JOHN C. BUGHER

PRNC 50

PUERTO RICO NUCLEAR CENTER

TRAINING AND EDUCATION PROGRAM OUTLINES

Volume I

AEC Ad Hoc Committee for Program Review October 15-16-17, 1964



OPERATED BY UNIVERSITY OF PUERTO RICO UNDER CONTRACT NO. AT (40-1)-1833 FOR U. S. ATOMIC ENERGY COMMISSION

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TRAINING & EDUCATION PROGRAMS

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October 1964

OUTLINE OF MATERIAL TO BE PRESENTED TO AEC Ad Hoc Committee for Program Review

RADIOISOTOPE APPLICATIONS DIVISION

Dr. Edwin Roig, Head

I. General Scope of Review

Emphasis will be given to the achievements of the Division in fulfilling its main function as training center.

II. Factors to be considered

A. Additional laboratory space

1. Organic Chemistry

a. A new temporary construction with an area of approximately 1600 sq. ft. at a cost of \$15,000 including laboratory benches, 4 hoods, and air conditioners, was finished at the beginning of this fiscal year. At present 7 persons are working in this laboratory; maximum capacity is 14.

b. Part of the original space that was used for organic chemistry is now being used by Dr. Odum; the remaining space we are using for instrumentation and office space.

2. Radiation Chemistry and Photochemistry

d. The 2700 curie Co-60 source was installed in the irradiation basement during last FY. Access to the room has recently been modified substituting the spiral staircase for a safer type along the sides of the wall. This modification allowed for the installation of a platform to be operated by a hoist thus providing a practical and safe means 6f transferring equipment to and from the basement. We are now providing safety requirements to allow for the utilization of the irradiation facilities.

b. Since January, 1964 this group has acquired a laboratory at the Chemistry Department (our old Radiochemistry laboratory) - 800 sq. ft. This lab is planned for organic photochemistry and flash photolysis under the NIH grant. Construction of the flash photolysis set-up is nearing completion. At present two persons are working in that laboratory; maximum capacity - 6. This laboratory at the University has released the crowdness in our facilities in this building.

B. Scientific Personnel

Please refer to Table I summarizing the present staff situation, including the level we expect to reach with the existing facilities...Reference is also made to number of students participating and maximum number of students that can be supervised under the different research programs. TABLE I

SCIENTIFIC PERSONNEL

Research Program	Scientific Staff	Desired Scientific Staff	Number of Trainees	Maximum no. Of Trainees
Organic Chemistry	2 senior scientists 5 res. assistants ²	3 senior scientists 3 res. assistants	l Latinam. 2 U.S.citizens	lo
Organic Photolysis and Flash Photolysis (NiH sponsored)	l senior scientist l res. assistant	2 senior scientists ³ 3 res. assistants ⁴	i i	~ 1
Inorganic Photolysis and Radiation Chemistry	2 res. assistants	2 res. assistants		1 1 1 1 1 1
Solid State Physics	l senior scientist l res. assistant l student assistant	3 senior scientists ⁵ 2 res. assistant	1	Q
¹ Dr. Castrillón is from Argentine and has a temporary appointment. ² The three research amistants are graduate students in Chemistry. ³ Dr. Wigg, from McMaster University, Canada, is expected in October. ⁴ Two additional assistants require increased grant support.		ntment. Histry. October. He is red by MIH grant	a post-doctoral fellow who	fellow who

Dr. Weisz from Hebrew University, Israel will arrive shortly to occupy one of these positions.

C. Collaboration given to UPR

Our staff participates actively in the activities of the science departments of the University of Puerto Rico. They participate in the teaching of university courses. The following teaching load of the present academic year is typical of our collaboration:

Staff member	Course	Credit hours
Dr. Edwin Roig Dr. H. Harry Szmant	Quantitative Analysis (undergraduate) Organic Chemistry (undergraduate)	3
	Theory of Organic Chemistry (graduate) Physico Chemical Basis of Biological	3
Dr. Malcolm Daniels	Processes (undergraduate) Advanced Physical Chemistry (graduate)	3 3

The following staff members are supervising Master's research:

Dr. H. H	. Szmant and Dr. E.	Roig - 1	graduate	student
Dr. H. H	 A — reconstruction of according 	-	graduate	
Dr. Male:	olm Daniels	- 1	graduate	student

D. Collaboration from UPR

The following staff members from the University of Puerto Rico hold ad-honorem appointments at PRNC and participate in the teaching of some of our courses, and in our research programs;

Name

Department

Dr. Juan Daniel Curet Dr. Alec Grimison Dr. Waldemar Adam Mrs. Graciela C. Candelas Dean, College of Natural Sciences Chemistry Biology

E. Formal instruction

1. Courses

a. Basic Radiolsotope Techniques course - has been incorporated in the graduate curriculum of Microbiology and Biochemistry at the School of Medicine as a two-credit course. Other participants receive no academic credit.

b. Radiochemistry - taken by advanced undergraduates and graduates of the Chemistry Department, 4 credits.

c. Nuclear Techniques in Biological Research - taken by advanced undergraduates and graduates of the Biology Department, 4 credits.

d. Radiological Physics - taken by Residents in Radiology from the University Hospital; offered when requested.

2. Teaching staff

Members of other PRNC divisions and of the science departments of the University of Fuerto Rico collaborate in the **teaching** of courses. The situation is well taken care of and the collaboration will continue since it is impossible for the Division to have among its members specialists for all the topics covered in our courses. The persons more involved in the teaching of courses follow:

Name

Division

Dr. E. Roig (Ph.D.) Radioisotopes

Mrs. Rosa S.Tirado (M.S.) Radioisotopes

Dr. R. Luse (Ph.D.)Agricultural Bio-sciencesMiss Z. Frías (M.S.)Radiotherapy and CancerMrs. G. Candelas (M.S.)Biology Dept. (U.P.R.)Mrs. M.P. Lozano (M.S.)Radiotherapy and CancerMiss H. Pabón (M.S.)Health Physics

3. Students

a. Please refer to tables II and III and Graph for an analysis of participants.

b. Comments and conclusions

(1) Significant increase in FY 1963 - due to ten students from the Dominican Republic who came as a group in an arrangement through the University of Puerto Rico to participate in our basic course. Also twelve PRNC employees took the basic course. This number, large as compared to other years, is not typical. Disregarding these two events, which may be considered as special, the general trend of increase noticeable since 1962 brought the total number of students to a figure in the low forties.

(2) The significant decrease in FY 1964 is mainly due to a sharp decrease in the U.S.A. citizens. We must wait until the end of this year to analyze this situation. It could be that the local demand is being satisfied. However, recently the local sugar industry has shown interest in having their scientists trained in nuclear techniques and we are already receiving applications for said training. This training will require the basic Radioisotope Techniques course as an introduction to more advanced training in the bio-agricultural division.

(3) As expected, the Latin American participation in the basic course (elementary level) has decreased.

(4) The participation in academic courses (University credit) has reached a plateau of approximately ten students. This will remain in coming years since it shows saturation of our laboratory facilities.

Special field

Radiochemistry and Instrumentation Radiochemistry and Instrumentation Radiobiology Statistics Radiobiology Physics and Health Physics Physics and Health Physics

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TABLE

DISTRIBUTION OF STUDENTS on the RADIOISOTOPE TECHNIQUES COURSE from FY-1958 to FY-1964

T are 1		Dit	Distribution of		students by fields of work	work			
Year	Nationality	Medicine	Medical Technology	Biology	Chemistry	Biophys. and Rfocham	Others	Total	
1958	U.S.A. Latinamerican Others	r.v.;	~ • •	5010	10 14	m H	KQ 1 r	37	
1959	U.S.A. Latinamerican Others	ц - ,	(V I I	1 10 0 I	1 10 CU 1	ו אש ו		∾ &£.	(9 4)
1960	U.S.A. Iatinamerican Others	CU CO (A)	러러 1	<u>ن</u> ا ن	-4 1 1	- 1 t	1010	61,0	(21)
1961	U.S.A. Latinamerican Others	401	F 1 3	к н н	0[1	мн -	MI	v 8.4	100
1962	U.S.A. Latinamerican Others	۲ n n	~~ •	01 1	10 1 1		1 OF 1	- 3 r o	(北)
1963	U.S.A. Latinamerican Others	© i i	ייש	オ・・	105	1.1.4	nai	32 75 15	(1 77
1961	U.S.A. Latinamerican Others	ו הארא		<u>ع</u> ا،			Q I I	י ב י	(14)
Total		ί	র	47	41	ଝ	35		(236)

TABLE ILI

DISTRIBUTION OF STUDENTS IN ACADEMIC COURSES

Fiscal Year	Radiochemistry	Nuclear Techniques in Biological Research	Total per FY
1960	5	t,	ŝ
1961	9	1	9
1962	6	ı	9
1963	4	7	Ħ
1961	3	8	ᆌ
	*77	15**	39

* 21. of these students were USA citizens, and 3 Latinamerican.

** All of these students were USA citizens.

PARTICIPANTS IN FORMAL COURSES (Basic course, Radiochemistry, and Nuclear Techniques in Biological Research)



(5) Latin Americans participating in our course are mainly from the medical field.

Biology.

