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RENEWAL RESEARCH PROPOSAL

for

EVALUATION OF THE ABSORBED DOSE FROM THE DIAGNOSTIC USE OF RADIOPHARMACEUTICALS

Submitted to

U. S. Atomic Energy Commission

Washington, D. C.

Proposed by

Edward M. Smith, D.Sc.

Division of Nuclear Medicine, Department of Radiology

University of Miami School of Medicine: Miami, Florida

August 1, 1969

Authentication

9/17/69
Date

Eugene E. Cohen
Vice-President for Financial Affairs
and Treasurer, University of Miami

8/6/69
Date

Edward M. Smith, D.Sc.
Assistant Professor of Radiology
University of Miami School of Medicine

The investigations encompassed by this application have been or will be approved by the Committee of Associates of the Investigator(s) in accordance with this institution's assurance on clinical research dated October 24, 1966.

1. Title of Project

Evaluation of the Absorbed Dose from the Diagnostic Use of Radiopharmaceuticals.

2. Institution

University of Miami School of Medicine, Department of Radiology, Division of Nuclear Medicine at:
a) The Mount Sinai Hospital, 4200 Alton Road, Miami Beach, Fla. 33142
b) Jackson Memorial Hospital, P.O. Box 875 Biscayne Annex, Miami, Fla. 33152

3. Project Abstract:

The evaluation of the absorbed dose received by a patient resulting from a diagnostic procedure employing a radiopharmaceutical is essential if the maximum benefit is to be derived by the patient. Even when the most sensitive and sophisticated instrumentation is used, the quantity of activity administered to the patient limits the quality of the diagnostic information extractable from the study. To obtain the necessary data to calculate the absorbed dose, the tissue distribution of the radionuclide incorporated into the radiopharmaceutical will be studied "in vivo", and the activity concentration in tissue specimens and body fluids will be measured. The physical parameters required for absorbed dose calculations will be experimentally determined, and correlated with theoretically calculated values. The results of these investigations will yield a reliable estimate of the absorbed dose received by various body tissues from new radiopharmaceuticals as they are introduced into use, as well as from the routine radiopharmaceuticals in current use. In addition, the interrelationship of the radiopharmaceuticals, radionuclides and organ visualization system on the resultant absorbed dose to a patient having a clinical study versus the clinical information that may be obtained from this study is being evaluated. These types of studies are essential if a given rad dose to a patient is to have any meaningful significance.

4. Scientific Background

The scientific background for this renewal research proposal was presented in the original research proposal dated December 1, 1966.

5. Scientific Scope

A. Objectives

(1) The collection of clinical data yielding information on the tissue distribution with respect to time of the radionuclide incorporated into the radiopharmaceutical under study.

(2) Experimental verification of the physical parameters such as absorbed fractions and energy buildup factors required in the absorbed dose calcuations.

(3) The actual absorbed dose calculations and the dissemination of the calculated values for the absorbed dose.

(4) Investigations on the interrelationship of radiopharmaceuticals, radionuclides and organ visualization systems on the resultant absorbed dose to a patient having a clinical study versus the clinical information that may be obtained from this study.

B. Relationship of proposed research to present knowledge and comparable work in progress elsewhere

This material was presented in the original research proposal dated December 1, 1966.

C. General Plan for the Work

The outlined presented in this section is for the third year of this project.

(1) Radiopharmaceuticals to be studied

(a) Work will be completed on the radiopharmaceuticals outlined in the -01 and -02 year of this research proposal

(b) The tissue distribution data for Hippuran labeled with Iodine-123 and I-131 will be collected. In addition, the literature will be searched for any information on this radiopharmaceutical.

(2) Collection of tissue distribution data

The methods to be employed in the collection of tissue distribution data were presented in the original research proposal dated December 1, 1966. These methods will be varied as required for the particular radiopharmaceutical under study

(3) Experimental determination of physical parameters required in absorbed dose calculations

The methods to be employed in these studies were described in our original research proposal. In addition, we will study the potential use of the thermoluminescent material $CaSO_4$(Dy). This material may prove sufficiently useful in the dosimetry of high energy (> 200 keV) photon emitters since it should have increased sensitivity over Lithium fluoride.

