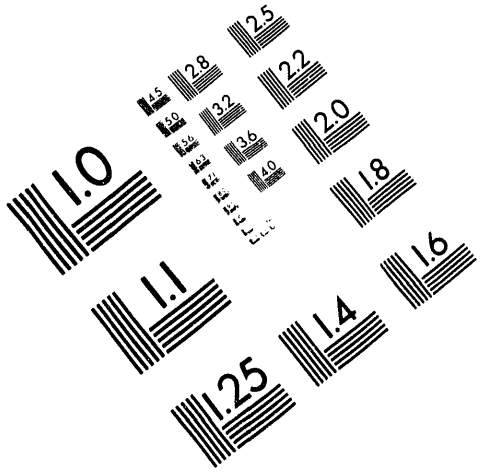

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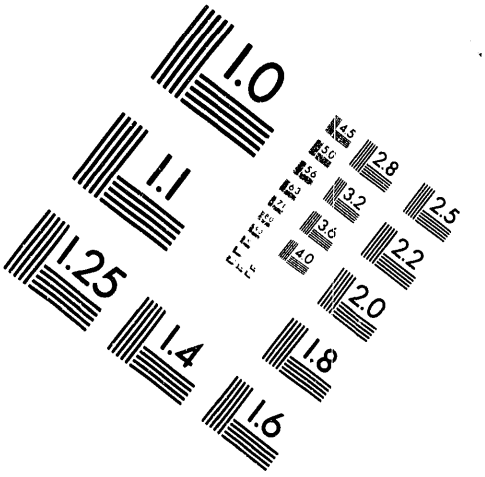

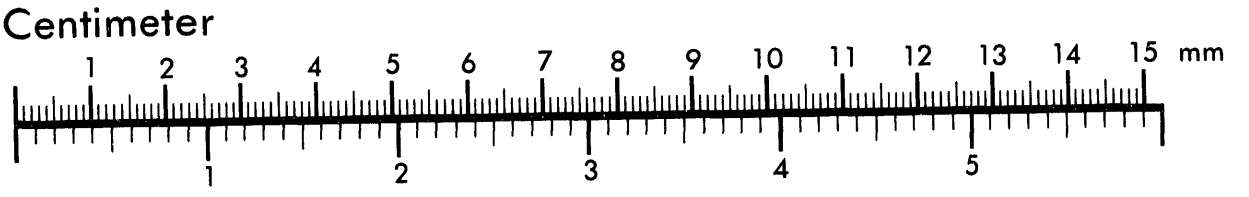

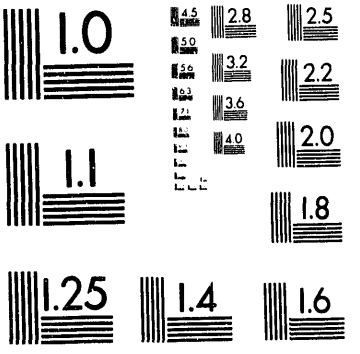

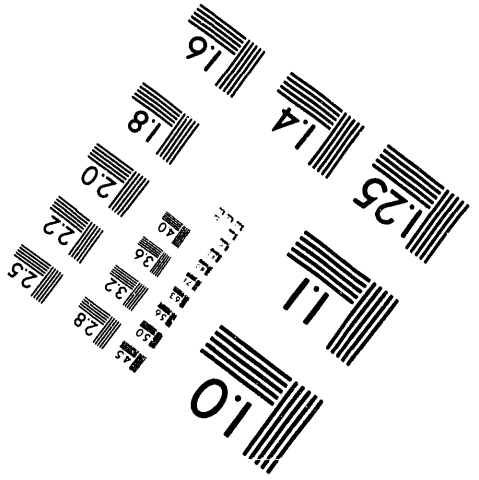

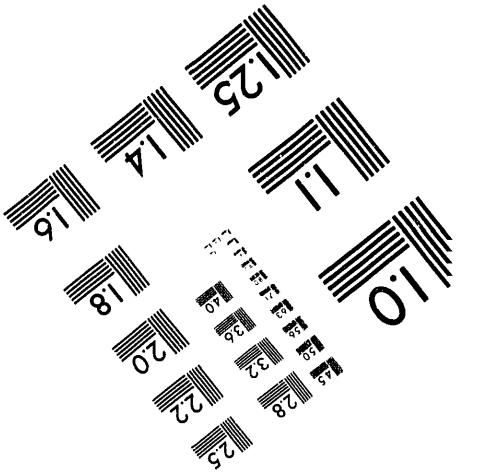

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THE RADIOLOGICAL RESEARCH ACCELERATOR FACILITY

Progress Report
for the Period December 1, 1992 - November 30, 1993

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Introduction

The Radiological Research Accelerator Facility (RARAF) is based on a 4-MV Van de Graaff accelerator, which is used to generate a variety of well-characterized radiation beams for research in radiobiology, radiological physics, and radiation chemistry. It is part of the Center for Radiological Research (CRR) - formerly the Radiological Research Laboratory (RRL) - of Columbia University, and its operation is supported as a National Facility by the U. S. Department of Energy (DOE). As such, RARAF is available to all potential users on an equal basis and scientists outside the CRR are encouraged to submit proposals for experiments at RARAF. The operation of the Van de Graaff is supported by the DOE, but the research projects themselves must be supported separately.