(6) Local participants come mainly from Chemistry and

F. Research

1. General comments

We are convinced that in order that we may contribute to the scientific development of Puerto Rico and of Latin America it is necessary that we first establish a continuous and high-level research program so that PRNC as an institution, on its own merits, becomes an attractive training center. The Radioisotope Applications Division believes to have come a long way in this direction and support for this belief will be presented to you by the individual program leaders. Some of the aspects which we planned to promote, such as the utilization of the nuclear reactor as a research tool in hot atom chemistry and due to different reasons: (i) the lack of space for organic chemistry (solved recently with the new laboratory); (ii) the delay in the Dr. Szmant's visit to Dr. Block's assignment to PRNC and also due to financial difficulties; (iii) the delay in modifying access to the Co-60 source.

2. Student participation - Refer to Table IV.

3. Research projects

a. Organic Chemistry - H. Harry Szmant

(1) Organic Boron Compounds (A. Carrasquillo, Research Assistant, PRNC and graduate student; Department of Chemistry, U.P.R.) - Preparation of water soluble derivatives of boric and sub-boric acid.

(2) Organic Sulfur Compounds

(a) Dr. Seymour S. Block, Oak Ridge Research Participation Program Fellow, July-August, 1964: Metallic Chelates of Sulfoxides.

(b) Dr. José P. A. Castrillón (Argentina), Associate Scientist, FRNC: (i) Exchange of oxygen between sulfoxides and sulfides. (ii) Rea duction of sulfoxides by triphenylphosphine and carbon tetrachloride.

(c) Mr. Osvaldo Cox, Graduate Student, Department of Chemistry, U.P.R.: Reaction of Sulfoxides by Triphenylphosphine.

(d) Miss Leilani Ortiz, undergraduate student, Department of Chemistry, U.P.R.; Petroleum Research Fund grant of the American Chemical Society: Reaction of Carbondiimides with thionyl chloride. TABLE IV

STUDENT RESEARCH PARTICIPATION

	FY-1964			* 1		6 1:**			× H	г	1
NODERT RESEARCH PARTICIPATION	FY-1963			1 1	·	10 1.			ı		4
DIUDENT RESERV	Program	Organic Chemistry	Post-doctoral	U.S.A. Latin American	Graduate students	U.S.A. Intin American	Radiation Chemistry and Photochemistry	Fost-doctoral	U.S.A.	Graduate students (U.S.A.)	Undergraduate students (U.S.A.)

* Sponsored by ORINS Participation Program. **One of these students was sponsored by the International Atomic Energy Commission.

(e) Mr. J. J. Rigau, Research Assistant, PRNC and graduate student, Department of Chemistry, U.P.R.: Structure of the isomeric 2-phenylsulfinylindanols.

(f) Mr. R. H. Figueroa, Research Assistant, PRNC, and graduate student, Department of Chemistry, U.P.R.; Dr. E. Roig: Association of Sulfoxides with Phenols.

(3) Nucleophilic Substitution Reactions of Imidates (National Institutes of Health Grant) - Mr. Luis Bravo Navarrete (Chile) and Miss Adele Mouakad, both graduate students, Department of Chemistry, U.P.R.

(4) Solvent Effects in Chemistry

(a) Mrs. Yolanda Vaillant de Candelario (Cuba), Research Assistant and graduate student, Department of Chemistry, U.P.R.: A study of the monosodium salt of phenolphthalein.

(b) Miss Mirta Román, graduate student, Department of Chemistry, U.P.R.: Solvent effects in the Wolff-Kishner reaction.

b. Photochemistry and Radiation Chemistry

(1) Oxyanion Solutions - Miss Vicki Meyers, Research Associate, PRNC, and Mrs. Ederlyna V. Belardo, Research Assistant, PRNC

(a) Photolysis of Nitrate at 304mu: Effects of Concentration, intensity, pH and scavenger.

(2) D.N.A. and Constituents

(a) Photo oxidation of thymine at 1849°A - Dr. Alec Grimison, Associate Professor, Chemistry Department, UPR, and Associate Scientist, ad honorem, PRNC; Miss Ederlyna V. Belardo, and Mrs. Awilda R. Sandoval, Research Assistant, Chemistry Department, U.P.R.

(b) Photodeamination of cytosine at 2537°A: Deamination kinetics - Dr. Alec Grimison and Mrs. Avilda R. Sandoval.

(c) Luminescence of cytosine in aqueous solution: discovery of, pH dependence, quenching kinetics. - Dr. Alec Grimison and Mrs. Awilda R. Sandoval.

(d) Luminescence of Thymine and D.N.A. - Dr. Alec Grimison and Mrs. Awilda R. Sandoval.

(e) Deamination of D.N.A. at 2537°A - German Santiago, Graduate Student, Chemistry Department, U.P.R. -11-

(f) Energy Transfer between Cytosine and Thymine - Dr. Alec Grimison and Mrs. Awilda R. Sandoval.

(g) Viscosity and Optical Studies on D.N.A. -Mrs. Ederlyna V. Belardo and Mrs. Awilda R. Sandoval.

c. Solid State Physics Project of Organic Crystals

(1) Equipment

Equipment has been built to purify anthracene by sublimation and zone refining and to make crystals from solution and from the melt. Equipment has been built to make steady state and transient measurements of electrical conductivity in anthracene crystals.

(2) Measurements

Steady state measurements of electrical conductivity of anthracene crystals using the Kallmann-Pope iodine electrode indicate that the conductivity increases after irradiation of neutrons. There does not seem to be changes in mobility of carriers measured using transient techniques. Plans are being made to make these measurements after irradiating with gamma and x-rays. Measurements will also be made in other organic crystals.

G. Publications

"The Thallous - Thallic Exchange at Various Acidities in Perchlorate Media" - E. Roig and Richard W. Dodson, J. Of Phys. Chem. <u>65</u>, 2175 (1961)

"Radioisotope Demonstration of Common Ion Effect on Solubility", E. Roig, I.G. Rieckehoff, C.S. Russo and J.D. Curet, J. Chem. Ed., Vol. 38, 1961, p. 350.

"The Radiation Chemistry of Arsenite, Pt. II, Oxygen-Free Solution", M. Daniels, J. Of Phys. Chem. 66, 1475 (1962)

"Photochemically-Induced Oxidation of Arsenite: Evidence for the Existence of Arsenic(IV)", M.Daniels, J. of Phys. Chem. <u>66</u>, 1473 (1962)

"Photochemistry of Thymine", M. Daniels and Alec Grimison, Nature, 197, 484 (1963)

"The Deuterium Isotope Effect in the Hydrogen Bonding of Imidazole in Naphthalene Solutions", Alec Grimison, J. of Phys. Chem., Vol. 962 (1963)

"Fluorescence of Cytosine in Aqueous Solutions", M. Daniels and Alec Grimison, PRNC.

"The Photochemical Deamination of Cytosine at 2537°A", M. Daniels and Alec Grimison, Biochem. and Biophys. Research Communications 16, 428 (1964) "Radiation Chemistry of Arsenite Solutions, Pt. III. Effect of Arsenite Concentration in Oxygen-Baturated Solution", M. Daniels, J. Phys. Chem. <u>68</u> 1867 (1964).

"The Wolff-Kishner Reaction of Hydrazones", H. H. Szmant, J. Am. Chem. Soc. <u>86</u> 2909 (1954).

"Informe Acerca de las Revistas Científicas y Técnicas Latinoamericanas - Química", in commemorative volume published by UNESCO, Centro de Cooperación Científica para América Latina, Montevideo, summarizing the activities of "Grupo de Trabajo para la Selección de Revistas Científicas Latinoamericanas", in San Juan, April 26-May 1st, 1964.

OUTLINE OF MATERIAL TO BE PRESENTED TO AEC Ad Hoc Committee for Program Review

CLINICAL APPLICATIONS DIVISION

Dr. Sergio Irizarry, Head

1. Purpose and Scope of Program

The main purpose of the program of this Division is teaching and training of Latin American physicians in the diagnostic and therapeutic uses of radioisotopes in humans. This goal is accomplished in two ways:

(1) providing special training courses of basic clinical radioisotopic techniques for the diagnosis and treatment of human disease.

(2) providing special training in clinical research.

2. Types Training Available

Introduction

Initially this Division began operating under the Direction of Dr. A. A. Cintrón Rivera in 1958 at the Radioisotope Unit of the School of Medicine at the San Juan City Hospital. A total of 36 trainees have completed the clinical course, of which 28 have come from various Latin American countries. Table I.

The average output of trainees during the past 7 years has been 5 per year. Graph I.

TABLE I

TRAINEES FROM LATIN AMERICA

-

Country	-	Number of Trainees
1. Argentina		6
2. Bolivía		1
3. Chile		3
4. Colombia		2
5. Costa Rica		1
6. Dominican Republic	,	3
7. Guatemala		1
8. México		5
9. Uruguay		1
10. Venezuela		5
	TOTAL	28

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1958 1959 1960 1961 1962 1963 1964	
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GRAPH I

Type Courses Available:

There are two general types of courses available according to breath and scope of the course: orientation courses and training courses. Considered in the light of duration and type of training desired two courses are offered:

A short 4 weeks or 8 weeks basic clinical applications training course or a long 6 months to 12 months clinical research training course.

Description of the Courses:

The Short Course

The short course is basically a 2 months formal program consisting of lectures, demonstrations, informal presentations, laboratory exercises for training and periods of discussion. Emphasis is placed on mastering of techniques, their indications and uses, correct interpretation, limitations and correlation with clinical problems.

The 8 weeks course contemplates the completion of 80 laboratory exercises in which a wide variety of techniques are employed. A list of the teaching units covered by the laboratory procedures utilized appears in table II.

