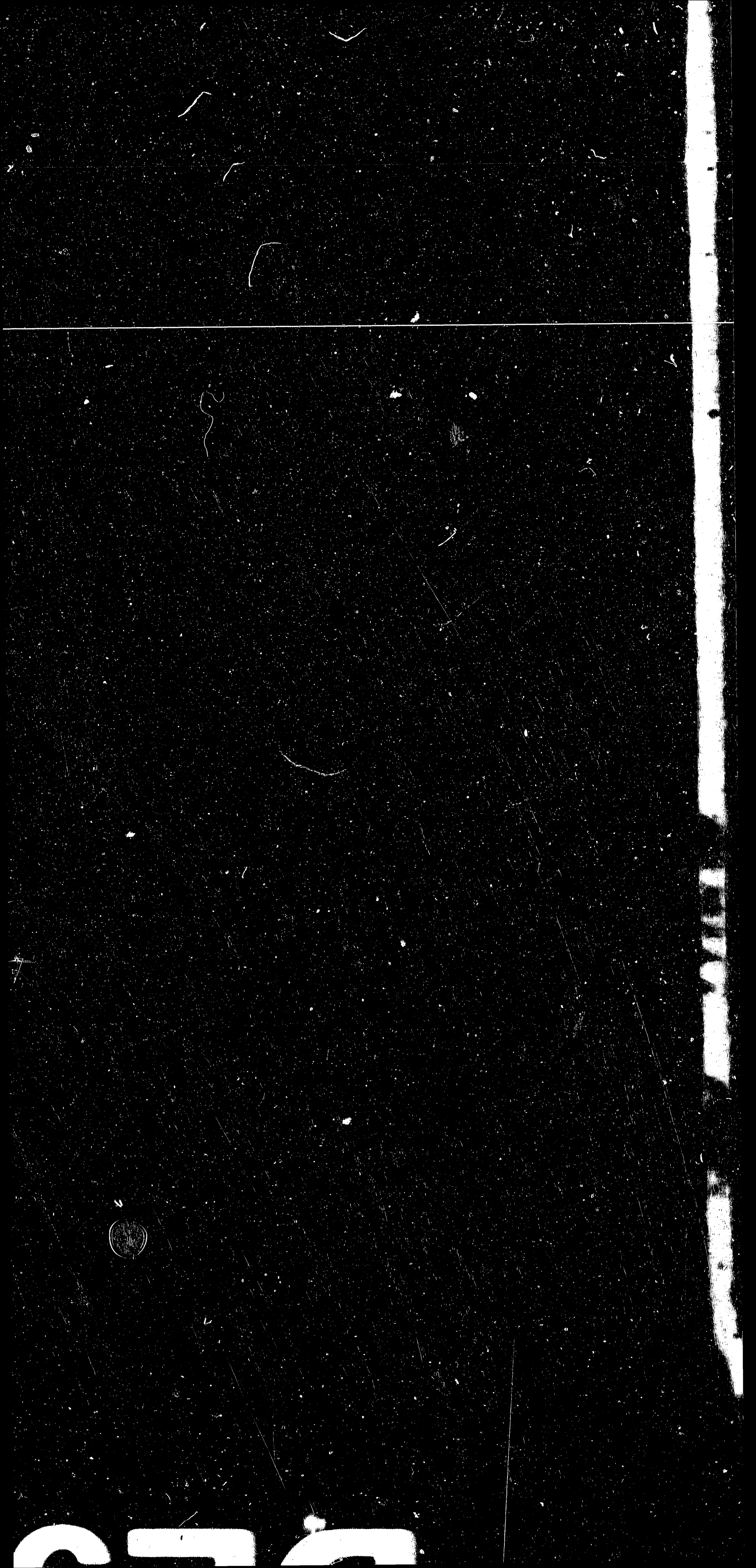

ORNL/FTR--3749

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OAK RIDGE NATIONAL LABORATORY

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ORNL

FOREIGN TRIP REPORT

ORNL/FTR-3749

DATE: October 3, 1990

SUBJECT: Report of Foreign Travel of Furn F. Knapp, Jr., Group Leader, Nuclear Medicine Group, Health and Safety Research Division

TO: Alvin W. Trivelpiece

FROM: Furn F. Knapp, Jr.

To visit the University of Bonn, Bonn, West Germany (9/8-11/90, 9/16-17/90), the University of Liege, Liege, Belgium (9/12-13/90), and the University of Metz, Metz, France (9/14-15/90) to coordinate continuing collaborations with colleagues at these institutions.

