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MASTER

**Nuclear Medicine Technology
Progress Report for Quarter
Ending June 30, 1979**

F. F. Knapp, Jr.

OAK RIDGE NATIONAL LABORATORY
OPERATED BY UNION CARBIDE CORPORATION • FOR THE DEPARTMENT OF ENERGY

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HEALTH AND SAFETY RESEARCH DIVISION

NUCLEAR MEDICINE TECHNOLOGY PROGRESS REPORT
FOR QUARTER ENDING JUNE 30, 1979

F. F. Knapp, Jr.

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ORNL/TM-6639

ORNL/TM-6771

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CONTENTS

	<u>Page</u>
Summary	1
Diffusion Chamber Assay System	2
Tin-117m	6
Tellurium-123m	7
Selenium-75	10
Platinum-195m	12
Radionuclides for Medical Cooperative Programs	17
Other Nuclear Medicine Technology Group Activities	18
Papers and Publications	19
Papers	19
Reports	19

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SUMMARY

Investigations with the diffusion chamber assay system have continued, and we now report the relative cytotoxicity and target cell uptake of ^{195m}Pt -labeled *cis*- and *trans*-dichlorodiammineplatinum(II) (*cis*- and *trans*-DDP). These two agents are excellent candidates for such studies since *cis*-DDP is an established potent antitumor agent while the *trans*-isomer exhibits little antitumor activity. Diffusion chambers containing KB tumor target cells were implanted in the peritoneal cavities of rats, which were later treated with ^{195m}Pt -labeled *cis*- or *trans*-DDP. The number of viable cells at various time intervals as well as the cellular uptake of ^{195m}Pt were compared for both agents. The KB tumor cell population in chambers from the *cis*-DDP-treated animals decreased while the cell population in chambers from the *trans*-DDP treated animals increased, although the levels of DDP were considerably greater in *trans*-treated cells for periods up to 24 hrs. Cytotoxicity data obtained in the study are similar to results from *in vivo* studies and indicate that the diffusion chamber technique is a simple assay system that may be used to determine the effects of toxic agents under controlled conditions.

In this progress report, the results of continuing studies with ^{117m}Sn , ^{123m}Te , ^{75}Se , ^{11}C , and ^{195m}Pt -labeled agents are also described. A series of five ^{117m}Sn -labeled steroids containing a variety of structural modifications have been prepared. Future tissue distribution studies in rats will determine the potential usefulness of these agents for adrenal imaging applications. Based upon our studies with ^{75}Se -labeled steroids (adrenal imaging) and fatty acids (myocardial imaging),

the potential use of the ^{73}Se -labeled agents for emission computerized axial tomographic applications is also discussed. Calculations of the estimated radiation dose to humans from two ^{123m}Te -labeled steroids which suggest the potential clinical usefulness of these agents for adrenal visualization have been completed. Additional patient studies in a Medical Cooperative Program with the Oak Ridge Associated Universities have continued with ^{11}C -aminocyclobutanecarboxylic acid (ACBC) and ^{11}C -tryptophan. Continuing studies with ^{195m}Pt -labeled antitumor agents are also reported.

DIFFUSION CHAMBER ASSAY SYSTEM

K. R. Ambrose

The diffusion chamber assay system initially described in ORNL/TM-6639 has been used to relate the cellular uptake and cytotoxicity of ^{195m}Pt -labeled *cis*- and *trans*-dichlorodiammineplatinum(II) (*cis*- and *trans*-DDP) in the KB (human nasopharyngeal carcinoma) cell line. In earlier studies, rats were injected with *cis*- or *trans*-DDP or with saline one day after intraperitoneal implantation of diffusion chambers containing KB target cells. Target cells within chambers of the *cis*-DDP treated animals decreased in number, whereas the cell population in chambers of saline or *trans*-DDP treated animals increased approximately tenfold within three days. These results are similar to those from numerous animal studies that have demonstrated the potent antitumor properties of *cis*-DDP and the ineffectiveness of the *trans* isomer. The diffusion chamber technique has also been demonstrated to be a sensitive and reproducible assay for dose-response studies of *cis*-DDP induced cytotoxicity (ORNL/TM-6771).