TABLE II

1

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1

2 months training program

Units of Study	Average number procedure per trainee
1. Thyroid Function routine uptake measurements (15) assay radioactive blood thyroid hormone levels (15) modified tests of thyroid function(5)	35
2. Dynamic functions of the hepatic, renal, and vascular systems	20
3. Hematologic applications of radioisotopes	5
4. Tumor localization studies	10
5. Gastro-intestinal absorption	5
6. Electrolyte and Fluid balance	2
7. Therapeutic procedures	_3_
	80

A 4 weeks course, of similar nature to the 8 weeks course, is also given. The procedures are similar but the total number of training exercises is cut in half, so that 40 teaching exercises are completed by each trainee.

The Long Course

There are two long term courses being offered by this Division:

A- Semester course for medical residents: orientation in medical uses of radioisotopes.

B- Semester to 1 year course in clinical research. Description of courses

The Semester course for medical residents is a non credit course designed for orientation in the medical aspects and uses of radioisotopes for diagnosis and therapy in clinical practice. The course consists of 20 hour lecture sessions and 12 sessions 2 hours each for laboratory demonstrations.

The Semester to 1 year clinical research course is offered to candidates who have had already gone thru the basic training at Puerto Rico Nuclear Center or elsewhere, and who want advanced specialized training in clinical research. The trainee would have no formalized teaching, but would be assigned special responsibility within a project being carried out at the Division and be supervised at regular intervals to evaluate progress being made and for the solution of problems that may arise during the course of the investigation. The trainee may have a special problem of his own that he would like to investigate. In this case he discusses his project with us for a

decision as to feasibility and scientific value. If approved he is given the necessary assistance and supervision for its completion. The trainee is responsible for the design of his project, selection and standardization of the method, collection of the data, analysis and reporting. A final report at the end of the year is submitted to the Director for evaluation and publication if it fulfills the requirements for a communication.

New Proposed courses

Following a previous recommendation of the Bio-Medical Advisory Committee, the Division is setting up a special advanced course for training in renal pathology. This is a 4 weeks course offered to candidates with previous experience in the field of nuclear medicine, who want a specialized training in the particular area of renal diseases. Registration capacity for full training is 4 trainees; the course may be offered twice a year, for at least 2 years, before another course of similar nature on another subject is prepared. The basic organization of the course allows the first week to a general review of nuclear physics, mathematics and statistics; the second week covers the pathologic and physiologic aspects of the renal apparatus; the third week defines the clinical pictures of various pathologic entities, and the fourth week is dedicated entirely to radioisotope techniques for the evaluation of renal function.

A second new proposed course is a general course of orientation in Nuclear Medicine of one week duration. This course is intended for the general practitioner and doctors in other medical specialties. The subject matter of this course will try to cover the

general applications of radioisotopes for diagnosis and treatment in current use in medical practice. Demonstrations and case presentations will be used to strengthen the theoretical presentations.

A program of each of the formal courses described above is appended. Appendix A.

Diagnostic Service Load and its relation to training courses

The laboratory, as already mentioned, began operations in 1957-58 at which time a total of 438 diagnostic procedures were performed. Since then, yearly reports indicate increase output in the diagnostic service load until the years 62-63 and 63-64 in which the output levelled off at or around 3,300 procedures - an 8 fold increase. This is illustrated in Chart I, graph 2.

The diagnostic load has always been considered a necessity for the training program. It is generally admitted that the necessities of the training program can be well met by a ceiling of 200 diagnostic procedures per month. This level of activity had already been reached by 1960-61. An increase beyond this level during the past 2 years can be explained by the combined operations of the University Radioisotope Unit and PRNC Clinical Applications laboratory. It should be mentioned that a semester course for medical residents of general orientation in the clinical uses of radioisotopes was completed by 26 participants of the University Hospital. A new course is scheduled for the next semester January - June, 1965.

Training procedures are performed by trainees and in all instances whenever possible, a parallel run is made by the instructor for control of technique.

CHART I

FLOW CHART DIAGNOSTIC PROCEDURES BY YEAR

		: 1957-58	58 :	1958-59		1959-60	 Q	1960-61		1961-62		1962-63		1963-64	•••••
THYROID FUNCTION		405	••	592	••	1337	••	1816	••	2086	••	1691		2349	••
LIVER		4	••	S		30	••	40	.,	54	••	68	λ.	75	••
HEART	**	29	••	62	••	13		110	۰.	70	••	80	••	65	••
KIDNEY		1	••	٠	••	32	••	252	•••	223	••	172	••	206	••
GASTROINTESTINAL		•	••	121	••	125	••	135	••	227	••	35	••	27	
B1.00D	••	:	••	7	••	50	••	16	••	34	•-	25	••	11	••
TUMOR LOCALIZATION	• •		••	٠	••	1	••	۲		12	••	118	÷	45	••
TRAINING PROCEDURES		*	••	*	••	¥	••	264	¥ N	309	••	690	••	630	
MI SCELLANE OUS	••	6	••	1	••	36	•••	47	••	77	••	7	••	4]
TOTALS		438		804		1623		2680		3092		3126		3412	

* No statistical data

September 17, 1964

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In the flow chart presented before, training procedures make a substantial figure of total diagnostic load from which it is taken. This is more apparent in the last two years during which time we have had better reporting of this activity.

The teaching procedures include the following techniques:

l. Thyroid Function Studies	 uptakes, 2, 24, 48 hours PBI-131 Conversion ratios PBI-131 plasma levels KCNS discharge test TSH stimulation test Triiodothyronine suppression test Iodine inhibition test Thyroid Scans
2. Cardiovascular	 Cardiac output Stroke Volume Circulation time Central Volume Circulatory rates for shunts Cardiac scanning
3. Kidney Function	 Hippurate I-131 renogram Neohydrin Hg 203 renogram Blood clearance Renalscans
4. Liver functions	 Hepatogram Liver uptake, excretion, intestinal entry time, Blood clearance Liver Blood Flow Liver scanning
5. Hematology	 <u>Cr-51</u> Blood volume, red blood mass, Red cell survival Splenic uptake In vitro Red cell uptake Gastro-intestinal blood loss Splenic scanning
	 Fe-59 Iron Plasma Clearance Daily plasma iron turnover Red blood cell iron uptake Red cell iron turnover Total red cell iron Percent hemoglobin renewal per day

12.

	- Total hemoglobin formed - Average red cell life span - Total circulating hemoglobin
6. Gastro-intestinal function	 Absorption Vitamin B-12 Absorption labelled neutral fat and fatty acids (Oleic I-131 and triolein I-131) Blood curve absorption levels Urinary excretion levels Stool, elimination of radioactive fat
7. Tumor Localization	 Gamma-scintigraphy Paper dot scanning Photo dot scanning Gamma-photo-radiography Other methods of tumor localization Progress in instrumentation
8. Electrolyte Balance and Fluid Compartments	 Plasma Volume Extracellular volume Total Body water Intracellular volume Sodium and Potassium turnover and exchangeable pools Sodium compartment
9. Therapeutic procedures	 Hyperthyroidism Cancer of the Thyroid Intractable Coronary Disease Polycythemia Vera Chronic Leukemia Pleural and Peritoneal Malignant Effusions

Research Program

A number of clinical research projects are being carried by the Medical Staff of the Division on patients referred for diagnostic studies or on patients undergoing treatment at the University Hospital or the I. González Martinez Oncologic Hospital. The rationale for this activity is that it enters into the teaching material offered the trainees in the various courses, in the formal presentations or at informal discussions. Trainees are encouraged to design and carry out their own projects. During the last training course given at this Division two new proposal or projects of investigation were submitted as a result largely, of initiative of the trainees. This 2 research proposals are:

 Clinical and Radioisotopic Evaluation of the Cardiovascular States in Diabetics - initiative in part of trainee Dr. Mario Iturralde from Bolivia.

2. Iodine Metabolism in Endemic Goiter in Mexico, initiative in part of trainee Dr. Antonio Quijano Blanca from Mexico.

The project of the clinical and radioisotopic evaluation of the cardiovascular states of diabetics patients was approved and is under way. The project for the study of endemic goiter in Mexico is under consideration for approval pending financial support.

All other projects are tuned to the needs of the teaching program. This relation is best shown if we compare the units of study of the various courses and the project title of the clinical studies. This is given below, table III.

TABLE III

Comparison Units of Study for Training and Projects of Investigation

Units of Study-Clinical Applications

Project

1. Tests of Thyroid Funtion

1

- Clinical and Laboratory Evaluation of Thyroid Disorders
- Evaluation of in vitro tests of thyroid function for use as diagnostic procedures.
- Study of the effect of anticonceptive therapy on the 24 hour I-131 thyroid uptake

2. Cardiovascular	 Coronary blood flow in anemia Cardiovascular studies in dia betics
3. Kidney function	 Renogram follow up Study in Cancer of the Cervix Combined clinical, renographic and scintigraphic studies in kidney diseases Renogram studies in diabetics
4. Liver function	- I-131 Rose Bengal localization studies - scintigraphy
5. Gastro-intestinal function	 The effect of radiotherapy on intestinal absorption of iodine 131 labelled fats and Vitamin A in humans. The thyroid gland as an indicator of intestinal absorption of I-131 labelled fats
6. Hematology	
7. Tumor Localization	- Instrumentation improvement

8. Electrolyte Balance and

-

- Fluid Compartments
- 9. Therapeutic procedures

- Electrolyte and fluid disorders in diarrhea.

- Organ and tumor localization

- -Electrolyte and Fluid Balance in women under anticonceptive therapy.
- Review of Patients treated with I-131.