(4) Comparison of the absorbed dose versus the information content of a a clinical study

This work was initiated during the first year of our contract and we are continuing along these original lines, however, we are incorporating an additional parameter, the system modulation transfer system. This will be determined by computing the modulation transfer function for the total system using the film densitometry method as described by Mozley (Mozley, J. M.: Quantitative Comparison of Radioisotopes Scanning and Scanners in Brain Tumor Imaging-Effects of Modulation Transfer Cuntion and Quantum Fluctuation. J. Nuc. Med. 10:359 (1969).

6. Scientific Personnel

A. Edward M. Smith, D.Sc., Principal Investigator

This information was provided in the original research proposal dated December 1, 1966. A minimum of 15 per cent of Dr. Smith's time will be devoted to this project.

B. Albert J. Gilson, M.D., Co-Investigator

This information was provided along with my letter dated May 15, 1967, to Dr. Robert Wood. A minimum of 20 per cent of Dr. Gilson's time will be devoted to this project.

C. Peter J. Kenny, Co-Investigator

Education

[redacted]

Professional Experience:

1. Department of Posts and Telegraphs; Dublin, Ireland (1952-1953); Communications Engineer
2. Department of Industry and Commerce, Dublin, Ireland (1953-54) Meteriological Officer.
3. St. Anne's Hospital, Dublin, Ireland (1953-1958) Physicist
4. University College, Dublin, Ireland (1955-1958) Lecturer in Radiological Physics.
5. Sloan-Kettering Institute for Cancer Research, New York, (1958-1961) Research Assistant

Professional Experience - Kenny - (continued)

6. Sloan-Kettering Institute, New York, New York (1958-1961) Research Associate in Biophysics.
7. Cornell University Medical College Graduate School (1961-1969) Instructor in Biophysics
8. University of Miami School of Medicine, Miami, Florida (1969-) Assistant Professor of Radiology, Division of Nuclear Medicine

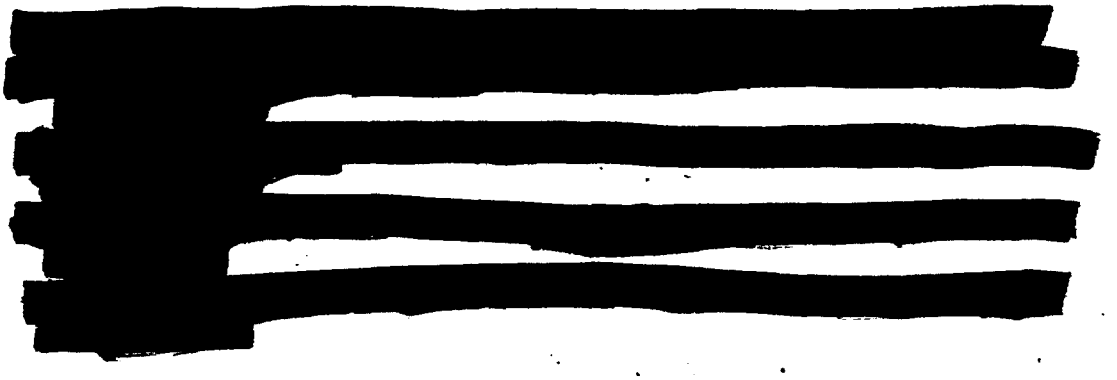
Publications

Twenty-six publications in quantitative organ visualization, metabolic studies and other related areas in Nuclear Medicine.

A minimum of 25 per cent of Peter Kenny's time will be devoted to this project.

D. Homer B. Hupf, Ph. D., Radiopharmacist

Education



Professional Experience

1. Abbott Laboratories (June, 1955 - September, 1957) Sales Representative
2. Abbott Radiopharmaceutical Division (June, 1959 - June, 1965)
3. Oak Ridge National Laboratory (June, 1965 - July, 1969) Research Radiochemist
4. University of Miami School of Medicine; Miami, Florida (1969-) Assistant Professor of Radiology

A minimum of 20 per cent of Homer Hupf's time will be devoted to this project.

7. Other Personnel

A. Pablo Larrea, B.S., Systems Programmer. This individual will devote 10 per cent of his time to this project in the area of programming and data processing.

B. Bea Weaver, B.S., Research Technologist. This individual will devote 100 per cent of her time to this project.

C. Marcine Parker, Medical Secretary. This individual will devote 25 per cent of her time to this project.

8. Other Financial Assistance

In addition to U.S.A.E.C. funds, the personnel involved in this project will be supported by University of Miami, Mount Sinai Hospital or Dade County funds.

