

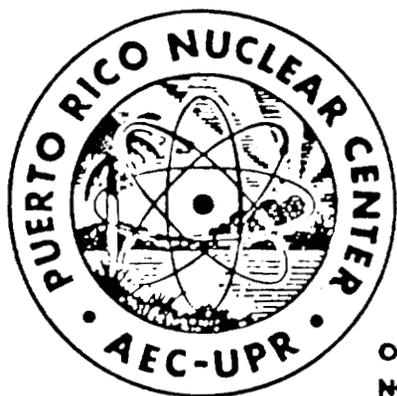
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# PUERTO RICO NUCLEAR CENTER

ANNUAL REPORT 1964



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PUERTO RICO NUCLEAR CENTER  
1964 ANNUAL REPORT

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## RADIOTHERAPY AND CANCER DIVISION

Víctor A. Marcial, M.D., Head

Training in all aspects of the applications of nuclear energy to cancer for physicians and allied personnel is offered. A research program designed to improve knowledge in the cancer and radiation fields is conducted to enhance the training program.

Dr. Arturo Valencia Serna from Colombia completed his second year of residency in the radiotherapy residency program, which is designed to qualify physicians as radiation therapists and is approved by the American Board of Radiology. Dr. Valencia is currently in his third year of residency at the Puerto Rico Nuclear Center.

Dr. Felipe N. de Jesús from Puerto Rico completed six months in the radiotherapy residency program during 1964. Dr. de Jesús is now in residence at University Hospital.

Dr. Manuel J. Caussi from Argentina completed a three-month radiotherapy training program in April, 1964. Dr. Caussi is the chief of radiotherapy services at Rawson Health Center Hospital in San Juan, Argentina. He is currently investigating the possibility of installing either a cobalt or cesium teletherapy unit and also installing a clinical radioisotopes laboratory at Rawson Hospital.

Mrs. Dominga Echevarría, a technical nurse at the Ponce District Hospital, completed in-service training in this division during 1964. Mrs. Echevarría is working with cancer patients at the Ponce District Hospital.

During 1964, fourth year medical students completed a one-month training course in radiotherapy designed to familiarize them with cancer and radiotherapeutic problems.

Angel Rodríguez Rodríguez	Hernán J. Cestero Aguilar
Leonardo Collazo López	Humberto J. Ortiz Suárez
Juan A. Castro Barnés	Ernesto Rivé Mora
Fermin C. Miranda Hernández	Neftalí Rodríguez Amadeo

The Radiotherapy and Cancer Residency Program at the Puerto Rico Nuclear Center has had seventeen participants since 1957. A list of the participants including the dates of participation, country of origin, and present position (if known) is presented:

PARTICIPANT AND COUNTRY OF ORIGIN	DATES OF PARTICIPATION	PRESENT POSITION
José M. Tomé, M.D. Spain (naturalized U.S. citizen August 28, 1960)	July 1, 1957- June 30, 1960	Chief Scientist, Radiotherapy and Cancer Division, PRNC
José T. Medina, M.D. Puerto Rico	July 1, 1958- June 30, 1959	Head, Radiology Depart- ment, Dr. I. González Martínez Oncologic Hos- pital, Río Piedras, Puerto Rico
Jeanne Ubiñas, M.D. Puerto Rico	July 15, 1957- August 14, 1961	Associate Scientist, Radiotherapy and Cancer Division, PRNC; Deputy Director, Cancer Contro Program, Puerto Rico Department of Health
Ernesto N. Amadey, M.D. Argentina	July 1, 1959- June 30, 1960	Director, Radiotherapy Department, J.R. Vidal Hospital, Corrientes, Argentina; Director of Radiology and Nuclear Medicine, Ministry of Education and Public Health, Corrientes, Argentina; Professor of Radiology, School of Medicine, Northwest National University, Argentina
Andrés Peralta, M.D. Dominican Republic	July 1, 1959 November 22, 1960	
Alberto Ceide, M.D. Puerto Rico	July, 1959- June, 1960	
Martina Castells, M.D. Spain (naturalized U.S. citizen)	July 1, 1959- June 30, 1963	Head, Radiotherapy Department, San Juan Municipal Hospital, Puerto Rico

PARTICIPANT AND COUNTRY OF ORIGIN	DATES OF PARTICIPATION	PRESENT POSITION
Juan Reusche, M.D. Peru	November 16, 1959 June 30, 1960	Head, Radiotherapy Department, "Instituto de Radiología Cayetano Heredia Loayza Hospital;" Head and Associate Professor, Radiotherapy Department, "Universidad Peruana de Ciencias Médicas Cayetano Heredia," Perú
Antonio Bosch, M.D. Mexico (Naturalized U.S. citizen, August 27, 1964)	July 1, 1960 June 30, 1962	Associate Scientist, Radiotherapy and Cancer Division, PRNC
Alvaro Rosas, M.D. Colombia	July 1, 1960 June 30, 1961	Radiotherapist, National Cancer Institute, Colombia
Efraín Navarro, M.D. Mexico	January 1, 1961 December 31, 1963	Cancer Institute, Mexico
Douglas Carrizo, M.D. Venezuela	July 1, 1961 June 30, 1962	Senior Resident, Radiotherapy Department, Jefferson Medical College Hospital, Philadelphia, Pa.
Mario Vuksanovic, M.D. Bolivia	July 1, 1961 July 30, 1962	Head and Assistant Professor, Radiotherapy Division, School of Medicine, University of Miami; Director of Radiotherapy, Jackson Memorial Hospital
Antonio Bullón, M.D. Peru	July 16, 1962 June 30, 1963	Radiologist, Peru

PARTICIPANT AND COUNTRY OF ORIGIN	DATES OF PARTICIPATION	PRESENT POSITION
Lucas Di Rienzo, M.D. Argentina	July 16, 1962 June 30, 1963	Director, Dr. Di Rienzo Radiological Clinic; Private Radiology School General Secretary of the Society of Nuclear Medicine and Roentgenology, Cordoba, Argentina
Arturo Valencia, M.D. Colombia	January 1, 1963 to present	In training at PRNC
Felipe de Jesús, M.D. Puerto Rico	July 1, 1964 to present	In training at PRNC

