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Nuclear Medicine Progress Report for Quarter Ending December 31, 1985

F. F. Knapp, Jr.
K. R. Ambrose
M. M. Goodman
P. C. Srivastava

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Work sponsored by
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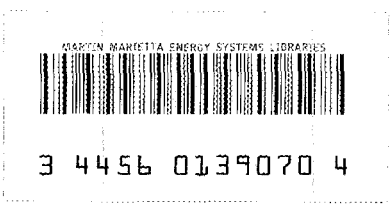

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CONTENTS

SUMMARY

The first clinical results with the new iodine-123-labeled methyl-branched fatty acid, 15-(p-iodophenyl)-3-R,S-methylpentadecanoic acid (BMIPP), are described in this report. These studies were conducted at the University of Vienna (Dr. R. Dudczak). A series of 19 patients were evaluated with [I-123]BMIPP by planar imaging studies. The groups consisted of patients with normal coronary arteries, and patients with single-, double-, and triple-vessel disease. The goal of these studies was to evaluate [I-123]BMIPP for the first time in patients, to analyze regional uptake and wash-out properties, and to compare the results of BMIPP with the straight-chain analogue, [I-123]IPP. As expected BMIPP showed delayed myocardial clearance, further demonstrated the apparent inhibitory effect of methyl-substitution on β-oxidation. The results of wash-out kinetic measurements are described in this report. An important finding was that, in addition to good myocardial images, abnormal (reduced) elimination was observed in patients with coronary artery disease (CAD) which is not observed with other agents such as IPP. Thus, the additional information obtained with BMIPP may be of useful prognostic value.

The results of methyl-branching on the subcellular distribution and incorporation into lipid pools of rat hearts using 3-monomethyl (BMIVN) and 3,3-dimethyl (DMIVN) analogues of 19-iodo-18-nonadecenoic acid (IVN) are also described in this report. Branching appeared to result in a higher association of radioactivity with the microsomal cell fractions when the subcellular distributions of DMIVN were compared to that for IVN. Branching also appeared to inhibit β-oxidation within the myocardial cell resulting in an increased conversion to storage (triglyceride and polar lipid) with the branched analogues (DMIVN and BMIVN).

During this report period seven shipments of osmium-191 were made to collaborators for Os-191/Ir-191m generator fabrication. Clinical studies in the bolus mode are now in progress in Belgium (Liege) and Germany (Bonn) and preclinical studies with continuous infusion are in progress in Boston (Massachusetts General Hospital) where generators fabricated at ORNL are supplied each month. Two shipments of Cu-64 were made to the Oak Ridge Associated Universities and four shipments of Pt-195m-cis-dichlorodiammineplatinum(II) (cis-DDP) were made on a cost-recovery basis through the ORNL Isotopes Distribution Office.

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EVALUATION OF REGIONAL MYOCARDIAL UPTAKE AND CLEARANCE IN CLINICAL STUDIES WITH NEW ^{123}I-LABELED β-METHYL FATTY ACID

Preliminary studies with iodine-123-15-(p-iodophenyl)-3-R,S-methyl-pentadecanoic acid, [^{123}I]BMIPP, have recently been conducted in nineteen patients at the Department of Nuclear Medicine, University Clinic, in Vienna, Austria (R. Dudczak, M.D., and colleagues). Patients were evaluated who underwent coronary angiography because of the onset of chest pain. These represent the first human studies conducted with this new structurally-modified fatty acid, in which methyl-branching was introduced to interfere with degradation by β-oxidation to delay myocardial clearance. Thallium-201 perfusion images dipyridamol stress (pharmacological vasodilitation) and 4 h redistribution scintigrams were also obtained. The myocardial scintigraphy was performed with 2-4 mCi of [^{123}I]BMIPP in patients who were fasted for at least 10 h after a light breakfast. Background corrected myocardial time activity curves were generated, using the vena cava region as the representative of blood background. In some patients plasma samples were also analyzed to evaluate the presence of possible BMIPP catabolic products.

The heart was clearly visualized in patients with normal coronary arteries (Fig. 1). As described earlier for animal studies (ORNL/TM-9343), pronounced heart uptake and good heart:blood ratios with little interference from the blood pool was observed. Several patients who had angiographically confirmed single-vessel, double-vessel or triple-vessel coronary artery disease (CAD) were also studied with [^{123}I]BMIPP. A typical scintiphoto of a patient with triple-vesel disease is shown in Fig. 2. In such gamma camera images reduced BMIPP uptake is clearly observed in the posterolateral posterior and in the anterior myocardial wall. The thyroid was not visualized as shown in the image of the neck region. Since thyroid-blocking agents were not administered, lack of thyroid image demonstrates the low in vivo deiodination of BMIPP.

The markedly reduced BMIPP uptake in the infarcted region (inferior) and in the postlateral wall of a patient with triple-vessel disease is shown in Fig. 3. In a number of such patients defects in BMIPP uptake were clearly seen in infarcted as well as in noninfarcted regions supplied

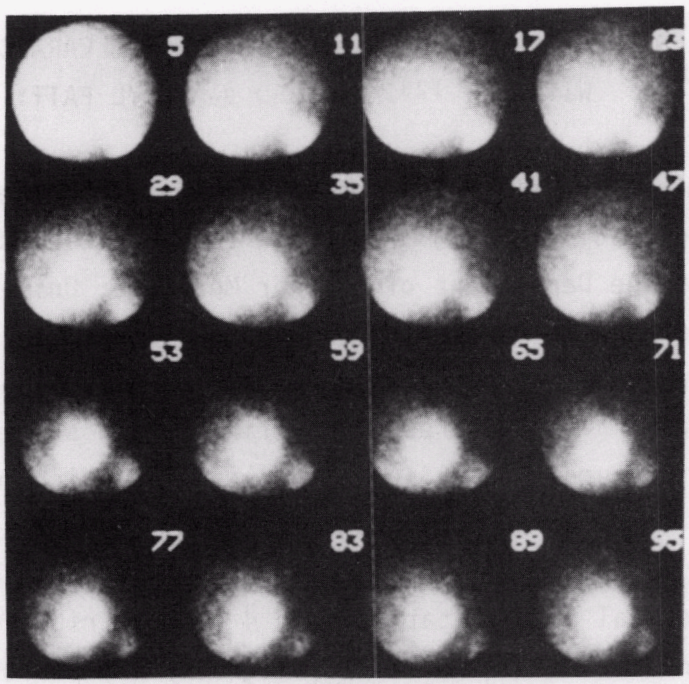

Fig. 1. Serial scintigrams after i.v. injection of 3 mCi [^{123}I]BMIPP in a patient with normal coronary arteries. Each image represents the sum of five 1 min frames. (Courtesy, R. Dudczak, M.D., University of Vienna, Austria).