Advanced Course in Nuclear Medicine;

RADIOISOTOPES IN RENAL DISEASES

The Clinical Applications Division of the Puerto Rico Nuclear Center will offer an advanced course in Nuclear Medicine applied to the study of diseases of the renal apparatus. The course contains an introduction unit which will review basic aspects of nuclear physics. This will be followed immediately by a work shop in anatomopathology study of renal morphology, normal and abnormal, with presentation of pertinent illustrative material derived from surgical specimens and related to clinical pictures and case discussions. This area will be taken up in two units:

A. Unit of anatomo-pathology studies of the kidneys, in which the basic considerations will be the study of normal anatomy of the kidney which includes: gross anatomy, histology, embriology, anatomypathology of the kidney, physio-pathology and special techniques of histopathology (histo-chemistry)

B. Special syndromes or clinical pictures of renal diseases. This includes: nephritis and nephrosis, metabolic diseases, vascular diseases and obstructive syndromes, including tumors and renal infectious processes.

The fourth unit will be dedicated to the study of the renal apparatus by the use of several radioisotopic techniques. Emphasis will be placed on methodology of the different tests and their interpretation and correlation with physio-pathatologic mechanisms presented or demonstrated in the various clinical pictures. The duration of the course is four weeks, with 18 hours for lecture time and 116 hours for practice, demonstrations, discussions, seminars and other activities.

The course will be offered utilizing various methods available for transmission of information. This will be based on the formal lecture, panel discussion and methods in which the active participation of the trainee will be encouraged, such as case presentations, bed-rounds, seminars, discussions, laboratory practice and clinical evaluation and work up of patients under supervision. Information will be presented using available audio-visual means, such as, movies, slides, surgical specimens, visits to autopsy rooms, recorded lectures, etc.

Requirements for diploma: Doctor or Senior Medical Student who have had previous training in radioisotopes (Basic Course Radioisotopes Techniques) or equivalent experience.

Requirements for other participants not entitled to diploma: Doctor, Medical Student or paramedical professional, for example: nurse, technician.

A certificate of participation may be issued in this category for full attendance to lectures and demonstrations but persons in this category are not responsible to perform or render any special assigned work.

Capacity of enrollment for diploma - 8 trainees.

Participants with no diploma - no limitations.

Stipends - A fee of \$25 will be charged to all enrollees to the formal course with credit. Other participants no charge.

A program of the course is submitted.

RADIOISOTOPES IN RENAL DISEASE

Program for the Special Advanced Course: I. Introduction: Biophysics 1. Mathematics review lecture - 1 hour laboratory - 3 hours 2. Statistics review lecture - 1 hour laboratory - 3hours 3. Review Basic Concepts Nuclear Physics lecture - 1 hour laboratory - 3 hours 4. Review Nuclear Physics lecture - 1 hour laboratory - 3 hours II. Anatomic Pathology of the Kidney 5. Anatomy of the kidney: Embryology lecture - 1 hour laboratory - 3 hours 6. Anatomic pathology of the kidney lecture - 1 hour laboratory - 3 hours 7. Histopathology of kidneys lecture - 1 hour laboratory - 3 hours 8. Renal Physiology and Clinical Laboratory lecture - 1 hour laboratory - 3 hours 9. Renal Physio-pathology lecture - 1 hour laboratory - 3 hours

10. Special histo-pathologic techniques (histo-chemistry)

lecture - 1 hour
laboratory - 3 hours

III. Clinical Syndrome: Renal Diseases

11. Nephritis and Nephrosis

lecture -lhour
laboratory - 3 hours

12. Metabolic diseases

lecture - 1 hour laboratory - 3 hours

13. Vascular diseases

lecture - 1 hour
laboratory - 3 hours

14. Obstructive Uropathies including tumors and infectious processes of the kidney

IV. Radioisotopes

11 contract of the local division of the loc

15. Renographic studies, part I

lecture - 1 hour
laboratory - 3 hours

16. Renographic Studies, part II

lecture - 1 hour laboratory - 3 hours

17. Gamma Scintigraphy, part I

lecture - 1 hour
laboratory - 3 hours

18. Gamma Scintigraphy, part II

lecture - 1 hour
laboratory - 3 hours

19. Electrolyte studies; Sodium turnover, Sodium space and Sodium excretion

> lecture - 1 hour laboratory - 3 hours

20. Fluid compartments - total body water

lecture - 1 hour laboratory - 3 hours

21. Differential test of renal function using stable sodium and radioactive sodium

-

lecture - 1 hour laboratory - 3 hours

22. Miscellaneous tests of renal function: renal cystogram and radiocystometry, excretion half time, renal clearance and renal blood flow.

ORIENTATION IN THE MEDICAL USES OF ISOTOPES FOR ONE WEEK DURATION

- 1. Introduction to basic concepts of Nuclear Physics and radioactive protection, and handling radioisotopes.
- 2. Radioactive applications in the study of thyroid diseases.
- 3. Study of dynamic functions of the cardiovascular apparatus, renal and hepatobiliary systems.
- 4. Studies of gastrointestinal absorption.
- 5. Tumor Localization

-

-

- 6. Body spaces and fluid compartments; electrolyte and fluid disorders.
- 7. Therapeutic applications.

Lecture time - 10 hours

Laboratory sessions - characterized mainly by demonstrations, case presentations and group discussions - 26 hours
OUTLINE OF MATERIAL TO BE PRESENTED TO AEC AD. HCC. COMMITTEE FOR PROGRAM REVIEW

MEDICAL SCIENCES AND RADIOBIOLOGY DIVISION

Dr. Maurice Paul Weinbren, Head

This division is composed of three theoretically separate programs, though, in fact, these have become interdependent in many ways. This interdependence avoids unnecessary duplication of skills and facilities and has enabled the division as a whole, to operate with considerably greater efficiency. The basic program was established to:

- a. To conduct training and research in radiobiology at the cellular and subcellular level with emphasis on medical applications.
- b. To establish and operate tissue culture facilities for its own program and also to serve others.
- c. To explore the utilization of nuclear energy in developing new knowledge of tropical diseases of man.
- d. To organize and operate a small animal laboratory needed for its own program and those of others.

In this area we have established a well-trained staff who are adept in most of the techniques of tissue culture. Little progress has been made with the program designed to study the effects on individual cells resulting from neutron capture by Boron 10, because no sconer did Dr. Szmant's group succeed in synthesizing some soluble B¹⁰ containing compounds, than we lost our standard cell lines due to persistent and refractory contamination.

A program to study human chromosomes in cultured leucocytes was established as a cooperative effort between the U.S. Army Tropical Medicine Research Laboratories (Col. M. Dacquisto), this Division (Dr. M. P. Weinbren) and the Division of Radiotherapy and Cancer (Dr. José Tomé). The program is designed primarily to establish a normal pattern and to compare this with material drawn from cases with "Tropical Sprue", Radiotherapy patients receiving radiation to the abdomen and in whom a "sprue-like" condition results, and patients receiving similar doses of radiotherapy to areas excluding the abdomen. The study is not, however, limited to this type of material and we have received a number of specimens from physicians at the University Hospital and the forces. Our first cultures were made on October 22, 1963 and we have now (September 14) processed 410 specimens. Now that this facility has been established it is proposed to establish a file of material from the members of the Puerto Rico Nuclear Center staff, and in particular to follow those individuals who were accidentally exposed to radiation in Mayaguez.

The Dengue Epidemic

This Division was invited to participate in a study of the epidemic of Dengue fever which was first recognized as being of epidemic proportions in the town of Manati in late August 1963. The part played by the Tissue Culture Unit was an attempt to isolate virus from 143 sera collected from patients in the first 12 hours of illness. The tissues used for this purpose were African Green Monkey (Cercopithecus) Kidney monolayers which were purchased in tubes from Flow Laboratories.

From 38 of the sera inoculated into the tissues a "positive reaction" was obtained. The term "reaction" has been used because as yet we have been unable to achieve the usual end point of specific cytopathogenic effect which is transmissible for an indefinite number of passages.

In tissue culture two types of changes were seen and may be referred to as "early" and "late". The early change consists of a fleeting cytopathogenic effect where areas of degeneration of the cell sheet occur and the affected cells detach and can be seen floating in the medium. This usually occurs on the 3rd. day following inoculation and would appear to be confined to a hypersusceptible cell population as the detached cells are replaced in a matter of hours by the cells not affected at this time. The "late" phenomenon occurs between the 8th and 10th post inoculation days when the monolayer's appearance becomes that of Madeira lace or drawn-thread needlework; there are "holes" of varying sizes up to 300u in diameter separated by bands of cells piled several deep. At this stage there is little or no increase in the number of cells floating free in the medium but if the process is allowed to continue for a further 2 or 3 days all the cells detach.

In many instances both "early" and "late" phenomena occur in the same cell sheet but this is not invariably the case. Sometimes, when the specimen was inoculated at different dilutions, the lower dosage resulted in only the "late" form while the more concentrated inoculum produced both types.

In some instances the "effects" are transmissible by means of the supernatant medium from the "early" stage and in others only from the "late". In any event after 2 or 3 passages the virus assumed a condition of latency and although demonstrable in the cells by means of the indirect fluorescent antibody technique, no overt manifestations of any type were seen. Altogether 299 fluorescent antibody tests were carried out in this unit in the course of testing tissue culture cells or mouse brain impressions for the presence of the Dengue virus.