SHORT TERM RADIOTHERAPY TRAINING

PARTICIPANT AND COUNTRY OF ORIGIN	DATES OF PARTICIPATION	PRESENT POSITION
Oriel Alva, M.D. Argentina	March 29 - August 17, 1958	Radiotherapist, British Hospital; Radiotherapist Roffo Cancer Hospital, Buenos Aires, Argentina
Alvaro Ariza, M.D. Colombia	February 1 - April 30, 1959	Radiotherapist, National Cancer Institute, Colombia
Napoleón Matos, M.D. Peru	September 29 - October 4, 1958	Radiotherapist, Cancer Institute, Lima, Peru
Modesto Rivero, M.D. Venezuela	February 1 - May 31, 1961	Head, Radioisotopes Division, University Hospital; Radiotherapist, Razetti Cancer Institute, Caracas, Venezuela
Manuel J. Causa, M.D. Argentina	January 28 - April 30, 1964	Chief, Radiotherapy Services, Rawson Health Center Hospital, San Juan, Argentina

Research projects conducted in this division contribute to scientific background for the trainees and to stimulate them to carry on their own investigations. In general, research is oriented toward making contributions in the clinical aspects of radiation therapy and in the fundamentals of radiotherapy, radiobiology, and cancer as a medical science.

1. "Evaluation of Radiation Response by Means of Exfoliative Cytology in Cases with Cancer of the Cervix Treated with Radiation" This study, active since fiscal year 1961, is designed to help evaluate exfoliative cytology as a tool for determining prognosis in cases with carcinoma of the cervix treated with radiation. During 1964, an analysis of cases with a minimum of two years continued observation was made correlating the presence of tumor cells in the vaginal smear at one month, two months, four months, six months, twelve months, and at the end of radiation therapy with two-year, tumor-free survival. A total of two hundred and forty-four cases were analyzed and the following information obtained. Some cases may show recognizable tumor cells in the vaginal smear as long as one year after therapy even though the patient may be healed of her disease at the end of two years. If the vaginal smear is free from tumor cells twelve months after radiotherapy, the patient will be well at the end of two years in eighty percent of the cases. The presence of tumor cells in the vaginal smear at the end of radiotherapy and one month afterward has no relationship to prognosis. Patients who consistently show positive smears for tumor cells after therapy will either die or suffer from persistent disease by the end of two years. Making the distinction between tumor cells and normal vaginal epithelium displaying pronounced radiation effect is very difficult in some cases.
2. "Surgical Adjuvant Breast Project" - Investigators: Víctor A. Marcial, M.D., and Jeanne Ubiñas, M.D. This division is collaborating with the departments of surgery and pathology of the Dr. I. González Martínez Oncologic Hospital in contributing cases to a national project designed to improve prognosis in patients with breast cancer treated with radical mastectomy by additional therapy. Post-operative irradiation of the lymph node areas and systemic chemotherapy are being tested. A total of thirty cases have been contributed to date. Final analysis of results at the national level will not be made until a minimum of five years observation time has elapsed; however, the initial impression that chemotherapy improves the

prognosis has been changed with further information on the cases studied. It now appears that the group treated with chemotherapy as adjuvant therapy has the same prognosis as patients submitted to radical mastectomy alone.

3. "Incidence of Leukemia in Patients with Cervical Cancer Treated with Radiation" - Investigators: Víctor A. Marcial, M.D., and Antonio Bosch, M.D. This division is collaborating with the Gynecology Department of the Dr. I. González Martínez Oncologic Hospital and the Department of Pathology of the University of Puerto Rico College of Medicine in contributing cases to an international study designed to determine the risk of developing leukemia in patients who have been irradiated for cancer of the uterine cervix. A total of six hundred thirty-nine cases were contributed to this study, as of December 31, 1964. A revision of the international experience in this project in 1964 indicated that 33,000 person-years had been contributed and that two cases had developed leukemia. This number of leukemia cases corresponds to what would be expected from the normal population.
4. "Chromosome Changes in Patients Undergoing Radiation Therapy for Cancer" - Investigators: José Tomé, M.D., Paul Weinbren, M.D., and Lt. Col. Michael Dacquisto, M.D. This is a collaborative study designed to determine the chromosome abnormalities induced by irradiation of patients for cancer. A total of fifty-eight cases have been included during 1964. The number, pattern, and reversibility of the chromosome changes are being analyzed and related to cancer location, irradiation quality, and dose. Blood samples were taken before, during, and after irradiation. Dicentric, ring, and grossly abnormal chromosomes have been observed.
5. "Fractionation of Weekly Doses in Cancer Patients Submitted to Irradiation" - Investigators: Radiotherapy staff. This is a clinical study designed to determine the optimal fractionation of weekly tumor doses in patients submitted to irradiation for cancer. Half of the patients receive a weekly tumor dose divided into three applications and the other half received their weekly tumor dose divided into five applications. Tumor effect, survival, and normal tissue reactions are being observed. Seven hundred and eighty-one patients have been incorporated into this study.

6. "Controlled Study of the Split-Dose Technique in Radiotherapy of Cancer" - Investigators: Radiotherapy staff. The purpose of this study is to compare the results obtained by the usual uninterrupted radiation treatment (6000 roentgens in six weeks with a similar dose given in two separate two-week periods with a rest interval of two to three weeks between (3000 roentgens in two weeks plus two to three weeks rest plus 3000 roentgens in two weeks). Tumors measuring five centimeters or more, excluding pelvis and esophagus, are included. Half the cases receive the usual uninterrupted treatment and half receive the divided treatment. Results will be evaluated in terms of tumor regression, abnormal tissue reactions, and curability. Seventy patients were included in this study during 1964.
7. "Carcinoma of the Cervix Uteri and Pregnancy" - Investigator: Antonio Bosch, M.D. This retrospective study is designed to determine the incidence of carcinoma of the cervix associated with pregnancy and the optimal management of this disease. In a group of 2,554 cases of uterine cancer treated at the Dr. I. González Martínez Oncologic Hospital, it was found that sixty-two patients had tumors associated with pregnancy. An optimal way of handling this complication was determined and the results will be reported at the annual meeting of the American Radium Society in April, 1965.
8. "Carcinoma of the Cervix Uteri in Sterilized Women" - Investigators: Antonio Bosch, M.D., and Zenaida Frías. The aim of this study is to analyze possible relationship of carcinoma of the cervix uteri and previous interruption of the reproductive capacity by surgical means. It has been observed that in patients under fifty years of age with carcinoma of the cervix uteri, 25.4 percent have had previous surgical sterilization. The true significance of this finding is being evaluated and a comparison is being made of its nature in a cancer population versus a normal population at the Pelvic Cancer Diagnostic Clinic of the Puerto Rico Department of Health.
9. "Adenocarcinoma of the Cervix Uteri" - Investigator: Jeanne Ubiñas, M.D. This retrospective clinical study is designed to determine if adenocarcinoma of the cervix uteri is more radioresistant than epidermoid carcinoma of this structure. A total of seventy-two patients were analyzed and it was found that the five years survival in this group of patients is no different from that encountered in epidermoid carcinoma.