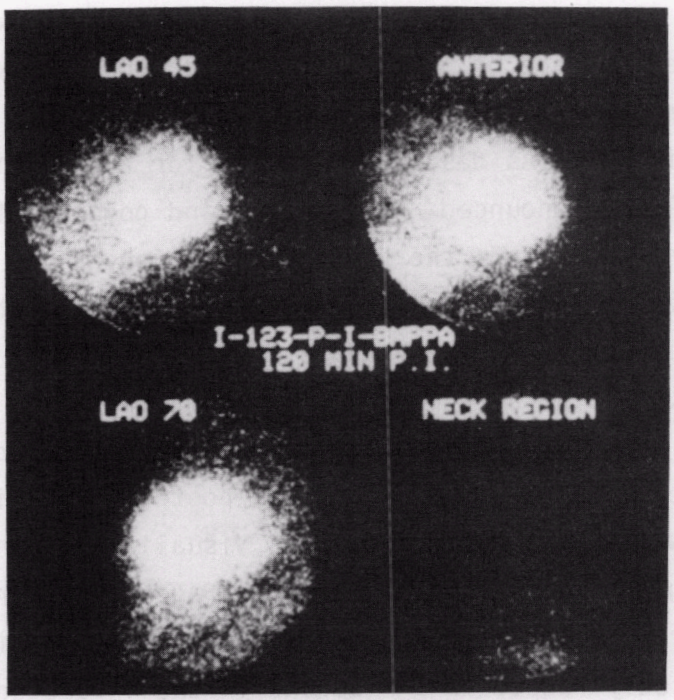

Fig. 2. Uncorrected scintiphotos in a patient with three vessel disease obtained 2 h after intravenous injection of 3 mCi [^{123}I]BMIPP. No premedication was given. (Courtesy, R. Dudczak, M.D., University of Vienna, Austria).

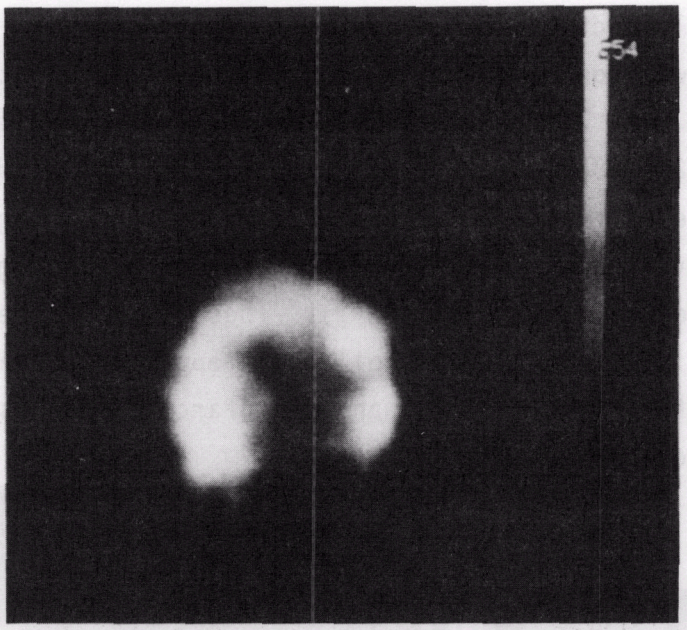

Fig. 3. Interpolated background corrected image from a patient with triple-vessel disease after injection of [^{123}I]BMIPP. (Courtesy, R. Dudczak, M.D., University of Vienna, Austria).

by stenosed vessels.

The evaluation of global myocardial time activity curves (e.g. regional myocardial "washout") complemented the visual interpretation of the gamma camera images. The background corrected time activity curves from heart and liver after intravenous administration of 3 mCi [^{123}I]BMIPP demonstrated a faster elimination from the liver than from the heart (Fig. 4). This different behaviour in organ washout of BMIPP was seen in all 19 patients studied. Obviously the metabolic fate of BMIPP is different in the heart than in the liver, and this observation will now be explored in more detail in animal models. In particular, the use of isolated heart models, which will circumvent the interference of blood levels and myocardial extraction of, for instance, hepatic metabolites, will give a more clear understanding of the myocardial metabolism and fate of this interesting new agent. These studies are in progress at the Institute for Clinical and Experimental Nuclear Medicine in Bonn, Federal Republic of Germany.

The elimination behaviour of BMIPP from those patients fitted a biexponential function ($T_{1/2}$ 11.4±4.4 min and 91.5±36.8 min). However, the elimination was monoexponential from the heart in eight patients (218.8±102.5 min) and biexponential in the remaining 11 patients (13.8±4.1 min and 187.2±49.8 min). Evaluation of "regional" elimination parameters indicated the half-time was prolonged from diseased regions as compared to the respective normal perfused region or the "best" region in patients with three vessel disease (Table 1). These findings were seen from regions with reduced (n=6) as well as an apparent normal BMIPP uptake, including both infarcted (n=5) and noninfarcted regions but supplied by stenosed coronary vessels (n=6).

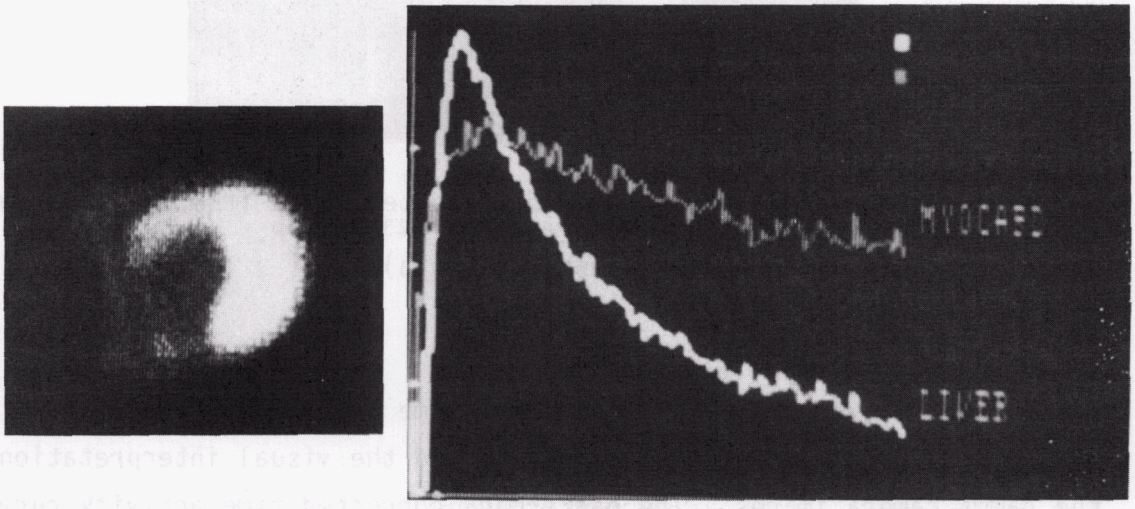

Fig. 4. Comparison of the time-activity curves for heart and liver wash-out from the [^{123}I]BMIPP study of the patient shown in Fig. 3. (Total study period, 100 min).