SITES VISITED:

9/8-9/11/90 9/16-17/90	University of Bonn, Bonn, West Germany	J. Kropp
9/12-13/90	University of Liege, Liege, Belgium	C. Brihaye M. Guillaume
9/14-15/90	University of Metz, Metz, France	G. Kirsch

ABSTRACT: The traveler visited the Clinic for Nuclear Medicine at the University of Bonn, West Germany, to review, organize, and plan collaborative studies. He also met with the editorial board of the journal *NucCompact—European/American Communications in Nuclear Medicine*, on which he serves as U.S. editor. He also visited colleagues at the Cyclotron Research Center (CRC) at the University of Liege, Belgium, to coordinate clinical applications of the ultrashort-lived iridium-191m radionuclide obtained from the osmium-190/iridium-191m generator system. The traveler planned and coordinated continuing collaboration with colleagues at the CRC for further applications of this generator system. He also visited the University of Metz, Metz, France, to organize a three-center project for the synthesis and evaluation of various receptor-specific cerebral imaging agents, involving the Oak Ridge National Laboratory (ORNL), CRC, and the University of Metz.

CLINIC FOR NUCLEAR MEDICINE, UNIVERSITY OF BONN
BONN, WEST GERMANY

The traveler visited the University of Bonn to review, coordinate, and plan various collaborative studies involving agents developed at the Oak Ridge National Laboratory (ORNL) and to meet with the editorial board of the journal, *NucCompact/European-American Communications in Nuclear Medicine*. He has served as one of the American editors since 1989 and was recently appointed as the coordinating editor for a special issue of the journal encompassing the 18 papers which were presented at the Second Amsterdam International Symposium on Radioiodinated Fatty Acids. Final editing of the papers was completed and the final package was prepared for the publisher, GIT Verlag, for publication in the October 1990 issue.

Collaborative studies in Bonn are expected to be initiated in November 1990 involving clinical evaluation of the iodine-123-labeled "BMIPP" fatty acid cardiac imaging agent [15-(p-iodophenyl)-3-R,S-methylpentadecanoic acid] developed by the traveler and his colleagues at ORNL. In addition, several collaborative projects utilizing a Langendorff isolated rat heart model are continuing to determine the metabolic fate of BMIPP, its incorporation into endogenous myocardial lipids, and the various physiological factors affecting its myocardial uptake, metabolism, and release. These studies in Bonn are being directed by Dr. J. Kropp in collaboration with medical student projects and are an extension of the work he conducted in conjunction with the traveler while completing a six-month guest assignment at ORNL. In Bonn, the data were analyzed and discussed, and the next series of experiments were planned for the beginning of the fall term in Bonn in October 1990. The results of these studies will continue to provide an important foundation for a better understanding of the behavior of the BMIPP myocardial imaging agent in human studies.

The traveler recently received the Senior American Scientist Award from the Alexander Von Humbolt Foundation from West Germany which will support a twelve-month stay at the Clinic for Nuclear Medicine in Bonn during the 1991-1992 period. While in Bonn, discussions also focussed on the planning and coordination of the experiments which will be conducted by the traveler in Bonn. The research will center on the development of animal and clinical protocols for the evaluation of agents developed by the traveler and his colleagues at ORNL involving, in addition to the cardiac imaging agents described earlier, radiolabeling and evaluation of the tungsten-188/rhenium-188 and osmium-194/iridium-194 generator systems.

The traveler also completed final drafts of several papers for submission for publication. These papers included work conducted in collaboration with Dr. Kropp while the traveler was on official offsite assignment at the University of Bonn during the 1985-1986 period and work conducted by Dr. Kropp in conjunction with the traveler and his colleagues while on guest assignment at ORNL during the July 1988-February 1989 period. The titles of the papers are:

Kropp, J., Reske, S. N., Knapp, F. F., Jr., and Biersack, H.-J., "Evaluation of the Preservation of Myocardial Viability by SPECT Imaging with [Iodine-123]-IPPA Before and After Coronary Bypass Surgery," for submission to the European Journal of Nuclear Medicine.

Kropp, J., Ambrose, K. R., Knapp, F. F., Jr., Nissen, H. P., and Biersack, H.-J., "Evaluation of the Incorporation of the Radioiodinated IPPA and BMIPP Fatty Acid Analogues into Complex Lipids from Isolated Rat Hearts by High-Performance Liquid Chromatographic Analysis (HPLC)," for submission to Chromatographia.