10. "Lymphangiography in Cancer Patients" - Investigator: Felipe N. de Jesús, M.D. In 1964, lymphangiography was introduced as a method for helping the radiotherapist localize malignant lesions prior to irradiation. The objectives of this procedure are to help in the diagnosis and localization of lymphomas in the pelvic and retroperitoneal spaces, to determine lymph node metastases in carcinoma of the cervix, and to localize post-irradiation persistence or recurrence of carcinoma of the cervix. Nine lymphangiographic studies have been performed.
11. "Cancer of the Nasopharynx" - Investigator: José Tomé, M.D. This is a retrospective clinical study in which forty patients with carcinoma of the nasopharynx were analyzed regarding correlation of clinical features with survival obtained using various treatment techniques.
12. "Cancer of the Breast and the Role of Radiation Therapy In Its Management" - Investigators: Víctor A. Marcial, M.D., and Graciela Serna, M.D. This retrospective clinical study is designed to determine the value of radiation therapy in the management of breast cancer patients. Patients with a minimum observation period of five years from the radiotherapy department of the Dr. I. González Martínez Oncologic Hospital are being analyzed. The results of this study will be presented at a symposium organized by the Puerto Rican Chapter of the American College of Surgeons on February 26, 1965.
13. "Study of the Optimal Tumor Dose in Radiation Therapy of Cancer of the Esophagus" - Investigators: Radiotherapy staff. This clinical study is designed to determine the optimal radiation tumor dose in the treatment of cancer of the esophagus. Half of the cases treated receive cobalt teletherapy doses of 5000 roentgens in four weeks and the other half received doses of 6000 roentgens in six weeks. Disappearance of dysphagia and twelve months survival are compared in each group. Seventy seven patients have been included in this study to date. It now appears that 5000 roentgens in four weeks gives better results than 6000 roentgens in six weeks. Additional observation is required before definite conclusions can be made.
14. "Fat Absorption Study on Patients Irradiated in the Abdomen" Investigators: Sergio Irizarry, M.D., and Víctor Marcial, M.D. This study is conducted in collaboration with the Clinical

Radioisotope Applications Division and is designed to determine the immediate and late effects of abdominal irradiation on the fat absorption of the intestine. Of an original group of twenty cancer of the cervix cases, fourteen showed changes in the intestinal absorption before treatment compared to the control group (patients with head and neck cancer) where three out of nineteen developed some diminution in the blood levels of tagged fat. Additional studies performed one year and one-and-a-half years later showed no difference in the fat intestinal absorption between the abdominal irradiated patients and the controls.

15. "Bio-Chemical Changes in the Blood of Patients Receiving Radiotherapy for Cancer - Serum Lipids, Serum Sodium and Potassium, and Urea" - Investigators: Barbara Weinbren, B.M., and Víctor A. Marcial, M.D. This project is designed to determine the bio-chemical changes in the blood of patients receiving radiotherapy for cancer. Initially, total protein, uric acid, alkaline phosphatase, acid phosphatase, calcium, phosphorous, albumin, and globulins were studied in a group of over 300 patients submitted to irradiation therapy for cancer. Data obtained were compared with values reported from normal Puerto Ricans aged twenty to sixty. Noteworthy findings: Total protein values in cancer patients in the study were found below the mean levels for normal Puerto Ricans; no significant changes were noted in the levels of uric acid or other constituents; notable lowering of alkaline phosphatase was observed during and after irradiation in cases with cervical cancer.

This part of the study is being conducted in collaboration with personnel from the Clinical Radioisotope Applications Division. Twenty cases with the diagnosis of cancer of the cervix and twenty cases with cancer of other regions are being studied. Blood samples are taken before, during, and after irradiation. Lipo proteins, total lipids, total proteins, urea, and serum sodium and potassium levels have been determined. Cholesterol determinations will be made in the same group.



Lecture on radiation therapy technique

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## CLINICAL RADIOISOTOPE APPLICATIONS DIVISION

Sergio Irizarry, M.D., Head

Various training courses for physicians and ancillary medical personnel were offered in the diagnostic and therapeutic uses of radioisotopes in humans. Courses range from general orientation to short term basic and advanced training in clinical radioisotope techniques or long term courses in clinical research.

These specialists received training in the clinical uses of radioisotopes from December 2, 1963 to January 24, 1964.

Dr. Alvaro Ortiz Ortiz, Ad Honorem Professor of Internal Medicine, is currently engaged in starting a clinical radioisotope laboratory at the San Juan de Dios Hospital in San José, Costa Rica.

Dr. Mario Iturralde is the Head of the Department of Endocrinology of the Central Hospital in La Paz, Bolivia. He is also working with the "Comisión Boliviana de Energía Nuclear" (Atomic Energy Commission of Bolivia).

Dr. Manuel J. Caussi is the chief of radiotherapy services at the Rawson Health Center Hospital in San Juan, Argentina.

Miss Marta García y Angulo had been a radioisotope technician in the National Cancer Research Laboratory in Bogotá, Colombia, prior to coming to Puerto Rico Nuclear Center for additional training. At present Miss García y Angulo is not working with radioisotopes.

From January 7, 1964 to February 14, 1964, Dr. Antonio Quijano Blanca, director of the Institute for Bio-Medical Research of Veracruzana University in Mexico, received training.

From December 7, 1964 to January 29, 1965, the following people received training:

- Dr. Norman Maldonado - Medical Resident at University Hospital
- Dr. Evelyn Cintrón - Physician at the Ponce District Hospital
- Dr. Graciela Serna - Visiting Radiotherapist from Mexico in the PRNC Radiotherapy and Cancer Division



Blood being prepared for radioactivity analysis

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The training consists of lectures, demonstrations, informal presentations, laboratory exercises, and discussion periods. Emphasis is placed on mastering techniques, their indications and uses, correct interpretation, limitations, and correlation with clinical problems. In the eight-week course, a total of eighty laboratory exercises representing a wide variety of techniques are employed. Table 2 shows the breakdown of training procedures by units of study. Table 3 presents information on the participants in the clinical applications course from 1958 through 1963.