RARAF was conceived in the mid-1960s by Drs. Victor P. Bond of Brookhaven National Laboratory (BNL) and Harald H. Rossi of Columbia University as a research resource dedicated to radiobiology and radiological physics and was officially established on January 1, 1967. RARAF's Van de Graaff accelerator originally served as the injector for the Cosmotron, a 2-GeV accelerator operated at BNL in the 1950s and early 1960s. The immediate aim was to provide a source of monoenergetic neutrons for studies in radiation biology, dosimetry, and microdosimetry. In other major projects the energetic ions produced were utilized directly. RARAF was located at BNL from 1967 until 1980, when it was dismantled and moved to the Nevis Laboratories of Columbia University, where it was then reassembled and returned to operation.

Data obtained from experiments using RARAF have been of pragmatic value to radiation protection and neutron therapy. At a more fundamental level, the research at RARAF has provided insight into the biological action of radiation and especially its relation to energy distribution in the cell. High-LET radiations are an agent of special importance because measurable cellular effects can be caused by single particles, eliminating some of the complexities of multievent action and more clearly disclosing basic features. This applies particularly to radiation carcinogenesis.

Facilities are available at RARAF providing different radiations having a wide range of linear energy transfers (LETs). In the track-segment facility, monolayer cultures of cells or other thin samples can be exposed to charged-particle tracks with well-defined LETs from 10 to 200 keV/μm. Cells can be irradiated with spatially correlated pairs or triplets of ions using the molecular-ion facility. There is also a charged-particle beam line for radiological physics or chemistry experiments. The charged-particle beams from the accelerator can be used to produce essentially monoenergetic neutrons in the range 220 keV to 15 MeV and broad-spectrum neutrons with a mean energy as low as 40 keV. Low-LET (photon) radiations are provided by a 250-kVp X-ray machine and a 50-kVp X-ray machine attached to the track-segment fixture. A facility is now available to provide soft X rays (0.3 to 3 keV) using proton-induced X-ray emission (PIXE).

Some of the support facilities available at RARAF include: cell culture laboratories, a minicomputer and a personal computer (PC) for controlling experiments and recording data, a CAMAC data acquisition system, a bio-preparation/animal-holding room, limited electronics for use by experimenters, and office space for users.

Members of the RARAF staff provide a variety of services in addition to operating, maintaining, and developing the accelerator. They perform most irradiations and are responsible for dosimetry and for developing specialized dosimetry devices and methods when needed. They also provide computer support, help design experiments and irradiation fixtures, and do collaborative research with some users. The CRR machine shop is available for the fabrication of necessary dosimetry and irradiation fixtures. Costs for special services and machine shop time are recovered from the user. All principal investigators are encouraged to request funds in their grant applications to cover the cost of accelerator use, unless the funding source is the Office of Health and Environmental Research of DOE.

In addition to the RARAF Staff, other CRR scientists are engaged in collaborative research with outside users of RARAF. Some of the most interesting and complex

experiments done by outside users have been made possible only by active and significant in-house collaboration far beyond the operation of the accelerator and provision of dosimetry.

The operation of RARAF through 1982 was described in RRL Annual Progress Reports. From 1983 to 1987, RARAF operated under a separate DOE Contract or Grant (first DE-ACO2-83ER60110, then DE-FG02-86ER60539), and operation of the Facility was described in separate RARAF Progress Reports (1-5). Since 1988 the operation of RARAF has been supported by part of a single grant to the CRR (DE-FG02-88ER60631), but since RARAF is a separate component, the reports are submitted separately (6-10).

RARAF User's Guide

To increase the utilization of RARAF by scientists outside CRR, a RARAF User's Guide was prepared in 1985 for distribution to potential users. The Guide contains detailed information about the Facility's research capabilities and how to plan an experiment at RARAF, and it includes an Experiment Request Form for submitting proposals for new experiments. The User's Guide was reproduced as an appendix to the RARAF Progress Report for 1985 (3). A copy of the Guide may also be obtained by contacting the Manager of RARAF.

Since the sections of the User's Guide covering the RARAF staff and the Scientific Advisory Committee are currently out of date and new capabilities and facilities have now become or will soon be available, it is expected that a new User's Guide will be prepared after the basic development of these new facilities is completed.