In order to relate cellular uptake of the platinum compounds with the observed cytotoxicity, chambers containing 1.4×10^4 viable KB cells were implanted into the peritoneal cavity of anesthetized female Fischer strain rats. One day after implantation, animals were injected intraperitoneally with $^{195\text{m}}\text{Pt}$ -labeled *cis*- or *trans*-DDP at the dosage of 2 mg/kg (0.16 mg/ml saline). The specific activities of the injected agents were 0.286 $\mu\text{Ci}/\mu\text{g}$ *cis*-DDP and 0.281 $\mu\text{Ci}/\mu\text{g}$ *trans*-DDP. Chambers were removed from the animals at 4, 8, 24, and 48 hr post-injection, and the number of target cells per chamber was determined microscopically. Following two centrifugations to separate the cellular and "free" radioactivity, the cells and supernatants from each chamber were counted in a gamma counter. In addition, blood and serum samples from chamber-bearing rats were assayed at the time of sacrifice for $^{195\text{m}}\text{Pt}$ radioactivity.

In Table 1, the calculated microgram levels of DDP per total cell population or per cell and the mean number of cells per chamber are shown for each assay period. Ratios of *trans:cis* bound to the target cells (micrograms of DDP/cell) at 4 and 8 hr were 3.8 and 2.3, respectively. At the latter time periods, the numbers of cells in the *cis*- and *trans*-treated groups differ markedly (i.e., increase in *trans*-DDP treated animals and decrease in *cis*-DDP treated animals), and a comparison of the micrograms of DDP/cell values is difficult to interpret. However, the progressive loss of DDP from the total cell population is evident from the data shown in Table 1.

Table 1. Uptake of *cis*- and *trans*-DDP in KB cells in diffusion chambers implanted in rats injected with 2 mg of DDP/kg body weight

Hours post-injection	Animals injected with	DDP/total cells ^a (μg)	No. of cells ^b	DDP/cell (μg)
4	<i>cis</i> -DDP	1.29×10^{-3}	23.0×10^3	0.56×10^{-7}
	<i>trans</i> -DDP	4.80×10^{-3}	22.6×10^3	2.12×10^{-7}
8	<i>cis</i> -DDP	1.31×10^{-3}	20.2×10^3	0.66×10^{-7}
	<i>trans</i> -DDP	3.52×10^{-3}	22.6×10^3	1.55×10^{-7}
24	<i>cis</i> -DDP	0.42×10^{-3}	20.0×10^3	0.21×10^{-7}
	<i>trans</i> -DDP	2.21×10^{-3}	47.0×10^3	0.47×10^{-7}
48	<i>cis</i> -DDP	0.63×10^{-3}	13.0×10^3	0.48×10^{-7}
	<i>trans</i> -DDP	1.21×10^{-3}	169.0×10^3	0.07×10^{-7}

^a Amount of DDP calculated from ^{195m}Pt radioactivity in cells from diffusion chambers, 5 chambers per test group.

^b Average number of viable cells per chamber determined by hemocytometer and trypan blue dye exclusion.

A comparison of the number of KB target cells within the chambers 48 hr after injection of *cis*- or *trans*-DDP (Table 1) shows 93% inhibition of cell growth in *cis*-DDP treated animals. This same cell inhibition value was obtained in earlier diffusion chamber studies where cell growth in animals injected with 2 mg/kg *cis*-DDP was compared to that observed in control animals injected with an equivalent volume of saline. In addition, the results reported here at 4 and 48 hr (i.e., micrograms of *cis*- and *trans*-DDP bound; 93% cell inhibition) have been confirmed in a second experiment in which a saline control group was included.

A comparison of the amount of cell-free *cis*- and *trans*-DDP in the chamber fluid demonstrated an even greater *trans*:*cis* ratio than that suggested from the cell-bound DDP calculations discussed above. Four hours after injection of the two agents into separate test animals the amount of *trans*-DDP detected in the extracellular fluid was 6 times greater than the value determined for *cis*-DDP. The rate of disappearance of *trans*-DDP from chamber fluid, approximated from values at the four time periods, was similar to the disappearance kinetics observed for loss of radioactivity from blood and serum of the chamber recipients, although the actual quantity was highest in the chamber fluid. In the *cis*-DDP treated animals, the disappearance rates of radioactivity were similar only for chamber fluid and serum; blood exhibited a slower clearance rate probably as a result of the established binding of *cis*-DDP to red blood cells.

The inverse relationship between the relative uptake and biological properties of the DDP isomers is an interesting finding. Similar *in vitro* results have been reported although *in vitro* studies do not as closely

resemble physiological conditions. Under the closed conditions of an *in vitro* system, the investigator must determine the optimal time period for target cell-DDP interaction as well as the amount of DDP that will elicit the most meaningful result.