TABLE 2

Clinical Applications of Radioisotopes  
Two-Month Training Program

Units of Study	Average Number Procedures per Trainee
Thyroid function	35
Routine uptake measurements	15
Assay radioactive blood thyroid	
Hormone levels	15
Modified tests of thyroid function	5
Dynamic functions of the hepatic, renal and vascular systems	20
Hematologic applications of radioisotopes	5
Tumor localization studies	10
Gastro-intestinal absorption	5
Electrolyte and fluid balance	2
Therapeutic procedures	3
	Total <u>80</u>

A substantially heavy diagnostic patient load with a variety of clinical material is necessary for the training program. Table 4 shows the volume of diagnostic procedures performed yearly since the clinical radioisotopes laboratory started functioning in 1957.

Clinical research projects are carried out by the medical staff to obtain information that may be incorporated into the training program. One result of this research is that it is now possible to teach the trainees what to expect when evaluating normal

TABLE 3  
Clinical Applications  
(Participants 1958-1963)

Name	Country of Origin	Dates of Training	Present Occupation (if known)
Oriel Alva, M.D.	Argentina	Mar. 3-29/58 (1 month)	Radiotherapist, British Hospital, Buenos Aires, Argentina
Carlos Stevenson, M.D.	Chile	June 1 - Aug. 1/58 (2 months)	Assistant Professor of Internal Medicine, Deputy Director, clinical radioisotopes training program for Latin American physicians - Salvador Hospital Santiago de Chile
Ulises Gelós, M.D.	Uruguay	Aug., 1958 (1 month)	
Zenón E. González, M.D.	México	Oct., 1958 (1 month)	
G. Cassah Hasfura, M.D.	México	Nov., 1958 (2 months)	
Mario Spinetti, M.D.	Venezuela	Dec., 1958 (1 month)	
Manfred Hartung, M.D.	Venezuela	Dec., 1958 (1 month)	

Peter Eberstadt, M.D.	México	Dec. 3, 1957 Feb. 7, 1959 (2 months)	Deputy Director Radiological Protection Program, National Nuclear Energy Commission, México - Director Clinical Radioisotope - Physiology Laboratory - Public Health and Welfare Hospital, México City, Mexico
A.R. Rodríguez Rosado, M.D.	Puerto Rico	1959 (2 1/2 months)	Head, Clinical Radioisotope Laboratory, San Juan City Hospital and Pavia Clinic
Aldo E. Lanaro, M.D.	Argentina	Aug., 3- Oct. 9, 1959 (2 1/2 months)	Associate Scientist-Clinical Applications Division, Puerto Rico Nuclear Center
César Arango Jaramillo, M.D.	Colombia	June 13 - Aug. 31, 1960 (2 1/2 months)	Chief, Radiotherapy Services, Hospital Universitario de Caldas - Manizales, Colombia
Guillermo Castillo, M.D.	Venezuela	June 13 - Aug. 31, 1960 (2 1/2 months)	Head, Radioisotopes Section, Hospital Vargas and Instituto de Diagnostico, Caracas, Venezuela
Italo Zanzi Cordova, M.D.	Chile	June 15 - Aug. 31, 1960 (2 1/2 months)	Head, Radioisotopes Laboratory, Hospital J.J. Aguirre, Universidad de Chile

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Héctor M. Forcher, M.D.	Argentina	Dec. 6, 1961 Jan. 29, 1962 (2 months)	President, Argentine Society of Nuclear Medicine, Head, Radioisotopes Department, Endocrinology and Metabolism Clinic - Hospital Escuela General San Martín - Buenos Aires, Argentina
Jorge R. López Verde, M.D.	Argentina	Dec. 6, 1961 Jan. 29, 1962 (2 months)	Chief, endocrinology section Hospital Escuela General San Martín-Centro de Medicina Nuclear - Buenos Aires, Argentina - Secretary, Argentine Society of Nuclear Medicine
Miss Sevil Modeste Valero	Dominican Republic	Oct. 1, 1962 Nov. 23, 1962	
Miss Mayra A. Sánchez Cabral	Dominican Republic	Oct. 1, 1962 Nov. 23, 1962	Department of General Studies University of Santo Domingo
Rafael González Massenet, M.D.	Dominican Republic	Oct. 1, 1962 Nov. 23, 1962	
Eduardo Mirabal Font, M.D.	Puerto Rico	April 1-30, 1963	
Martina Castells López, M.D.	Spain (naturalized U.S. citizen)	April 1-30, 1963	Head, Radiotherapy Department, San Juan Municipal Hospital, Puerto Rico

Marcelino A. Rispoli, M.D.	Argentina	Aug. 1 - Sept. 24, 1960 (2 months)	Cardiologist, Alvear Hospital, Buenos Aires, Argentina
Modesto Rívero González, M.D.	Venezuela	Dec., 1960 Jan., 1961 (2 months)	Head, Radioisotopes Division, University Hospital Caracas; Radiotherapist, Razetti Cancer Institute. Caracas, Venezuela
Rodolfo Arroyave, M.D.	Guatemala	Dec., 1960 Jan., 1961 (2 months)	
Mrs. Lia Kohn de Merenfeld	Venezuela	June 27 Aug. 5, 1961 (1 1/2 months)	Physicist, Vargas Hospital Caracas, Venezuela
Rodolfo Aguilera Cuenca, M.D.	México	Aug. 7 - Oct. 9, 1961 (2 months)	Chief, Radioisotopes Depart- ment Clinica Ruiz, Puebla, México
Mario Vuksanovic, M.D.	Bolivia	Dec. 6-28, 1961 (1 month)	Head and Assistant Professor, Radiotherapy Division, Depart- ment of Radiology, School of Medicine, University of Miami Director of Radiotherapy Jackson Memorial Hospital

Efraín Navarro López, M.D.	México	June 3-29, 1963	Cancer Institute, Mexico
Miss Nydia E. Muriel	Puerto Rico	June 10 - Aug. 2, 1963	
Miss Norma Cándara	Puerto Rico	July 29 - Aug. 28, 1963	Research Technician, Clinical Applications Division, Puerto Rico Nuclear Center
Jeannie Ubiñas, M.D.	Puerto Rico	Oct. 15 - Nov. 26, 1963	Associate Scientist - Radio- therapy and Cancer Division, Puerto Rico Nuclear Center; Deputy Director, Cancer Control Program, Puerto Rico Department of Health