CYCLOTRON RESEARCH CENTER (CRC), UNIVERSITY OF LIEGE LIEGE, BELGIUM

The traveler visited the University of Liege to discuss and coordinate on-going collaborative clinical studies with the ultrashort-lived iridium-191m radioisotope which is available from the osmium-191/iridium-191m radionuclide generator system developed at ORNL. Osmium-191 production and radionuclide generator fabrication were temporarily interrupted during the last 18-month period both at ORNL and the University of Liege due to the unavailability of production facilities and the hiatus encountered during the design and testing of new processing equipment. Generator fabrication has resumed in Liege, and collaborative studies coordinated between Liege (Dr. C. Brihaye) and the traveler with several institutions in Germany can now proceed. These institutions include the Departments of Nuclear Medicine at the Universities of Bonn (Dr. J. Kropp and Dr. H.-J. Biersack), Passau (Dr. N. Schad), and Mainz (Dr. A. Bockisch), where approval from the institutional committees has been received for patient studies. Studies in Passau and Mainz will focus on the use of the multicrystal camera systems. The referring cardiologists at these institutions are anxious to use the iridium-191 radioisotope for the evaluation of cardiac ejection fraction and wall-motion studies in various patient groups in conjunction with the iodine-123-labeled fatty acids. These dual isotope studies will uniquely provide both functional and metabolic data in one study period, which precludes positioning and physiological changes which inherently occur when data obtained from two different study periods are compared. The traveler also met with collaborators in Liege to coordinate the design and development of new serotonin receptor agents for cerebral imaging involving the synthesis of analogues being pursued at ORNL. Several new agents have been developed by Janseen, Inc., a pharmaceutical company in Belgium, and collaborators in Liege have unique access to several analogues and intermediates required for the syntheses being developed at ORNL.

CHEMISTRY DEPARTMENT, UNIVERSITY OF METZ METZ, FRANCE

While in Liege, the traveler was invited to visit Dr. G. Kirsch, professor of organic chemistry at the University of Metz, to discuss several collaborative projects. While on sabbatical leave at ORNL for two six-month periods in 1981 and 1987, Professor Kirsch

had worked with the traveler, and a productive collaboration has continued since that time. The traveler organized a three-center project involving ORNL, Liege (*vide ante*), and Metz for the synthesis and evaluation of various receptor-specific cerebral imaging agents. Professor Kirsch and his colleagues are expected to play a key role in synthesizing and providing various key intermediates and starting materials. These will be used at ORNL for fabrication of the intact pharmacologically active agents, for radiolabeling with iodine-125 and iodine-123, and for evaluation of the radioiodinated analogues in animal models. Kits for the preparation of the most promising new agents will also be developed. Collaborators in Liege have the capability of further developing the radiopharmaceutical preparation of these agents and obtaining approval for initial volunteer and patient evaluation in conjunction with the clinical center in Liege.

SUMMARY AND RECOMMENDATIONS

The traveler visited colleagues in Bonn, Liege, and Metz to coordinate collaborative projects on the development of a variety of radiopharmaceuticals for applications in nuclear cardiology. Because of the opportunity for timely introduction of new radiopharmaceuticals for clinical studies in Europe, the ORNL Nuclear Medicine Program has been very successful over the last several years in introducing new agents developed under the Department of Energy (DOE) support at ORNL into clinical studies at various institutions in Europe. Such successful interaction with investigators at clinical and research institutions in Europe provides an effective mechanism for initiation of clinical testing of agents developed under DOE funding and will continue to provide the foundation for approval and subsequent introduction of these agents into the United States. These successful programs clearly illustrate the effectiveness of international collaboration and the successful leadership provided by the traveler in the transfer of technology from the laboratory to the clinic.

ITINERARY

1990

9/8-11	Travel from Oak Ridge, Tennessee, to Bonn, West Germany
9/12-13	Liege, Belgium
9/14-15	Metz, France
9/16-17	Travel from Bonn, West Germany, to Oak Ridge, Tennessee

PERSONS CONTACTED

Bonn, West Germany

B. Ammari, M.D.
H.-J. B ersack, M.D.
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B. Bo elte, B.S.
B. Briele, M.D.
F. Gruenwald, M.D.
R. Knoop, Ph.D.
J. Kropp, M.D.

Liege, Belgium

C. Brihaye, Ph.D.
R. Cantinaue, Ph.D.
C. Delandshere, M.D.
M. Guillaume, Ph.D.
C. Lamiere, Ph.D.

Metz, France

G. Kirsch, Ph.D.

COVER SHEET
FOR TRIP REPORTS SUBMITTED TO THE OFFICE OF ENERGY RESEARCH

Destination(s) and Dates for Which Trip Report Being Submitted: Bonn, FRG (9/8-11/90, 9/16-17/90)
Liege, Belgium (9/12-13/90)
Metz, France (9/14-15/90)

Name of Traveler: Furn F. Knapp, Jr.

Joint Trip Report ☐ Yes
☒ No

If so, Name of Other Traveler(s): _____

_____

DISCLAIMER

-END-

DATE FILMED

10 / 31 / 90