In two patients with a biexponential behaviour in the normal region, the decline in myocardial activity was monoexponential in a diseased region. These included the "chronic" ischemic region in a patient with single vessel disease and an infarcted region in a patient with double vessel disease. A typical background (vena cava region) corrected myocardial time activity curve fitting a biexponential function is shown

Table 1. Myocardial elimination half-time after intravenous injection of [^{123}I]BMIPP in six patients with coronary artery disease showing a monoexponential time activity curve.

Region	T/2, Minutes
Normal (N=6)	150.5 ± 45.6 111 - 230
"Chronic Ischemic" Region (N=6)	234.8 ± 107.1 140 - 407
"Acute Ischemic" (Infarcted) (N=5)	417.6 ± 352 165 - 990

for a patient with three vessel disease and previous myocardial infarction in Fig. 5. Gamma camera images of this patient showed a reduced BMIPP uptake in the septal and inferior (infarcted) wall. These data demonstrate a delayed washout of BMIPP from the septal region compared to the posterolateral wall. The regional myocardial elimination parameters

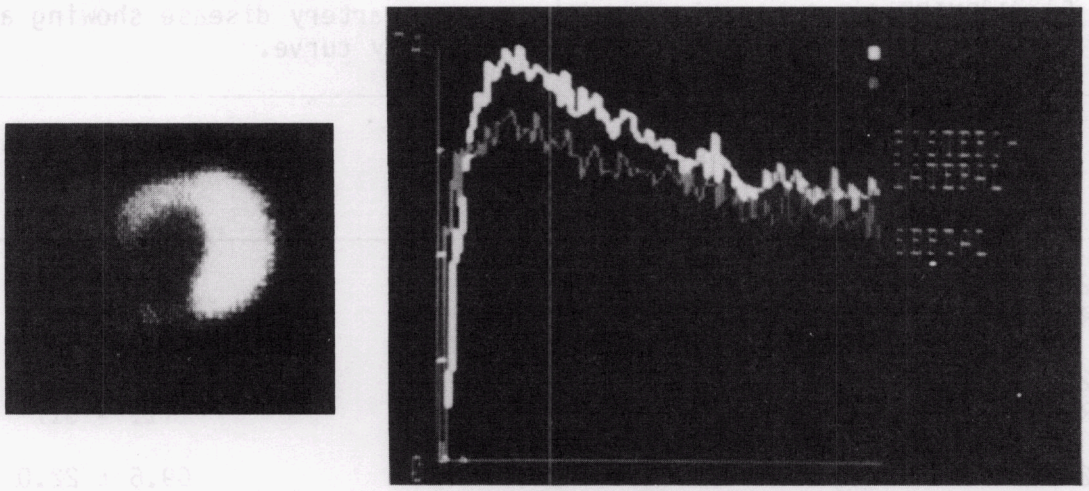

Fig. 5. Time-activity curves (total study period, 100 min) for a patient with three-vessel disease after injection of [^{123}I]BMIPP. (Courtesy, R. Dudczak, M.D., University of Vienna, Austria).

evaluated in this subset of patients with CAD, where the myocardial time activity curve fitted a biexponential function, are summarized in Table 2. By intraindividual comparison of normal and diseased myocardial regions significant differences were found both for the initial elimination half-time and the component ratio ($p<0.01$), being prolonged and/or reduced, respectively, from diseased regions. These changes were observed in all patients with CAD, including those with normal BMIPP elimination behaviour. These preliminary findings with the new BMIPP agent appear promising. Since in addition to visual interpretation of myocardial images, the regional analysis of myocardial time-activity curves may add to the diagnostic feasibility of BMIPP for recognizing patients with heart disease. In a large number of patients studied with the presently used straight-chain fatty acid agents, 15-(p-[^{123}I]iodophenyl)pentadecanoic acid (IPP) and 17-[^{123}I]iodoheptadecanoic (HDA), a regional abnormal elimination behaviour was not seen in all patients with CAD. Thus, the additional information obtained with BMIPP may have some prognostic value.

Table 2. Myocardial elimination half-time after i.v. injection of [^{123}I]BMIPP in nine patients with coronary artery disease showing a biexponential time activity curve.

	Normal Region (+Best Vessel 3VD) (N=13)	Diseased Region (N=14)
T/2 I Min:	11.2 ± 4.3	19.7 ± 12.7
Range	6.7 - 18.2	9.4 - 44
T/2 II Min:	153.7 ± 47.9	160.1 ± 64.2
Range	109 - 222	111 - 317
T/2 I' Min:	62.4 ± 20.7	69.6 ± 22.0
Range	43 - 96	48 - 119
C-I/C-II:	0.36 ± 0.15	0.28 ± 0.14
Range	0.18 - 0.73	0.18 - 0.55

The availability of the new methyl-branched BMIPP agent also allowed a comparison of the absolute uptake and time-activity curves of [^{123}I]BMIPP and the [^{123}I]IPP straight-chain analogue which is used in a much larger patient population at a number of European institutions. Comparing the findings obtained with BMIPP to those with IPP in a similar study population, Dr. Dudczak has found that peak myocardial activity occured later with BMIPP than with IPP. Myocardial extraction, as estimated from the myocardium/background ratio, is slightly less for BMIPP than for IPP. Background corrected time activity curves of the heart and liver after intravenous injection of [^{123}I]IPP are shown in Fig. 6, showing a nearly parallel activity decline from these two organs. In contrast, the background corrected time activity curves of heart and liver after intravenous injection of [^{123}I]BMIPP show, as mentioned previously, a faster elimination from the liver than from the heart (Fig. 4).

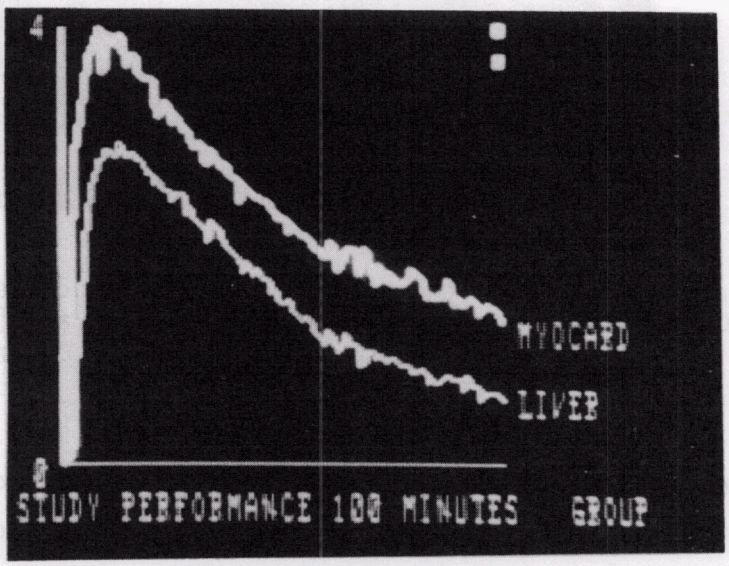

Fig. 6. Time activity curves for the heart and liver after injection of [^{123}I]IPP to a patient with normal coronary arteries (Total study period, 100 min). (Courtesy, R. Dudczak, M.D., University of Vienna, Austria).