Radioactivity measurements have shown that significantly greater levels of *trans*-DDP are present in chamber fluid compared with values from animals injected with the *cis* isomer. Moreover, more *trans*-DDP than *cis*-DDP was found associated with the KB cells although *cis*-DDP is the isomer that exhibits potent antitumor activity. These results suggest that the absolute amount of the DDP isomers present in the cells is not responsible for the relative cytotoxicity induced by *cis*- and *trans*-DDP and indicates that either the degree or mode of interaction of DDP with important cellular substituents determines the relative cytotoxicity.

TIN-117m

F. F. Knapp, Jr., K. R. Ambrose, and T. A. Butler

Our studies with a unique class of trimethyltin-substituted steroids have continued, and several ^{117m}Sn -labeled ($^*\text{Sn}$) compounds have been prepared for tissue distribution studies in rats. Since ^{117m}Sn -labeled $\text{Me}_3\text{Sn-Li}$ is an important intermediate for the preparation of the radiolabeled steroids, the conversion of the primary $\text{Me}_3^*\text{Sn-Cl}$ product to the crucial $\text{Me}_3^*\text{Sn-Li}$ intermediate has been investigated. The reaction of lithium with $\text{Me}_3^*\text{Sn-Cl}$ has been studied in both liquid ammonia and dry tetrahydrofuran. The liquid ammonia system has proven cumbersome, and yields of the $\text{Me}_3\text{Sn-Li}$ are not reproducible. In contrast, $\text{Me}_3^*\text{Sn-Li}$ can be obtained in high yields by reaction of lithium metal with $\text{Me}_3^*\text{Sn-Cl}$ in

tetrahydrofuran at room temperature. The ^{117m}Sn -labeled steroids that have been prepared include: 24-(trimethylstanna)-chol-5-en-3 β -ol (analog of cholesterol); 23-(trimethylstanna)-24-nor-5 α -cholan-3 β -ol (saturated nucleus); 23-(trimethylstanna)-24-nor-5 β -cholan-3 α -ol (cis-A/B ring juncture); 3 β -methoxy-24-(trimethylstanna)-5-ene (hydrophobic C-3-substituent); and 17 β -[(trimethylstanna) methyl]-androst-5-en-3-ol (short sidechain). These compounds were prepared by reacting ^{117m}Sn -labeled $\text{Me}_3\text{Sn-Li}$ with the brominated steroid substrates. The results of future tissue distribution studies with these agents in rats will determine the structural features required for maximal adrenal uptake of these agents.

TELLURIUM-123 m

F. F. Knapp, Jr. and K. R. Ambrose

We have reported earlier the results of extensive tissue distribution and excretory studies in rats using ^{123m}Te -labeled 24-nor-23 (isopropyl telluro)-5 α -cholane-3 β -ol (23-ITC) and ^{123m}Te -24-(isopropyl telluro)-chol-5-en-3 β -ol (24-ITC) (ORNL/TM-5809, 5936, 6044) (Fig. 1). These two agents show dramatic adrenal uptake in rats, and the adrenal glands of rats and rabbits have been visualized clearly after intravenous administration of the ^{123m}Te -labeled steroids. In order to assess the potential clinical usefulness of these agents for human adrenal visualization, calculations of the expected radiation dose to human organs from ^{123m}Te -labeled 23-ITC and 24-ITC have been carried out.

The organ distribution and biological half-life properties of ^{123m}Te -labeled 23-ITC and 24-ITC determined in rats were assumed to be

ORNL-DWG 79-14524

Fig. 1. Structures of two new ^{123m}Te -labeled adrenal imaging agents.

similar in humans. The estimated radiation dose values to various human organs were then calculated using the decay parameters for the ^{123m}Te radionuclide by employing the standard Medical Internal Radiation Dose (MIRD) method. The estimated dose values for several organs are compared in Table 2 with dose estimates for other radiolabeled steroids presently in clinical use for the diagnosis of adrenal disease. These results indicate that the estimated radiation dose from ^{123m}Te -(23-ITC) is similar to the calculated doses from NP-59 and Scintidren. The potential use of ^{123m}Te -(23-ITC) is being discussed with several clinical investigators.

