717670

PROPOSAL AND AUTHORIZATION
FOR RESEARCH OR DEVELOPMENT

NYO-149

1. Project Title: Medical Research			2. Date May, 1958
3. Budget Activity No: Summary 6120,6310,6320	4. Budget Item No:	5. Contractor's No:	6. Method and Time of Reporting Progress: Quarterly & Special Reports
7. Contractor: Associated Universities, Inc. Brookhaven National Laboratory		8. Working Location: Upton, New York	9. Contract No: AT-30-2-GEN-16
10. Persons in Charge: L. E. Farr, M.D.		11. Starting Date: Continuing	

SUMMARY

The research program of the Medical Department concerns itself with the biological effects of radiation and in particular with particle radiation of very short range or of very short duration. The researches thus must inherently be concerned with studies of precise isotope localization, kinetics of distribution and redistribution, metabolism of organic compounds, functions of inorganic compounds and the effect of excited atoms on the stability of large molecules of complexes. Since the investigations are carried out in a medical atmosphere by members of a medical department, the researchers must always be concerned with ultimate effects upon intact or originally intact human beings. This is so even though the experimental observations may be carried out on isolated organ systems, tissue cells in culture, or identical or analogous body chemical reactions observed in the test tube, cell preparations, or isolated organ systems. Advantage is sought of special situations which may be applicable to medical therapy such as neutron capture therapy of glioblastoma multiforme. Isotopes used are largely those of short half life--less than three hours--in order that progression through a metabolic complex can more satisfactorily be followed and that radiation dose may be held to a minimum. Gamma and X-radiation studies are also carried out that similarities and differences may be closely examined in the same fashion that effects are observed in single cells, multicelled and highly organized species. Diagnostic studies in the widest sense are carried out on suitable disease states under study in the hospital. Such studies are concerned primarily with elucidation of the nature of the disturbance and the proper selection of individuals in a general population for a uniform response rather than with specific diagnostic routines for use in a large general medical clinic. The entire program of the department is integrated with each scientist having awareness of, interest in, and frequently, participation in his colleagues' investigations and can be summarized by stating that it is directed at the application of short-lived radioactive isotopes to diagnosis, to therapy, and to the study of medically significant effects of radiation of whole-body, regional, cellular, and microsomal dimensions.

The over-all scope of the medical program will not change through any budget year; however, in any given year the emphasis will be in those portions of the program for which unusual capabilities exist in the staff at that time or for which most promising leads have been developed. Since the work is part of the Department's continuing program, break-throughs will be exploited when warranted with imagination and determination. In other instances, the knowledge will be brought to the attention of collaborators or others for further development elsewhere.

Specifically, the program contains several component parts which relate the general statement as given above to the several fields of medicine. The continuing intensive exploration of particle radiation of short range has brought out the necessity for further dosimetric and instrumental developments. In the application of a therapeutic procedure such as neutron capture therapy, it becomes important to know the effect of a single fission event on a single cell so that the probability of biological effect can be estimated by a summation of knowledge of the probability of the capture reaction occurring together with the probable atomic distribution of the boron in the tissue of interest. Thus, it becomes important to know dose effects in terms not of tissue volumes but of cell population of varying types, closely intermingled, and for the larger part of their metabolism, carrying on identical biochemical reactions. Hence, from time to time, greater emphasis must be placed upon differing particle bombardments ranging from cosmic rays, through boron-10 neutron capture with slow neutrons, to neutron and charged particle bombardment itself.

Brookhaven National Laboratory
REPOSITORY
COLLECTION
BOX No.
FOLDER

(See Continuation Sheet)

4001774

OFFICIAL USE ONLY

To elucidate effects, an intimate knowledge must be obtained of cell, organ, or tissue, and of entire mammalian metabolism so that not only is the specific reaction known and identifiable, but its relation and interrelationship to a whole host of other reactions is clearly known. While this is necessary to assess effects, other knowledge, together with a precise statement of the laws governing passage across cell membranes, must be sought out and established that specific isotopes may be placed in specific situations that specific effects may be observed. To the general area of knowledge concerned with such target placement, we have applied the term "selective kinetics."

It is clear that capacity to place and fix an atom on a specific cellular target without diversion, wandering, or delay implies a concise knowledge which in the reverse could be employed to remove an atom from a cell, organ or tissue effectively and expeditiously and without engendering harm to the body as a whole or its constituent parts. While much work will be concerned with specific body constituents added under experimental conditions, it is clear that additional useful, extremely accurate, and rapid analytical methods are necessary. In part they will be pioneered through the further adaptation of machines, devices, and products of nuclear physics to the solution of specific biological, analytical problems. The exploration and development of activation analysis is an example of this effort.

When explorations deriving from this program of substantive investigations give clear promise of useful application to therapy or diagnosis of a specific disease state under conditions which with some development could be met in an advanced medical center, the specific adaptive maneuvers or practical results obtained with a given procedure and resulting modifications are reported either as an effort directed toward clinical control of cancer or as an effort directed toward effective control of other disease states.

For convenience in charging research endeavor to specific budget allotments, the various projects included in this program are divided into two large groups and one smaller group designated as I. Substantive Investigation, that is, those researches undertaken to prove or disprove specific scientific hypotheses or to add systematically to the sum of medical knowledge; II. Applied Research and Development, wherein specific products, compounds, devices, procedures, or maneuvers are utilized to improve present procedures relating specifically to diagnosis or treatment of a recognized disease entity; and III. Special Projects, which are enterprises approved by the Department and operated as part of its program though not necessarily integrated in its endeavor to the same degree. Substantive Investigation is within budget activity 6120; Applied Research and Development, in 6310 or 6320. Special projects are covered by special funds and are so indicated or are a part of general operating expense in which case funds derive from the research projects.

For convenience in presentation, the various endeavors included in this program are divided into five groups. A. Radiation Effects, that is, studies concerned with the mechanism, extent or prediction of radiation effects in man; B. Selective Kinetics, that is, studies on metabolic pathways which may most advantageously be used to permit placement of isotopes on specific cell targets or target structures within cells, or conversely, specifically and effectively to remove isotopes already fixed in specific cells; C. Instrumentation Development, that is, improvement of devices and machines for specific medical uses such as development of a medical reactor or specific components of a medical unit in a general research reactor, coincident circuitry for patient use, etc.; D. Methodology, that is, the establishment of methods or standard preparations to be used in methods or procedures for ultimate application in a study of radiation effects or selective kinetics and the necessary studies of a disease condition to permit of its useful classification in such a program.

REPOSITORY Brookhaven Natl Lab
COLLECTION FM189 Med. Dept 1950-61
BOX No
FOLDER

(See Continuation Sheet)

4001775

Brookhaven National Lab
REPOSITORY
7M/89 Med. Dept. 1950-61
COLLECTION
BOX No.
FOLDER

Distribution of effort in the department and its contribution to the several ABC Activities is provided in the following table:

% Distribution of Department Activity
by Areas of Effort and by ABC Activities

	---% to ABC Activity-- 6120	6310	6320	% BNL Dept. Total
A. Radiation Effects	25	10	7	42
B. Selective Kinetics	22	9	7	38
C. Instrumentation Development	3	1	1	5
D. Methodology	9	4	2	15
Total	59	24	17	100

The fifth group, under the heading of "Special Projects," gives details of certain self-contained projects carried out by the Department, such as the operation of an occupational medicine clinic, educational conferences, and the continuing medical study of the Marshall Islanders. While very important and significant in their own right, they derive from staff competence gained by Brookhaven experience rather than basically providing that experience for the scientists concerned. Costs for operating the occupational medical clinic are included in the general and administrative costs of the Laboratory and are distributed as Indirect Expense. On the other hand, costs for such Special Projects as the Marshallese studies are included in the costs of Radiation Effects with the major expense being borne by ABC Activity 6120.

In 1952 the definitive plan for the ultimate staffing of the Medical Department was presented and approved in principle. Since that time additions to the staff have been made to fulfillment of that plan. In 1952 there were four scientists on the Senior Staff. By June 30, 1957, the Senior Staff had increased to 15 and during Fiscal 1958, to 16. In 1952 the total scientific staff was 19, at end of fiscal year 1957, it was 34, and by the end of fiscal year 1958, it is expected to be 39. The increase in staff to final size should be as rapid as possible that the potentialities of the new medical center may be promptly realized. The additional facilities provided by the new building lend significant energy to the provisions of technical assistance and equipment required to maintain the momentum achieved in the research program. Realistic estimates of capital equipment are constantly reviewed so that items considered most useful in the program are available as the research requires.

The participation in work at Brookhaven by scientists from universities and teaching hospitals continues as a most promising aspect of the Brookhaven program in medicine. In 1952 eleven medical scientists participated for varying lengths of time in the collaborative program. By March of fiscal 1958 this program included 50 research collaborators and guests. This program will be more effective with the new building since more scientists can be accommodated for longer periods of time. The increasing requests for appointment to this medical department both as regular staff members and as research collaborators indicates strongly that the Brookhaven program is filling a need of universities and teaching hospitals both for fully qualified individuals and for opportunities for research experience in the field of atomic medicine.

The Medical Department has now developed its program in outline. During 1959 there should logically be an increase in intensity of work on most of the basic divisions of investigation particularly the following: 1) Neutron capture therapy and RBE studies of heavy particles; 2) the study of kinetics of distribution of metals as pioneered by work in Mn^{56}; 3) the application of mathematics to description of kinetics of distribution for further development of tracer theory with its manifold immediate applications such as capacity to alter fixation or to remove fixed isotopes; 4) the usefulness of short-lived isotopes in cancer therapy; 5) the effects of radiation as a carcinogenic and mutagenic agent with development of better methods of determining whole-body burdens and their relation to fallout; 6) the effects of radiation on hematopoietic tissue and methods for prevention or amelioration; 7) intensive study of specific metabolic reactions both for placement of radioactive isotopes and for understanding and control of mechanisms involved therein; 8) the effects of radiation on production of antibodies and allergies.