Research Using RARAF

Table 1 lists the experiments performed at RARAF during the period May 1, 1992 through April 30, 1993 and the number of days each was run in this period. The numerical order of experiments is based on the date of submission of the Experiment Request Forms. Fractional days were assigned to experiments when two or more were run on the same day or

Table 1. Experiments Run at RARAF, May 1, 1992 - April 30, 1993

Exp. No.	Experimenter	Institution	Exp. Type	Title of Experiment	No. Days Run
37	D. J. Brenner	CRR	Phys/Bio	Towards the new Q	7.7
41	R. C. Miller/ S. Martin	CRR	Bio	Oncogenic transformation induction by high-LET radiation	6.7
43	T. K. Hei	CRR	Bio	Cellular and molecular studies on the mutagenesis of charged particles using human-hamster hybrid [A_{L1} cells	5.0
50	R. C. Miller	CRR	Bio	Oncogenic transformation as a function of dose protraction of particles of defined LET	1.0
52	R. C. Miller	CRR	Bio	Short-range radiation induced oncogenic transformation	11.3
53	J. C. Willey	University of Rochester	Bio	Evaluation of the cytotoxic and oncogenic transforming effects of simulated radon daughter products using human bronchial epithelial cells	0.5
54	L.G. Littlefield	ORISE (Oak Ridge)	Bio	Cytogenic indices - direct vs indirect action	2.0
55	R. C. Miller/ S. Martin	CRR	Bio	Isolation of cells transformed by neutrons and charged particles of defined LET	1.7
56	R. C. Miller	CRR	Bio	Transformation of synchronized $C_3H10T_{½}$ cells by neutrons and charged particles of defined LETs	3.0

Table 1. (Continued)

Exp. No.	Experimenter	Institution	Exp. Type	Title of Experiment	No. Days Run
58	B. Loucas	CRR	Bio	Breakage and rejoining of interphase chromatin in non-cycling human fibroblasts as a function of LET	8.0
59	D. Grunberger	Columbia University	Bio	Induction by radon daughter alpha particles of mutations in the dihydrofolate reductase gene of Chinese hamster ovary cells in culture	3.0
60	I. B. Weinstein	Columbia University	Bio	Effects of alpha-particle irradiations on mammalian cells [mutation]	0.5
62	Z. Ronai	American Health Foundation	Bio	Radon effects on gene expression in hamster clara cells	1.0
63	L. Chasin	Columbia University	Bio	[Mitotic)]Recombination induced by simulated radon	1.0
64	S.G. Martin	CRR	Bio	Human epithelial cell transformation	4.0
---	A. Lindgren	Bemidji State University	Bio	Effects of neutrons the lenses of mice and rats.	1.0
				TOTAL	57.3

when an experiment ran more than 10 hours on a single day. Sixteen different experiments were run during this 12-month period. While this is less than either of the last two years, it is about the same as the three years prior to 1990-91.

Nine experiments were proposed by members of the CRR, supported by grants from NIH and DOE DE-FG02-88ER60631, and seven were proposed by outside users, supported by various grants and awards from the Department of Energy (DOE) and the National Institutes of Health (NIH). In addition to research conducted by three other groups from Columbia University, experiments were performed by researchers from three other universities, a national laboratory, and a foundation. Only one sixth of the experimental time was used by outside users, the rest was used by CRR scientists. This is the first year in the last four in which outside researchers have not utilized half or more of the experimental time.

The problem of radon exposure continues to be a topic of considerable concern and interest. More than one-third (6) of the experiments run at RARAF this year used ^{3}He and ^{4}He ions to investigate the effects of radon-daughter alpha particles (Exp. 41, 53, 59, 60, 61, 62). Most of these experiments are investigating biological changes, but there is also one chemistry experiment (Ward, Exp. 61). Another six experiments (Exp. 37, 43, 50, 55, 56, 58) are not specifically looking at radon effects but include a range of He-ion LETs which would provide sufficient data for that purpose. Among these are measurements of both microdosimetric and nanodosimetric spectra for He ions with various LETs.

A brief description of the experiments that have been run at RARAF since May 1, 1992 is given below.

A project proposed by David Brenner, in collaboration with other CRR scientists, to obtain some of the basic data necessary for the estimation of the quality factor, Q, as a function of the microdosimetric quantity lineal energy, y, (Exp. 37) continued this year. Measurements of the yield of chromosome aberrations and mutations in mammalian cells exposed to a series of radiations (mostly charged-particle track segments) are being made spanning the entire range of lineal energies of interest in radiation protection. About half of

the radiations can be obtained at RARAF (10 to 200 keV/μm) and those lineal energies not available at RARAF have been obtained at the Tandem Van de Graaff Accelerator at BNL. Paul Kliauga is measuring the microdosimetric spectra for each radiation. A simple wall-less right-circular cylindrical proportional counter, consisting only of a center wire and a 1/8-inch diameter helix in a 9-inch diameter brass and aluminum housing, is irradiated with the charged particle beam. The beam enters the chamber through an aperture covered with 6-μm thick mylar to simulate the bottom of the cell dishes. Spectra for 0.5- and 1-μm simulated site sizes were measured at RARAF this year for several ^{4}He-ion LETs. Irradiations of human skin fibroblasts with 180- and 200-keV/μm ^{4}He ions have been performed to observe mutations in the HGPRT gene. Biological results will be unfolded using the measured microdosimetric spectra to give a response function, q(y), which can be used to predict the effect of any radiation whose microdosimetric spectrum is known. This will be tested using the results of irradiations with 14-MeV neutrons which produce secondary particles having a wide range of LETs.

