States Government nor any agency thereof, nor any of their employees, makes any warranty, express or implied, or assumes any legal liability or responsibility for the accuracy, completeness, or usefulness of any information, apparatus, product, or process disclosed, or represents that its use would not infringe privately owned rights. Reference herein to any specific commercial product, process, or service by trade name, trademark, manufacturer, or otherwise does not necessarily constitute or imply its endorsement, recommendation, or favoring by the United States Government or any agency thereof. The views and opinions of authors expressed herein do not necessarily state or reflect those of the United States Government or any agency thereof.

DISCLAIMER

Portions of this document may be illegible in electronic image products. Images are produced from the best available original document.

Background

Our program was aimed primarily at understanding the basic picture of the "physical stage" in the interaction of neutrons with tissue and biological materials. Quantitative description of the processes and spectra involved in the transfer of energy from neutron radiation to the biological material helps in understanding the biological effects of neutron radiation. Physical information on the generation of secondary particles and the ultimate delivery of the energy to biological material provides a basic input for biophysical models of the biological effects of neutrons, and for neutron radiobiology. The question of radiation quality is very important for neutron protection and is generally expressed by the quality factor, Q , or the radiation weighting factor, w_R , which are believed to be much higher for neutrons than for x or gamma rays. Our studies of the energy deposition spectra of neutrons in small volumes should help to determine improved means for specifying the radiation quality of neutron fields. It is important that as good a scientific basis as possible exist upon which to make decisions concerning permissible levels of neutron radiation. The role of this project is to apply the basic research data generated by the OHER (now OBER) Radiological and Chemical Physics program to practical problems in radiation protection, such as improved measurement techniques and a better prediction of the health effects of neutrons.

Program of Work:

Study neutron interactions with biological tissue through neutron-generated secondary particles (p , α , C , N , O)

- Develop methods and computer programs for neutron interaction and track structure calculations.
- Calculate neutron-induced secondary particle spectra
 - Used as input to biophysical models of neutron biological effects
- Determine γ spectra and parameters
 - Basis for practical radiation hazard determination
 - Biology at cell nucleus level
- Calculate energy deposition and ion yield spectra on the nanometer scale (work begun when project ended)
 - Neutron effects at level of DNA and nucleosomes
 - Nanometer studies of energy deposition, ionization clusters (e.g. pairs).

Applications of Work

Applications Already in Use

- Neutron kerma coefficients (energy transfer coefficients) used worldwide for neutron dosimetry
- Katz used neutron-induced secondary particle spectra to predict cellular neutron effects by delta-ray interaction model
- γ spectra serve as standard for health physics analysis of radiation fields using tissue-equivalent proportional counters (state-of-the-art method)
- Neutron code led to radon code. W. Hofmann (U. of Salzburg) uses our results with his effect-specific track-length model to predict radon carcinogenesis in bronchial epithelium.

Future Applications

- Predict neutron biological effects from calculations + biophysical model
 - Hit-size effectiveness model
 - Elemental dose model
 - Study mechanisms of radiation action through testing models
- Elucidate neutron interactions on the nanometer scale
 - Determine neutron energy deposition spectra and ionization clusters for DNA and nucleosomes
 - Study nanometer-scale information as predictor of neutron RBE.

Some Accomplishments

1. Track structure effects in neutron microdosimetry and nanodosimetry. This is an investigation of the effect of proton energy-loss straggling and the associated transport of energy by secondary electrons on neutron event-size distributions in small sites. W. Wilson of Pacific Northwest Laboratory and H. Paretzke of GSF, Munich have

developed an analytic model for the ionizations or energy depositions produced in nanometer-size sites for protons and alpha particles which summarizes the results of hundreds of Monte Carlo calculations. The Wilson-Paretzke model has been used to generate event-size distributions for monoenergetic protons with a given chord length within a sphere of fixed diameter. Their distributions have been fitted with log normal distribution functions and the parameters of the log normal function are fitted analytically as a function of proton energy, sphere diameter, and chord length. These proton spectra are then used in a modified Caswell-Coyne code to generate event-size distributions for neutrons which include not only the effect of energy-loss straggling but also the transport of energy out of and into the cavity by the secondary delta rays. Wilson and Paretzke have also analyzed data for "touchers" or "passers" for protons and these are included in our calculations as well.