(See Continuation Sheet)

This list could be extended usefully, but it may be more desirable to summarize the effort to two main areas; 1) the biological effects and medical implication of radiation exposure; 2) the effect of development of reactors on medical concepts of their use and hazards. The planned increase in staff year by year to a total of 48 scientists is to augment and intensify the effort in these areas and to fill in the important segments of the stated program. The importance of the first is currently exemplified by the present controversy on the effects of fallout. One or two suitable whole-body counters, a multiple-foci chrono-intensity detector, and additional animal facilities will enable the increased staff productively to work on these problems. The importance of the problem regarding reactors is pointed up by the number of reactors built, building or planned for the United States and the world. Some additional instrumentation and operating personnel again could profitably build on the present solid foundation. The cost increment while significant in terms of present budget is very small in terms of expenditures making these studies of importance.

Medical Department

Effort Sub-Divisions	Page No.
Radiation Effects	6000 - 5
Selective Kinetics	6000 - 14
Instrumentation Development	6000 - 20
Methodology	6000 - 25
Special Projects	6000 - 30

REPOSITORY Brookhaven Natl Lab
COLLECTION 7M189 Med. Dept. 1950-61
BOX No
FOLDER

PROPOSAL AND AUTHORIZATION
FOR RESEARCH OR DEVELOPMENT

NYO-149

1. Project Title: The Determination of Radiation Effects of Medical Significance			2. Date: May, 1958
3. Budget Activity No: 6120, 6310, 6320	4. Budget Item No:	5. Contractor's No:	6. Method and Time of Reporting Progress: Quarterly & Special Reports
7. Contractor: Associated Universities, Inc. Brookhaven National Laboratory		8. Working Location: Upton, New York	9. Contract No: AT-30-2-GEN-16
10. Persons in Charge: Drs. Farr, Bond, Robertson, Cotzias, Stickley, Cronkite, Hughes, Dahl		11. Starting Date: Continuing	

12. Background:

The medical significance of radiation particulate in nature and of very short range in tissue requires much more elucidation. In many instances means do not even exist to detect results of such experiences by cells. Evolution of effects in terms of lifetime happenings of man is of the greatest importance. For convenience in reporting, this category of radiation effects is broken down into the following subgroupings determined by the main pertinence of observation:
1. Radiation effects, general; 2. Radiation effects, therapeutic use of; 3. Radiation effects, therapeutic control of; 4. Radiation effects, validation of tolerance dose; 5. Radiation effects, carcinogenic; 6. Radiation effects on longevity and on immune and genetic mechanisms.

As noted in the summary, the Department's endeavors are divided into several groups. The following tables reflect the distribution of the Department's efforts within these groups, the contribution to the several AEC Activities, and a more detailed distribution within the group:

% Distribution of Department Activity
by Areas of Effort and by AEC Activities

	---% to AEC Activity-- 6120	6310	6320	% BNL Dept. Total
A. Radiation Effects	25	10	7	42
B. Selective Kinetics	22	9	7	38
C. Instrumentation Development	3	1	1	5
D. Methodology	9	4	2	15
Total	59	24	17	100

% Distribution of Radiation Effects
by Specific Fields of Effort and by AEC Activities

		---% to AEC Activity-- 6120	6310	6320	% BNL Dept. Total
A.	Radiation Effects	25.0	10.0	7.0	42.0
50.0%	General (Incl. Marshall)	11.6	2.4	7.0	21.0
37.5	Therapeutic use of	10.1	6.0	—	16.1
.5	Therapeutic control of	—	0.2	—	0.2
1.0	Validation of tolerance dose	—	0.4	—	0.4
5.0	Carcinogenic	1.3	0.7	—	2.0
6.0	Longevity, immune and genetic mechanisms	2.0	0.3	0.3	2.6
100.0%					

REPOSITORY Brookhaven National Lab
COLLECTION 7M189 Med. Dept. 1950-61
BOX No.
FOLDER

4001778

13, 14, 15. Status as of April 1958 and future programs:

a. General Radiation Effects and RBE of Capture Particle Bombardment of Cellular Structures (6120, 6310, 6320)

To determine radiation effects, the similarities and differences between particulate and electromagnetic radiation must be established. This is of particular importance in the evaluation of neutron capture therapy. Consequently, studies are being carried out over a long period of time to explore the relation of particle energy, change and size of cellular effects. In general whole-body studies are preferred but specialized laboratory situations will be utilized when they give promise of more understandable results.

The general effectiveness of particle radiation related to electromagnetic radiation will be given by an RBE (relative biological effectiveness ratio). However, because of the discrete nature of particle and cell, when the effects are limited to cellular dimensions, comparisons are difficult. A variety of approaches must be used with a realization that one may give quite a different response than another without conflict.

As part of this problem, studies were made of RBE in several experiments separately done using spleen thymus weight loss, using testis weight loss, using pathological effects on swine skin, using carcinogenesis, using rate of recovery of mice from heavy particle radiation and using mortality as a common measure. The RBE for recoil particles from B^{10}, Lithium-6, and Uranium-235 were estimated on one or more of the above bases. Under the conditions of observation the RBE of the alpha and lithium-7 particles from boron-10 capture reaction approach a value of 2.0. The carcinogenesis studies were terminated because of a severe mite infestation after eight months but a second experiment is planned. Considerations brought to the fore by these studies are given careful attention, particularly in relation to neutron capture therapy.

V. P. Bond, O. D. Easterday, E. E. Stickley, E. P. Cronkite, S. W. Lippincott

b. General Radiation Effects of Accelerator Generated Particles

(See also under Instrumentation Development) (6120)

Because the cyclotron makes possible the generation of particles having a pure spectrum of energy by suitable selection, it is a device of great usefulness in determining particle radiation effects in tissue. These studies are now in part getting under way and in part have been under way by collaborators during the past year.

It has been demonstrated that clean laminar lesions can be produced in the cerebral cortex of the rabbit which is a sharply limited response. By the use of absorbers of suitable thickness, it is possible to shift the dose to any chosen level of the cortex. Studies on dose effects are now under way.

REPOSITORY Brookhaven National Lab
COLLECTION Med. Dept. 1950-61
BOX No.
FOLDER

L. I. Malis, L. Kruger, and J. E. Rose

During the coming year it is planned to ~~utilize the small cyclotron and~~ Van de Graaff generator to produce fast neutrons to expose mice and compare effects with a standard gamma or X-ray source. A gas target will permit optimal flux. Device development is necessary.

V. P. Bond, E. E. Stickley, H. H. Rossi, G. N. Glasoe (Physics) and additional staff members

c. Studies on the Toxicity of Irradiated Intestine (6120)

The intestinal syndrome produced by supralethal doses of ionizing radiation is associated with 3- to 5-day deaths in most animals. The syndrome is characterized by extreme toxicity which seems greater than would be accounted for on the basis of fluid and electrolyte imbalance alone. The present studies were undertaken to determine whether any toxic agent (or agents) which might contribute to the syndrome is present in the irradiated intestine.

Many experimental approaches have been tried with, for the most part, negative results. Early toxicity of mucosal scrapings from unirradiated mice when injected

(See continuation sheet)

4001779

13, 14, 15. Status as of April 1958 and future programs: (continued)

intraperitoneally was found to be due largely to sepsis. Lethality from intravenous injections (very small amounts) is thought to be due to potassium toxicity.

Attempts are being made to determine toxicity by a more normal route of injection such as directly into the intestines of irradiated mice. Studies are under way on the influence of an increase in body levels of potassium and sodium (by addition of the elements to the drinking water) on the survival time in the acute intestinal syndrome. An attempt is also being made to protect irradiated mice from the intestinal syndrome by intralumen injections of normal mucosal cells into the small intestine in the hope of producing seeding.

R. A. Conard and H. Quastler

REPOSITORY Brookhaven Nat'l Lab
COLLECTION FM 89 Med. Dept. 1950-ed
BOX No.
FOLDER

4001780

13, 14, 15. Status as of April 1958 and future programs:

a. Particle Radiation Generated by Neutron Capture

(1) Neutron Capture Therapy of Glioblastoma Multiforme (6310)

(See also Methodology, Selective Kinetics, and Instrumentation Development)

The application of thermal neutron capture reactions to therapy of malignant tumors remains very attractive. Boron-10 as a capture element appears satisfactory for trials. The procedure is still complicated, and various alternative maneuvers must be tried to determine which is most efficacious.

During the past year, intra-arterial injection through the ipse lateral internal carotid artery was tried. Ten patients were treated by this alternative method. Sodium pentaborate, a new Brookhaven-developed borate compound, was used as the vehicle for the first time in patients. Exposure time was ten minutes, and infusion of pentaborate was continuous during nine of the ten minutes. A remotely controlled infusion pump was used to introduce the pentaborate solution. This maneuver successfully eliminated the skin lesions previously so troublesome. Tentative results on survival suggest the procedure is at least as effective as the prompt injection procedure. Complete pathological studies will be done, and until these are completed, definitive conclusions cannot be made. This procedure will continue during the coming year to obtain a comparative test of the Medical Research Reactor.