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TABLE 4

Diagnostic Procedures Carried Out At  
 Puerto Rico Nuclear Center Clinical Radioisotopes Laboratory  
 Fiscal Year 1958 Through One-Half Fiscal Year 1965

	:1957-58:	1958-59:	1959-60:	1960-61:	1961-62:	1962-63:	1963-64:	1964-65**
THYROID FUNCTION	: 405	: 592	: 1337	: 1816	: 2086	: 1931	: 2349	: 1462
LIVER	: 4	: 5	: 30	: 40	: 54	: 68	: 75	: 58
HEART	: 29	: 79	: 13	: 110	: 70	: 80	: 65	: 7
KIDNEY	: -	: -	: 32	: 252	: 223	: 172	: 206	: 100
GASTROINTESTINAL	: -	: 121	: 125	: 135	: 227	: 35	: 27	: 9
BLOOD	: -	: 7	: 50	: 16	: 34	: 25	: 11	: 61
TUMOR LOCALIZATION	: -	: -	: -	: -	: 12	: 118	: 45	: 21
TRAINING PROCEDURES	: *	: *	: *	: 264	: 309	: 690	: 630	: 182
MISCELLANEOUS	: -	: -	: 36	: 47	: 77	: 7	: 4	: -
TOTALS	438	804	1623	2680	3092	3126	3412	1900

\* No statistical data

\*\*Data for first 6 months only

TABLE 5

Comparison Between Units of Study in Training Program  
With Current Research Projects

Units of Study Clinical Applications.	Project
1. Thyroid Function	<ul style="list-style-type: none"> <li>- Clinical and laboratory evaluation of thyroid disorders.</li> <li>- Evaluation of in vitro tests of thyroid function for use as diagnostic procedures.</li> <li>- Study of the effect of anticonceptive therapy on the 24-hour I-131 thyroid uptake.</li> </ul>
2. Cardiovascular	<ul style="list-style-type: none"> <li>- Cardiovascular studies in diabetics.</li> </ul>
3. Kidney function	<ul style="list-style-type: none"> <li>- Renogram followup study in cancer of the cervix.</li> <li>- Combined clinical, renographic and scintigraphic studies in kidney diseases.</li> <li>- Renogram studies in diabetics.</li> </ul>
4. Liver function	<ul style="list-style-type: none"> <li>- I-131 Rose Bengal localization and dynamic studies - scintigraphy, hepatogram.</li> </ul>
5. Gastro-intestinal function	<ul style="list-style-type: none"> <li>- Effect of radiotherapy on intestinal absorption of iodine 131 labelled fats and vitamin A in humans.</li> <li>Thyroid gland as an indicator of intestinal absorption of I-131 labelled fats.</li> </ul>
6. Hematology	

and abnormal functions of various organs or systems of patients in Puerto Rico in comparison with similar evaluations carried out in patients in other parts of the world. Examples of this are:

- a. Average twenty-four hour radioiodine uptake in euthyroid individuals is generally much lower in Puerto Rico than in the continental United States (twenty-five percent versus thirty percent) and higher in Puerto Rico than in Jamaica, by about twelve percent.
- b. Patients treated with I-131 for thyroid disorders in Puerto Rico respond with much smaller doses than patients with similar disorders treated elsewhere.
- c. Short term or long term use of anticonceptive substances have no measurable effect on the twenty-four hour radioiodine uptake by the thyroid gland.
- d. Iodine-131 oleic acid and triolein I-131 blood absorption levels may be determined reliably by using the thyroid gland I-131 trapping function as an indicator. This makes the withdrawal of serial blood samples unnecessary and avoids the pitfall of a false positive test in patients with a delayed absorption, which occurs in about twenty percent of the normal patients.
- e. Radiation injury to the intestinal wall during radiation therapy may induce a state of temporary malabsorption from which the patient appears to recover soon after cessation of therapy.

Trainees are encouraged to design and carry out their own research projects. Table 5 shows the relationship between the units of study in the training program with the current research projects.

7. Tumor localization - Instrumentation improvement-combined x-ray photoscanning unit for gamma-photo-radiography. Organ and tumor localization brain scanning, others.
8. Electrolyte balance and fluid compartments - Electrolyte and fluid disorders in diarrhea. Electrolyte and fluid balance in women under anticonceptive therapy.
9. Therapeutic procedures - Review of patients treated with I-131.

A brief description of the current research projects is included.

1. "Clinical Evaluation of the Twenty-Four Hour I-131 Uptake by the Thyroid Gland in Puerto Rican Patients." - Investigator: Sergio Irizarry, M.D. This study to evaluate the range of euthyroid, hyperthyroid and hypothyroid function in Puerto Rican patients was completed on 263 individuals with unequivocal clinical pictures of thyroid dysfunction or eufunction. Results were:

	Number	24-Hour I-131 Uptake	
		Average + Standard Deviation	Range
Euthyroids	93	25.3 + 8.4	13.2 -67
Hyperthyroids	84	69.1 + 13.9	31.6 -97
Hypothyroids	24	6.6 + 5.7	1.1 -20.7
Non-toxic nodular goiter	62	27.3 + 12.9	7.7 -81.9

Diagnostic precision is estimated for the twenty-four hour I-131 uptake test on the basis of this analysis to be in the neighborhood of ninety-five percent confidence for the hyperthyroid state, eighty-seven percent for euthyroid function and seventy percent for hypothyroidism.

2. "Scintigraphic and Histopathologic Study of Thyroid Nodules"  
Investigators: Sergio Irizarry, M.D., and Aldo Lanaro, M.D.

A partial report based on sixty-four patients for whom it was possible to correlate scintigraphic isotopic images of thyroid nodules and the histopathologic findings at surgery was presented at the First Argentinian Symposium of Nuclear Medicine held at Mendoza on November 19-21, 1964, by Dr. Aldo E. Lanaro from this division.

The thyroid nodules were classified by their isotopic images as "cold" or devoid of any activity, "hot" or hyperactive or as "warm" or intermediate in activity. They were also classified by histopathologic findings as being malignant, benign, Hashimoto's, cystic, hemorrhagic, adenomatous, of non-thyroid origin and so forth.