We have recently been able to obtain a supply of BHK (Baby Hamster Kidney) cells through the kindness of Dr. Michael Siegel of the Variety Children's Research Foundation, Miami. Dr. Siegel obtained this established diploid cell line from its originator, Dr. Stoker, in Scotland. Our particular interest in these cells lies in the fact that they have been shown to be unusually sensitive to the Dengue viruses and we hope to use then to further on study of the material collected during the Dengue epidemic. Another approach to the problem of unmasking the latent dengue virus has been to use irradiated infant mice as a medium. The mice received 300 or 400 rad. before inoculation. The system used was one of continuous passage in both irradiated and normal mice. On some occasions the virulence appeared to be enhanced but this effect was temporary though it is true that larger quantities of the virus may be demonstrated into the brains of the mice from the irradiated series by the indirect fluorescent antibody technique (I.F.A.). Up till now this I.F.A. technique has been carried out on impressions made from the cut surface of the brain being studied but in the last few days we have received a cryostat microtome and will now be able to use tissue sections for the purpose and this should be much more satisfactory.

The dosage of 300 or 400 rad was derived from an estimated LD₅₀ in the region of 650 rad (based on previous experience with rats). It was further assumed that the R.B.E. for baby mice of radiation from a 350 KVP "Maxitron" would be similar to that from Cobalt 60 . Subsequent experiments have shown however that this is not so, at least for the units at the Puerto Rico Nuclear Center and the Oncological Hospital. The attached table shows the results of the experiments which may be summarized as follows:-

DATE		MAXITRON DEATHS-DAYS	LD ₅₀	Co ⁶⁰ DEATHS-DAYS
7/14/64 (PRNC)	456	5-14	(PRNC) 912	6-14
8/11/64 (PRNC)	456	4-10	(PRNC) 912	4
8/28/64 (PRNC)	456	4-11	(HOSP) 920	4-15
HOSP	455	4-11		

<u>.</u>

In all cases the animals were observed for 3 weeks and no deaths occurred after those noted above.

7-14

MAXITRON (PRNC)

Co⁶⁰ (PRNC)

Dose r	.# Dead	# Alive	Time of Death	Dead	Alive	Time of Death
1200	16	0	5-7	9	0	6-12
1000	16	0	5-9	15	1	5-9 9-14
800	16	0	7-10	0	16	
600	16	0	7-14	0	14	
400	0	8		0	16	
200	0	16		, o	16	2) 2
	LD	456 r			LD 912 50	r
	5	10	8/11			
1600	14	0	4-6	14	0	4-8
800	14	0	7-10	o	14	
400	0	14		0	14	
200	0	14		0	14	
	rD ¹	45 6	r		LD 912 50	r
	MAX.	PRNC				
1600	14	· 0	4			
800	14	0	8-11			
400	0	14				
	LD 456 50					

- 4 -

	MAX H	OSP			со ⁶⁰	HOSP
1 600	14	0	4-6	14	0	4-6
800	12	1	9-11	2	12	13-15
400	0	14		0	14	
	^{LD} 50 45	5			LD ₅₀	920

OUTLINE OF MATERIAL TO BE PRESENTED TO AEC AD HOC COMMITTEE FOR PROGRAM REVIEW

RADIOTHERAPY AND CANCER DIVISION

Dr. Victor A. Marcial, Head

A. RADIOTHERAPY RESIDENCY PROGRAM

1. Training Program

The purpose of this program is the training of radiation therapists. Cancer, the second most common cause of death in the nation requires that radiation therapy be utilized at sometime in the disease in over 50% of patients. Adequate radiation therapy is best provided by properly trained specialists with full-time interest and dedication to this aspect of medicine. This program attempts to train academically and research oriented radiation therapists. The ultimate goal is to serve the cancer patient better, providing him with well trained specialists and more efficient treatment methods.

The present program of training constitutes a collaborative project between the Puerto Rico Nuclear Center, the I. González Martínez Oncologic Hospital, and the University of Puerto Rico School of Medicine. The main objective of the Puerto Rico Nuclear Center and the University of Puerto Rico School of Medicine are training and research, and that of the Oncologic Hospital is the service to cancer patients; consequently, the efforts of these institutions complement each other.

The total training period last three years, but trainees are required to take an additional fourth year of supervised practice before admission to the Board certification exams. The program enjoys full approval from the American College of Radiology.

Trainees acquire a solid background in clinical cancer through supervised work with new, follow-up, and hospitalized cancer patients. They learn to diagnose the disease, determine the extent of the same, choose the appropriate treatment, and plan and conduct radiological therapy. Radiation the rapy experience is acquired by working with roentgentherapy machines of various voltages and teletherapy units, which include cobalt and cesium, and with the application of radioactive material such as: radium, strontium, cobalt, and iridium.

The present program permits trainees to become familiar with non-radiological cancer treatment methods, such as surgery and chemotherapy. In addition, they learn of cancer control activities in Puerto Rico, this includes the operation of a Central Cancer Registry, tumor clinic work, cancer detection, and public and professional education in cancer. Since July 1, 1964 some changes have been introduced in the curriculum that affect mainly the first year trainees. Radiotherapy trainees in the first year will be offered a course of cancer pathology for three months, a course in radiological physics for three months, and a course in radiobiology. In addition, they will take the Basic Radioisotopes Techniques Course and will be given radioisotopes clinical training for two months. A lecture course in bio-statistics and refresher conferences in biochemistry will be offered during the training period.

Latin-american trainees have faced three major obstacles in coming to receive long term radiotherapy training at American centers. These are: the certification from the Council on Foreign Medical Graduates of the American Medical Association, which is a requisite for training in approved residency programs, licensure by the State Board to practice medicine on a temporary basis, and adequate financing during the training period. Since the requirement of certification by the ECMFG was introduced, the number of trainees has decrease in all American centers.

B. SHORT TERM RADIOTHERAPY TRAINING

The short term radiotherapy trainees are those that come to the Division as observers for a period of a month or longer. As a rule they are experienced radiologists who want to become familiar with our program. This constitutes a less desirable type of training for Latin-americans in view of the fact that they do not acquire a solid basis in radiotherapy. Short term trainees face the following problems: as a rule they have permanent positions at home and cannot afford to leave their departments for long periods of time and they are older individuals who cannot afford to bring their families with them in view of the limited economic support they receive while away.

C. FOURTH YEAR MEDICAL STUDENTS TRAINING

The fourth year medical students have been offered a training period of one month in the Radiotherapy and Cancer Division on a voluntary basis. The students do not enjoy free time in their fourth year other than a month of vacation. During the vacation some students choose to come to the Radiotherapy Division to learn about cancer and radiation therapy.

D. RADIOTHERAPY TECHNICIANS COURSE

A recent law in Puerto Rico requires that personnel associated with the operation of radiation equipment be physicians or qualified radiology technicians. Radiotherapy technicians are required to take a formal course of training for two years. Our Division has prepared a training course that will be offered to a group of nurses from the Oncologic Hospital and the Puerto Rico Nuclear Center beginning early in fiscal year 1964-65. The proposed course follows the pattern required by the American Board of Radiology; it consits of four hundred hours of didactic activities and over a thousand hours of supervised experience.

E. VISITING RADIOTHERAPISTS

Young radiotherapists from Latin America have been given the opportunity to work as visiting radiotherapists for periods of one year or longer. This has permitted them to become familiar with our program and has proved stimulating to our staff.

2. Research Activities

The research activities at the Radiotherapy and Cancer Division continue being of clinical nature in the majority of projects. As no laboratory facilities are available in the Division, we have to request the help of the Medical Sciences Division for such services. It is expected that when the animal house be finished, basic research facilities will be enhanced considerably.

The following projects are underway in the Division:

1. Evaluation of Radiation Response by Means of Exfoliative Cytology in Cases with Cancer of the Cervix Treated with Radiation.

This is a long term project which is being carried out at the Radiotherapy Division with the objective of determining the value of exfoliative cytology as a prognostic tool in cases with carcinoma of the cervix treated with radiation. An initial analysis relates to patients with a minimum of two years follow-up who showed the presence of persistent tumor cells in the vaginal smear after irradiation. The significance of this finding and its relationship to tumor free survival has been determined.

2. Surgical Adjuvant Breast Project.

This is a national project with the objective of improving prognosis in patients with breast cancer treated with radical mastectomy with additional therapy. Postoperative irradiation of the lymph node areas, and systemic chemotherapy are being investigated. So far, 29 patients from the 1. González Martínez Oncologic Hospital have been contributed to the study.

3. <u>Study of the Incidence of Leukemia in Patients with Cervical Cancer Treated</u> with Radiation.

This is an international study with the objective of determining the risk of developing leukemia in patients who have been irradiated for cancer of the uterine cervix. As of the end of June 1964 all the collaborating institutions have contributed 33,000 persons-years to the study and 2 cases have developed leukemia. The expected number of leukemia cases based on normal population incidence would be 2 cases.

4. <u>Study of Chromosome Changes in Patients Undergoing Radiation Therapy</u> for Cancer.

The aim of this study is to determine chromosome changes in irradiated cancer patients that may have prognostic value. The samples are taken before, during, and after irradiation and the lymphocytes are separately cultured, the cultures are then treated with colchicine and the lymphocytes are stained and observed for chromosome abnormalities.

5. Study of Fractionation of Weekly Doses in Cancer Patients Submitted to Irradiation.

This is a clinical study aimed at determining the optimal fractionation of weekly tumor doses in patients submitted to irradiation for cancer. Half of the patients seen at the Department are receiving the weekly tumor dose divided in three applications vs. five applications in the other half. Tumor effect, survival, and normal tissue reactions are being observed. Six hundred and twenty two patients have been incorporated in this study.