It has been clear for some time that, although the cell nucleus is of the scale of microns, say 8 μm , to understand the biological effects of ionizing radiations we need to consider as well smaller structures such as DNA (2 nm spacing between the strands) and nucleosomes (5-10 nm). For neutrons the situation is more complicated than for protons, for example, because of the many secondary particles produced by neutron interactions, the most important being p, α , C, N, and O.

Using the Wilson-Paretzke model combined with our analytic neutron code, we have calculated the spectra of neutron energy depositions in nanometer-size cavities for neutron energies from 0.5 MeV to 20 MeV. Most of our calculations are for site sizes ranging from 10 nm to 1000 nm. Our latest work has been summarized in a paper, "Monte Carlo and Analytic Methods in the Transport of Electrons, Neutrons, and Alpha Particles" (Caswell and Seltzer, 1994).

We have made some comparisons of our results with other calculations (Morstin and Olko) and experimental measurements (Kliauga). Calculations were carried out on the Cray Y-MP computer at NIST.

2. Improved Calculations of Microdosimetric Spectra for Low-Energy Neutrons.

Improved calculations of microdosimetric spectra for low-energy neutrons were carried out by separating the elastic and non-elastic nuclear reaction channels. Ion yield calculations for low-energy neutrons were also improved by using a better set of W (energy per ion pair) values at low energies. A program for Monte Carlo calculation of the penetration of low-energy neutrons was developed and the results were used to show the effect of the thickness of tissue-equivalent proportional counter build-up caps on the nuclear reactions which contribute to the energy deposition and ionization produced in these chambers.

3. Energy deposition spectra and their moments for fast neutrons. Using calculated charged particle initial spectra and slowing-down spectra we calculate the energy deposition in spherical cavities. The spectrum obtained is sometimes called the single event spectrum or a distribution of dose versus y , the lineal energy. The frequency mean of this spectrum, $\bar{y}_F$, the dose average, $\bar{y}_D$, and the dose average including saturation correction, $\bar{y}^*$, can then be calculated. These quantities are closely related to the Kellerer-Rossi parameters $\bar{z}_F$, ζ , and ζ^* . We calculate these spectra and their moments for neutron energies up to 20 MeV and for cavity sizes in the range of .5 μm to 30 μm . Systematic calculations have been carried out of the energy deposition spectrum, $f_1(\epsilon)$, and the parameters $\bar{y}_F$, $\bar{y}_D$, and $\bar{y}^*$ over the range of energies and sensitive volume sizes cited using bin-averaged neutron cross sections.

A library of y spectra as a function of neutron energy has been generated for a 1 μm cavity for energy deposition in tissue and for ionization yield for a inhomogeneous tissue-equivalent proportional counter. This work has not been published due to the unavailability of funding.

Collaborations and Outreach

Dr. Walt Wilson of Pacific Northwest National Laboratory has been most helpful in supplying a computer program based on the Wilson-Paretzke model which enabled us to extend our calculations to the nanometer region.

Dr. J. Joseph Coyne was a very active participant in this program until his retirement from NIST in 1991. He contributed broadly in the field of microdosimetry, and also carried out much of the work on the analysis of the physics involved in the calculation and computer programming.

Stephen M. Seltzer, who is well-known in the field of radiation transport calculations, and Lisa R. Karam, who has broad experience in radiation biochemistry, and R. S. Caswell, all participants in this project, formed a small study group on biophysical and biochemical models of radiation interaction. Dr. Karam taught the two physicists molecular biology and radiation biochemistry, and Seltzer and Caswell discussed neutron microdosimetry, neutron nanodosimetry, and biophysical models of radiation interaction.