Two experiments initially proposed by Richard Miller were concluded by Stewart Martin, also of the CRR. Oncogenic cell transformation by ^{4}He ions to simulate radon daughters (Exp. 41) was examined using fresh explants of Syrian hamster embryo cells instead of $C_3H10T_{1/2}$ cells. Irradiations with six different lineal energies of ^{4}He ions from 90 to 200 keV/μm were made at doses as low as 10 mGy. Results statistically different from background were obtained at 20 mGy. The maximum transformation rate for cells at risk appears to be between 30 and 40 mGy and is about the same as the maximum rate for x rays, in contrast to the $C_3H10T_{1/2}$ system where the maximum rate for neutrons is considerably higher than for x rays. ^{4}He ions were more carcinogenic at 90-keV/μm than at other LETs even though the RBEs for cell inactivation were similar. Morphologically transformed colonies have been isolated and cloned (Exp. 55). The clones were examined to see if they are immortalized and were injected into in nude mice to observe whether they would form tumors.

Richard Miller of the CRR performed three other investigations this year, all involving $C_3H10T_{1/2}$ cell transformation. An investigation to determine the effect of dose fractionation on transformation using charged particles with different LETs (Exp. 50) was continued. Cells were irradiated with 70-keV/μm deuterons in three fractions with separation times between fractions ranging from 18 seconds to 1½ hours. Previous data has indicated an increase in transformation only for irradiations using particles with LETs between 40 and 120 keV/μm. The level of enhancement increases with the time between fractions until 90 minutes separation time, after which it remains constant. An experiment investigating the effects of short-range radiations, "soft" x rays and low-energy neutrons (Exp. 52), was resumed. Cells were irradiated with 0.35-MeV neutrons either attached to the surface of a standard T-25 cell flask or as a centrifuged pellet at the bottom of a small plastic tube in order to determine if there is a difference in cell survival or mutation between the two methods. In the future, cells will be irradiated in the small plastic tubes with neutrons having energies of 50 keV or less. A third experiment to determine cell transformation as a function of cell cycle (Exp. 56) was also continued. Cells synchronized by mitotic shake-off were irradiated with 0.6 Gy of 6-MeV neutrons at various times after synchronization. Little variation in cell survival was observed with position in the cell cycle. Initial results indicate that the radiosensitive period for transformation of cells by 6-MeV neutrons is the G_1 phase as opposed to x rays for which transformation peaks in G_2. Separately, Miller also performed an irradiation to determine if there is a difference in the rate of cell transformation when cells are irradiated with 70-keV/μm deuterons, which are near the Bragg peak, or 70-keV/μm ^{3}He ions which have a much higher velocity and are far from the Bragg peak.

Tom Hei of the CRR, in collaboration with Charles Waldren of Colorado State University, has temporarily completed the examination of the LET response of a line of human-hamster hybrid cells containing human chromosome 11 (A_L cells) over the full range of available LETs (Exp. 43). Cells are scored at both the HGPRT and S1 loci. Southern blot analysis of both types of mutants is being performed by Li Zhu of the CRR. HGPRT$^-$ mutants

induced by ^{4}He ions have shown mostly multilocus deletions in contrast to spontaneous mutants which showed either no apparent change in the sequence or partial deletions. Similar analysis of S1$^-$ mutants using probes that map to both the long and short arms of human chromosome 11 indicated that the majority of mutants suffered massive chromosomal changes.

A collaboration between James Willey of the University of Rochester and Tom Hei and Chang Qing Piao of the CRR is examining the oncogenic transformation of an immortalized human bronchial epithelial cell line using 150-keV/μm ^{4}He ions (Exp. 53). After a single irradiation of 0.3 or 0.6 Gy, anchorage-independent colonies have been isolated in soft agar. Of the 13-14 mice inoculated with these putatively transformed cells, 4-5 small nodules have developed. Molecular studies looking for activated oncogenes have indicated that k-*ras* is not present.

The examination of chromosome aberrations in human lymphocytes irradiated with monoenergetic neutrons (Exp. 54) by Gayle Littlefield of Oak Ridge Institute for Science and Education (ORISE, formerly part of Oak Ridge Associated Universities) continued this year. Cells were irradiated using 0.4-MeV monoenergetic neutrons with and without the addition of the OH radical scavenger WR-1065. Changes in cell cycle delay with neutron energy were examined as well as how cell cycle kinetics are ameliorated under conditions of maximum OH-radical scavenging. Micronuclei production as a function of dose was determined.