The availability of both [^{123}I]IPP and [^{123}I]BMIPP also allowed a comparison of the relative behaviour of these two fatty acids in the same patient in which the studies were performed one week apart. Myocardial time-activity curves obtained after intravenous injection of either IPP or BMIPP are compared in Fig. 7. Peak activity appears higher and

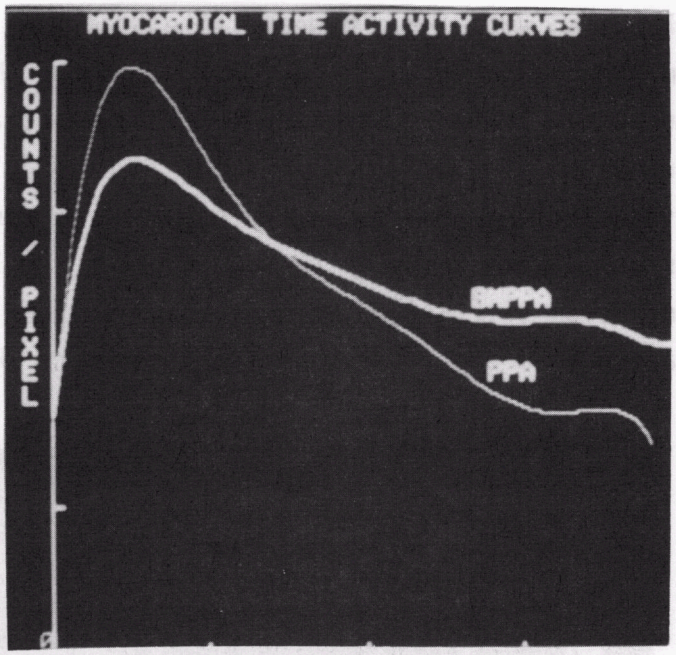

Fig. 7. Comparison of the heart time-activity curves (total study period, 100 min) after administration of [^{123}I]IPP and [^{123}I]BMIPP to patients with three-vessel disease. (Courtesy, R. Dudczak, M.D., University of Vienna, Austria).

elimination faster with IPP than with BMIPP. The respective myocardial images of this patient with three vessel disease are shown in Fig. 8 and 9. The interpolated background corrected images show a slightly reduced uptake in the posterolateral wall in the BMIPP study (Fig. 8), whereas IPP uptake appears normal (Fig. 9).

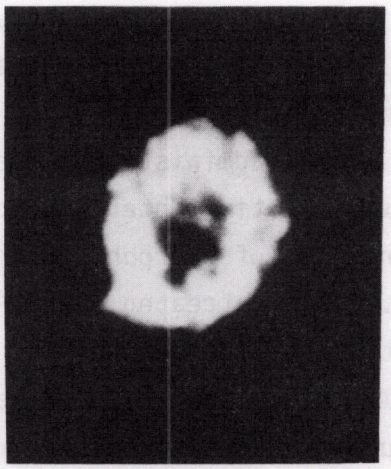

Fig. 8. Interpolated background corrected image for [^{123}I]BMIPP (Courtesy, R. Dudczak, M.D., Vienna, Austria).

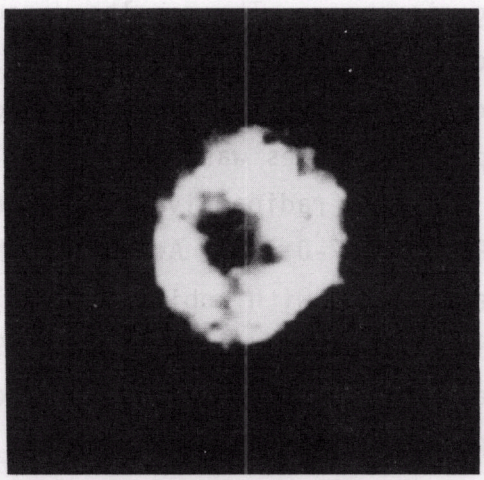

Fig. 9. Interpolated background corrected image for [^{123}I]IPP (Courtesy, R. Dudczak, M.D., Vienna, Austria).

Because of the importance of analyzing both blood and liver to evaluate metabolism of BMIPP, both plasma and urine samples from several patients were analyzed to evaluate the potential catabolism of [^{123}I]BMIPP. In ten patients, blood clearance and urinary excretion for 0-2 h and 2-16 h after tracer administration were evaluated. Blood samples were drawn at various time intervals to determine total activity and to evaluate the formation of hydrophilic and lipophilic metabolites from BMIPP degradation. Both untreated (pH 7.4) and acidified (pH 2) plasma samples were extracted with chloroform. Five minutes after injection, 76.7% ± 3.9% of the radioactivity was extracted into the organic phase. The aqueous- and solid phases contained 3.6% ± 1.9% and 19.8% ± 4.2% of the remaining radioactivity, respectively. With time the ^{123}I content of the aqueous phase increased to 39.1% ± 5.8% after 20 min while the organic phase decreased to 32.9% ± 6.3%. For later periods the ^{123}I content of both phases remained nearly constant. By extraction of the acidified plasma samples, nearly all the aqueous radioactivity was extracted into the organic phase. The results demonstrate the presence of radioiodinated weak acids in the aqueous phase.

The distribution of radioactivity in the organic phase of both 5 min and 90 min acidified plasma samples was further analyzed by thin layer chromatography (TLC). A major radioactive component was observed at 5 min corresponding to BMIPP (R_f 0.67-0.75). At 90 min, however, three radioactive peaks were observed with mobilities (R_f) corresponding to the unmetabolized BMIPP (R_f 0.70), benzoic acid (R_f 0.59) and the triglyceride (R_f 0.85) region. These findings demonstrate catabolism of BMIPP by human tissues. It is probable that the identification of short-chain catabolites such as benzoic acid results from hepatic metabolism. In animal studies at ORNL, a radioactive component with the mobility of hippuric acid was shown in the urine after administration of both radioactive BMIPP and the dimethyl DMIPP analogue. Such catabolism could result from initial α-hydroxylation as described earlier (ORNL/TM-9609). In ten patients, extraction with chloroform/methanol was performed in untreated and acidified urine and the organic phase of the latter procedure then analyzed by TLC. By extraction of untreated urine

with chloroform/methanol most of the radioactivity was found in the aqueous phase. Extraction of acidified urine revealed nearly equal amounts of radioactivity in the aqueous and organic phase (Table 3). By TLC analysis a radioactive component was observed with a mobility corresponding to hippuric acid (R_f 0.15-0.20). The urine from one patient (20 µl) was also analyzed by reversed phase high performance liquid chromatography and a radioactive component with the same retention as for [^{131}I] orthoiodohippuric acid was observed. Surprisingly, these data demonstrate that [^{123}I]BMIPP is catabolized to a product with a TLC mobility similar to the glycine conjugate of 4-[^{123}I]iodobenzoic acid (hippuric acid). The possible catabolism of BMIPP from an initial α-hydroxylation has been discussed earlier (ORNL/TM-9609).

