^{69m}Zn-CHLORIDE—A NEW SCANNING AGENT: A STUDY OF ITS DOSIMETRYAND BIOLOGICAL FATE

Steven A. Lorber, Fred M. Gold, Anthony A. Maglione and Sidney Rubenfeld

Bellevue Hospital, New York University School of Medicine, New York, New York

A great deal of information is available on the metabolism of zinc in animals and man. Much of this knowledge was gained by studying radioactive zinc in the form of ^{65}Zn (*1–4*). The recent introduction of ^{69m}Zn (*5*) with a 13.8-hr physical half-life and a 0.438-MeV gamma-ray emission has permitted, in addition to metabolic studies, a detailed evaluation of the organ concentration by radioisotope scanning techniques. Figure 1 shows the decay scheme (*6*) of ^{69m}Zn. Zinc-69m decays by isomeric transition to ^{69}Zn which, in turn, decays to the ground state of ^{69}Ga. The ^{69m}Zn-^{69}Zn isomeric decay mode is equivalent to a transient type equilibrium where the daughter ^{69}Zn decays with the half-life of the parent ^{69m}Zn after reaching equilibrium which is approximately 4.8 hr after production.

This study was undertaken with the objectives of determining the amount of radiation from ^{69m}Zn absorbed by various target organs, of providing additional data on the biological fate of zinc and of exploring the possible applications of this radionuclide as a prostatic scanning agent.

MATERIALS AND METHODS

Twenty-five mature male mongrel dogs, previously anesthetized with sodium pentobarbital, were injected via a femoral vein with ^{69m}Zn-chloride in 0.1 *N* HCl diluted in 5 cc normal saline in doses of 7 μCi/kg. A group of 18 female rabbits were similarly studied by ear-vein injection of the ^{69m}Zn-chloride in 0.1 *N* HCl (Union Carbide Corp., Sterling Forest, N.Y.) in larger doses of 33 μCi/kg to provide ample counting statistics (zinc-chloride from Union Carbide, Sterling Forest, N.Y.).

To establish the rate of accumulation and elimination of the zinc radionuclide, the dogs and rabbits were sacrificed at predetermined intervals. The dogs were sacrificed at 30, 60, 120, 180, 240 and 360 min after injection, while the rabbits were sacrified at 2, 4, 8, 16 and 20 hr postinjection. Aliquots of liver, prostate, kidney, pancreas, eye, lung, muscle, testes, fat, intestine, heart and blood were counted and compared with a standard of the administered dose prepared from the original ^{69m}Zn-chloride solution.

In vivo counting as well as scanning of animal organs were carried out by using a Nuclear-Chicago Pho/Gamma III Scintillation Camera. The scintillation camera was adapted with a high-energy pinhole collimator to allow magnified images of the small animal organs with good resolution. Aliquots of organs and blood were measured by a Nuclear-Chicago Auto/Gamma Scintillation Well with a 2 × 2-in. NaI(Tl) crystal having a sensitivity of 3.3×10^5 cpm/μCi.

The ^{69m}Zn tissue absorbed doses were calculated using the following equation (*7,8*):

$$D\,(v \leftrightarrow v) = \tilde{C}_v \sum_i \Delta_i\, \phi_i\, (v \leftrightarrow v)$$

Received Aug. 15, 1969; revision accepted Jan. 29, 1970.

For reprints contact: Steven A. Lorber, New York University Medical Center, School of Medicine, 550 First Ave., New York, N.Y. 10016.

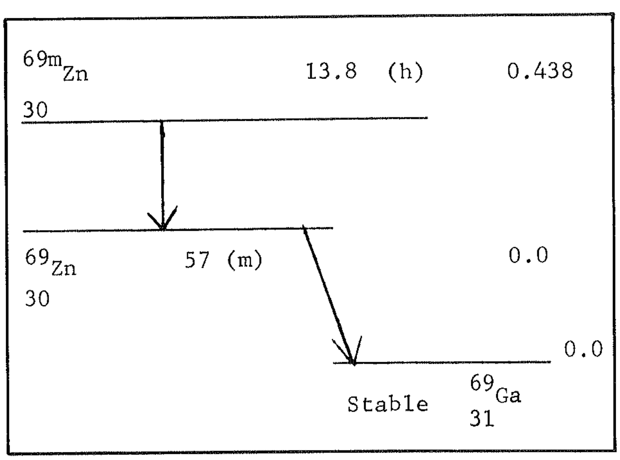

FIG. 1. Decay scheme of ^{69m}Zn.