Bradford Loucas of the CRR is continuing a study of chromosome breakage and rejoining kinetics as a function of charged-particle LET (Exp. 58). Using the technique of premature chromosome condensation (PCC), chromosome aberrations can be observed without requiring cells to be in mitosis so that a long time delay does not occur between the radiation damage and the observation, during which repair might occur. Confluent cultures of AG1522 human fibroblasts in G_0 phase are placed in ice within 5 minutes of irradiation to observe "initial" damage or incubated for various times after irradiation to observe repair. Initial breaks as a function of dose increase with LET, peaking at about 90-120 keV/μm. As a

function of fluence, initial breaks increase with increasing LET, possibly peaking around 180 to 200 keV/μm.

An experiment to examine the mutational effects of radon (Exp. 59), proposed by Dezider Grunberger of the Institute of Cancer Research of Columbia University, was continued. Adelaide Carothers of the Institute has irradiated Chinese hamster ovary (CHO) cells hemizygous for the dihydrofolate reductase (*DHFR*) gene with 150-keV/μm ^{4}He ions using the track-segment facility. DNA is isolated and hydrolysed by enzyme digestion and damaged nucleosides are separated by Christina Frankel at NYU using HPLC. They have observed what appears to be a novel damage product not seen with chemicals and as yet unidentified. This compound is detectable by both ultra-violet and electro-chemical means, the quantity is proportional to dose, and it is detectable at 10 mGy. The product is also observed after x-irradiation but produces only half the yield at twice the dose as for ^{4}He ions .

An investigation of the effects of ^{4}He ions on gene rearrangement of rat fibroblast cells (Exp. 60) was completed by Bernard Weinstein and Gabrielle Windgasse of the Comprehensive Cancer Center of Columbia University. The cells contain a single copy of a transcriptionally silent reporter gene (*hph*) which is activated by the insertion of a promoter sequence in the region from the 5' end to *hph*. Hygromycin-containing medium was used to select the expressed gene and surviving colonies were expanded and analyzed for genetic changes using the Southern blot technique. Unfortunately, no mutated colonies were observed.

An experiment to examine the response of a DNA-damage inducible gene, termed clone 3, in immortalized hamster clara cells to ^{4}He ions (Exp. 62) continued this year. Zeev Ronai and Susan Rutberg of the American Health Foundation in Valhalla, N. Y. are trying to determine the possible role of this gene in cell transformation as an aid to understanding the molecular events that occur during radon-induced transformation of human lung cells.

A study of mitotic recombination in hybrid Chinese hamster ovary (CHO) cells irradiated with ^{4}He ions (Exp. 63) was resumed by Lawrence Chasin of the Department of

Biological Sciences of Columbia University. This CHO cell line contains two mutant alleles of the *hprt* gene located on two separate X chromosomes, one with a deletion at the 3' end and the other with a deletion at the 5' end of the gene. It is believed that at least 20 kb of overlapping sequence are retained on each gene. Cells were irradiated with 150-keV/μm ^{4}He ions and surviving cells were subjected to selection by HAT medium for the HPRT$^+$ phenotype indicating a recombination of the two defective genes.

Stewart Martin of the CRR has begun studies involving immortalized human uroepithelial cells (SV-HUC-1) and a human epidermal keratinocyte (RHEK-1) cell system developed by C. A. Reznikoff (Exp. 64). Irradiated HUC cells are injected into nude mice as the assay for tumorigenicity since they do not show morphological transformation in culture. Explanted tumor cell lines from a tumor obtained as result of single-dose irradiation are currently being examined for radiation sensitivity, chromosomal alterations, and oncogene activation/suppressor gene loss. Additional irradiations will be performed with 0.4 MeV neutrons. It appears from preliminary results that RHEK-1 cells irradiated with 0.1 Gy of 120-keV/μm ^{4}He ions are yielding a number of tumors at the injection sites in nude mice with latency periods significantly shorter than the 6 months required for HUC cells. Studies related to obtaining a quantifiable human transformation assay system are proceeding with both these cell lines.

An experiment to observe the effects of neutrons on the lenses of the eyes of mice and rats was begun by Alice Lindgren of Bemidji State University in Minnesota. C3H/He and C57 Black mice and Sprague-Dawley rats will be irradiated with 0.4-MeV neutrons. Four weeks after irradiation the lenses of the animals' eyes will be wounded, causing the cells in the epithelium of the lens to start to progress through the cell cycle from G_0. The cells are cultured and examined for mitotic abnormalities. As a preliminary experiment, passage 1 explanted cells from both strains of mice were irradiated with 0.4-MeV neutrons to observe transformation. Preliminary results indicate that the cells more resistant to inactivation show a higher transformation rate per survivor.

Accelerator Utilization and Operation

Accelerator usage is summarized in Table 2 and Figure 1 for the current report period as well as the seven previous periods. The accelerator was used for 35% of the normal schedule time (8 hours per day, 5 days per week, excluding holidays) this year, about half last year's use and a little less than half the average use from 1986 to 1992. Maintenance and repairs, which required over 18% of the scheduled time last year, were reduced below the 1986-92 average in part due to the reduced accelerator use, but mainly due to the correction of the continuing accelerator problems that plagued us last year.