L. B. Farr, H. J. Bagnall, O. D. Easterday, E. B. Stickley, J. S. Robertson, S. W. Lippincott, H. J. Webster, P. I. Yakovlev, W. Haymaker.

(2) Neutron Capture Therapy Effectiveness and ~~Tissue Effects~~ Thermal Neutron Exposures (6120 6310)

COLLECTION Brookhaven Nat'l Lab M 189 Med. Dept. 1950-61
BOX No.
FOLDER

(See also Methodology and Selective Kinetics)

Extensive histological studies are required in the exploration of this new therapeutic modality for not only must the efficacy ~~of control of the tumor be~~ established, but the harmlessness of the procedure in relation to all other central nervous system structures must be unequivocally demonstrated. Physiological and clinical studies will ultimately find their support in careful histological documentation. Extensive methodology development is simultaneously required. For full evaluation it is necessary to know both the alterations which may be encountered in central nervous system structures of so called normal man and the effects of a tumor on all other structures of the brain as well as for comparison of the effects of other therapeutic procedures which are used.

During the past year there have been sectioned 19 brains after first fixing in celloidin. These are being examined independently and then conjointly by neuroanatomists, pathologists, and experimenters to determine what effects, if any, can be attributed to the neutron capture procedure. Approximately one year is required for full preparation of a serially cut specimen. Only preliminary data are now available which are encouraging in suggesting a high specificity for the procedure and an effective one when neutron exposure was high. Further studies on the natural history of the disease and the effects of procedure modifications will be continued.

S. W. Lippincott, W. Kahle, L. B. Farr, H. J. Bagnall, P. I. Yakovlev, H. de F. Webster, W. Haymaker

(3) Neutron Capture Therapy Procedures in Control of Tumor (6120)

(See also Selective Kinetics, Methodology, Instrumentation Development)

A tumor induced by us through the use of methyl cholanthrene in the brain of the mouse is transplantable and is highly invasive. For seven years it has been used as a test tumor in the study of maneuvers for neutron capture therapy and the evaluation of certain concepts in this therapeutic procedure.

During the past year this transplantable tumor has been used both as an intracerebral transplant and as an intra-muscular transplant. Effectiveness of

(See continuation sheet)

13, 14, 15. Status as of April 1958 and future programs: (continued)

neutron exposure has been explored with variations in 1) time of exposure after boron injection, 2) total neutron exposure, 3) total dose of boron. This is in an attempt to determine the parameters which may be expected to be required for successful conclusion of patient therapy.

During the past year for the first time extraordinary success has begun to appear. With a neutron exposure of 10^{12} neutrons and a boron dose of 100 mg. per kilogram, effective elimination of the tumor can be achieved in over half of the animals. Sodium pentaborate appears more effective than previously used sodium tetraborate (borax). Latest time evaluation studies suggest that possibility of achieving control with a smaller boron dose and of the same order as presently being given to patients. These studies will be continued during the coming year.

L. E. Farr, O. D. Easterday, H. J. Bagnall

b. Particle Radiation from Radioactive Isotopes

(1) Metastatic Cancer Control in Liver with Manganese-56 (6120, 6310)

Two findings have dictated the utilization of radiomanganeses in two different diseases.

1. Radiomanganese can be injected intraportally into animals, and this results in a prolonged location of the isotope in the liver. This maneuver permits the avoidance of injury to other tissues which hitherto has constituted a limiting factor in the treatment of liver malignancy with radiomanganese. It is proposed to investigate further the partition of radiomanganese between cancers and normal liver in order to see whether more selective injection of tumor can be achieved. During these experiments, it was found that the isotopes of zinc might be as useful as those of manganese in the palliation of liver tumor.

2. It has been observed that drugs which benefit patients with Parkinson's disease are potent chelating agents for manganese. This chelation occurs both in the test tube and in the living animal. In the latter, a marked redistribution of manganese tags is seen following administration of anti-Parkinsonian compounds. These findings lead to a study of manganese metabolism in treated and untreated Parkinsonian patients. It is proposed to investigate whether a primary disturbance of managnese metabolism does indeed exist in the Parkinson state and to correlate this with the finding of the change selective kinetics encountered in the treatment of the disease.

G. C. Cotzias, D. C. Borg

REPOSITORY Brookhaven Nat'l Lab
COLLECTION 7M189 Med. Dept. 1950-61
BOX No.
FOLDER

4001782

13, 14, 15. Status as of April 1958 and future programs:

a. Cancerogenic Action of Graded Doses of Whole-Body Irradiation (6120)

The major tumor that has been induced by whole-body irradiation in the lethal and sublethal range is a mammary tumor that varies in appearance from a fibroadenoma to an adenocarcinoma with a few fibrosarcomata. The one-year incidence of mammary tumors is dose dependent and extrapolates back to approximately zero dose. The mechanism of induction appears to be indirect and requires the presence of a functioning ovary, but the latter need not be irradiated.

The tumors are in part transplantable. Both autonomous and hormone-dependent tumors exist. The rapidly growing autonomous tumor is clearly a carcinoma. Some tumors are metastasizing upon transplantation.

It may be possible in the near future to provide both autonomous and hormone-dependent mammary tumors for cancer chemotherapy testing programs.

V. P. Bond, R. A. Conard, E. P. Cronkite, J. Furth, S. W. Lippincott

b. Combined Effects of Beta Irradiation of the Skin and Whole-Body X-Irradiation on Carcinogenesis in the Skin (6120, 6310)

The possible additive effects of whole-body radiation and localized beta radiation of the skin in regard to carcinogenesis of the skin have not been determined. The problem is of both theoretical and practical interest, since the Marshallese people who were accidentally irradiated with fallout developed beta lesions of the skin and received a substantial dose of whole-body irradiation.

Groups of 50 female mice have been given 20,000 rep of beta radiation from a Sr^{90} source (750 rep/min) to a flap of skin on the back (area $\approx$ 0.9 cm^2). Other groups of 50 mice have been given the same beta doses to the skin plus 400 r of whole-body x-irradiation. Still other groups of 50 mice were given 6,000 rep of beta radiation to the skin, and corresponding groups received the same beta doses to the skin plus 400 r of whole-body irradiation. Another group of mice have received only a whole-body dose of 400-r x-irradiation. Preliminary results indicate that in the 6,000-rep group which received in addition 400 r of whole-body x-irradiation, there was more skin damage at the site of the beta irradiation than in the group receiving the 6,000 rep alone to the skin. A few malignant skin tumors are appearing which have been verified by histological study. The incidence of such tumors in the various groups will be determined in the near future.

R. A. Conard, E. P. Cronkite, V. P. Bond

REPOSITORY Brookhaven Natl Lab
COLLECTION HM189 Med. Dept. 1950-61
BOX No
FOLDER

4001783

Project Title: Radiation Effects, Therapeutic Control of

13, 14, 15. Status as of April 1958 and future programs:

Frequently, following radiation exposure, a lesion develops which requires treatment. The type of lesion encountered and treated will in part depend on other researches though from time to time general efforts will be made therapeutically to control effects of specific radiation such as beta.

Effectiveness of Aloe vera Extract in Beta Lesions of the Skin (6310)

The therapeutic efficacy of local daily application of an Aloe vera plant extract to acute beta burns of the skin of mice and rats is being tested. Results are inconclusive at this time. The extract (furnished by Forkas Chemical Corporation) is said to be of benefit in the healing of thermal burns.

R. A. Conard

REPOSITORY Brookhaven Natl Lab
COLLECTION FM 189 Med. Dept. 1950-61
BOX No
FOLDER

400118

13, 14, 15. Status as of April 1958 and future programs:

In using radioactive isotopes as tracer materials or diagnostic agents, it is mandatory that the resulting radiation exposure be within the capacity of the molecules, physiological system, organ or mammal to accept without disturbance. Thus, in a manner each tracer study becomes a test of assumptions of radiation exposures which will not alter metabolic events. Specific genetic effects are separately catalogued.

Bone Marrow Function of Irradiated Dogs (6310)

Dogs given nonuniform irradiation have been studied at various intervals following exposure to determine the degree of bone marrow function in the heavily and lightly irradiated regions. Pathology and radioactive iron uptake were used as criteria of function. This work is a joint project with Boston College.

V. P. Bond, J. Flavin, B. P Cronkite

4001785

REPOSITORY Brookhaven Natl Lab
COLLECTION TM 189 Med. Dept. 1950-61
BOX No.
FOLDER

13, 14, 15. Status as of April 1958 and future programs:

a. Radioautograph Studies of Cell Proliferation in Animals Utilizing Tritium-Labeled Thymidine (6210, 6310)

Tritium-labeled thymidine, developed by W. L. Hughes of this Department, has proved to be most effective in labeling the desoxyribonucleic acid (DNA) of proliferating tissues of the mouse. These studies are being made in collaboration with the BNL Biology Department and the National Institutes of Health (G. Brecher). To date the appearance and disappearance of labeled blood cells in the peripheral blood following single injections of labeled thymidine have been followed, as has their appearance in all tissues throughout the body as a function of time. In addition, transfusion of labeled leukocytes has been accomplished and promises to be useful in studying the life span and fate of leukocytes. To date it appears that this agent will be most helpful in unraveling various time features of the generative cycle (intermitosis and mitosis).

V. P. Bond, R. A. Conrad, B. P Cronkite, W. L. Hughes, R. Painter, and H. Quastler.

b. Recovery of Fish from Irradiation (6120)

Preliminary work has indicated that an initial sublethal exposure increases the survival time and probably the LD50 of goldfish. Experiments are under way to verify and extend these observations. This work is a joint project with Columbia University.