Radiochemical apparatus being prepared for  
tracer analysis

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Based on the combined histopathologic and isotopic classification, the following correlation was found:

<u>Number</u>	<u>Scan Characterization</u>	<u>Histopathology</u>	<u>Percentage</u>
31	Cold nodules	Malignant (15)	49
		Benign (12)	39
		Hashimoto (1)	
		Non-thyroid (3)	
21	Warm nodules	Malignant (7)	33
		Benign (13)	62
		Hashimoto (1)	
4	Hot nodules	Benign (3)	
		Hashimoto (1)	

Comment: This study will continue since more information of this kind is needed in Puerto Rico. The significance of the work immediately becomes apparent by demonstrating the relatively high frequency of malignant tumors in the group of so called "cold and warm" nodules, twenty-two nodules out of a group of fifty-two lesions turned out to be malignant, an incidence rate of approximately forty-two percent. This incidence is much higher than the average incidence reported in other places.

### 3. Clinical and Radioisotope Evaluation of the Cardiovascular and Renal States in Diabetics.

A partial report dealing with the evaluation of normal and abnormal function of the kidneys in diabetics was completed on sixty-three patients and presented by Dr. Aldo E. Lanaro before the First International Congress of Biology and Nuclear Medicine held at Sao Paulo, Brazil, from September 21 to 25, 1964.

The renogram was useful in detecting renal abnormalities in about ten percent of the sixty-three patients who showed no clinical or laboratory evidence of renal disease. However, the opposite also occurred in which seven percent of the patients with manifest renal disease failed to show abnormal renographic tracings. All abnormal tracings were confirmed by repeating the procedure under x-ray localization.

4. Clinical Evaluation of Twenty-Four and Forty-Eight Hour I-131 Thyroid Uptake With Concurrent Assay of Labelled Blood Hormone Levels.

The uptake at twenty-four and forty-eight hours is being studied in relation to simultaneous determination of the protein-bound conversion ratios and protein-bound plasma levels of labelled thyroid hormone at twenty-four and forty-eight hours. The radioisotope values will then be correlated with the clinical data in an attempt to define the boundaries of normal and abnormal function of these parameters in Puerto Rican patients. Two hundred and five patients have entered this project to date.

5. The Renogram and Other Tests of Renal Function.

The variations of normal or abnormal pattern in renographic studies would be better understood if other tests of renal function are run as a control group. To gain more knowledge about the renogram and its variations, a group of patients with known renal disease and healthy controls are being studied serially with simultaneous determinations of blood creatinine levels, creatinine or phenolsulphonphthalein clearance and urinalysis. The renographic alterations will be correlated with the other parameters. Kidney localization is done with the help of an upright film of the abdomen. Twenty-five patients have entered the study to date.

6. Fat Absorption Studies on Patients Irradiated in the Abdomen.

Observations of patients irradiated in the abdomen and their external controls (patients with head and neck carcinoma) for the possibility of developing malabsorptive defects under long term observations showed no significant trend in that direction. The original group with cancer of the cervix was twenty patients, fourteen of which apparently developed malabsorption of fat during the administration of radiotherapy in the abdomen. The control group being irradiated in the neck showed three out of nineteen patients who developed low blood levels of tagged fat.

During later examinations at one year and one and a half years after irradiation, the control group showed one patient out of thirteen with low fat blood levels, and none out of a group of seven.

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The experimental group irradiated in the abdomen showed one patient out of a group of fifteen who presented low fat blood levels one year after treatment, and one out of a group of eleven after one and a half years of post-therapy.

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This clearly indicates that the frequency of low fat blood levels is of the same order of magnitude for the controls and experimental group at one year and one and a half years post-therapy follow-up examinations.

About a hundred patients irradiated in the abdomen will be followed for a longer time to clarify the effect of radiation as used in current practice on the intestinal function over several years. Information on this point is not yet available.

7. "Fat Absorption Studies: The Use of Thyroid Trapping of Iodide as an Indicator for Absorption of I-131 Labelled Fat"

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I-131 labelled fats - triolein or free oleic acid - have been useful tools for examination of gastrointestinal digestion and absorption in patients suspected of having pancreatic steatorrhea or the malabsorption syndrome. Although blood absorption curves have been used extensively, in practice they may be difficult to follow on all patients since a substantial group of patients with good intestinal absorption may absorb rather late, and be misrepresented as malabsorbers if the blood curve is not followed long enough.

3  
Results: A group of twenty-one healthy Puerto Rico Nuclear Center employees were investigated. Thyroid gland uptake of I-131 at twenty-four hours was determined on all subjects. The next morning, after noting residual activity in the thyroid gland, a dose of I-131 labelled fat was administered. Blood samples were drawn three and five hours later for assay and a thyroid uptake of the I-131 set free from fat was determined twenty-four hours later. The assumption was made for practical purposes that the peak of iodine trapping occurs at about twenty-four hours and that the day-to-day variation is not great, in this laboratory, about  $\pm 4$  units of uptake.

-The 24-hour radioiodine uptake was 21 percent  $\pm 1.6$ .

-The 24-hour radioiodine (set free from fat) uptake was  $13.7 \pm 3.9$ .

-The ratio of I-131 from fat uptake to predetermined I-131 thyroid uptake is 66.4 percent  $\pm 17.9$ .

-Fat absorption - blood curve - percentage of dose per blood volume 13.4 percent  $\pm$  6.7.

Application to patients: A group of seventeen patients have been examined by this technique and results correlated with blood levels at five hours. Four patients out of seventeen showed low blood levels at five hours, but all of them showed normal thyroid iodide levels from the I-131 set free from the absorbed labelled fat.

The technique can distinguish the group of late absorbers from the group of early absorbers if blood samples are collected. More patients will be examined and special application of this technique should be helpful in malnourished children and adults with various gastrointestinal disorders of digestion and absorption here in the tropics.

#### 8. Tumor Localization

The X-ray photoscanning unit has been completed and is now operational. Additional modifications of the scaler analyzer are contemplated by introducing a system of differential counting techniques to enhance isotopic images. At present, good radiographic gamma photoscans in one film are being obtained by double exposure. The technique is being improved for immediate application to resolution of brain tumors and other organs.

Liver tumor localization: Thirteen patients with biopsy or surgically documented liver disease were correlated with I-131 Rose Bengal liver scans. Diagnosis was positive for carcinoma in nine patients; the scan was successful in detecting the presence of tumors in seven; the two that did not show up in the scan were beyond the power of resolution of the instrument because they were single metastatic tumors, less than two centimeters in diameter. The other four patients had non-neoplastic disease of the liver; three had jaundice due, in each instance, to a different etiology such as gallstones, hemolysis or cirrhosis, but it is interesting to note that the defect seen was quite compatible in appearance with the presence of a destructive lesion. This is important because the defect in jaundice may falsely masquerade as a tumor or space occupying lesion. The fourth patient with a fatty liver showed a diffusely abnormal scan.