Table 3. Summary of extraction studies of urine from patients administered with [^{123}I]BMIPP.

Untreated urine	Phase	Acidified urine
86.8 ± 3.8%	aqueous	48.8 ± 3.9%
10.4 ± 3.4%	organic	48.9 ± 4.1%
3.1 ± 0.6%	solid	2.3 ± 1.2%

These comparative studies clearly indicate a different uptake and elimination behaviour of IPP and BMIPP in various organs. The 3-methyl-branching in BMIPP must result in a different metabolism of this agent which is consistent with the results of earlier studies (ORNL/TM-9609). The interpretation of organ clearance curves with BMIPP in terms of specific metabolic pathways is not yet possible, and no conclusions can be drawn as a detailed understanding of the relationship between metabolism and clearance curves with other radioiodinated fatty acid analogues also remains unclear. The steps required for degradation of BMIPP are more complex than for IPP. In addition to the possibility of α-hydroxylation for the degradation of BMIPP as described earlier (ORNL/TM-9609), other pathways for oxidative degradation of branched chain fatty acids may resemble those established for branched chain amino acids such as leucine. In this case an ATP dependent carboxylation may occur which is catalyzed

by an enzyme using biotin as a cofactor. If such a mechansim is encountered during catabolism of BMIPP, ^{123}I-benzoic acid will eventually be generated, as a result of β-oxidation. The occurrence of these more complex catabolic pathways for BMIPP may indicate that this agent may be more effective in recognizing patients with heart disease. In addition, the longer myocardial retention observed with BMIPP may facilitate SPECT studies and the recent animal studies with the new 3,3-dimethyl analogue recently described (ORNL/TM-9609) indicate this agent may be even more promising.

EFFECTS OF 3-METHYL-BRANCHING ON INCORPORATION OF RADIOIODINATED IODOVINYL FATTY ACIDS INTO LIPIDS AND SUBCELLULAR FRACTIONS FROM RAT HEARTS

In the last quarterly report (ORNL/TM-9784) the results of initial studies on the metabolism of radiolabeled iodovinyl long chain fatty acids in rat hearts were described. These studies have continued and are designed to investigate the effects of methyl-branching, and in some cases dietary status, on the subcellular distribution and the lipid pool distribution of various analogues in rat hearts. The analogues tested include the straight chain agent, 19-iodo-18-nonadecenoic acid (IVN), and the monomethyl-branched, 19-iodo-3-(R,S)-methyl-18-nonadecenoic acid (BMIVN), and dimethyl-branched, 19-iodo-3,3-dimethyl-18-nonadecenoic acid (DMIVN), analogues. Earlier subcellular distribution studies with BMIVN and IVN showed a significant difference between the subcellular profiles of these two analogues at 30 min post-injection in rats fasted for 24 h (ORNL/TM-9784). Methyl-branching in the BMIVN analogue results in prolonged heart retention and a high association of radioactivity with the mitochondrial fraction. The subcellular distribution of the dimethyl-branched DMIVN analogue more recently evaluated was expected to also show the relatively high mitochondrial association compared to the straight chain IVN analogue. With DMIVN, however, the difference appears to be a high association of radioactivity with the microsomes in contrast to the predominance of radioactivity from IVN in the cytoplasm when tested in fasted rats (Fig. 10). In fed rats the situation is reversed, since the

DMIVN shows a higher percentage of radioactivity in the cytoplasm. This finding may correlate with a suggestion that DMIVN is released more rapidly from the myocardium of fed rats. Future studies on DMIVN retention in hearts of fasted and fed rats will further evaluate this observation.

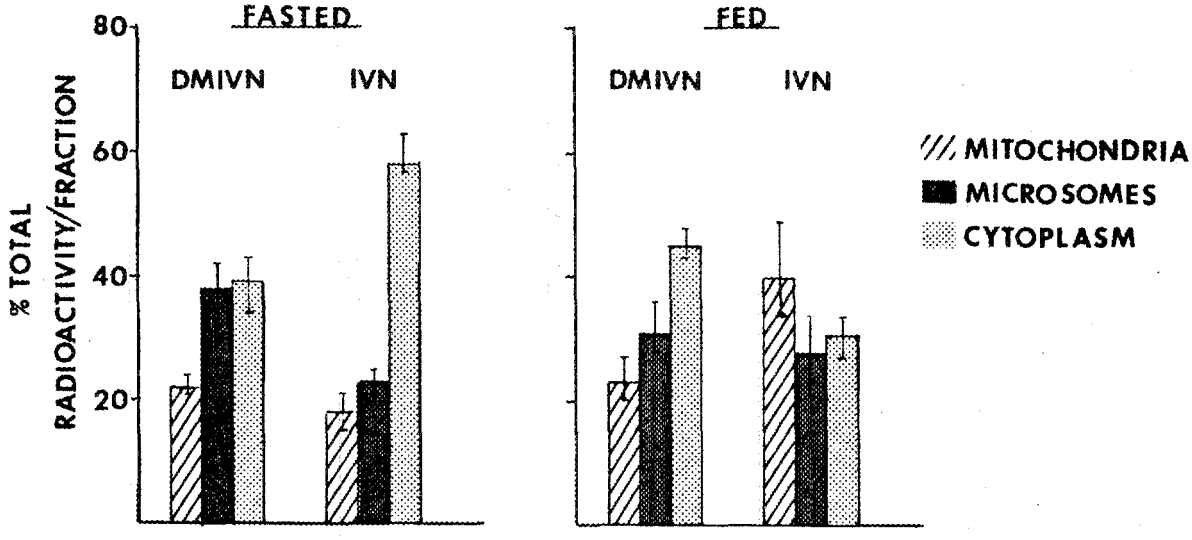

Fig. 10. Distribution (with ranges) of radioactivity in subcellular fractions from rat hearts after injection of ^{125}I-labeled DMIVN or IVN.

Studies on the lipid pool distribution of BMIVN and IVN in the hearts of fasted rats have also now been completed. The results of these studies are compared here with those obtained earlier with DMIVN (ORNL/TM-9784). The differences in heart uptake and retention of the three analogues are shown in Fig. 11. The prolonged retention of the methyl-branched analogues (BMIVN and DMIVN) up to 1 h post-injection is reflected in the persistently high level of activity extractable into the organic fraction by the Folch procedure (Fig. 12). Similarly the release of IVN activity from the heart (Fig. 11) is mirrored by the fall in radioactivity in both the aqueous and organic fractions (Fig. 12). Radioactivity in the aqueous fraction may represent fatty acid metabolites. Thus, the ability of the straight chain IVN analogue to undergo β-oxidation within the myocardium may result in the comparatively high levels of activity in the aqueous fraction.