We also interacted with Professor Werner Hofmann of the University of Salzburg, Austria on biophysical models of radiation carcinogenesis, which are primarily for the radon problem, but are relevant to neutron health effects.

R. S. Caswell was Chairman, Science Panel, Committee on Interagency Radiation Research and Policy Coordination (CIRRPC), Office of Science and Technology Policy; also alternate member of the main committee of CIRRPC from 1984-1994.

S. M. Seltzer was a member of the CIRRPC Science Subpanel on the Use of Particle Fluence for Radiation Risk Assessment. He reported on the Lethal, Potentially Lethal (LPL) model of radiation action of Stan Curtis to this Science Subpanel studying Fluence-Based Risk Assessment.

R. S. Caswell was a member and Secretary of the International Commission on Radiation Units and Measurements (ICRU).

S. M. Seltzer was a member and R. S. Caswell was a sponsor of the ICRU Committee which prepared ICRU Report 49, Stopping Power for Protons and Alpha Particles (1993).

R. S. Caswell is an honorary member of the National Council on Radiation Protection and Measurements (NCRP).

Budget

<u>Agreement</u>	<u>Period Covered</u>	<u>Funding</u>
DE-AI-05-86ER60389	Dec. 1, 1985 - Nov. 30, 1992	\$325,300

The average yearly funding was about \$46,500.

Publications

Key Publications Leading to This Program:

R.S. Caswell, "Deposition of Energy by Neutrons in Spherical Cavities," *Rad. Res.* **27**, No. 1, 92 (1966).

R.S. Caswell and J.J. Coyne, "Interaction of Neutrons and Secondary Charged Particles with Tissue: Secondary Particle Spectra," *Rad. Res.* **52**, No. 3, pp. 448-470 (1972).

R.S. Caswell and J.J. Coyne, "Microdosimetric Spectra and Parameters of Fast Neutrons," *Proc. Fifth Symp. on Microdosimetry, Verbania-Pallanza, Italy, Euratom Document EUR 5452 d-e-f*, p. 97 (1976).

R.S. Caswell, J.J. Coyne, and M.L. Randolph, "Kerma Factors for Neutron Energies Below 30 MeV," *Rad. Res.* **83**, 217-254 (1980).

Publications from This Program:

R.S. Caswell, J.J. Coyne, and H. M. Gerstenberg, "Recent Improvements in Neutron Energy Deposition Calculations," *Proc. 5th Symp. on Neutron Dosimetry EUR 9762, CEC Luxembourg*, pp. 255-262 (1985).

R.S. Caswell and J.J. Coyne, "Neutron Kerma Values," *Encyclopedia of Physics in Medicine and Biology*, Pergamon Press, T.F. McAinsh, ed. 521-523 (1985).

R.S. Caswell, "Nuclear Data for Biomedical Applications," *Radiation Effects* **94**, 1-11 (1986). Also published in *Nuclear Data for Basic and Applied Science*, Proceedings of the International Conference, Santa Fe, New Mexico, 13-17 May 1985, Volume 1, Gordon and Breach Science Publishers, 675-685 (1986).

R.S. Caswell, J.J. Coyne, H.M. Gerstenberg, and R.B. Schwartz, "Refinement of Neutron Energy Deposition and Microdosimetry Calculations," *Proc. International Conference on Fast Neutron Physics, Dubrovnik, Yugoslavia*, pp. 122-134 (1986).

H.M. Gerstenberg, R.S. Caswell, and J.J. Coyne, "Initial Spectra of Neutron-Induced Secondary Charged Particles," *Radiat. Prot. Dosim.* **23**, No. 1/4, 41-44 (1988).

R.S. Caswell, J.J. Coyne, H.M. Gerstenberg, and E.J. Axton, "Basic Data Necessary for Neutron Dosimetry," *Radiat. Prot. Dos.* **23**, 11-17 (1988).

R.S. Caswell and J.J. Coyne, "Effects of Track Structure on Neutron Microdosimetry and Nanodosimetry," Nuclear Tracks and Radiation Measurements **16D**, 187 (1989).