Many more liver scans have been performed in this division, but since most of them have not undergone surgery or a liver biopsy, the correlation has remained clinical. Depending on the degree of suspicion of the referring physician or the source of hospital population, the yield of abnormal scans with isotopic images compatible with tumors varies enormously: for example, in a group of twenty patients from the I. Gonzalez Martinez Oncologic Hospital referred for scans the yield was seven with abnormal scans, whereas a group from the University Hospital, which specializes in patients with non-neoplastic liver disease, the yield of abnormal scans compatible with tumor was one out of thirteen.

Brain scanning: Brain scanning for tumor localization is being offered on a consultation basis to neurologists and neurosurgeons who need this type of diagnostic procedure in the island. Since there is no other facility performing this type of work, patients are scheduled on a merit basis of urgency at the time of consultation requests. Response of neurosurgeons to this type of procedure is good at present and it is contemplated that with their cooperation in referring patients for examination we may obtain a large volume of clinical material from which to derive useful information in this needed area of tumor localization. So far, we have been able to study twelve patients, and we anticipate studying two patients each week, so that in a year we will be able to study about one hundred patients.

9. Renogram: Post Therapy Studies of Urinary Flow Alterations in Patients with Cancer of the Cervix.

Thirty-eight patients have entered the study, and of these, twenty-two have been followed consistently some from several months to several years. A summary of changes observed:

No change	
Normals	10
Abnormals	5
Change	
Normal to abnormal	3
Abnormal to normal	3
Abnormal to normal to abnormal	1
	<u>22</u>

The purpose of this study is to relate changes in renogram with clinical progression or regression of the disease after the initial attempt at its control following a full course of radiotherapy. More patients are needed before useful conclusions can be obtained.

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## MEDICAL SCIENCES AND RADIOBIOLOGY DIVISION

Maurice Paul Weinbren, M. D., Head

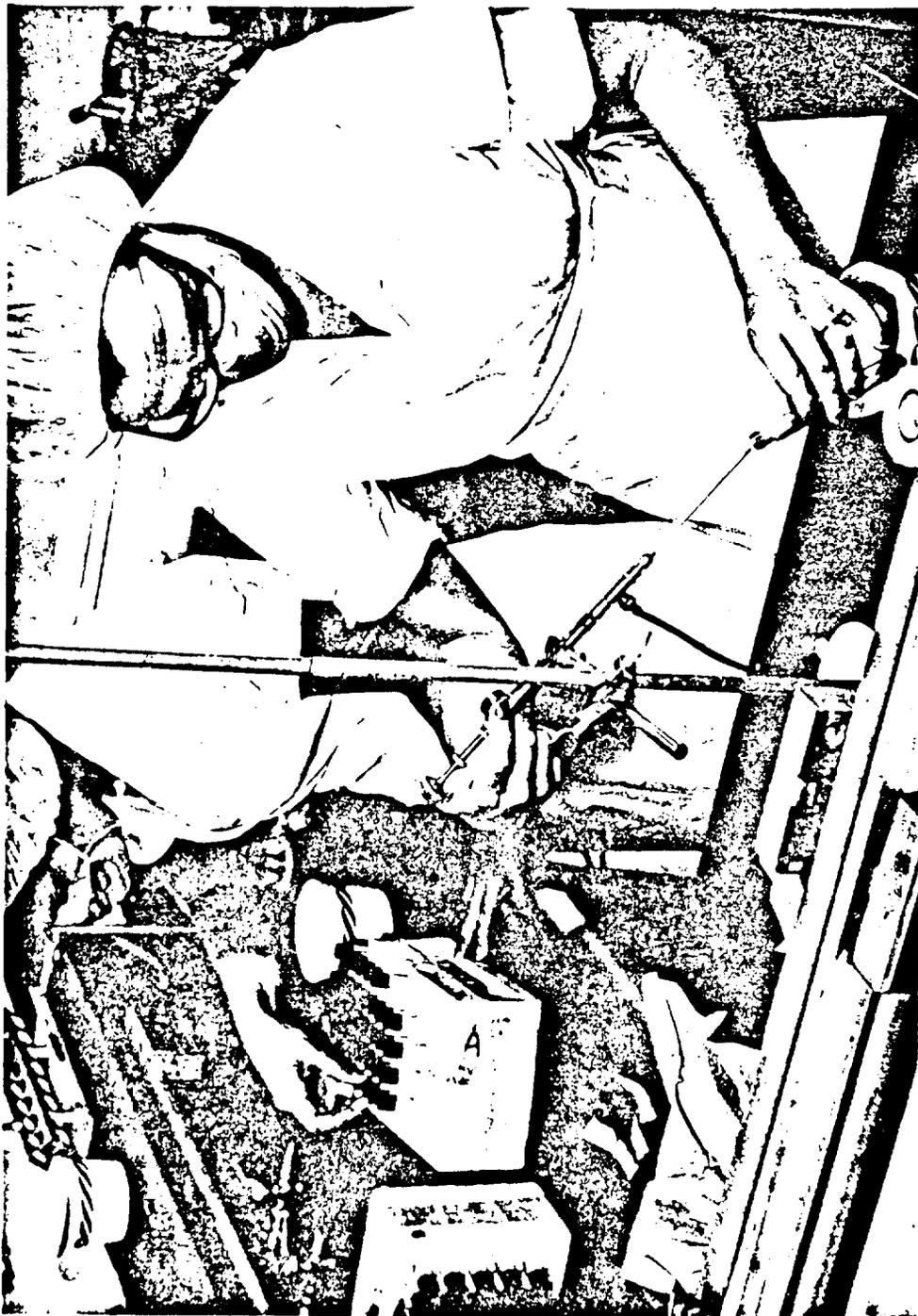
Tissue culture facilities and a small animal laboratory are operated for several programs. A training and research program in radiobiology at the cellular and sub-cellular level with emphasis on medical applications is carried out. Utilization of nuclear energy in developing new knowledge of tropical diseases of man is being explored.

The training activities of this division have been directed principally toward laboratory technicians who needed to learn the highly specialized techniques used in tissue culture and virology. A short course in radiobiology was offered for twelve students from the Radiotherapy and Cancer Division.