6. Study of Optimal Tumor Dose in Radiation Therapy of Cancer of the Esophagus

This is a clinical study to determine the optimal radiation tumor dose in the treatment of cancer of the esophagus. Half of the cases have been treated with cobalt teletherapy doses of 5000r in 4 weeks vs. 6000r in 6 weeks in the other half. Disappearance of dysphagia and twelve month survival will be compared in each group. Fifty four cases have been included in the study.

7. The Influence of Whole Body Irradiation in the Enzyme Activity of the Intestine.

This is a project to determine changes in enzyme levels in the intestinal wall caused by radiation. Mice have been studied as to acid and alkaline phosphatase levels in the small intestine which has been divided in two equal halves. Acid phosphatase levels have been found equal in both halves, but alkaline phosphatase in the upper half is twice in amount of what is found in the lower half. Total irradiation of the animal, up to 500r, 48 hrs. before the animal is killed, hasshown no change in phosphatase levels. S.G.O.T. and S.G.P.T. levels will be investigated.

8. Controlled Study of the Split-Dose Technique in Radiotherapy of Cancer.

The purpose of this study is to compare the results obtained by means of the usual uninterrupted treatment (6000r in 6 weeks) vs. a similar dose given in two separate two-weeks periods with a rest interval of two to three weeks halfway in the treatment (3000r in two weeks $\neq 2$ to 3 weeks rest $\neq 3000r$ in 2 weeks). Only tumors measuring 5 cm or more (excluding pelvis and esophagus) are included in this study. Half of the cases in

the study are being treated with the usual technique and the other half receives the split-dose technique. Results will be evaluated in terms of tumor regression, normal tissue reactions and curability. Fifty cases have been included.

9. Adenocarcinoma of the Cervix .

This is a retrospective clinical study which has as objective to corroborate the clinical impression that adenocarcinoma of the cervix uteri is more radioresistant than epidermoid carcinoma of this structure. Eventually we wish to determine whether the combined use of radical hysterectomy after radiation would improve the survival.

10. Carcinoma of the Cervix Uteri and Pregnancy.

In this retrospective study the incidence of carcinoma of the cervix uteri associated with pregnancy was determined in a group of 2554 cases of uterine cancer treated at the I. González Martinez Oncologic Hospital. Sixty two patients had their cancer associated with pregnancy. The optimal way of handling this complication has been determined from the revised material.

11. Carcinoma of the Cervix Uteri in Sterilized Women.

The aim of this study is to analyze the possible relationship of carcinoma of the cervix uteri and previous interruption of the reproductive capacity by surgical sterilization. It has been observed that in patients under 50 years of age with carcinoma of the cervix uteri 25.4% have had previous surgical sterilization. The true significance of this finding is being evaluated.

Future Projects:

1. Combined Irradiation and Chemotherapy in the Treatment of Carcinoma of the Esophagus.

This study has the objective of improving the curability of carcinoma of the esophagus by irradiation therapy adding mexotrexate. The study will include controls and will be initiated during fiscal year 1964–65.

2. Study of Dose Fractionation and the Combination of Radiation and Chemical Agents on a Mouse Tumor.

The objective of this study is to observe the effects of various fractions of radiation alone or in combination with chemical agents on chondro-sarcoma grown in mice. A correlation of radiation dose and histologic changes in the transplantable chondrosarcoma will be attempted.

3. A Controlled Study to Determine the Usefulness of Oxygen Administration During Radiation Therapy.

Available radiobiological and clinical data suggests that the response of anoxic tumors is best when the patients receive oxygen while being irradiated. The study is being suggested for discussion with the Advisory Committee. Patients with bulky anoxic tumors will be selected and half will be administered oxygen during radiation while the other half receives identical dose of radiation but no oxygen. Tumor regression and one year curability will be evaluated.

III. SERVICE ACTIVITIES

An adequate load of clinical cases is necessary for good training and for clinical cancer research. As there exist hundreds of different types of cancerous tumors, the trainee must be exposed to a significant and varied load of patients to be able to become familiar with all types of neoplasia and the problems involved. Most clinical studies require a good volume of cancer patients to be able to accumulate data of statistical

The Radiotherapy and Cancer Division has not suffered from lack of good clinical material, as it has access to all the patients seen at the Dr. I. González Martínez Oncologic Hospital. During last year 21,794 teletherapy applications were given, 207 curietherapy insertions were made, and 723 new patients were registered for radiation

OUTLINE OF MATERIAL TO BE PRESENTED AT

AEC REVIEW OF PRNC PROGRAMS

October 15-17, 1964

REACTOR DIVISION

Presented by Mr. Héctor Barceló Head of Reactor Division

A. Functions

110

i

This program includes the operation and maintenance of a 1 megawatt swimming pool reactor and a 10 watt homogeneous reactor and the associated equipment necessary to operate these facilities.

B. Organization

l Division Head

- 1 Reactor Supervisor
- **1** Associate Reactor Supervisor
- 4 Reactor Operators
- 1 Mechanic
- 1 Janitor
- 1 Secretary

C. History

1. Operation

The 10 watt homogeneous reactor was first made critical on August 12, 1959.

The 1 megawatt swimming pool reactor was made critical for the first time on August 16, 1960. The test period for this reactor extended through November 1950, after which it was turned over to the PRNC for operation. - 2 -

2. Megawatt-hours of operation

Year	1961-1962	287.19	Megawatt-hours
Year	1962-1963	996.76	Megawatt-hours
Year	1963-1964	1,163.67	Megawatt-hours

3. Long term beam tube experiments

In July, 1962, the first long term experiment was inserted in the reactor in beam tube No. 2. In this experiment a graphite calorimeter is used to measure the effects of radiation on graphite with respect to its emissivity.

In October, 1962, the first neutron spectrometer for the Neutron Diffraction Program was installed in beam tube No. 4 and the second neutron spectrometer was installed in beam tube No. 3 in July, 1963.

4. Training

1959-1960 Training course given to four reactor operators for the PRNC

- 1961-1962 a. Training course given to twelve reactor operators for the BONUS reactor
 - b. Short course in instrument trouble diagnosis offered to two PRNC electronic technicians.
- 1962-1963 Reactor supervision training program given to six BONUS supervisors
- 1963-1964 On-the-job training of two reactor supervisors from Colombia, South America
- D. Improvements and developments
 - 1. Beam tube No. 1 has been provided with a fast flux collimator and a borated-water neutron shutter
 - 2. The thermal column was improved to provide a higher and more uniform flux distribution over the vertical access opening
 - 3. A new core configuration has been developed which provides a higher neutron flux density at the beam tubes and gives a higher value of rod worth.

- 4. Rod vibration caused by water flow has been reduced without the reduction in size of the water channels
- 5. A mechanized system was installed to permit the transfer of radioactive material from the swimming pool into the hot cells under water.
- 6. A voltage regulator was designed and built by the reactor division for the safety amplifiers to correct rise in magnet current with power increase
- 7. A Nitrogen 16 detector was installed in the primary water outlet to monitor power level more accurately than is possible with the equipment for the differential temperature method originally installed
- 3. A wire scanner was built by the division to scan copper wires used for flux mapping
- 9. Techniques have been developed for constructing and overhauling rod magnets. One overhauled magnet has been in service for a period of four months with no indication of deterioration
- 10. An analog computer is under construction for the calibration of rods
- 11. Studies of a liquid gamma-loop using iodo-benzene have been completed
- 12. A new instrument is being designed to enable the instrumentation console to be checked without removal from the system
- E. Publications and papers

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- 1. PRNC reports completed
 - a. Record Keeping H. Barceló
 - b. Hazards Summary Report for the L-77 Reactor H. Barceló and R. Brown
 - c. Operating Limits for the L-77 Reactor H. Barceló
 - d. Reactor Operating Procedures H. Barceló
 - e. Reactor Operators Training Course (Academic Phase) H. Barceló
- 2. PRNC reports in progress
 - a. Summary of the Hazards Report for the 1 Megawatt Reactor
 - b. Operating Limits for the 1 Megawatt Reactor
- 3. Papers presented at "Light Water Moderated Research Reactors" meeting*
 - a. Comparison of Rod Worth by Period and Analog Computer Methods
 - b. Elimination of Control Rod Vibration Caused by Water Flow
- * Presented by H. Barceló at Gatlinburg, Tennessee in June, 1962

- F. Engineering assistance to others
 - 1. BONUS reactor, Rincón
 - a. Calibration of ionization chambers for power reactor
 - b. Participation on BONUS Safety Committee
 - 2. Participation as guest member on the Oak Ridge Reactor Safety Committee during 1963 for the inspection of ORR, LITR and X-10 reactors (H.Barceló)
 - 3. Sugar mill operations in Puerto Rico Development of production control methods using radioisotopes
 - a. Control of crusher feed input for constant density instead of constant volume
 - b. Monitoring of feed to detect 'tramp iron'
 - c. Interstage crusher output monitoring to improve crusher efficiency

G. Future plans for increase in megawatt-hour output

The present operation of the 1 megawatt reactor is limited to one shift (9 hours) per day at a maximum power level of 1 megawatt. It is expected that in the near future the hours of operation and the power level of this reactor will be increased according to the following schedule:

- 1. Two-shift operation 1 megawatt power level
- 2. Two-shift operation 2 megawatt power level
- 3. Three-shift operation 2 megawatt power level
- 4. Three-shift operation 5 megawatt power level

OUTLINE OF MATERIAL TO BE PRESENTED TO AEC AD HOC COMMITTEE FOR PROGRAM REVIEW

October 15-17, 1964

NUCLEAR SCIENCE AND TECHNOLOGY

Dr. Owen H. Wheeler, Head

A. FUNCTION

Is teaching and research in Chemistry and Physics in support of M.S. programs offered by the Departments of Chemistry and Physics of the University of Puerto Rico in Mayaguez.