Aliquots of the organic fractions were evaluated by thin-layer chromatography (ORNL/TM-9207) to separate the lipids into polar lipids,

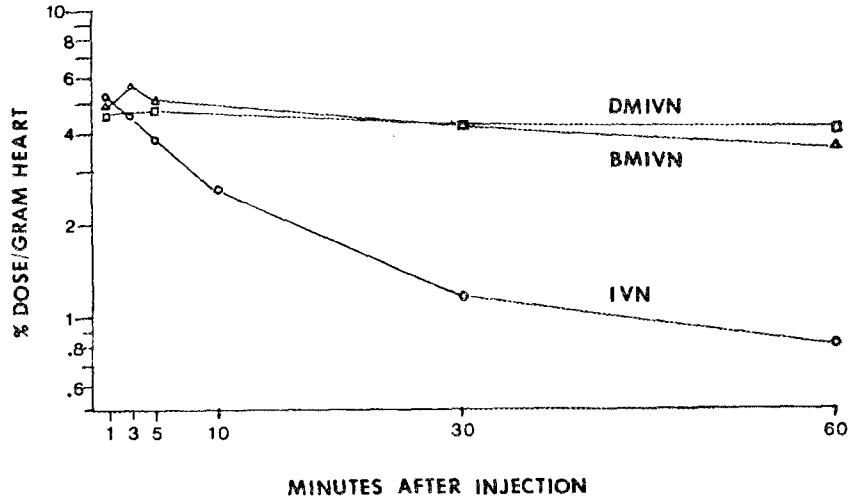

Fig. 11. Comparison of the myocardial uptake and retention of radioiodinated staight chain (IVN), mono methyl-branched (BMIVN) and dimethyl-branched (DMIVN) analogues.

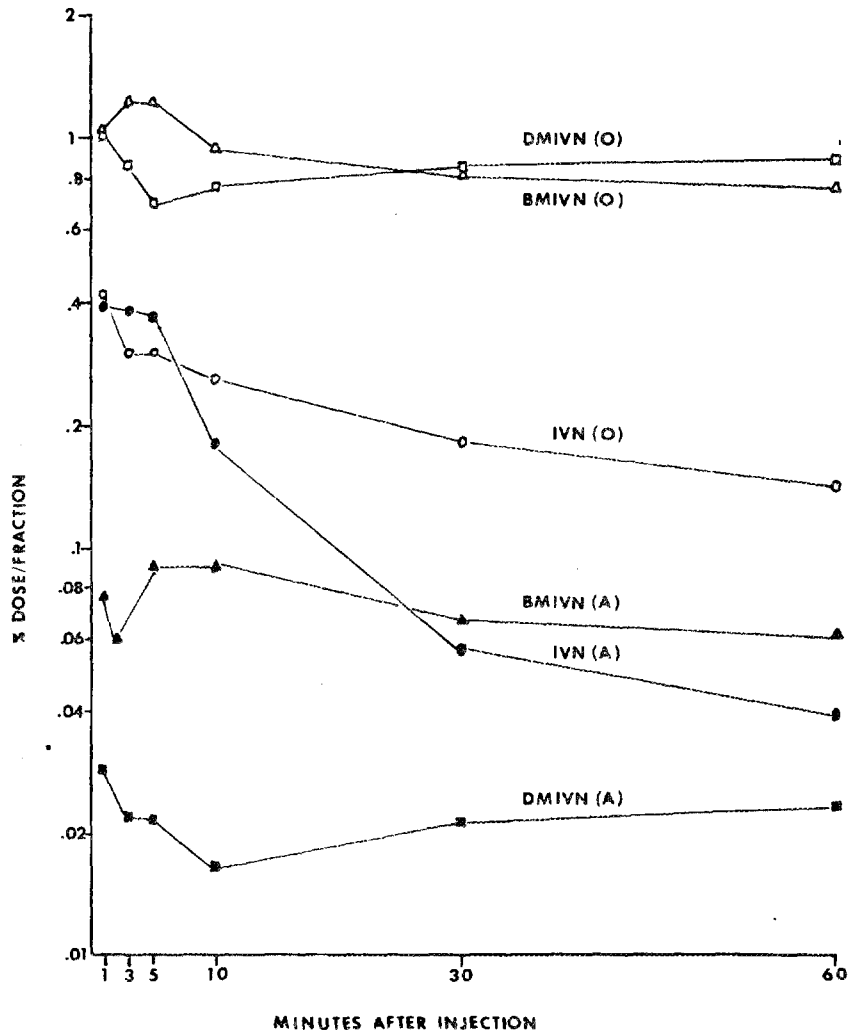

Fig. 12. Compartmentalization of myocardial radioactivity into organic (O) and aqueous (A) fractions following Folch lipid extraction of rats injected with radiolabeled fatty acid analogues.

diglycerides, free fatty acids and triglycerides. The relative percentage of radioactivity in each lipid pool was combined with the % dose uptake value for each heart to obtain a % dose/lipid pool value as a means of comparing the flux of the various analogues through the various lipid pools. The polar lipid pool appears to be a major storage depot for all the iodovinyl analogues (Fig. 13), in contrast to the minimal storage of the iodophenyl fatty acid metabolites within the polar lipids in the myocardium (ORNL/TM-9207). With BMIVN the majority of radioactivity at all time intervals was found in the polar lipid fraction, whereas with DMIVN there was a slower rate of incorporation into this fraction. The straight chain IVN showed relatively high incorporation into polar lipids initially, but a decrease in activity over the 60 min assay period.