The principal research activities are:

1. "Study of the Biological Effects of Neutron Capture by B-10 at the Cellular Level." - Investigators: Paul Weinbren, M.D., and H. Harry Szmant, Ph.D. New cell lines established in the tissue culture unit are HeLa (origin: human carcinoma of the cervix), KB (origin: human carcinoma of nasopharynx), and BHK (origin: baby hamster kidney). Boron compounds suitable for study were received and some pilot tests were conducted. It was decided to run the pilot studies with two mono-boron compounds, which are the prototypes of those synthesized at the Puerto Rico Nuclear Center, but which are available in greater supply, from United States Borax Research, and of known purity and stability in aqueous media. For greater ease of handling in the laboratory when labelling tubes, they are known as compounds A and B. A is Triethanolamine Borate  $\left[ \text{B}(\text{OCH}_2 - \text{CH}_2)_3\text{N} \right]$ . B is Triisopropylamine Borate  $\left[ \text{B}(\text{OCHCH}_3 - \text{CH}_2)_3\text{N} \right]$ . Both compounds were supplied as 0.1M aqueous solutions.

Because KB and BHK cells are more rapidly growing and easier to handle than the HeLa, which are destined for the main study, the pilot toxicity tests were run in tubes of BHK and KB. In these tissues we obtained identical results. The 0.1M solution was diluted serially in two-fold steps and then 0.1 milliliter of the parent solution and each of the



Tissue culture medium is dispensed to tubes  
for growing cell suspensions

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for growing cell suspensions

dilutions was added to the freshly fed culture tubes, each of which contained 2.0 milliliters of medium or approximately a 1:20 further dilution.

The results are:

CONCENTRATION	CELLS LOST	CELLULAR CHANGE
0.1 ml of 0.1 M in 2.0 ml=0.005M	5.0%	Frequent
Two fold dilutions	2.5%	Occasional
0.00125M	Nil	Rare
0.000625M	Nil	Nil
0.0003125M	Nil	Nil
0.00015625M	Nil	Nil
0.000078125M	Nil	Nil

A four-fold dilution of the 0.1 Molar solution, when used as 0.1 milliliter to 2.0 milliliter of culture medium was at the lower limit of toxicity for both compounds. A parallel experiment in which 2.0 percent of dimethylsulphoxide was added to the medium gave identical results. The dimethylsulphoxide was used because it has the ability to potentiate the passage of some substances through cell membranes - it is not known at this time whether compounds A or B are affected in this way. The next step to be accomplished was a check on the length of exposure necessary to achieve a demonstrable effect on the cells in the presence of boron compounds. For this purpose, BHK cells and compound A were chosen. The BHK cells were grown in small flat-bottomed plastic flasks and, when fully sheeted the medium was changed for one containing five percent of compound A at 0.1M or 0.025M (final concentrations of 0.005M and 0.00125M). Controls consisted of cells with normal medium and those with the boron compounds at both concentrations. These were incubated at the same temperatures and for the same periods as test flasks exposed to the neutron flux for eight, sixteen, or twenty-four hours. The neutrons were provided by a Plutonium-Beryllium source. The flasks were exposed to the neutrons at thirty-seven degrees centigrade in groups consisting of pairs with 0.005M and pairs with 0.00125M compound A. Flasks with normal medium could not be irradiated simultaneously for lack of space in the window through which the neutrons were obtained. At eight, sixteen,

and twenty-four hours these groups, together with non-irradiated controls were transferred from the incubator to the refrigerator to stop any further growth. At the end of the experiment the supernatant medium was decanted, and the cells in the sheets removed with the aid of trypsin. The free cells from each flask were suspended in a volume of ten milliliters of balanced salt solution and then replicate counts were made in a Coulter Model B counter using a 140  $\mu$  aperture tube, lower threshold setting of fifteen, upper threshold setting of seventy-seven, the amplitude control at four and aperture current control at 0.707. These counts were made on a volume of 0.5 milliliters.

The mean counts obtained corrected to the nearest 1000 are:

TREATMENT	MEDIUM		
	Normal Medium	Medium + 0.005M of A	Medium + 0.00125M of A
37°C for			
8 hours	50,000	53,000	53,000
16 hours	53,000	53,000	Spec. spoiled
24 hours	54,000	48,000	e 50,000
Neutrons + 37°C for			
8 hours		44,000	49,000
16 hours		23,000	43,000
24 hours		Spec. spoiled	19,000

e tube blocked

Further experiments are in progress to confirm the effect shown where it appears that, at the higher concentration, the cell loss is evident about eight hours ahead of that seen in the lower concentration.

2. "Cooperative Cytogenetic Study" - Investigators: Paul Weinbren, M.D. and Lt. Col. Michael Dacquist, M.D.

Three hundred and thirty-four successful cultures have been made from four hundred and ninety-five specimens submitted to date. The percentage of successful cultures of whole blood, about eighty is comparable to those obtained in other laboratories. As in other laboratories, it has been found here that leucocytes from patients with blood dyscrasias are difficult to culture and from patients with leukemia, multiple myeloma and so on, successful cultures are obtained in about thirty percent of the cases.

A report on results obtained to date by Lt. Col. Dacquist, who has been responsible for the diagnostic efforts, is given.

\* Effects on Human Chromosomes Brought About by Therapeutic Radiation to Selected Regions. \*

This project was designed to determine the relative efficiency of radiation from cobalt<sup>60</sup>, 300KVP x-ray and radium in causing damage, and also to determine whether there are any different effects, depending upon the site of radiation, such as pelvis, chest, head and neck. Patients are selected to fit each of these categories and in all cases control, mid-therapy, end of therapy and follow-up samples are collected. Available for study so far are twenty-five cases of pelvic radiation, twenty-five in which radiation was given to the head and neck, and fifteen to the thorax. While no definite conclusions are yet possible, we see dicentric, ring and grossly abnormal chromosomes, all of which can be attributed to ionizing radiation. In a few cases, we have also seen a drop in the percentage of normal modal number metaphases during therapy with a rise in the follow up period. Conclusions will be based primarily on statistical considerations, and final opinion will be formulated after counting and studying hundreds of metaphases.

Klinefelter's Syndrome. Six cases of suspected Klinefelter's were studied, one by direct marrow smear and five by culture. All showed forty-seven chromosomes and an XXY pattern.

Mongolism. Six cases have been submitted. From one, no leucocytes could be cultured although three separate attempts were made. Of the remaining five, two showed the typical twenty-one trisomy, one was normal and two remain to be studied.