Table 2. Estimated mean radiation dose values for the various radiolabeled adrenal imaging agents calculated from female rat tissue distribution data

Compound	Dose (rad/mCi injected dose)				
	Adrenals	Liver	Kidney	Ovaries	Spleen
^{131}I -6 -Iodomethyl-19-nor-cholest-5(10)-en-3 β -ol ("NP-59") ^a	151.40	0.12	0.55	7.27	1.74
^{75}Se -19-(Methylseleno)cholest-5-en-3 β -ol ^b	60.80	1.03	1.09	10.01	0.62
^{75}Se -6-(methylseleno)methyl-19-norcholest-5(10)-en-3 β -ol ("Scintidren") ^c	93	2.1	2.0	14	
^{123m}Te -(23-ITC)	97.85	1.58	3.24	8.00	1.42
^{123m}Te -(24-ITC)	210.20	2.00	3.78	12.93	3.38

^aS. D. Sarkar et al., *J. Nucl. Med.* 16: 1038-1042 (1975).

^bS. D. Sarkar et al., *J. Nucl. Med.* 17: 212-217 (1976).

^cJ. A. Peacegood et al., in *Proceedings*, British Institute of Radiology Meeting, London, February 16, 1976.

SELENIUM-75

F. F. Knapp, Jr., K. R. Ambrose, and T. A. Butler

As a result of our potential interest in the use of ^{73}Se -labeled agents for positron emission computerized axial tomography, preliminary studies have continued with ^{75}Se -labeled fatty acids and steroids to determine if the use of the ^{73}Se -labeled agents would be feasible. Recent studies with ^{75}Se -(24-ITC) have shown that this agent has distribution properties in rats very similar to those reported earlier for ^{123m}Te -(24-ITC) (ORNL/TM-6916). The adrenal:tissue ratios for various rat organs following injection of these two agents are shown in Table 3.

Table 3. Adrenal:tissue ratios determined one day following the intravenous administration of ^{123m}Te -(24-ITC) and ^{75}Se -(24-ITC)

Tissue	Adrenal:tissue ratios	
	^{123m}Te -(24-ITC)	^{75}Se -(24-ITC)
Blood	54.8	67.3
Liver	27.1	27.1
Ovaries	4.9	9.0
Lung	18.7	10.9
Kidneys	56.2	30.0
Spleen	14.0	19.2
Pancreas	122.8	46.4

The use of ^{73}Se -labeled steroids for tomographic visualization of adrenal masses is a potentially powerful tool for the diagnosis of adrenal disease. Studies using adrenal agents labeled with positron-emitting radionuclides have not been previously reported probably since the human adrenals cannot be visualized until at least 48 hr after administration of either of the ^{131}I - or ^{75}Se -labeled agents presently in clinical use. It is therefore impractical to consider the use of short-lived positron-emitting radionuclides such as ^{11}C , ^{15}O , or ^{13}N that could conceivably be covalently incorporated into adrenal-specific steroid imaging agents. The ^{73}Se radionuclide is sufficiently long-lived ($T_{1/2}$ 7.2 hr) and decays with a high positron yield (65% β^+). Tissue distribution studies in rats have shown high adrenal:tissue ratios within 24 hr after administration of ^{75}Se -(24-ITC) (Table 3). These ratios would not be sufficiently high for optimal adrenal visualization by single photon techniques. During emission tomographic counting techniques, however, only coincident events are detected and significantly higher background levels can be tolerated. Moreover, liver uptake would not present as serious a problem as it poses in conventional single-photon techniques.

The chemical synthesis and purification of ^{75}Se -labeled 24-(isopropyl tellurol)-chol-5-en-3 β -ol can be easily completed within a 4-hr period, indicating that the ^{73}Se -labeled agent could be available in considerably less than one half-life after end of bombardment (E.O.B.) of the cyclotron target. If adrenal visualization were not possible until after an additional 14 hr after administration of this agent (3 half-lives E.O.B.), sufficient radioactivity would be retained

(12.5% of the injected dose) to indicate that the expected 2.3% adrenal uptake would be sufficient for adrenal visualization. Thus, administration of 10 mCi of ^{73}Se -(24-ITC) would result in the accumulation of about 29 μCi of the radioactive label in the adrenal glands after 21 hr. At this period, an extrapolation of the rat tissue distribution data would indicate an estimated adrenal:liver ratio of 27:1 and an adrenal:blood ratio of 67:1.

An additional important factor which must be considered in determining the potential usefulness of the ^{73}Se -labeled tissue imaging agents is the estimated radiation dose values. The 511 keV positron emission from the ^{73}Se radionuclide would not be the only contribution to the total dose since the ^{72}As daughter has an 80-day physical half-life. In addition to the low-energy gamma emissions, all of the decay parameters of the ^{72}As radionuclide would have to be considered in our calculations and could contribute substantially to the total dose. These dose calculations are being carried out in conjunction with our collaborators both at ORNL and ORAU and should indicate if the estimated doses from the ^{73}Se -labeled steroids and fatty acids are within the acceptable limits to warrant the synthesis and testing of these agents.