Accelerator use for radiobiology and associated dosimetry was just over half both last year's use and the average since 1986. This is by far the lowest percentage of scheduled time for radiobiology that has been experienced since RARAF began operating at Nevis Laboratories and was not due to the loss of a single, major experiment but appears to have been the result of several experiments winding down or reaching completion while few new ones began. The amount of radiobiology and dosimetry should increase markedly this coming year as the low-energy neutron and single-particle irradiation facilities become operational.

Utilization of the accelerator by radiological physics and chemistry was also significantly lower this year than any time in the past. This was due to a great extent to the absence of the variance-covariance experiment (Exp. 34) of Paul Goldhagen at the Environmental Measurements Laboratory of the DOE. Since DOE shut down the tritium-target manufacturing facility at Oak Ridge National Laboratory, we have been unable to find a source of suitable targets and have been using three received in early 1990. Because these have been depleted by extensive use in addition to the radioactive decay of the tritium, they cannot be used to produce the high dose rates desired for Goldhagen's experiment and consequently there has been no utilization. Lack of fresh neutron-producing targets has, of course, also impacted on radiobiology by increasing the time necessary to deliver the required doses. We have now located a DOE facility in Pinellas, Florida which appears to be ideally

Table 2. Accelerator Use (percent of normal schedule time[1])

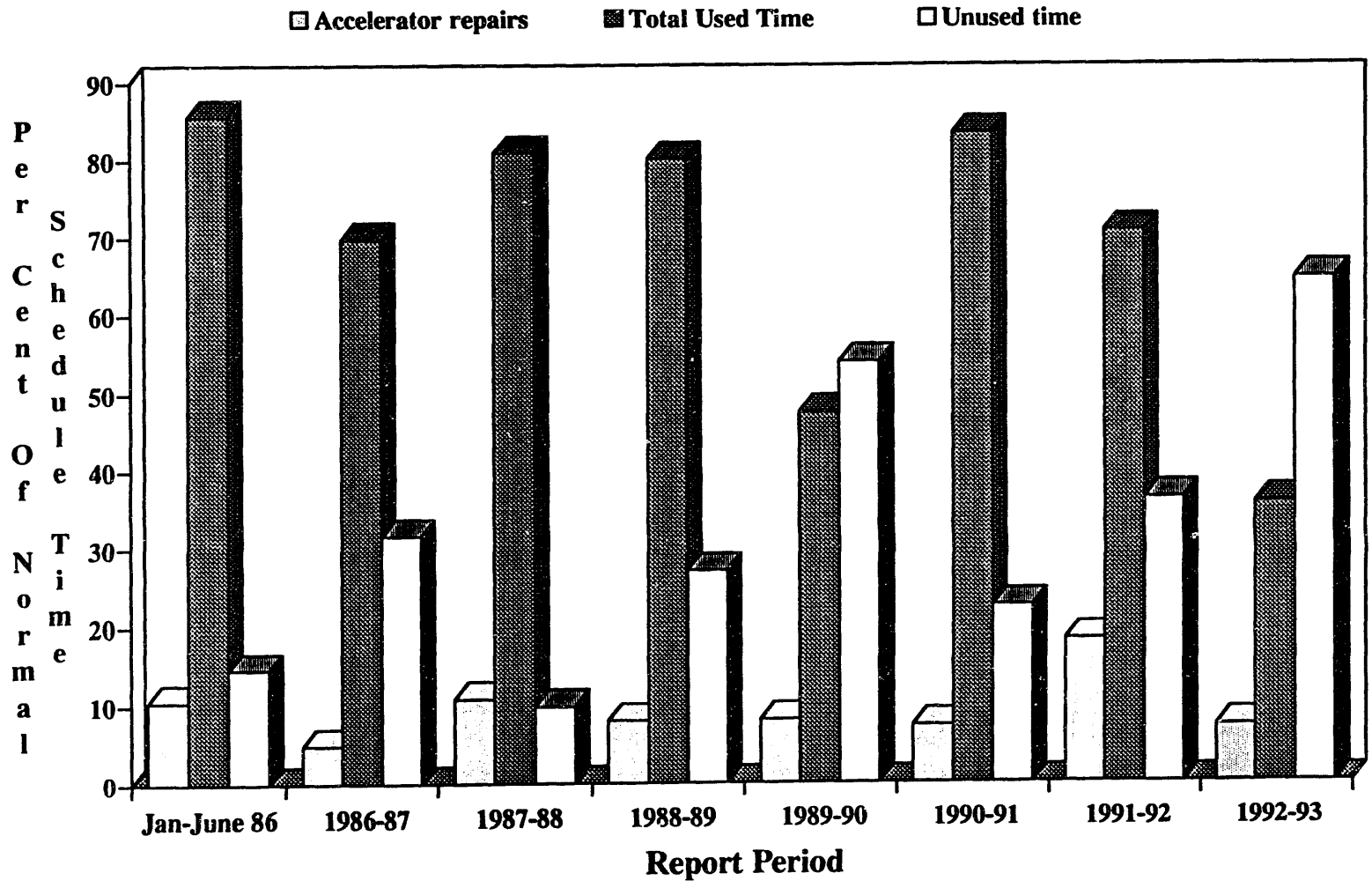
	Jan-June 1986	July 1986-April 1987	May 1987-April 1988	May 1988-April 1989	May 1989-April 1990	May 1990-April 1991	May 1991-April 1992	May 1992-April 1993
Radiobiology and associated dosimetry	41.6	34.4	40.8	34.3	31.5	43.8	36.2	20.2
Radiological physics and chemistry	31.2	26.7	27.0	35.1	2.4	29.9	12.5	2.8
Target, beam and radiation tests	0	1.4	0	0.4	3.2	0	0.8	3.2
Safety system tests	2.4	2.4	2.4	2.4	2.4	2.4	2.8	2.4
Accelerator-related repairs and maintenance	10.4	4.8	10.7	7.9	8.0	7.3	18.2	7.2
Total used[2]	85.6	69.7	80.9	80.1	47.5	83.4	70.5	35.8
Unused[3]	14.4	31.5	9.7	27.1	54.0	22.6	36.8	64.7
Unavailable due to 1/18/88 fire	---	---	12.3	2.2	---	---	---	---
Total days	125	208	248	247	250	248	253	249