B. STAFF

Scientists: Chemistry - O. H. Wheeler (1/2 time), J. F. Facetti Physics - E. Ortiz (1/10 time), J. A. Gonzalo Chemical Technology - J. Muñoz (Special Projects) Research Assistants - Chemistry-2, Physics-1/2 Technical Assistants - Chemistry-2, Physics-1, Other-1 1/2 Graduate Students (PRNC) - Chemistry-2, Physics-2, (Other) Chemistry-5

Future plans call for the addition of another physicist and another research assistant in physics and an increase to $\underline{6}$ graduate student appointments.

Later developments envisage increases to 3 chemists and 3 physicists with a supporting group ratio of 2 assistants and 2 graduate students per scientist. C. TEACHING

The staff members of the Division teach courses in Chemistry and Physics directly related to Nuclear Science (radiochemistry, nuclear physics) and other courses as a service to the University (statistical mechanics, inorganic chemistry).

The Division also organizes the weekly general seminars and special seminars in solid state physics and radiochemistry. The orientation of groups of visitors, including local high school students, on the activities of the Center in Mayaguez, is also carried out by Division members.

D. RESEARCH

Is offered for graduate students in the U.P.R., M.S. programs in chemistry and physics, and currently most of the research in these programs is carried out through PRNC. In addition research for a Ph.D. is available through the ORINS program. B. Cruz (Physics Dept.) is candidate for Ph.D. (Physics) at Harvard.

Staff members and visiting scientists also carry out independent research.

E. RESEARCH FIELDS

Include radiochemistry, nuclear chemistry, hot-atom chemistry, synthetic organic chemistry, physical organic chemistry, radiation chemistry, chemical technology, solid state physics, neutron physics, radiation physics.

- 2 -

Members of the Division, including graduate students, also cooperate with the Neutron Diffraction and Resonance in Radiation Effects programs.

The addition of research in neutron inelastic scattering and other fields of neutron physics is expected in the future.

It is hoped to cooperate in these fields with newly established groups in Colombia, Venezuela and Mexico.

F. RESEARCH ACTIVITIES

Cover the study of (u_{i},α) reactions in heavy elements, range of fission products in aluminum, hot-atom chemistry of tin, antimony and rhenium compounds and of organic phosphorus compounds, mechanism of organic reactions using isotopic tracers, radiation induced brominations and hydroxylations of steroids, synthesis of steroids of radiological interest, use of ultrasonics in uranium extraction, chemical dosimetry, photomultiplier fatigue, radiation damage in ferroelectrics, radiation damage in alkali halide crystals and neutron diffraction study of magnetic structures.

G. FUBLICATIONS

During the last year 15 publications have appeared or have been accepted for publication in the following journals: Journal of Physics and Chemistry of Solids, Journal of Inorganic and Nuclear Chemistry, Nuclear Science and Engineering, Bulletin of American Physical Society, Radiochimica Acta, Transactions of the American Nuclear Society, Journal of Organic Chemistry, Tetrahedron, Canadian Journal of Chemistry, International Journal of Applied Radiation and Isotopes, Zeitschift fur Physik.

CUTLINE OF MATERIAL TO BE PRESENTED TO AEC AD HOC COMMITTEE FOR REVIEW OF PRNC PROGRAMS

October 15-16-17, 1964

NUCLEAR ENGINEERING

Dr. José Luis García de Quevedo, Head

- A. Master's Degree Programs in Mayaguez in which PRNC Cooperates Through Provision of Support, Laboratory and Research Facilities and/or Teachers of Advanced Subjects:
 - 1. Nuclear Engineering
 - 2. Health Physics
 - 3. Biology
 - 4. Chemistry
 - 5. Physics
 - 6. Agriculture
 - 7. Mathematics
- B. Master's Degree Program Requirements of ORINS Fellowship in Nuclear Science and Engineering (originally Nuclear Science and Technology)
- C. Original Organization of Nuclear Science and Technology Program and Division Within the University and Within PRNC:
 - 1. Use of sub-specialties under Nuclear Science and Technology to cover all fields of graduate studies.
 - 2. Lack of direct academic cognizance over degree programs.
- D. New Organizational Structure
 - 1. Direct cooperation with department with cognizance over general discipline involved, and with program orientation toward nuclear topics. (Biology, Chemistry, etc.)
 - 2. Creation of new degree program and new academic department by the University to cover truly new discipline created by advent of nuclear energy - Department of Nuclear Engineering.
 - 3. Creation of new PRNC division to meet engineering research and teaching requirements within PRNC - Division of Nuclear Engineering.

- E. Division of Nuclear Engineering
 - 1. Teaching responsibilities
 - a) cooperation with Department of Nuclear Engineering in supporting development of nuclear engineering degree.
 - b) cooperation with other departments of the College of Engineering in developing the nuclear aspects of their discipline.
 - (1) electrical engineering
 - (2) mechanical engineering
 - (3) chemical engineering
 - (4) civil engineering
 - c) development of specialized terminal training programs to serve requirements of AEC and Puerto Rico nuclear energy development in the power and engineering areas. PRWRA is now planning a reactor power plant per year for the next ten years, starting 1970.
 - (1) Reactor Operators Training
 - (2) Reactor Supervisors Training
 - (3) Nuclear Engineering Training
 - (In this case, degree may be granted simultaneously to academically qualified students through Nuclear Engineering Department of the College. PRNC issues certificates only.)
 - 2. Research responsibilities
 - a) thesis research for graduate students in Engineering.

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- b) engineering faculty research on educational and tutorial subjects.
- c) open research and development in Engineering. (PRWRA is negotiating for combined electricity desalination plant)

3. International

- a) development of exchange teaching and research proposals with Latin-American engineering schools and laboratories.
- b) development of residence training and research program at PRNC for Latin-American engineers.
- c) development of tutorial and training opportunities for engineers in Puerto Rico nuclear energy installations such as Bonus, PRWRA, etc.

- d) development of conference and institute activity in engineering pertaining to Nuclear Energy development. This will be based on:
 - (1) special interest, facilities and capability at PRNC.
 - (2) ditto for Puerto Rico
 - a. IAEA Conference on Medium Size Reactor Power Plants. February 1965.
 - b. Participation in UPADI Conference in Caracas, 1964, San Juan, 1962. PRNC participants: Soderstrom, Knight, Gomberg. (Also representing United States Atomic Energy Commission and Energy Joint Council).
 - c. Projected Institute on the Bonus Reactor Plant, for Latin America and United States participants.
 - (3) support and development of activity in new areas.
 - a. Projected A.S.E.E. C.D. Institute for Instructors on Shelter Requirements (joint project with CAAM).
- 4. Present Status of Engineering Teaching Activity in Division and Laboratory

a) students working toward M.S. - Current enrollment

(1) Bonus trainees - 10
(2) Local - 8
(3) Latin America
a. self or government - 1
b. IAEA - 1
TOTAL - 20
b) special trainees (Primarily Reactor Division)
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(1) Reactor operator training - Summer 1964

- a. Bonus 10
 b. Local 1
 c. PRNC 1
 TOTAL 12
 New group expected by January 1
- (2) Reactor Supervisor training (men are graduates of Nuclear Science and Technology program) Two from Colombia.

- c) special engineering research and study within Division and Laboratory
 - (1) Thermal emissivity of graphite
 - (2) Neutron monochromator based on total reflection
 - (3) Nuclear afterheat in case of water loss PRNC reactor
 - (4) Development of Reactor Lab teaching manual for issue in Spanish
 - (5) Rework of sections Hazards Summary Report
 - (6) Leaching of Uranium Ores with help of Ultrasonics
 - (7) Use of tracers in Chemical Engineering Processes
 - a. Study of mixing
 - b. Determination of Particle velocity in Rotary Kilus
 - c. Diffusion in Metallurgy
- d) personnel of Nuclear Engineering Division
 - Head: Dr. José Luis García de Quevedo*, Ph.D., also Chairman, Department of Nuclear Engineering.
 - Members: Dr. Donald S. Sasscer*, Ph.D., Iowa; Department of Mechanical Engineering.

Dr. Aviva E. Gileadi (full time starting October 15, 1964).

Dr. Peter Paraskevoudakis (on loan from Health Physics Division).

Dr. Phillip W. Osborne*; Department of Mechanical Engineering Metallurgy.

Prof. Kenneth Soderstrom*; Department of Mechanical Engineering.

Prof. Carlos V. Wheeler*; Department of Mechanical Engineering.

- F. Laboratory Assistance in Nuclear Engineering to Others.
 - 1. Bonus

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- a) Calibration of Ionization Chambers for Power Reactor
- b) Participation on Bonus Safety Committee: Gomberg, Barceló

^{*} CAAM Faculty - Part Time PRNC

- c) Construction of N.A.D. equipment (Other non-engineering services in health physics and operations area also supplied)
- 2. Sugar Mill Operations in Puerto Rico Development in Production Control using Radioisotopes.
 - a) Control of feed for constant weight input to crusher.
 - b) Foreign material detector for sugar mill feed line.