A. Gorbman, V. P. Bond

REPOSITORY Brookhaven Nat'l Lab
COLLECTION 7M189 Med. Dept. 1950-61
BOX No.
FOLDER
4001786

13, 14, 15. Status as of April 1958 and future programs:

1. Charting of Metabolic Pathways

To determine how an isotope may be used, it is necessary to know its metabolic and therefore physiological pathways within the body. In most instances these remain to be charted before an application can be developed.

a. Neutron Capture Therapy of Glioblastoma (6310)

(See also Radiation Effects, Methodology, and Instrumentation Development)

The relative rate of movement of boron salts from blood to tissues under varying conditions of administration remains to be explored. Under the assumption that a larger total transfer will occur at high concentration, a continuous infusion procedure was initiated in patients. Because of the total lack of similar circulatory pathways in mammals, the full effects of the procedure could be tested only under exceedingly carefully controlled conditions. Initial trials were at infusion rates maintaining concentration of boron within previously experienced levels from known blood concentrations. Rate of addition of boron was then very gradually increased from a dose of 25 milligrams per kilo to 67 milligrams per kilo with a total infusion time of 10 minutes. No clinical or physiological results suggest that qualitative distribution of boron was significantly altered by the constant infusion techniques. Additional studies are planned to compare original prompt infusion technique with present delayed infusion technique when Medical Research Reactor becomes operational.

L. E. Farr, H. J. Bagnall, J. S. Robertson, O. D. Easterday

b. Metabolism of Co^{60}-labeled Vitamin B_{12} in Animals and Patients (6120, 6320)

Studies on the distribution and excretion of Co^{60}-labeled B_{12} in dogs and other animals have been completed and reports are being prepared. Further work on plasma clearance and excretion of labeled B_{12} in various blood dyscrasias and "normal" controls has been completed. Plasma concentration curves of Co^{60} after the intravenous injection of the labeled B_{12} show a periodic and an aperiodic component, which indicates that clearance is progressing simultaneously with mixing. The aperiodic portion consists of a fast and a slow component. Curve analyses are under way. Urinary and fecal excretion show two clear components, one with a half-time of 2½ days and the other with a half-time of more than 300 days. The earlier suggestion of fast and slow plasma clearances in various blood dyscrasias must be reconsidered in view of the difficulty of curve analysis in the presence of simultaneous mixing and clearance.

E. F. Cronkite, E. Henley, L. M. Meyer, J. R. Rubini, D. A. Willigan, W. Wolins

c. The Sites of Catabolism of Plasma Albumin (6120)

In an extension of the study reported a year ago (W. L. Hughes, Proc. 8th Ann. Conf., National Nephrosis Foundation, 1956, p. 22) on the effect of nephrectomy on the catabolic rate of labeled plasma albumin, the effect of removing the intestines or large portions of the liver has been investigated. Removal of the intestines had no effect, but removal of portions of the liver decreased the rate of catabolism in proportion to the amount of liver removed. This effect can be much greater than that seen following nephrectomy and suggests that the liver must be the major site of catabolism for plasma albumin.

D. Gitlin, J. R. Klinenberg, G. Terres, W. L. Hughes

REPOSITORY Biochemistry Dept
COLLECTION Medical Dept 1950-61
BOX No.
FOLDER

d. Essential Fatty Acid Deficiencies in Swine ~~(6120)~~

Fatty acid deficiency induced in swine results in dermatosis resembling psoriasis in human beings. These lesions are being studied for pathology, fatty acid cholesterol metabolism, and distribution of C^{14}-labeled unsaturated fatty acids.

D. K. Sorenson, L. I. Gidez

(See continuation sheet)

4001788

13, 14, 15. Status as of April 1958 and future programs: (continued)

e. Catabolism of Serum Albumins in Mice (6120)

The comparison of data obtained in this laboratory for the half-life of crystalline bovine serum albumin (BSA) with the data for human serum albumin (HSA) reported by Melcher et al. (J. Immunol., 71, 275, 1953) shows nearly a twofold difference. These investigators, using iodinated HSA and following the catabolic rate by serum sampling, have found a half-life of 1.5 days. At BNL, by using whole-mouse counting, the biological half-life for iodinated BSA has been found to be between 0.6 and 0.7 days. Although it would be surprising if mice could distinguish between HSA and BSA to the extent noted (short of an immune response), various preparations of HSA (crystalline, Fraction V, and commercially prepared RISA) were tested in BNL mice with whole-body counting. The results indicated no significant difference in half-lives between the different HSA preparations; they had half-lives of 0.75 days, slightly longer than those for BSA. Further studies in which the catabolic rate was determined both by whole-mouse counting and by serum sampling ruled out the possibility of differences based on methods of determination. Since it is felt that Melcher's group has reported an accurate value, and that the results obtained at BNL also merit confidence, the present line of investigation is being continued in an attempt to resolve this discrepancy. The approach now being followed is one of testing various strains of mice.

G. Terres, W. Wolins

f. Tryptophan Metabolism in Neoplastic Diseases (6310)

A study is planned of the influence of neoplastic diseases on the quantities of tryptophan metabolites appearing in the urine of afflicted patients. Compounds related to the tryptophan-niacin metabolism scheme are being synthesized with tritium or C^{14} labels. It is also proposed to measure the tryptophan metabolite fluctuations in the urines of patients before and after exposure to large doses of radiation used in the treatment of neoplastic diseases.

L. V. Hankes

g. Metabolic Formation of Niacin from Tryptophan (6120)

The present work was undertaken to determine whether kynurenine can serve as a source of niacin (nicotinic acid) or one of its derivatives in the metabolism of the rat.

Kynurenine, $O\text{-}NH_2\text{-}C_6H_4\text{-}COCH_2CH(NH_2)COOH$, was labeled in the ring with tritium. The labeled compound in amounts of 1 to 12 mg. was injected intraperitoneally into rats, and the urine was collected for 24 hours. Both quinolinic acid and N^1-methylnicotinamide labeled with tritium were isolated from the urine. Their purity was demonstrated by the constancy of specific activity on recrystallization. Since the rat excretes niacin as N^1-methylnicotinamide, the results show that kynurenine is a step in the formation of niacin, with quinolinic acid as an intermediate.

Of the kynurenine administered, only 5% appeared in the 24-hour urine; apparently, the greater part was either catabolized or incorporated. Further studies on tryptophan metabolism are planned.

L. V. Hankes, I. H. Segel

REPOSITORY Brookhaven Nat'l Lab
COLLECTION TM189 Med. Dept. 1958-61
BOX No.
FOLDER (6120)

h. Metabolism of C^{14}-labeled Amino Acids by Trichinella spiralis Larvae. See under Methodology.

i. The Role of Carbohydrate and Mineral Metabolism in Control of the Cerebral Excitatory State (6120)

The importance of the nature of the substrate in regard to the inhibiting action of the antihistamine drugs on the respiration of rat brain cortex slices is being investigated by Warburg respirometry. Preliminary trials have not

4001789

(See continuation sheet)

13, 14, 15. Status as of April 1958 and future programs: (continued)

verified certain specific distinctions reported by others.

P. G. Lefevre and G. F. McGinniss

j. In Vitro Synthesis of Lipids by Human Red Cells (6120)

Fifteen μC of C^{14}-labeled sodium acetate were incubated with 50 ml. of whole blood containing acid-citrate-dextrose anticoagulant, Versene, penicillin, and streptomycin for 17 hours at 37°C. Lipids were extracted from the plasma and the washed red cells and were fractionated into major lipid fractions on a silicic acid column by means of gradient elution. In plasma the free cholesterol was labeled, whereas the esterified sterol had no radioactivity, which suggests that cholesterol can be synthesized but not esterified in plasma. Free fatty acids in plasma were highly labeled, but triglycerides exhibited negligible incorporation. In the red cells the activity of the triglycerides was quite high, being seven times that of the free fatty acids, which were only one-ninth as radioactive as the plasma fatty acids. Also unexpected was the relatively high specific activity of red cell esterified cholesterol, which was about eight times that of the free cholesterol. The phosphatide fatty acids of both red cells and plasma had nearly equal activities, which might indicate free exchange in vitro. The incorporation of other lipid precursors will also be studied in this system.

L. I. Gidez, H. A. Eder

k. Fatty Acid and Sterol Synthesis Using Carbon-14 (6120, 6320)

The mechanism by which fatty and sterol compounds are produced in the body may be of great significance since age-associated diseases notably arteriosclerosis show localized deposits of lipid materials. Patients were studied using mevalonic acid-2-C^{14} for cholesterol synthesis and glycerol 1, 3-C^{14}, acetate-2-C^{14}, and palmitate 1-C^{14} for incorporation into cholesterol and fatty acids of various serum lipoprotein fractions. Peak activities of label incorporation occurred at different times for the various fractions. Additional work is planned more closely to define the specific pathways by which the label enters the compounds of interest.

L. I. Gidez, W. W. Shreeve, H. A. Eder

l. Metabolic Pathways of Formation of Hexoses and Pentoses by Mammalian Species (6120, 6320)

The exact mechanism is not known of synthesis of carbohydrate from fat or amino acid compounds in the body or from other metabolites. An extended, comprehensive study has begun using largely carbon-14-labeled compounds to elucidate these pathways in patients.