[1] 8 hours per day, 5 days per week,excluding holidays.

[2] The sum of the used and unused time may add to more than 100 percent due to experiments which run significantly longer than the normal eight-hour scheduled time per day or are run on weekends.

[3] Includes user cancellations and meetings.

Fig. 1 RARAF Accelerator Use



suited to our needs and we are working our way through the red tape to obtain new targets as soon as possible. It is therefore anticipated that there will be considerably more use of RARAF for radiological physics this coming year.

The track-segment experiment at the BNL Tandem Van de Graaff Facility, related to RARAF Experiment 37, required the absence of Stephen Marino for several one-week trips to BNL, as well as significant amounts of time for Paul Kliauga, Stewart Martin, and Richard Miller, all RARAF. users. This experiment continued to have some effect on the RARAF schedule this year, but will no longer interfere since it has now been completed.

Development of Facilities

As in the previous three years, there has been considerable time spent on the development of new capabilities. It is expected that this level of effort will continue for least one more year.

Irradiations with the "soft" x-ray facility constructed in 1989-90 have been extended to carbon x rays (277 eV) using methane as a target gas. An attempt is being made to produce a usable beam of boron x rays (183 eV) with protons incident on a solid target because of the high toxicity of borane (BH_4), the only target gas that won't produce contaminant x rays with a higher energy.

There has been a significant amount of interest in recent years in radon exposure and the radiobiology and molecular biology of carcinogenesis and mutations caused by radon-daughter alpha particles. The CRR received a grant from NIH in 1990 to improve the radon-simulation facilities at RARAF. Construction of a single-particle irradiation facility, to irradiate the nuclei of individual cells with a precise number of charged particles, is a part of this project.

The 50°N charged particle beam is bent an additional 70° horizontally and elevated 20° vertically (by tilting the magnet out of the horizontal plane) with one magnet, then bent an additional 70° vertically with a second magnet into the new cell lab on the second floor.

Because these two magnets are identical in construction and bend the beam through the same angle (70°), they can be operated in series using a single existing power supply. This avoided the purchase of a 90° bending magnet and a power supply, both expensive pieces of equipment. New vacuum chambers have been constructed and installed to replace the existing ones which were only intended for a 37.5° bend. The magnet stands and magnets have been installed and power and control wiring and cooling lines have been connected. The beam line has been completed as far as the floor of the cell lab and a low-current proton beam was transported to the end of the beam line in December, 1992.

Modifications to the suspension of the 3' by 4' air-cushion vibration isolation table, have been made to reduce horizontal motions of the final aperture relative to the charged particle beam caused by any small changes in position of the table surface due to shifting of the load on the table.

It is expected that testing of the single-particle beam and preliminary irradiations will begin this Fall.

Because of disagreements in the literature over the RBE of 25-keV neutrons and an interest in the interaction between short proton-recoil tracks, a facility is being developed to irradiate cells with low energy neutrons. Much of the development for this project has been done by Chun-Zhang Chen of the CRR.

The Li(p,n) reaction will be used to produce neutrons with energies below 50 keV at dose rates usable for radiobiology. An lithium evaporator has been constructed and used to make thin (0.1 mg/cm^2) targets. The thickness of these targets have been measured using a Li(p,γ) resonance. Static beams of up to 10 μA of 1.96-MeV protons produced only a slow reduction in target thickness due to ablation and evaporation, although this was dependent on beam focusing.