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OUTLINE OF MATERIAL TO BE PRESENTED AT

AEC REVIEW OF PRNC PROGRAMS

October 15-17, 1964

HEALTH PHYSICS

Presented by Dr. José A. Ferrer Monge, Ph. D. Head of Health Physics Division

- I. Health Physics Division
 - A. AEC Operating Requirements
 - B. Service and training objectives

II. Services

- A. Present services
 - 1. Puerto Rico Nuclear Center
 - a. Personnel and area monitoring
 - b. Consulting
 - c. Environmental surveillance
 - d. Medical service
 - e. Instrument calibration
 - f. Waste disposal
 - 2. BONUS reactor at Rincón
 - a. Film badge service
 - b. Environmental surveillance
 - c. Consulting
 - 3. Advising government agencies, private companies, and various departments of the University of Puerto Rico in Health Physics matters
- B. Future plans
 - 1. Immediate completion of a disaster center for determination of dosages received in criticality incidents
 - 2. Development and construction of instruments for calibration of research equipment and for highly accurate dosimetry.

III. Education

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- A. Current program
 - 1. Special features of PRNC and its relationship to Latin America
 - 2. Status of Health Physics in Latin America
 - Re-evaluation of the Atomic Energy Commission Fellowship program in Health Physics
 - 4. Degree program in Health Physics in cooperation with Biology Department
 - 5. Cooperation with departments of physics, chemistry, and nuclear engineering to develop aspects of Health Physics as related to these fields.
- B. Future programs in education for Latin America
 - 1. Exchange teaching
 - 2. Training in residence for Health Physicists from Latin America
 - 3. Development of Health Physics conferences and institutes in Latin American countries
- C. Staff
 - 1. Personnel for regular Health Physics program
 - 2. Specialized personnel for advanced electives

IV. Research

- A. Areas of concentration
 - 1. Interaction of radiation with matter
 - 2. Medical aspects of Health Physics
 - 3. Radiation protection and dosimetry
 - 4. Radiation ecology
 - 5. Radiobiology

B. Present programs

- 1. Ecological studies
- 2. Supervision of thesis research for graduate students in Health Physics

C. Future plans

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1. Cooperative programs with various laboratories in Latin American countries

- 3 -

2. Research programs for Health Physicists in residence from Latin America

OUTLINE OF MATERIAL TO BE PRESENTED TO AEC AD HOC COMMITTEE FOR PROGRAM REVIEW

October 15-17, 1964

Agricultural Bio-Sciences Division

I. Activities in Education and Training

A. Courses given by ABS Division personnel in FY-1964

1. In Mayaguez

a. Bi	iology	617		Advanced Genetics (Linden, 3 credits)
b. Bi	iology	618		Cytogenetics (Koo, 3 credits)
c. Bi	lology	645	-	Special Problems in Nuclear Biology
				(Linden, 3 credits)
d. B:	iology	670	-	Research Thesis (Koo, 4 credits)
e.B:	iology	690	-	Graduate Seminar (Linden, 1 credit)
f.B:	lology	691	-	Seminar in Radiobiology (staff, 1 credit)
2. In San	Juan			

a. Biology 372 -	Nuclear Techniques in Biological Research
	(Luse, Roig, 4 credits)
b. Biochemistry 311	Seminar in Biochemistry and Nutrition
	(Maretzki, et al, 2 credits)

B. Masters degree thesis programs with ABS staff participation (in Mayaguez only). (Linden, Koo)

1. Supported by PRNC

a. Full-time assistants who are taking one course per semester

- 5 in Biology
- 2 in Agriculture
- 2 in Chemistry

b. Part-time assistants who are working toward M.S. degree

2 in Biology

2. Thesis work at PRNC but no financial support given to student

College of Agriculture plans new program with 23 students, 10 of which wish to do thesis at PRNC.

- C. Special training, as a part of research activities
 - Project "Isotope Applications in Soils Research" given to IAEA Fellow (Luse)
 - Project "Radiation Effects on Forest Structure" -Ph.D. thesis by ORINS graduate Fellow (Luse, Odum)
 - 3. Other Oak Ridge Graduate Fellowships and Research Participants are potential trainees.
- II. Research Projects of ABS staff
 - A. Within PRNC
 - 1. Acerola Metabolism Andrew Maretzki
 - 2. Mechanism of Back Mutation Francis K.S. Koo
 - 3. Radiation and Chemical Effects in Plant Chromosomes -Francis K.S. Koo and Edith Robles de Irizarry
 - 4. Uptake of Sr and Ca by Sorghum vulgare and Pueraria hirsuta in Pure Stands and in Combination in Relation to the Relative Concentration of these Elements in the Soil - Flavio Padovani under joint supervision of Francis K.S. Koo and Frank G. Lowman
 - 5. Nuclear Volume and Radiosensitivity in Rain Forest Tree Species -Francis K.S. Koo and Edith Robles de Irizarry
 - 6. Biochemistry of Sugar Cane Robert A. Luse
 - 7. Element Cycling in the Tropical Rain Forest Robert A. Luse and Howard T. Odum
 - 8. Insect Control by Induced Sterility David Walker
 - 9. <u>Rearing, and Radiation Studies of Diatrea Saccharalis</u> -David Walker and Adela V. de Alemañy and Miguel Figueroa
 - 10. Trailing Indigo Project Jean García
 - 11. Service Irradiation with Co⁶⁰ José Cuevas Ruíz
 - 12. <u>Tropical Fruit Irradiation</u> Duane B. Linden and José Cuevas Ruíz.

B. In cooperation with other organizations

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1. U.P.R. Agricultural Experiment Station staff (Mayaguez and San Juan)

Azzam - Gamma Radiation in Plant Breeding Abrams de Leon - Gamma Radiation in Plant Breeding Pennock - Gamma Radiation in Plant Breeding Alexander - Isotope applications Roldan - Isotope applications

2. U.P.R. College of Agriculture staff (Mayaguez):

Gamma radiation and isotope techniques

3. U.P.R. College of Medicine staff:

Enzyme characterization

4. U.S. Army Tropical Research Medical Laboratory staff:

Autoradiography

C. Publications, as index of increasing productivity

1961 - Division established

- 1962 8
- 1963 13
- 1964 20 (including in press)

Participation of the Puerto Rico Nuclear Center in the Atomic Energy Commission "Atoms at Work" exhibit program in Latin America

Fausto J. Muñoz Ribadeneira, Director

The Atomic Energy Commission has assigned to the Puerto Rico Nuclear Center responsibility for conducting investigations in the physical and biological sciences as part of the new program of "Atoms at Work" exhibits in Latin America during the fiscal year 1965-1966. The program will be inaugurated in San Salvador, El Salvador, C. Am. on February 23, 1965.

As PRNC coordinator for the exhibits, the author of this report was invited by the AEC Division of Special Projects to visit El Salvador and Guatemala during the last part of June, 1964, as part of an advance team. This group visited officials of the Ministry of Agriculture of El Salvador and the University of San Salvador. Information concerning the special needs and interests of El Salvador was gained at this time and has been used as a basis for selecting research and lecture topics for the exhibit.

The program of research to be performed at El Salvador suggests the possibility of cooperation in the future between the University of El Salvador and the Puerto Rico Nuclear Center. A tentative follow-up program in which students of the University of San Salvador might carry on graduate study at the University of Puerto Rico has been outlined. Activities of the PRNC Scientist Lecturers and PRNC Coordinator at the AEC "Atoms At Work" exhibit in San Salvador, El Salvador, Central America.

1) General Introductory Lectures

Person in Charge: Fausto J. Muñoz Ribadeneira

Dates Title of Lectures February 11, 1965 "The Nuclear Sciences and the Liberal Frofessions" February 12, 1965 "Chemical Dosimetry of Gamma Radiation" February 18, 1965 "Uses of Tracers in Unit Operations of Chemical Engineering" February 19, 1965 "Gamma Radiation and Industrial Processes" 2) Lectures on Entomology Person in Charge: Dr. David W. Walker Dates Title of Lectures February 25, 1965 "Application of Radiation Effects on Entomological Studies" February 26, 1965 "Studies of Entomological Problems in Sugar Cane in Puerto Rico" 3) Lectures on Genetics and Food Conservation Problems Person in Charge: Dr. Duane B. Linden Dates Title of Lectures March 4, 1965 "Radiation Effect on Genetics" March 5, 1965 "Preservation of Tropical Fruits by Gamma Radiation at the PRNC" 4) Lectures on Radiochemistry Person in Charge: Dr. Juan F. Facetti Dates Title of Lectures March 11, 1965 "Activation Analysis" March 12, 1965 "Szilard-Chalmers Reactions"

5) Lecture on Neutron Dynamics

Person in Charge: Dr. Eddie Ortiz

Date

Title of Lecture

March 16, 1965 (afternoon) "Descriptive Experiments Using a Neutron Source"

6) Lectures on Applied Mathematics in Engineering Problems

Person in Charge: Dr. Eddie Ortiz

Dates

Title of Lectures

"Finite Difference Applications"

March 16, 1965 (morning) "Boundary Value Problems"

"Transform Calculus"

(afternoon) March 18, 1965

March 18, 1965 (afternoon)

March 17, 1965

March 19, 1965 (morning)

"Matrices and Tensors"

7) Lectures on Muclear Power Economics

Person in Charge: Dr. Modesto Iriarte (Power Authority of P. R.)

DatesTitle of LecturesMarch 19, 1965"Factors to be Considered in Economics
of Nuclear Power Plants"March 22, 1965"The BONUS Reactor and the Nuclear
Power Program in Puerto Rico"