Zaider, M., Dicello, J., and Coyne, J. J., The Effects of Geometrical Factors on Microdosimetric Probability Distributions of Energy Deposition. Nucl. Instrum. Meth. Phys. Res. **B40/41**, 1261-1265 (1989).

Coyne, J. J., Caswell, R. S., Zoetelief, J., and Siebert, B.R.L., Improved Calculations of Microdosimetric Spectra for Low-Energy Neutrons, Radiat. Prot. Dosim. **31**, Nos. 1-4, 217-221 (1990).

Coyne, J. J., Gerstenberg, H. M., Hansen, J., and Zoetelief, J., Calculations of the Relative Effectiveness of Alanine for Neutrons with Energies up to 17.1 MeV, Radiat. Prot. Dosim. **31**, Nos. 1-4, 85-89 (1990).

Schuhmacher, H., Kunz, A., Menzel, H. G., Coyne, J. J., and Schwartz, R. B., "The Dose Equivalent Response of Tissue-Equivalent Proportional Counters to Low- Energy Neutrons," Radiat. Prot. Dosim. **31**, Nos. 1-4, 383-387 (1990).

Zoetelief, J., Eisenhauer, C. M., and Coyne, J. J., Calculations on Displacement Corrections for In-Phantom Measurements with Ionization Chambers for Mammography, Phys. Med. Biol. **35**, 1287-1299 (1990).

Coyne, J. J. and Caswell, R. S., "Neutron Energy Deposition on the Nanometer Scale", Radiat. Prot. Dosim. **44**, 49-52 (1992)

Caswell, R. S. and Lewis, V. E., "Neutron Measurement Intercomparisons Sponsored by CCEMRI Section III (Neutron Measurements)", Radiat. Prot. Dosim. **44**, 105-110 (1992).

R.S. Caswell and S.M. Seltzer, "Monte Carlo and Analytic Methods in the Transport of Electrons, Neutrons, and Alpha Particles," Monte Carlo Methods, (Eds. A Chatterjee and M. N. Varma) Plenum Press, 115-131 (1994).

Publications from the DOE-Sponsored Radon Program, "Energy Deposition and Radiation Quality of Radon and Radon Daughters", an outgrowth of this Neutron Program:

Caswell, R. S. and Coyne, J. J., "Microdosimetry of Radon and Radon Daughters," Radiat. Prot. Dosim. **31**, 395-398 (1990).

Caswell, R. S. and Coyne, J. J., "Alpha Particle Spectra and Microdosimetry of Radon Daughters," Proc. 29th Hanford Symp., Indoor Radon and Lung Cancer: Reality or Myth?, Richland, Washington, October 15-19, 1990, Part 1, 279-290 (1992).

Karam, L.R. and Caswell, R.S., "Radon in the Lung: Computer Code Developed," U.S. Department of Energy, Radon Research Notes, 12, 6-8 (1993).

Caswell, R. S., Karam, L. R., Coyne, J. J., Systematics of Alpha-Particle Energy Spectra and Lineal Energy (Y) Spectra for Radon Daughters, Radiat. Prot. Dosim., 52, 377-380, 1994.

Hofmann, W., Nösterer, M., Ménache, M. G., Crawford-Brown, D. G., Caswell, R. S., Coyne, J. J., Microdosimetry and Cellular Radiation Effects of Radon Progeny in Human Bronchial Airways, Radiat. Prot. Dosim., 52, 381-385, 1994.

Karam, L. R. and Caswell, R. S., Fluence-Rate and Y Spectra of Radon Daughter Alpha Particles in Rat and Human Lung Models, poster paper presented at the Forty-second Annual Meeting of the Radiation Research Society, April 29-May 4, 1994, Stouffer Hotel, Nashville, Tennessee.

Hofmann, W., Heistracher, T., Caswell, R. S., and Karam, L. R., "Track Structure Predictions of Radon-Induced Biological Effects in Human Bronchial Epithelium," Environment International 22, Suppl. 1, S949-S957 (1996)