9. Premises, Facilities, Equipment and Materials to be Furnished by the Contractor

The facilities and equipment described in the original research proposal are still in use. Additional equipment and facilities have been made available to us at Mount Sinai Hospital, which is a University affiliated hospital. These facilities include an Anger Camera which will be connected on a real-time basis to a 2116B Hewlett-Packard computer as well as additional clinical and research laboratory space.

AEC Contract No. AT-(40-1) 3734
Dr. Edward M. Smith, Radiology
University of Miami
10/15/69 - 10/14/70

10. Budget

1. Salaries and Wages

	Name	Position	Per Cent of Effort Funded	Requested from AEC	University of Miami Contribution
a.	Edward M. Smith, D.Sc. Asst. Prof. of Radilogy	Principal Investigator	15	$3,000	-0-
b.	Albert J. Gilson, M.D. Assoc. Prof. of Radiology Dir., Div. of Nuc. Medicine	Co-Investigator		-0-	-0-
c.	Peter J. Kenny, M.S. Asst. Prof. of Radiology	Co-Investigator	25	$5,000*	-0-
d.	Homer B. Hupf, Ph.D. Asst. Prof. of Radiology	Radiopharmacist	20	$1,700*	-0-
e.	Pablo A. Larrea, B.S.	Systems Programmer	10	$1,500	-0-
f.	Bea Weaver, B.S.	Research Technologist	100	$4,000	-0-
g.	Retirement at 5.5%			$ 836	
			Total	$16,036	-0-
	Employee Benefits F.I.C.A. (4.8) *Group Insurance (0.7)			222 84	
				306	

2. Supplies		
a. Radionuclides and radiopharmaceuticals	$1,300	-0-
b. Glassware and Chemical Supplies	$ 500	-0-
c. Thermoluminescent Dosimetry Material	$1,200	-0-
d. Phantom Material	$1,000	-0-
e. Electronic Components	$1,000	-0-
f. Office Supplies, Reference Materials, etc.	$ 200	-0-
Total	$5,200	-0-
3. Equipment		
Film Densitometer and Micromanipulators	$1,000	-0-
Collimators	$2,100	-0-
Nuclear Instrumentation	-0-	$2,000
	$3,100	$2,000
4. Publications and Communications	$ 750	-0-
5. Travel	$ 750	-0-
6. Other		
Computer time	$2,000	-0-
Subjects for Study and Travel for Subjects (20 at $100)	$2,000	-0-
	$4,000	$2,000
Total Direct Costs	$30,142	$2,000
7. Indirect Cost at ~~46~~ 49 ** salaries/retirement	~~7,858~~ 7,377	-0-
Total Project Costs	~~$38,000~~	$2,000
Second year funding AEC funds requested	~~$38,000~~ 37,519 (95%)	
Univ. of Miami contribution	2,000 (5%)	
	~~$40,000~~ (100%) 39,519	

** University of Miami Medical School at ~~46~~ 49 salaries - DCAA Provisional

Justification and Description of Items in Third Year Budget

1. Film Densitometer and Micromanipulators - These items of equipment will be used in the measurement of the modulation transfer function, and are not available in our laboratory.

2. Collimators - The 14 collimators will be used on the Multifunction Digital Research Scanning System. These will be specially designed for this system to perform the isoresponse (constant response through a patient) total body distribution studies.

3. Subjects for study and travel for subjects:

   This item in our budget is so that we may reimburse subjects who participate in our body distribution studies for their expenses as well as provide them with a small honorarium. It is anticipated that these subjects will spend one to three days on the Metabolic Ward of the National Children's Cardiac Hospital.

September 17, 1969
Modification No. 1

UNIVERSITY OF MIAMI
Coral Gables, Fla.