During the past year the effects of adrenal steroid hormones was studied on pathways of formation of carbohydrate from 1-C^{14}-acetate. The results indicate there was no deviation from usual pathways induced by adrenal steroid hormones. When C^{14} pyruvate was used, the results indicate extensive conversion of pyruvate to intermediates of the Krebs cycle prior to formation of glucose. The effect of adrenal hormones on utilization of 2-C^{14} acetate was also observed. Results were in general in agreement with predictions. A patient with lipotrophic diabetes was also studied with 2-C^{14} acetate. There was also observed the glucogenic, lipogenic, and ketogenic properties of ethanol 1-C^{14} in comparison with acetate. Differences were observed. Pentose sugars are also being studied because of their importance as a constituent of nuclear material as desoxyribose. Further studies are planned in this general field as data from completed experiments can be fully analyzed.

W. W. Shreeve, A. R. Hennes, R. Schwartz, M. Conowitz, Z. Grossman

REPOSITORY Brookhaven Nat'l Lab.
COLLECTION 7M189 Med. Dept. 1950-61
BOX No.
FOLDER
4001790

13, 14, 15. Status as of April 1958 and future programs:

When it is known in a measure of detail how a substance is distributed within the body and how it enters metabolic reactions, advantage can be taken of this knowledge to modify its behavior to secure target placement, or conversely, its removal and excretion from the body.

a. Neutron Capture Therapy Effectiveness and Tissue Effects of Thermal Neutron Exposures (6120, 6310)

(See also Radiation Effects and Methodology)

Cellular examination of tissues exposed for a known time to thermal neutrons at a known interval in relation to boron-10 administration is capable of yielding information of value when boron concentration and neutron concentration are high. This in turn permits some testing of hypotheses of movement of boron-10 under therapeutic conditions. Examination of tissues for necrosis, fibrous and giant cell formation that can be related to known intensity exposures will give information regarding rates of boron accumulation in structures under study. This data will be obtained during the coming year when the specimens are ready for examination.

S. W. Lippincott, L. E. Farr, W. Kahle, W. Haymaker, P. I. Yakovlev

b. Human Manganese Metabolism (6120, 6320)

Metabolis studies with radiomanganese tracers in humans have progressed to the first study of long-lived radioisotope (Mn^{54}) metabolism in patients. Data currently being gathered and evaluated indicate that employment of this isotope will be profitable and may allow correlation of human studies with animal experiments previously reported.

D. C. Borg and G. C. Cotzias

c. Uptake of Tritium-labeled Thymidine by Embryonic Tissues (6120)

CF-1 mice at various stages of pregnancy have been injected with tritium-labeled thymidine, and the embryos have been sectioned and prepared for autoradiography. This work is a joint project with Yeshiva University.

V. P. Bond, M. Atlas, and E. P. Cronkite

d. Copper Metabolism (6120, 6320)

Copper metabolism has been studied in mice by use of Cu^{64}. These studies include the distribution of inorganic copper, its conversion to ceruloplasmin, and its elimination both at tracer levels and at much higher levels up to those causing acute toxicity. The results show a striking resemblance to the abnormalities of copper metabolism seen in Wilson's disease and strongly suggest that the primary defect in Wilson's disease lies in the mechanism of copper excretion.

D. Gitlin

e. Thymidine Metabolism (6120)

Thymidine uptake and distribution in the mouse following intravenous administration have been studied. Thymidine leaves the blood stream rapidly (within a few minutes) and then appears within cells in a phosphorylated form. It seems to be absorbed by all cells of the body, but somewhat higher than average values are found in the liver and kidney. Immediately following its entry into cells, catabolism to water begins, resulting in about 50% destruction of the thymidine within the first hour. The activity remaining appears to be incorporated into DNA. Chemical procedures for better quantitation [illegible] developed.

W. L. Hughes

REPOSITORY Blackburn Hall Hall
COLLECTION MU189 Med Dept. 1950-cl
BOX No.
FOLDER
4001791

Project Title: Selected Kinetics Tracer Theory

13, 14. 15. Status as of April 1958 and future programs:

The general principles governing the movement of substances across cell membranes and throughout body compartments can be expressed mathematically. Thus, on the one hand, data may be tested to develop theory, and on the other, to determine whether behavior is in accordance with theory.

a. Neutron Capture Therapy Procedure in Control of Transplantable Mouse Tumors (6120)

(See also Radiation Effects, Methodology, Instrumentation Development)

A tumor induced by us through the use of methyl cholanthrene in the brain of the mouse is transplantable and is highly invasive. For seven years it has been used as a test tumor in the study of maneuvers for neutron capture therapy and the evaluation of certain concepts on this therapeutic procedure.

The movement of the boron into the several body compartments of interest can be approximated by chemical analysis and by neutron exposure following boron administration. Comparison of time interval effects gives information relative to the movement of boron from blood to tissue and back.

During the past year, what were thought initially to be ovservations in concentration changes have been verified as bona fide reflections of a movement. These have significance in the choice of an optimal time for exposure. Further data are being obtained to meet reliability tests for mathematical analysis.

L. B. Farr, J. S. Robertson

b. Water and Electrolyte Exchange: Halide Metabolism (6120)

During the quarter, analysis of data from experiments already completed was the principal activity in this field. Design of further experiments will be postponed until this phase has been completed.

J. S. Robertson

c. Tracer Theory (6120)

An analogue computer is being constructed for the Medical Department by the Instrumentation Division. The existing analogue computer is being used by the Physiology Division (D. C. Borg) in the analysis of data on manganese metabolism.

J. S. Robertson

d. Active Transfer of Metabolites Through Cell Membranes (6120)

(See also Methodology)

Interest continues to center on the steric specificity of the monosaccharide carrier system in the human red cell membrane. Although the widely differing carrier affinites of the various sugars do not seem to follow a consistent pattern in relation to molecular configuration, a distinct correlation has been established between these affinities and the pyranose conformational stabilities of all available aldohexoses and aldopentoses. This correlation is such as to imply that the C1 form may be essential in the substrate if it is to make use of the carrier. The extent of the generality of the conformational correlation is being investigated with some of the rarer sugars obtained from private sources.

The study is continuing as the new compounds become available and also is being tested with inhibitory compounds such as phlorizin.

P. G. LeFevre

REPOSITORY Brookhaven Nat'l Lab
COLLECTION JM189 Med. Dept. 1950-61
BOX No.
FOLDER
4001792

PROPOSAL AND AUTHORIZATION
FOR RESEARCH OR DEVELOPMENT

NYO-149

1. Project Title:	2. Date:
Instrumentation Development	May, 1958

3. Budget Activity No:	4. Budget Item No:	5. Contractor's No:	6. Method and Time of Reporting Progress:
6120, 6310, 6320			Quarterly & Special Reports

7. Contractor:	8. Working Location:	9. Contract No:
Associated Universities, Inc. Brookhaven National Laboratory	Upton, New York	AT-30-2-GEN-16

10. Persons in Charge:	11. Starting Date:
Drs. Farr, Robertson, Stickley, Bond, Cotzias	Continuing

12. Background:

The completion of many substantive investigations as well as the applications of the researches to diagnosis and therapy depend in many instances upon the development of instrumentation not heretofore available. Continued improvement and development of existing devices and machines is necessary that the exciting results of any given investigation may be fully exploited. The total resources of the Laboratory as well as those available to research collaborators and subcontractors are drawn upon when necessary to enable advancement in the instrumentation required by promising leads.

As noted in the summary, the Department's endeavors are divided into several groups. The following tables reflect the distribution of the Department's efforts within these groups, the contribution to the several AEC Activities, and a more detailed distribution within the group:

% Distribution of Department Activity
by Areas of Effort and by AEC Activities

	-% to AEC Activity-- 6120	6310	6320	% BNL Dept. Total
A. Radiation Effects	25	10	7	42
B. Selective Kinetics	22	9	7	38
C. Instrumentation Development	3	1	1	5
D. Methodology	9	4	2	15
Total	59	24	17	100

% Distribution of Instrumentation Development
by Specific Fields of Effort and by AEC Activities

	-% to AEC Activity-- 6120	6310	6320	% BNL Dept. Total
C. Instrumentation Development	3.0	1.0	1.0	5.0
40.0% Reactor	1.5	0.5	--	2.5
10.0 Accelerator	0.5	--	--	0.5
50.0 Ancillary	1.0	0.5	1.0	2.5
100.0%				

REPOSITORY Brookhaven Nat'l Lab
COLLECTION 111189 Med. Dept 1950-61

13, 14, 15. Status as of April 1958 and future programs.

a. Neutron Capture Therapy of Glioblastoma FOLDER (6310)

(See also Radiation Effects, Methodology, and Selective Kinetics)

The application of neutron capture therapy to individual patients requires extensive instrumentation development in all its phases. During the past year attention has centered upon design, construction, and development of a remotely controlled infusion pump which provides two solutions either to be used at will

(See continuation sheet)

4001193

13, 14, 15. Status as of April 1958 and future programs: (continued)

by proper manipulation remotely and also provides for control of rate of infusion from 0.25 ml. per minute to 50 ml. per minute. This pump would appear to have many uses other than in this specific program.

Further instrumental development will intensify when the Medical Research Reactor becomes operative, since many new adaptive devices will be required.

L. B. Farr, J. S. Robertson, B. B. Stickley, O. D. Easterday

b. Neutron Capture Therapy Procedure in Control of Transplantable Mouse Tumors (6120)

(See also under Radiation Effects, Selective Kinetics, Methodology)

The utilization of a small test animal like the mouse for purposes of developing neutron capture therapy required design and development of instrumentation that will permit procedures of meaning to be carried out on the mouse. At present this requires a device permitting full exposure of the tumor-bearing tissue to the thermal neutron stream with full protection of other regions of the mouse. The dimensions introduce severely difficult problems, but headway is now being made. These efforts will continue.