To achieve the dose rate desired, a beam current of at least 100 μA on the target is required and consequently the proton beam will be rotated in a 2-cm diameter circle to prevent the lithium from being evaporated off the target surface. Even with this beam current, the

cells will have to be confined to a 3-mm diameter volume and placed in the center of the annular ring formed by the rotating beam at an angle of approximately 90° relative to the beam direction. The shape of the target surface is arranged to minimize the change in dose rate with sample position. The design of the complex target required has been completed and will be constructed soon, after which it will be tested.

Personnel

The Principal Investigator of the RARAF Grant is Eric J. Hall. The personnel of the RARAF staff, their positions, and the percent support they receive from the RARAF Grant are given in Table 3.

TABLE 3. RARAF Staff

Name	Position	Per Cent of Support
Stephen Marino, M.S.	Manager, Dosimetrist	60
Gerhard Randers-Pehrson, Ph.D.	Accelerator Physicist	70
Marie Burchett	Senior Secretary	64[1]
Jesus Perez	Accelerator Technician	100

[1] Part time (64%), until December 31, 1992.

Our secretary, Ms. Marie Burchett, left at the end of December, 1992. She is sorely missed.

Several people not supported by the RARAF Grant also work at the Facility. Dr. Stewart Martin works essentially full-time at RARAF. In addition there are two full-time biology technicians, Ms. Marcia Richards and Mr. Zenin Kurunthottical, and a part-time biology technician, Mr. Marcus Geard. Dr. Richard Miller has returned to the CRR and

RARAF, continuing many of the research projects on which he had been working. Dr. Bradford Loucas currently spends a portion of his time at RARAF and should be spending considerably more time here when the single-particle facility is fully operational. Dr. Chun-Zhang Chen, a new Research Associate in biology, has a Ph. D. in physics and is currently assisting in the development of the low-energy neutron irradiation facility.

RECENT PUBLICATIONS OF WORK PERFORMED AT RARAF

Brenner, D.J., Miller, R.C., Marino, S.A., Geard, C.R., Randers-Pehrson, G., and Hall, E.J. Inverse dose rate effects for neutrons: General features and biophysical consequences. Radiat. Prot. Dosim., 44: 45-48, 1992.

Brenner, D.J., Miller, R.C., Marino, S.A., Geard, C.R., Randers-Pehrson, G., and Hall, E.J. Dose rate effects for oncogenesis by medium LET radiations. In: Low Dose Irradiation and biological Defense Mechanisms, Elsevier Science Publishers, Amsterdam, 1992.

Geard, C.R. Induction of sister chromatid exchanges as a function of charged-particle linear energy transfer. Radiat. Res. 134: 187-192, 1993.

Hei, T.K., Piao, C.Q., Willey, J.C., and Hall, E.J. Malignant transformation of human bronchial epithelial cells by radon-simulated alpha particles. [submitted].

Hei, T.K., Zhu, L.X., Vannais, D., and Waldren, C.A., Molecular analysis of mutagenesis by high LET radiation. Advances in Space Research [in press].

Hei, T.K., Zhu, L.X., and Waldren, C.A., Molecular mechanisms of mutagenesis by radiation of different qualities. NATO ASI series [in press].

Littlefield, L.G. and Hoffman, G.R. Modulation of the clastogenic activity of ionizing radiation and bleomycin by the aminothiol WR-1065. Environ. Molec. Mutagen. [submitted].

Littlefield, L.G., Joiner, E.E., Colyer, S.P., and Frome, E.L. Radioprotective chemicals as tools for studying mechanisms of radiation-induced chromosome damage in human lymphocytes. To be published in the proceedings of the Second International Symposium on Chromosome Aberrations, Essen, Germany.

Willey, J.C., Hei, T.K., Piao, C.Q., Apostoiakos, M.J., and Hukku, B. Radiation induced deletion of chromosomal regions containing tumor suppressor genes in human bronchial epithelial cells. Carcinogenesis [in press].

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3. Rossi, H.H., Goldhagen, P., and Hall, E.J. Radiological Research Accelerator Facility. USDOE Progress Report DOE/ER/60110-3 (1986).

4. Hall, E. J. and Goldhagen, P. Radiological Research Accelerator Facility. USDOE Progress Report DOE/ER/60439-1 (1986).

5. Hall, E.J. and Goldhagen, P. The Radiological Research Accelerator Facility. USDOE Progress Report DOE/ER/60439-2 (1987).

6. Hall, E.J. and Goldhagen, P. The Radiological Research Accelerator Facility. USDOE Progress Report DOE/ER/60631-T1 (1988).

7. Hall, E.J., Goldhagen, P., and Marino, S.A. The Radiological Research Accelerator Facility. USDOE Progress Report DOE/ER/60631-T4 (1989).

8. Hall, E.J., and Marino, S.A. The Radiological Research Accelerator Facility. USDOE Progress Report DOE/ER/60631-6 (1990).

9. Hall, E.J., and Marino, S.A. The Radiological Research Accelerator Facility. USDOE Progress Report DOE/ER/60631-8 (1991).

10. Hall, E.J., and Marino, S.A. The Radiological Research Accelerator Facility. USDOE Progress Report DOE/ER/60631-9 (1992).

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