U.S. Atomic Energy Commission, Research and Development Division
Post Office Box E, Oak Ridge, Tennessee

FINANCIAL STATEMENT- Contract AEC AT 40-1-3734 Modification 1 — Period 10/15/68 - 10/14/69

	Budget	Expenditures thru 7/31/69	Estimated Expenditures thru 10/14/69	Total Estimated Expenditures	Estimated Balance 10/14/69
Salaries & Wages	$ 20,800.00	$ 8,525.00	$ 10,333.00	$ 18,858.00	$ 1,942.00
Employee Benefits	2,172.00	863.00	914.00	1,777.00	395.00
Materials and Supplies	7,200.00	270.00	2,730.00	3,000.00	4,200.00
Equipment	3,500.00	1,906.00	12,394.00	14,300.00	(10,800.00)
Publications & Comm.	500.00	40.00	210.00	250.00	250.00
Travel	500.00	344.00	156.00	500.00	00
Other	2,000.00	791.00	209.00	1,000.00	1,000.00
Services	2,600.00	507.00	593.00	1,100.00	1,500.00
Overhead (49%-S&W)	10,753.00	4,177.00	5,063.00	9,240.00	1,513.00
Total Estimated Project Cost	$ 50,025.00	$ 17,423.00	$ 32,602.00	$ 50,025.00	$ 00
University of Miami 28%	$ 14,095.00	$ 4,878.00	$ 9,217.00	$ 14,095.00	
AEC 72%	$ 35,930.00	$ 12,545.00	$ 23,385.00	$ 35,930.00	

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PUBLICATION BY AEC AUTHORIZED ☐

NOTICE OF RESEARCH PROJECT
SCIENCE INFORMATION EXCHANGE
SMITHSONIAN INSTITUTION

U.S. ATOMIC ENERGY COMMISSION

SIE NO.

AEC CONTRACT NO.
AT-(40-1)-3734

SUPPORTING DIV. OR OFFICE:

NAME & ADDRESS OF CONTRACTOR OR INSTITUTION: (State the division, department, or professional school, medical, graduate or other, with which this project should be identified.)

Division of Nuclear Medicine; Department of Radiology; University of Miami School of Medicine; Miami, Florida

TITLE OF PROJECT:

EVALUATION OF THE ABSORBED DOSE FROM THE DIAGNOSTIC USE OF RADIOPHARMACEUTICALS

NAMES, DEPARTMENT, AND OFFICIAL TITLES OF PRINCIPAL INVESTIGATORS AND OTHER PROFESSIONAL SCIENTIFIC PERSONNEL: (not including graduate students) engaged on the project, and fraction of man-year devoted to the project by each person.

Edward M. Smith, D.Sc., Asst. Prof. of Radiology	15 per cent
Albert J. Gilson, M.D., Assoc. Prof. of Radiology	20 per cent
Peter J. Kenny, M.S., Asst. Prof. of Radiology	25 per cent
Homer B. Hupf, Ph.D., Asst. Prof. of Radiology	20 per cent
Pablo Larrea, B.S., Research Assoc.	10 per cent

NO. OF GRADUATE STUDENTS ON PROJECT: _____ NO. OF GRADUATE STUDENT MAN-YEARS: _____

SUMMARY OF PROPOSED WORK: (200-300 words, omit Confidential Data). Summaries are exchanged with government and private agencies supporting research, are supplied to investigaters upon request, and may be published in AEC documents. Make summaries substantive, giving initially and for each annual revision the following: OBJECTIVE; SCIENTIFIC BACKGROUND FOR STUDY; PROPOSED PROCEDURE; TEST OBJECTS AND AGENTS.

The evaluation of the absorbed dose received by a patient resulting from a diagnostic procedure employing a radiopharmaceutical is essential if the maximum benefit is to be derived by the patient. To obtain the necessary data to calculate the absorbed dose, the tissue distribution of the radionuclide incorporated into the radiopharmaceutical will be studied "in vivo", and the activity concentration in tissue specimens and body fluids will be measured. The physical parameters required for absorbed dose calculations will be experimentally determined, and correlated with theoretically calculated values. The results of these investigations will yield a reliable estimate of the absorbed dose received by various body tissues from new radiopharmaceuticals as they are introduced into use, as well as from the routine radiopharmaceuticals in current use. In addition, the interrelationship of the radiopharmaceuticals, radionuclides and organ visualization system on the resultant absorbed dose to a patient having a clinical study versus the clinical information that may be obtained from this study is being evaluated.

RESULTS TO DATE:

	PROGRAM CATEGORY NO.
BUDGET	
PRIMARY	
SECONDARY	

Edward M. Smith, D.Sc.
Signature of Principal Investigator

DATE: 6/4/65

INVESTIGATOR – DO NOT USE THIS SPACE

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