L. B. Farr, B. B. Stickley

c. Reactor Neutron Beam Evaluation (6120, 6310)

(1) Tissue-equivalent ionization chamber

A new series of neutron comparison measurements was made for standardization purposes by using the tissue-equivalent ionization chamber in the medical facility and in the biology facility at the reactor. This instrument was also used in the middle energy neutron experiments on mice at the small cyclotron. Standardization under x-ray was also included in the series.

The probe ionization chamber, guard-ring type, has been modified for application in the present reactor medical facility. X-ray testing and calibration have been carried out for both the graphite and tissue-equivalent electrode arrangements in the preparation for use of the chamber as a cross-calibration instrument between the present reactor facilities and those in the new medical research reactor.

B. B. Stickley

(2) Ionization chamber for gases (6320)

The triple ionization chamber designed by Rossi has been reassembled. The new gas-handling apparatus enables the ionization chamber to be evacuated and filled with the significant gaseous elements occurring in tissue in the correct proportions. The system provides for adequate pressure measurement, gas storage, and mixing. At the present stage of development, a variety of the accessory instruments can be used to measure the ionization current output, depending on the radiation level of the field in which measurements are being made. This instrument is designed to provide differential measurements of the several components present in the mixed radiation pattern characteristic of reactor exposures. It is provided with a remote manipulating device for scanning within liquid phantoms under exposure conditions.

Newly acquired electrometers were tested with the ionization chamber and gamma sources. Three electrometers have given evidence that they may produce reliable measurements when used with the ionization chamber. After calibration of the tissue-equivalent ionization chamber with existing gamma sources, the apparatus will be ready for use in thermal neutron dosage studies.

R. I. Weller and B. B. Stickley

REPOSITORY Northwestern University Medical Dept. 1960-61
COLLECTION
BOX No
FOLDER

(See continuation sheet)

480179

13, 14, 15. Status as of April 1958 and future programs: (continued)

(3) Gold wire activation technique (6310)

An immediately practical study of neutron flux patterns for the brain tumor neutron capture experiment has been begun by using the gold wire activation technique in a phantom constructed within a human skull. Simulation of skin and brain tissues is being developed in order to provide the most accurate picture possible of the neutron flux density at internal positions of greatest interest, in terms of both desired treatment regions and regions where protection is of critical importance.

B. B. Stickley

d. Medical Research Reactor (6120, 6310, 6320)

Since the reactor itself is well on the way toward completion, design effort is directed toward detailing plans for accessory apparatus which was presented in conceptual form only in the early phases of the planning program.

B. B. Stickley

e. Radiation Dosimetry (6120)

(1) Isotope Comparator

A precision isotope comparator was completed for general use with routine materials. In this instrument an air ionization chamber is used with an electrometer circuit for the rate-of-drift measurement procedure. A second instrument was completed for evaluation of flat beta-ray applicator sources in which use is made of an extrapolation chamber of Failla's design previously built by the Instrumentation Division.

B. B. Stickley

(2) In Vivo Radioactivity Scanner (6120)

Efforts are being continued to modify and adapt a commercial in vivo radioisotope scanning unit to provide the precision and dependability necessary at BNL. Further electronic and mechanical improvements are required before satisfactory performance can be achieved.

B. B. Stickley

(3) Beta Applicator Calibration (6120)

A report has been completed on this measurement. Of most interest is a description of a 125-mC Sr^{90}-Y^{90} beta applicator, calibrated with an extrapolation ionization chamber and by the use of nuclear film. Surface and depth doses determined by the two methods were in good agreement. By use of a polystyrene phantom, the surface dose was found to be 26.2 esu/cc-sec or 1430 rad/min with an estimated accuracy of ± 3%. The half-value thickness was determined to be 0.13 cm.

R. I. Weller

(4) Radiation Detection and Analysis (6120)

Pulse height analyzer techniques are being explored for use in activation analysis and simultaneous multiple isotope tracer studies. Existing equipment has been studied for this work, as an aid in prescribing the design of more suitable circuitry.

J. S. Robertson, B. B. Stickley

REPOSITORY Brookhaven Nat'l Lab
COLLECTION FMB9 Med. Dept. 1953-61
BOX No.
FOLDER
4001795

(See continuation sheet)

13, 14, 15. Status as of April 1958 and future programs: (continued)

f. Chemical Dosimetry (6120)

This work was initiated as a contributing phase in the energetic heavy particle (neutron capture) radiation studies, as well as for its usefulness in gamma-ray and other applications. Development is concomitant with those biological projects with which it is directly associated.

V. P. Bond, E. E. Stickley

g. RBE of Low Energy Monoenergic Neutrons (6120)

Data on the RBE of fast neutrons in the region of 100 to 1,000 kev are much needed. Preliminary work has indicated the feasibility of performing such studies with the 18-in. cyclotron at BNL. This work is a joint project with Columbia University.

V. P. Bond, E. E. Stickley, H. Rossi

h. Cobalt-60 Source (6120)

The 800,000 r/hr Co^{60} source previously used in the Microbiology Division is being replaced by a new source. Whereas the old source consisted of multiple slugs of Co^{60}, the new one is a single tube of Co^{60} clad in stainless steel. Although the new source was designed to be interchangeable with the old one, it proved impossible to extricate the old one from its lead shield; therefore, a new shield is being constructed.

J. S. Robertson

i. Basic Physiology of Manganese (6120)

Development of neutron activation methods for the determination of manganese in biological materials in which its concentration is very low has been postponed because of the temporary unavailability of certain necessary equipment. Preliminary evaluation of new analytical apparatus is anticipated for the coming quarter, however.

Pilot studies have been completed on the application of electron magnetic resonance techniques to the measurement of tissue manganese and the determination of its valence state in situ. At present the sensitivity of this method appears insufficient for application to most biological samples; however, certain alterations in the magnetic spectrometer and proposed changes in the sample preparation procedures will permit a re-evaluation of this approach within the next several months.

REPOSITORY Brookhaven National Lab
COLLECTION TM 189 Med. Dept. 1950-a
BOX No.
FOLDER

D. C. Borg, G. C. Cotzias, M. Birnbaum, L. Grodzins

j. Development of the Use of Europium-155 in Portable Diagnostic X-ray Devices (6120)

A series of radiographs has been made, the source being about 5 mC of Eu^{155} prepared by activating 100 mg. of Sm^{154} in the BNL research reactor. A second source, activated at the MTR, was broken during transfer for shipment. The 4-mC source was used by placing it in a shutter designed for use with similar Tm^{170} sources which was kindly lent to BNL by the Army Medical Equipment Development Laboratory, Fort Totten, New York. Because of the low activity of the source relative to that required in an operational device, the exposure times have necessarily been very long (hours to days), and it has not been feasible to use human beings as subjects. Radiographs of metallic objects, isolated bones, and a leg of lamb, however, indicate that a satisfactory degree of contrast and good resolution can be obtaine with Eu^{155}. As has been the case with Tm^{170} sources, the quality of the radiographs is inferior to that obtainable with a good x-ray machine, but is satisfactory for projected field uses.

4001796

(See continuation sheet)

13, 14, 15. Status as of April 1958 and future programs: (continued)

Investigation of the separation of Eu^{155} from Sm has continued. The use of cation exchange columns appears to be unsatisfactory, but other column methods are being tried.

J. S. Robertson

k. Isotopes Used in Tracer Studies (6120,6310,6320)

The use of several isotopes is being developed by members of the staff requiring instrumentation for the special problems as they arise, and by providing consultation service.

Projects in hematology have been begun on the application of Co^{58} as well as Co^{60}, along with Fe^{59} and Cr^{51}-labeled compounds, separately and in combination. The isotopes Mn^{52}, Mn^{54}, and Mn^{56} continue to be used in research studies of diagnostic and therapeutic interest. Attempts are still being made to develop the Ca^{47} isotope, because of its great potential value in a wide variety of research fields; reactor production from enriched Ca^{46} and cyclotron activation from Ca^{48} are possible approaches. Mg^{28} had been used for many studies, but the specific activity available, either from reactor or cyclotron production methods, precludes valid results in vivo, since the carrier burden of magnesium is still so great that interfering pharmacologic effects are produced.

H. B. Stickley and J. S. Robertson

REPOSITORY Brookhaven Nat'l Lab
COLLECTION TM 189 Med. Dept. 1950-1
BOX No.
FOLDER

4001797

PROPOSAL AND AUTHORIZATION
FOR RESEARCH OR DEVELOPMENT

NYO-149

1. Project Title: Methodology			2. Date: May, 1958
3. Budget Activity No: 6120, 6310, 6320	4. Budget Item No:	5. Contractor's No:	6. Method and Time of Reporting Progress: Quarterly & Special Reports
7. Contractor: Associated Universities, Inc. Brookhaven National Laboratory		8. Working Location: Upton, New York	9. Contract No: AT-30-2-GEN-16
10. Persons in Charge: Drs. Farr, Bond, Cronkite, Cotzias, Hughes, Robertson, Van Slyke, Lippincott		11. Starting Date: Continuing	

12. Background:

The development of methods of analysis or synthesis of observations of experimental design or of procedure modifications are included under the category of methodology. Exploration of a new approach is required before it can usefully be incorporated into a well tried usage.