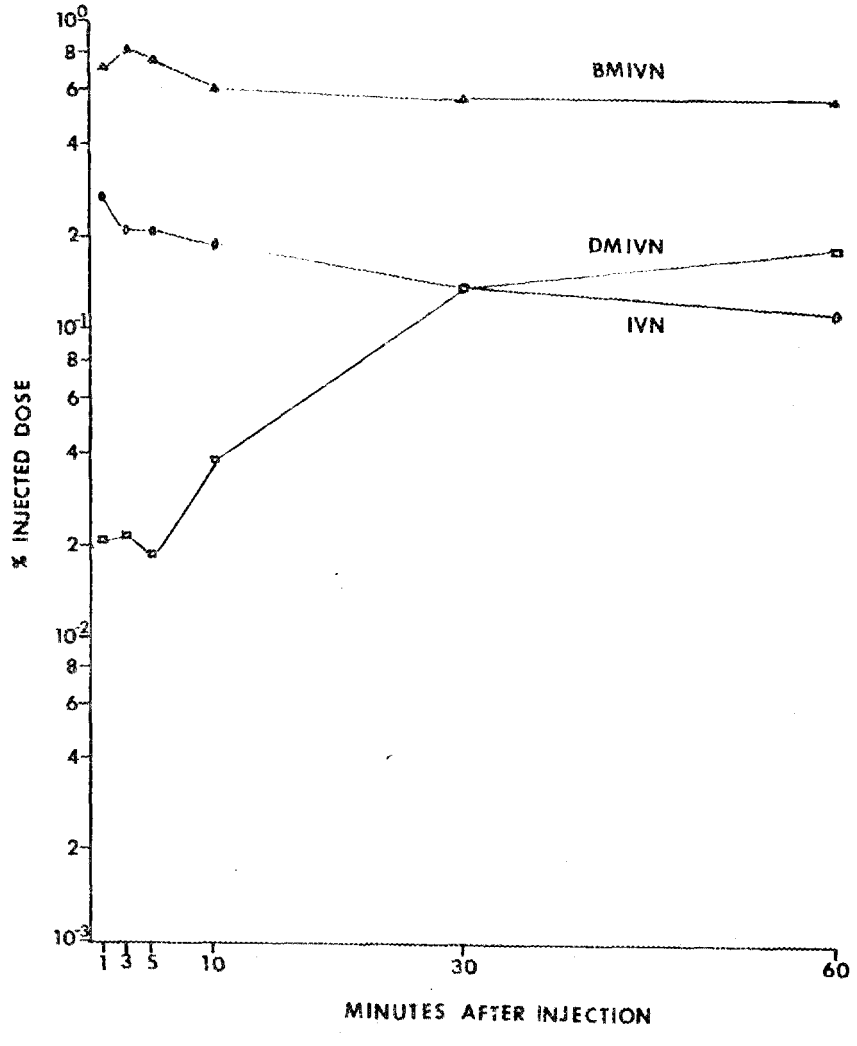

Fig. 13. Comparison of the prevalence of radioactivity in the polar lipid pool of rat hearts following intravenous injection of radiolabeled IVN (○), BMIVN (Δ), or DMIVN (□).

None of the iodovinyl fatty acids showed significant radioactivity in the diglyceride fractions (data not presented). The triglyceride fractions, however, contained a significant amount of radioactivity for all three analogues (Fig. 14). The differences in the patterns of incorporation and release for each analogue were very similar to those observed for the polar lipid pool. In the case of DMIVN, triglycerides seemed to predominate over polar lipids as the favored form of storage.

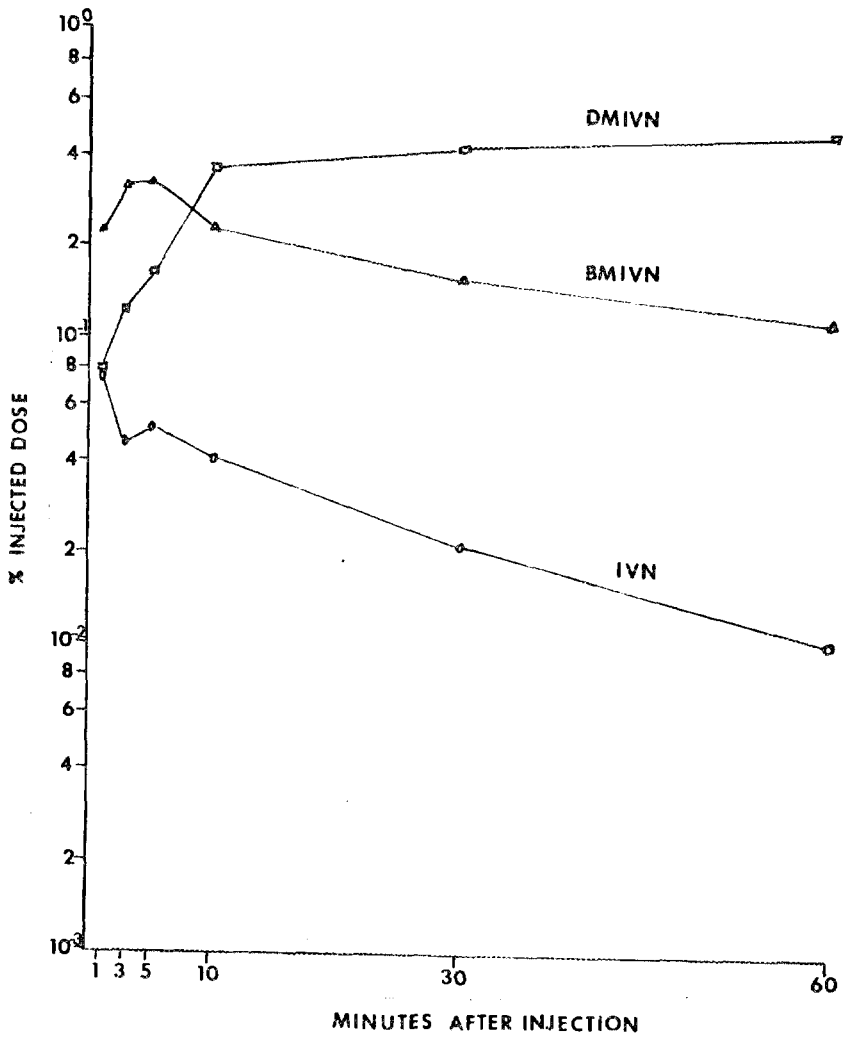

Fig. 14. Comparison of the prevalence of radioactivity in the triglyceride lipid pool of rat hearts following intravenous injection of radiolabeled IVN (O), BMIVN (Δ), or DMIVN (□).

The radioactivity within the free fatty acid fraction may inversely reflect the ability of the analogue to be oxidized (Fig. 15). The IVN analogue, which is thought to undergo β-oxidation, showed an early low level of radioactivity in this fraction. Monomethyl-branching in the BMIVN analogue appears to prevent β-oxidation but may allow for α-oxidation, hence the delayed onset and the slower rate of decrease of free fatty acid radioactivity for this analogue. The dimethyl-branched DMIVN analogue, in which both α- and β-oxidation are presumably inhibited, showed a predominance of radioactivity in the free fatty acid pool within the first 5 min after injection.