PLATINUM-195_m

J. D. Hoeschele and T. A. Butler

It has been reported (ORNL/TM-6410) that platinum retention in the kidney 24 hr after injection of a single dose of *cis*-DDP is (1) directly proportional to the dose administered over a sixfold dose

range, (2) independent of the concentration of the *cis*-DDP administered (at a given total dose), and (3) enhanced in most organs when the diuretic furosemide (10 and 24 mg/kg) is used in conjunction with *cis*-DDP chemotherapy (2 and 4 mg/kg). Studies of the various factors which may influence nephrotoxicity associated with *cis*-DDP chemotherapy have continued and it is now possible to report the results of experiments involving the use of sulfur-containing agents to effect *in vivo* removal ("rescue therapy") of bound platinum.

Previous attempts to minimize nephrotoxicity by prehydration in combination with osmotic diuresis techniques have been only partially successful. Consequently, alternative approaches for modifying platinum nephrotoxicity are being pursued and include the potential use of sulfur-donor ligands as agents to block platinum binding and removal of bound platinum by "rescue therapy." The rationale for this approach is that sulfur donor molecules in general react rapidly with Pt(II) and have a very high binding affinity for platinum and other heavy metals. Such agents have been used successfully for Hg(II) detoxification and have recently also shown promise in reducing kidney toxicity from *cis*-DDP in mice. In addition, N-acetylcysteine (NAC) has been shown to enhance urinary excretion of gold (Au). Since the chemistry of Au(I) and Pt(II) is similar, the potential use of NAC and thiourea (TU) in reducing kidney damage in rats from *cis*-DDP has been investigated.

The experimental approach adopted was to treat rats with a therapeutic dose of ^{195m}Pt -labeled *cis*-DDP (2 mg/kg), allow the maximum amount of drug to bind to the kidney over a 24-hr period, and then

attempt removal of the bound platinum using high doses of these relatively non-toxic sulfur compounds (platinum:ligand molar ratios >100; millimolar amounts of NAC and TU). The rats were sacrificed 48 hr after *cis*-DDP injection, the kidneys and other selected organs excised, and the platinum retention (percent injected dose/g tissue) determined by radio-metric assay. The potential effectiveness of these agents under experimental conditions as rescue agents has been evaluated by determining the percent reduction of platinum retention in the kidney for the treated group (platinum + sulfur-agent) compared to the controls (platinum only) 24-hr post-ligand therapy on the assumption that the level of platinum retention is a direct measure of kidney toxicity.

The preliminary tissue distribution data are compiled in Table 4 and indicate that there is essentially no difference in platinum retention in the kidney and all other tissues between treated and untreated groups after the intravenous administration of TU and NAC at either dose. Platinum retention in the lungs appears to have been reduced by TU treatments particularly at the 400 mg/kg dose; however, the total ^{195m}Pt activity in the lung is approximately the same as for the controls. It was noted that the lungs from both the TU- and NAC-treated animals contained considerable fluid. Therefore, the apparent decrease in retention could be the result of the added fluid weight. Hence, both TU and NAC appear to be ineffective for the *in vivo* removal of organ-bound platinum under the conditions employed. Higher initial doses of either of these agents (>800 mg/kg) produced lethal lung edema. It was subsequently learned that lung edema produced by TU, and to a lesser extent by NAC, is unique to the rat. Although this rat-specific edema

Table 4. Platinum retention (% dose/g tissue) in selected rat tissues following thiourea (TU) and N-acetylcysteine (NAC) 48 hr post-*cis*-DDP (Pt) administration. Doses administered (i.v.): Pt (2 mg/kg), TU(200, 400 mg/kg), and NAC (200, 400 mg/kg)