As noted in the summary, the Department's endeavors are divided into several groups. The following tables reflect the distribution of the Department's efforts within these groups, the contribution to the several AEC Activities, and a more detailed distribution within the group:

% Distribution of Department Activity
by Areas of Effort and by AEC Activities

	-% to AEC Activity-- 6120	6310	6320	% BNL Dept. Total
A. Radiation Effects	25	10	7	42
B. Selective Kinetics	22	9	7	38
C. Instrumentation Development	3	1	1	5
D. Methodology	9	4	2	15
Total	59	24	17	100

REPOSITORY Brookhaven Nat'l Lab
COLLECTION MU of Med Dept. 1958-01
BOX No.
FOLDER

% Distribution of Methodology by
Specific Fields of Effort and by AEC Activites

	-% to AEC Activity-- 6120	6310	6320	% BNL Dept. Total
D. Methodology	9.0	4.0	2.0	15.0

13, 14, 15. Status as of April 1958 and future programs:

a. Neutron Capture Therapy of Glioblastoma (6310) (See also under Radiation Effects, Selective Kinetics and Instrumentation Development.)

The almost universal occurrence of a severe skin lesion in the patients comprising treatment Series 2 highlighted the necessity for a change in procedure to overcome this problem. The alternative chosen was intra-arterial administration of the boron solution. It was to be injected into the internal carotid artery on the same side as the tumor. It was necessary to establish a procedure with minimum trauma and maximum certainty of placement. Placement of the infusion was determined by the injection of fluorescein into the vessel followed by facial examination with an ultra violet lamp. When the infusion was limited to the internal carotid artery, the fluorescein could be detected only over the invert canthus of the eye and superior to it in a spot about the size of one half dollar. Various fixative procedures were tried. The final procedure is an operative approach to expose the artery, insertion of a plastic cannula, fixation by suture, test with fluorescein, simple pull out removal and hemorrhage control by pressure. The remotely controlled infusion pump was used.

H. J. Bagnall, A. J. Bertinchamps, R. W. Christie
(See continuation sheet)

13, 14, 15. Status as of April 1958 and future programs: (continued)

b. Neutron Capture Therapy Procedure in Control of Transplantable Mouse Tumors (6120) (See also under Radiation Effects, Selective Kinetics, Instrumentation Development)

Standardization of procedure of transplantation of the invasive tumor used experimentally is mandatory for statistical analysis. The procedure as now used consistently yields takes in 92-95 per cent of all hosts. Deviation from this harvest can be attributed to effects of alterations in procedure or treatment. Injection procedures for the mouse have also been standardized as well as exposure procedures. The analytical method for tissue boron determination has likewise been further modified until now it appears to have reached a satisfactory status for the procedure used and the results necessary. As a result it is now possible to undertake evaluation studies with confidence. Several years experience were required to reach this point. Other aspects of the study will be standardized in like manner.

L. E. Farr, T. Konikowski

c. Neutron Capture Therapy Effectiveness and Tissue Effects of Thermal Neutron Exposures (6120, 6310) (See also under Radiation Effects and Selective Kinetics)

To permit study of effects in brains of thermal neutron exposure the specimens to be studied must be unchanged if possible from their original state. The fluid nature of brain tissue interposes problems of handling and eliminates certain types of study such as location of compounds of boron. Only a whole brain technique permits studies encompassing spatial relationships. This is a very unusual but potentially rewarding approach.

Procedures have been worked out for removal of whole brain specimens followed by suitable fixation then inbedding in celloidin for sectioning. A variety of staining procedures is being developed. Specific stains are being sought. Further continuing refinements in procedure will be sought.

S. W. Lippincott, L. E. Farr, W. Kahle, (P. I. Yakovlev, H. deF. Webster)

d. Organo-boron Toxicity in Mice (6310)

The determination of solubilities for a number of organometallic compounds, including organic boron, is in progress. These studies will be followed by toxicity investigation in mice.

O. D. Easterday

e. Boron toxicity in Mice (6310)

Studies are being continued in which the toxicity of various complexing agents of the carbohydrate group is under investigation. Approximately one half of the agents chosen for examination have been screened. The data are being subjected to probit analyses and relative potency evaluation.

O. D. Easterday

f. Clinical Studies of Labeled Protein Fractions (6310)

Clinical studies of labeled protein fractions are being carried out on normal individuals, patients with miscellaneous diseases, and patients with various types of carcinoma, as a possible diagnostic aid in detecting early cancer.

S. W. Lippincott, W. L. Hughes, W. Wolins, and C. T. O. Fong

g. Tissue Culture (6120)

Studies on the dynamics of cell proliferation in the mouse, using tritium-labeled thymidine, have been initiated. To augment these studies tissue culture of hematological cells has been initiated. The [illegible] techniques to be a valuable research tool but is of aid in clinical diagnosis of blood dyscrasias as well.

V. P. Bond and B. P. Cronkite

REPOSITORY [illegible]
COLLECTION [illegible]
BOX No.
FOLDER

(See Continuation Sheet)

4001799

13, 14, 15. Status as of April 1958 and future programs: (Continued)

h. Preparation of H^3-Cytidine and Deoxycytidine (6120)

Cytidine and deoxycytidine have been labeled with tritium by the same procedure which has proved successful for thymidine, and materials have been obtained with specific activities of several hundred mC/mM. Studies on the utility of these materials for labeling nucleic acids are under way in the Brookhaven National Laboratory Medical Department and Biology Department and at Columbia University.

W. L. Hughes and J. H. Taylor

i. Preparation of DL-Arginine Labeled with Tritium (6120)

Arginine has been labeled in the alpha position via racemization of its acetyl derivative in the presence of tritium oxide and excess acetic anhydride (procedure of Bergmann). Specific activity of the order of 1 mC/mg was easily obtained, and considerably higher activity should be easily attainable if necessary. The present material appears quite satisfactory for autoradiographic study of protein formation in living tissues.

D. Shemin and W. L. Hughes

j. Effect of Incorporated Tritium-Labeled Thymidine Upon Growth of Cultured Human Tissue Cells (6120)

Studies on the effects of tritium incorporation into the nucleus of human tissue cells (HeLa) have been continued. Results show that inhibition of growth by tritium oxide can be duplicated by tritiated thymidine in concentrations in the medium of the order of 1/1000th of T_2O. The possibility that growth inhibition is due to toxic contaminant (or contaminants) or to nonradioactive thymidine has been eliminated. Attempts are under way to detect the effects of the incorporated radioactivity upon individual cells by autoradiographic methods.

R. B. Painter and R. M. Drew

k. Radiation Effects on Antibodies (6120)

Work is being extended on study of the effects of continuous (chronic) exposure to Co^{60} gamma radiation on antibody production and susceptibility to anaphylactic shock in mice. Preliminary findings indicate that continuous exposures at dose rates of 1 and 4 rep per hr. depress the secondary tetanus antitoxin response. Continuous exposure to gamma radiation greatly enhanced the susceptibility of actively and passively sensitized mice to anaphylactic shock. Acute and fractional acute doses of gamma radiation are being compared to accumulated doses of chronic radiation with respect to their depressant action on antibody production. The time of secondary antigenic stimulus in relation to the above radiation conditions is also being considered.

R. D. Stoner

l. Nomogram for the Calculation of Total Beta and Gamma Dose Rate (6120)

A nomogram has been developed by means of which almost instantaneous calculations can be made of the dose rate for all the biologically important isotopes provided that an estimate is available of the weight of [illegible] organ for which this value is sought.

A. J. Bertinchamps

REPOSITORY Brookhaven Nat'l Lab
COLLECTION FM 189 Med. Dept. 1958-61
BOX NO.
FOLDER

n. Hemorrhage Control--Radiation Effects on Platelets (6320)

High levels of a physiologically active substance, serotonin, are found in blood platelets and parts of the gastrointestinal tract. Serotonin levels of tissues and platelets will be measured colorimetrically from tissues of normal and irradiated animals and platelet preparations to assess further the role of this substance in radiation injury and the effectiveness of platelet preparations in controlling radiation hemorrhage.

Urine levels of 5-hydroxyindoleacetic acid, the excreted metabolite of serotonin, will be measured in normals, leukemics, and other blood dyscrasias.

4001800

(See Continuation Sheet)

13, 14, 15. Status as of April 1958 and future programs: (continued)

m. Hemorrhage Control--Radiation Effects on Platelets (6320) (continued)

In addition, the comparative effectiveness of fresh and lyophilized platelets in the control of radiation bleeding will be evaluated.

V. P. Bond, R. A. Conard, B. P. Cronkite, J. R. Rubini and D. K. Sorensen

n. Determination of Vascular Volume in Normal and Neoplastic Tissue by Use of Suitable Radioactive Isotopes as Labels of Vascular Components (6120)

Chromium, phosphorus, and tritium are at present being used as labels. Preliminary studies are necessary to establish conditions whereby either reproducible blood volumes or an estimate of deviation from the mean can be obtained; and to determine the influence of the sacrificial method and the handling of the specimen on the results.

H. J. Bagnall

o. Procedures for Study of Metabolism of C^{14}-labeled Amino Acids by Trichinella Spiralis Larvae (6120)

Preliminary *in vitro* experiments have been conducted to determine optimum procedures for studying protein, lipid and carbohydrate turnover by *Trichinella spiralis* larvae. Encysted muscle larvae were labeled by intra-abdominal injection of infected mice with glycine-2-C^{14} and tryptophan-2-C^{14}. It was previously shown that *Trichinella* muscle larvae incorporated C^{14} when the host was fed a diet containing these C^{14}-labeled amino acids. *In vitro* turnover studies were done on the larvae isolated from the infected host. The C^{14}-labeled larvae were incubated in a Krebs-Ringer-mouse serum medium, the larval samples were obtained periodically to determine turnover rates. Isolated *Trichinella* larvae also incorporate C^{14} when cultured *in vitro* in the presence of C^{14}-labeled amino acids. This procedure is also being used to label isolated muscle larvae and follow subsequent turnover of protein lipids and carbohydrate. Several fractionation procedures are being studied for separating the various components of larval material.