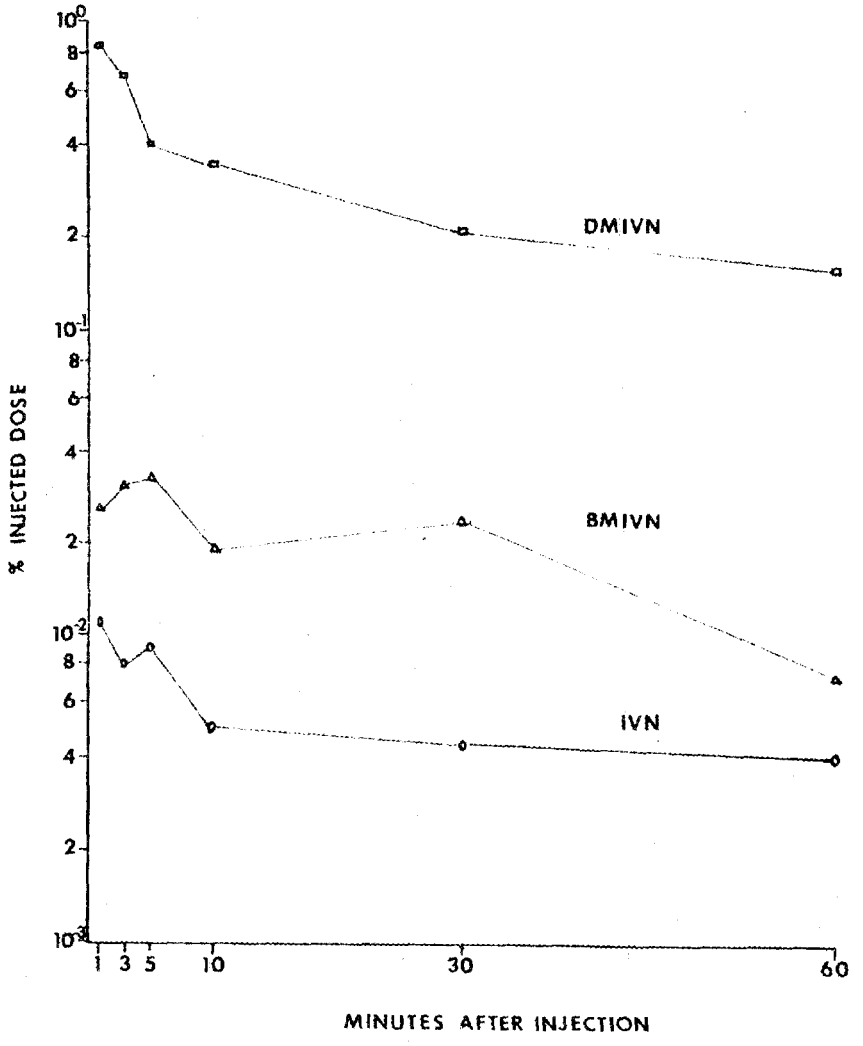

Fig. 15. Comparison of the prevalence of radioactivity in the free fatty acid pool of rat hearts following intravenous injection of radiolabeled IVN (O), BMIVN (Δ), or DMIVN (□).

The different patterns of lipid distribution and subcellular distribution of these iodovinyl fatty acids in the heart demonstrated by these studies may offer a metabolic basis for the retention of methyl-branched fatty acids within the hearts of fasted rats. Identification of metabolites in the aqueous fractions of the heart and lipid analyses of the blood of animals injected with the methyl-branched iodovinyl and iodophenyl fatty acids will help to further define the mechanism for metabolism of these promising myocardial imaging agents.

AGENTS FOR MEDICAL COOPERATIVE PROGRAMS

Osmium-191

Seven shipments of ^{191}Os-potassium osmate were made to the Medical Cooperative Programs for further development of the ^{191}Os→^{191m}Ir generator system and to study clinical applications of ^{191m}Ir ($T_{1/2}$ = 4.96 s). Applications being studied recently include the use of the generator system in the "bolus" as well as the continuous infusion mode for the steady-state perfusion of the myocardium and the arterial system. Two shipments were made to the Cyclotron Center, University of Liege, Belgium (Drs. C. Brihaye and M. Guillaume), two shipments to the University of Bonn, Federal Republic of Germany (Dr. S. Reske), one shipment to Massachusetts General Hospital, Boston, MA (Dr. H. W. Strauss), and two shipments to the Children's Hospital Medical Center in Boston, MA (Drs. S. Treves and A. Packard).

Copper-64

Two shipments of ^{64}Cu were made to collaborators at Oak Ridge Associated Universities, Oak Ridge, TN (Dr. J. Crook), where ^{64}Cu-citrate is being prepared and evaluated by PET as a myocardial and tumor imaging agent.

Platinum-195m

Four shipments of ^{195m}Pt-labeled cis-dichlorodiammineplatinum(II) (cis-DDP) were made on a cost recovery basis to study the pharmacokinetic properties and mode of antitumor activity of this agent. Investigators at the Harvard Medical School, Boston, MA (Dr. A. Jones), City of Hope Medical Center, Duarte, CA (Dr. K. Scanlon), University of Iowa, Iowa City (Dr. Burns), and National Institutes of Health, Bethesda, MD (Dr. C. L. Litterst) received one shipment each.

PRESENTATIONS AND PUBLICATIONS

Oral Presentations

F. F. Knapp, Jr., K. R. Ambrose, and M. M. Goodman "New Radioiodinated Methyl-Branched Fatty Acids for Cardiac Studies," Symposium on Assessment of Myocardial Metabolism by Cardiac Imaging, Vienna, Austria, Oct. 26, 1985.

P. C. Srivastava, M. M. Goodman, and F. F. Knapp, Jr. "Incorporation of Radiohalogens via Versatile Organometallic Reactions: Applications in Radiopharmaceutical Chemistry," Second International Symposium on the Synthesis and Applications of Isotopically Labeled Compounds, Sept. 3-6, 1985, Kansas City, MO.

P. C. Srivastava, M. L. Tedjamulia, and F. F. Knapp, Jr. "Synthesis and Intracellular Delivery of Dihydropyridine Coupled Radioiodinated Aromatic Amines for Evaluation of Cerebral and Myocardial Blood Perfusion," Second International Symposium on the Synthesis and Applications of Isotopically Labeled Compounds, Sept. 3-6, 1985, Kansas City, MO.

Journal Articles

R. D. Okada, F. F. Knapp, Jr., M. M. Goodman, D. Elmaleh, and H. W. Strauss "Tellurium-Labeled Fatty Acid Analogues: Relationship of Heteroatom Positions to Myocardial Kinetics," Eur. J. Nucl. Med., 11, 156-161 (1985).

P. C. Srivastava, H. G. Hay, and F. F. Knapp, Jr. "The Effects of Alkyl and Aryl Substitution on the Myocardial Specificity of Radioiodinated Arsonium and Ammonium Cations," J. Med. Chem., 28, 901-904 (1985).

P. C. Srivastava, M. L. Tedjamulia, and F. F. Knapp, Jr. "Potential Applications of the Phenylamine-Coupled Dihydropyridine System for the Brain Specific Delivery of Iodine-123-Labeled Amines," J. Med. Chem., 28, 1574-1580 (1985).

Reports

F. F. Knapp, Jr., K. R. Ambrose, M. M. Goodman, and P. C. Srivastava, Nuclear Medicine Progress Report for Quarter Ending September 30, 1985, ORNL/TM-9784.

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