Tissue	% dose/g tissue ^a				
	Control Pt only	Agent and dose (mg/kg)			
		Pt + NAC 200	Pt + NAC 400	Pt + TU 200	Pt + TU 400
Blood	0.140±0.009	0.134±0.0175	0.161±0.020	0.140±0.009	0.141±0.023
Liver	0.264±0.028	0.253±0.030	0.280±0.034	0.256±0.023	0.238±0.057
Spleen	0.210±0.0205	0.200±0.019	0.245±0.036	0.200±0.023	0.211±0.035
Kidneys	1.02±0.06	1.06±0.09	1.23±0.30	1.08±0.14	1.20±0.38
Heart	0.056±0.004	0.050±0.007	0.060±0.010	0.052±0.006	0.056±0.006
Lungs	0.146±0.014	0.134±0.016	0.119±0.008	0.097±0.008	0.097±0.017
<u>Organ ratios</u>					
Kidney:Blood avg = 7.81	7.31	7.89	7.66	7.69	8.52
Kidney:Liver avg = 4.3	3.88	4.18	4.40	4.21	5.05

^aMean values for three animals ± the standard deviation. Only two animals were used for the control group.

can be controlled by certain drugs, the rat would not appear to be a suitable animal model for these studies since an intravenous dose of 2000 mg/kg of NAC is tolerated well in the mouse but is 100% lethal in the rat (intraperitoneal). Further studies of platinum kidney "rescue therapy" are not presently planned.

RADIONUCLIDES FOR MEDICAL COOPERATIVE PROGRAMS

F. F. Knapp, Jr., J. D. Hoeschele, and T. A. Butler

In support of the continuing cooperative program with the ORNL Biology Division to study the translocation of asbestos fibers in rodents following deposition in transplanted tracheas, additional neutron activated chrysotile "A" asbestos fibers have been supplied. Six batches of ^{11}C -labeled L-aminocyclobutane carboxylic acid (^{11}C -ACBC) have been prepared and tested in patients at the ORAU Medical Division for tomographic visualization of a variety of solid tumors. In addition, three batches of ^{11}C -DL-tryptophan have been prepared and used to study various types of pancreatic disease. As part of the continuing Medical Cooperative Program to investigate platinum antitumor compounds, the following $^{195\text{m}}\text{Pt}$ -labeled compounds were synthesized and provided to our collaborators: two shipments of Na_2PtCl_6 to the Medical School at the University of Kentucky (Dr. P. DeSimone) for the study of nephrotoxicity and protein binding of *cis*-dichlorodiammineplatinum(II) (*cis*-DDP); two shipments of *cis*-DDP to the Radiopharmacy Department at the University of Southern California (Dr. W. Wolf) for radiopharmacokinetic studies; and one shipment of *cis*-DDP to the Medical School at the University of California at Los Angeles (Dr. E. Petrilli) for preclinical nephrotoxicity studies in dogs. It is anticipated that future clinical investigations with $^{195\text{m}}\text{Pt}$ -labeled *cis*-DDP will be conducted at the latter institution.

OTHER NUCLEAR MEDICINE TECHNOLOGY

GROUP ACTIVITIES

Three shipments of ^{43}K were made to the University of Mississippi Medical Center for coronary disease studies. Three shipments each were also made to both the V.A. Center, Wood, Wisconsin, and the National Institute for Environmental Protection at Research Triangle Park in North Carolina. One shipment was made to the Children's Hospital Medical Center in Boston, Massachusetts, for microdosimetry studies.

Visitors for this period included Professor R. A. Zingaro from the Chemistry Department at Texas A&M University who visited the Nuclear Medicine Technology Group on May 21 to discuss potential studies of the toxic effects of arsenic. In addition, a group of Nuclear Technology majors from the Chattanooga State Technical Community College visited on May 10 and were given an overview of the nuclear medicine research program. On June 4, R. A. Grigsby joined the Nuclear Medicine Technology Group as a summer research student to continue selected aspects of work initiated during his stay in the summer of 1978. Mr. Grigsby is a graduate student in chemistry with Dr. K. J. Irgolic at Texas A&M University. A research and development subcontract has been established recently with Dr. Irgolic to investigate the preparation of $^{123\text{m}}\text{Te}$ - and $^{117\text{m}}\text{Sn}$ -labeled radiopharmaceuticals.

PAPERS AND PUBLICATIONS

Papers

R. O. Rahn, N. P. Johnson, A. W. Hsie, J. F. Lemontt, W. E. Masker, J. D. Regan, W. C. Dunn, Jr., and J. D. Hoeschele, "The interaction of platinum compounds with the genome: Correlation between binding data and biological end points," Symposium on the Scientific Basis of Toxicity Assessment, Gatlinburg, Tennessee, April 15-19, 1979.

Reports

F. F. Knapp, Jr., *Nuclear Medicine Progress Report for Quarter Ending September 30, 1978*, ORNL/TM-6771.

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