L. V. Hankes and R. D. Stoner

p. Development of Analytical Methods for Glyco-proteins and Observations on Their Occurrence (6120)

Mucoproteins are an important yet neglected biochemical constituent of many mammalian tissues. Methods are lacking for analysis of these compounds and their behavior in health and disease has been only very sketchily outlined. The present study is in part an endeavor to characterize these compounds in a biochemical mixture that their identification may be facilitated.

The structure of orosomucoid, the alpha-1 acid glycoprotein of human plasma has been further investigated with the periodic acid reaction and an enzyme obtained from clostridium perfringens which splits off sialic acid. The data enable one to restrict the number of possible carbohydrate structures and point to specific linkages. A bovine alpha glycoprotein has been investigated with an exchange resin and with the Tiselius apparatus. It appears that the bovine glycoprotein contains galactosamine and glucosamine while the human alpha-1 glycoprotein contains only glucosamine. Further studies are planned with I^{131} in tritium labels on the protein.

REPOSITORY Brookhaven National Lab
COLLECTION MN 189 Med. Dept 1958-61
BOX No

B. A. Popenoe and M. Newman

q. The Specificity of Collagen (6120)

Continuing studies on the mechanism of formation of hydroxylysine, an amino acid which can be used to characterize collagen, have been pointed to elucidation of the mechanism by which lysine is hydroxylated in the formation of collagen. It has now been shown that in rats the hydroxylysine is formed by the addition of an oxygen atom to lysine in the body and that there is no other quantitatively significant source of hydroxylysine in collagen. Even dietary hydroxylysine itself is not incorporated into the collagen. Lysine labelled with C^{14} was used. Data suggest that present collagen may be two or more protein species. This problem will be further studied with labelled structures to determine this point more specifically.

D. D. Van Slyke, F. M. Sinex

4001801

(See continuation sheet)

13, 14, 15. Status as of April 1958 and future programs: (continued)

r. Protein Determination by Light Scattering Methods (6120)

The use of light scattering to characterize a protein is a method giving promise of high sensitivity to small changes. It may prove to be of great usefulness in observing radiation effects. Certain parts of the procedure need development and various native proteins must be satisfactorily characterized before the significance of differences can be determined. During the past period two urinary mucoproteins were studied and hemocyanin from squid. The usefulness of the procedure became evident in comparison studies with the ultracentrifuge. Further development of the method is planned.

M. Maxfield

s. Mechanism of Transfer across Body Membranes (6120)

The mechanism by which substances are transferred across membranes is of the greatest importance in any study of kinetics and specificity. Various membranes must be used as test substances and different approaches tested for productive results. The transfer of sugars from the vascular bed to the brain involves a special mechanism not yet known. Specific mechanisms are being tested by using sugars of various configurations. Once satisfactory hypotheses are developed, it becomes of moment to study the actual mammalian system. For this an isolated brain-lung preparation seems desirable. An effective perfusion pump had to be adapted and in particular a procedure is needed for separation of perfusate from mechanism to obviate clot formation and radioactive contamination of the pump. Further development will include increased speed of preparation, synchronization of perfusion with tissue demands, development of suitable perfusate, adaptation of electroencephalographic recording selection of anesthetic acid and sundry mechanical improvements.

P. G. LePevre and G. F. McGinniss

t. Induction of a State of Receptivity to Foreign Protein (6120)

The problem of tissue transplantation depends upon development of a means whereby reaction to protein of tissue not homologous can be suppressed or minimized to limits compatible with normal function of host and foreign tissues. Mice were studied to determine the effect of neonatal exposure to a foreign protein on behavior at a later age. Crystalline bovine serum albumin was used. At six months of age these treated mice when presumably sensitized to the protein by routine injection and then challenged showed 13 per cent fatalities as compared with 75 per cent for the controls. Further investigation is planned in order to characterize better this modified immunological response and to determine whether or not this phenomenon is identical with that described for acquired tolerance to tissue transplantation.

G. Terres

REPOSITORY Brookhaven Natl Lab
COLLECTION FM189 Med. Dept. 1953-61
BOX No
FOLDER

4001802

PROPOSAL AND AUTHORIZATION
FOR RESEARCH OR DEVELOPMENT

NYO-149

1. Project Title: Special Projects			2. Date: May, 1958
3. Budget Activity No: 6120	4. Budget Item No:	5. Contractor's No:	6. Method and Time of Reporting Progress: Quarterly & Special Reports
7. Contractor: Associated Universities, Inc. Brookhaven National Laboratory		8. Working Location: Upton, New York	9. Contract No: AT-30-2-GEN-16
10. Persons in Charge: Drs. L. E. Farr, R. A. Conard, V. P. Bond, E.P. Cronkite, S.W. Lippincott, R.A. Love.		11. Starting Date: Continuing.	

12. Background:

Enterprises approved by the Medical Department though not necessarily integrated in its endeavor to the same degree as undertakings in substantive investigations and applied research and development are reported in this category.

13, 14, 15. Status as of April 1958 and Future Program.

a. Studies on the Marshallese People Exposed to Fallout Radiation

The annual expedition to the Marshall Islands for the medical examination of the 82 Marshallese people exposed to significant fallout radiation in 1954 was carried out in March , 1957, three years after exposure. The findings of this survey will be published in a joint BNL-Naval Medical Research Institute report. Preparations have been completed for a four-year survey in the Spring of 1958. Hematological and other examinations are contemplated for this survey, which will be made at Rongelap, where these people now live. In addition, a whole-body gamma analyzer will be set up aboard a Navy LST for the purpose of carrying out gamma spectrographic analyses on the exposed and unexposed people on Rongelap. These will be correlated with urinary excretion rates of isotopes. As in the past, the United States Navy is assisting the Atomic Energy Commission, Brookhaven National Laboratory, and agencies of the Department of Defense in this survey. Costs are included in Radiation Effects, General. See table, Determination of Radiation Effects.

R. A. Conard, B. Cannon, Col. A. Lowrey, J. E. Rall, Lt. Col. S. Bach, L. Meyer and E. Carter.

b. Civil Effects Testing Program (See Project Sheet for 6600)

Depth dose measurements in human-sized phantoms were obtained at one nuclear detonation at the Nevada proving ground. These gamma and neutron measurements are now being confirmed and extended. This work was a joint project with the Naval Medical Research Institute. No activity is budgeted for fiscal years 1959 and 1960.

V. P. Bond, E. P. Cronkite, E. E. Stickley.

REPOSITORY Brookhaven National Lab
COLLECTION MB9 Med. Dept. 1958-61
BOX No.
FOLDER

c. Educational Conferences

A stated educational effort of the Department is ~~the organization of at least~~ one special conference each year in conjunction with the Division of Biology and Medicine of the Atomic Energy Commission. These conferences will in general be for educators to examine with active investigators specific responsibilities in the field of atomic medicine. The exact format of the conference will be altered in each case to meet the specific needs of the group concerned.

In February, 1958, such a conference was held to which were invited all of the Chairmen of the University Departments of Pathology in all of the accredited medical schools of the United States and Canada. Over 85% of the invitees attended. The conference was adjudged most successful. Its title was the Responsibility of the Hospital Practice in the Field of Nuclear Energy.

(See continuation sheet)

4001803

13, 14, 15. Status as of April 1958 and Future Program.

c. Educational Conferences (Continued)

It has been assumed that AEC will finance separately any future conferences. Therefore, no cost estimates have been included in FY 1959 and 1960 budget requests.

d. Occupational Medicine Clinic

The largest Laboratory-supported activity of the Medical Department is the Occupational Medicine Clinic. This organization provides to the Laboratory as a whole the necessary industrial medical services for proper operation. The work of the clinic has risen steadily with each year of the Laboratory's operation and the ultimate size of the operation cannot yet be determined. Within two years additional professional and technical personnel will be required. The total number of visits to the occupational medicine clinic during Fiscal 1956 was 9,711, and during Fiscal 1957 was 10,692. Similarly, the total number of x-ray examinations increased from 1,595 to 1,780. Costs are included in the General and Administrative costs of the Laboratory and are distributed as Indirect Expense.

REPOSITORY Brookhaven Natl Lab
COLLECTION 7M 89 Med. Dept. 1950-61
BOX No.
FOLDER

PROPOSAL AND AUTHORIZATION
FOR RESEARCH OR DEVELOPMENT

NYO-149

1. Project Title: Civil Effects Test Program (Nevada Studies)			2. Date: May, 1958
3. Budget Activity No: 6600	4. Budget Item No:	5. Contractor's No:	6. Method and Time of Reporting Progress: Quarterly & Special Reports
7. Contractor: Associated Universities, Inc. Brookhaven National Laboratory		8. Working Location: Upton, New York	9. Contract No: AT-30-2-GEN-16
10. Persons in Charge: B. P. Cronkite, V. P. Bond, E. E. Stickley		11. Starting Date:	

Brookhaven has undertaken spot assignments for the Civil Effects Test Program as appropriate. Work was carried out during the 1957 Nevada Test Series by members of the Medical Department. Their work is reported as part of the Medical Department program (see Special Projects, page no. 6000-30).

No continuing budget request has been submitted since the work is of a spot assignment type and will develop in relationship to a test program.

REPOSITORY Brookhaven Nat'l Lab
COLLECTION 7M189 Med. Dept. 1950-61
BOX No.
FOLDER

4001805