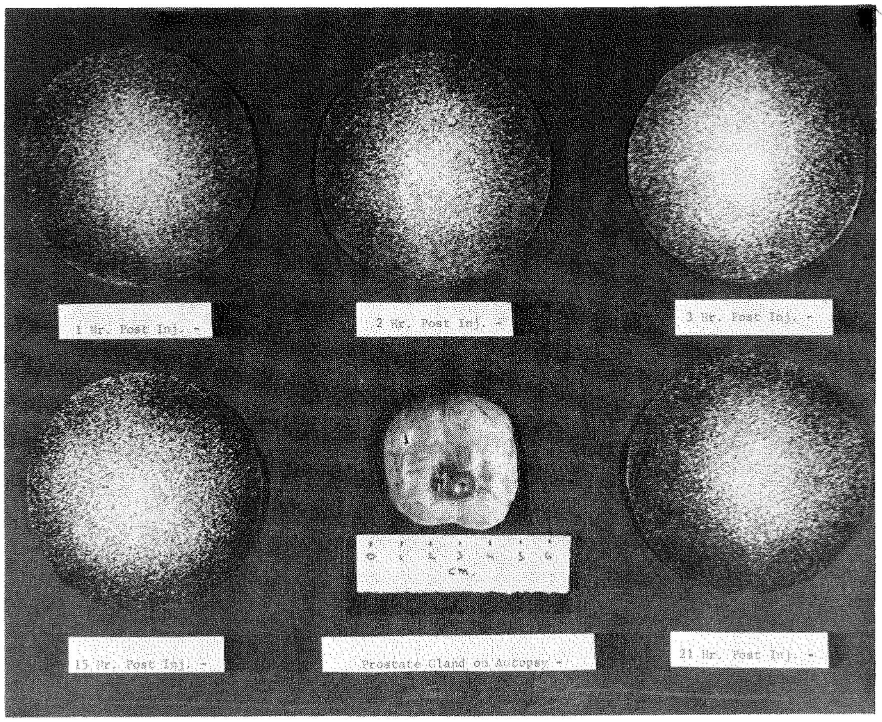

FIG. 2. *In vivo* gamma-camera prostate scans using ^{69m}Zn.

TABLE 1. Δ_i EQUILIBRIUM ABSORBED DOSE CONSTANTS FOR ^{69m}Zn EMISSIONS (9)

Type of emission	Δ_i
Beta-I	0.6923
Gamma-I	0.8861
Internal Con. Gamma I	0.0479
Ch. X-rays and Auger electrons	0.0008

In which

Δ_i = equilibrium absorbed dose constant for radiation of type i = 1, 2, 3 . . . . with a fractional frequency n_i per disintegration, and a mean energy, $n_i\bar{E}_i$ in MeV. $\Delta_i = 2.13\ n_i\bar{E}_i\left(\frac{\text{gm-rads}}{\mu\text{Ci-hr}}\right)$.

$$\phi_i\ (v \leftarrow\rightarrow v) = \frac{\text{energy from the i}^{\text{th}}\text{ type of radiation in the source v absorbed in volume, v.}}{\text{energy of the i}^{\text{th}}\text{ type radiation emitted by the source volume, v.}}$$

$\tilde{C}_v$ = cumulated concentration of activity in volume, v, in $\frac{\mu\text{Ci-hr}}{\text{gm}}$.

$$\tilde{C}_v = 1.44\ c(0)\ [T_{\text{elim. eff.}} - T_{\text{up. eff.}}]$$

in which

$c(0)$ = Maximum concentration of radionuclide in the tissue of interest if there were instantaneous uptake of the radionuclide.

$T_{\text{elim eff}}$ = The effective half-time for elimination of the radioisotope in the tissue of interest.

$T_{\text{up eff}}$ = The effective half-time for uptake of the radioisotope in the tissue of interest.

The values of Δ_i and ϕ_i used to calculate the ^{69m}Zn tissue absorbed doses are given in Tables 1 and 2.

RESULTS

In dogs the accumulation of radioactive zinc in the time interval of 30–180 min postinjection was found to be greatest in the liver. The concentrations

TABLE 2. ϕ_i ABSORBED FRACTION VALUES FOR THE 0.438-MeV GAMMA EMISSION OF ^{69m}Zn (10)

Organ	ϕ_i
Liver	0.1227
Prostate	0.0736
Kidney	0.1717
Pancreas	0.1223
Testes	0.0738
Retina/eye	0.0061
Lung	0.3680
Muscle	0.3288
Spleen	0.1396
Blood	0.3288
Heart	0.1721
Fat	0.4917
Intestine	0.7375
Total body	0.3288

TABLE 3. AVERAGE PERCENT (× 10^2) TOTAL DOSE/GRAM IN DOG TISSUES OF ^{69m}Zn

Sacrifice time after injection (min)	Organ									
	Liver	Prostate	Pancreas	Kidney	Spleen	Retina	Lung	Muscle	Testes	Blood
30	3.6	0.94	1.2	1.2	0.50	0.56	0.33	0.09	0.11	0.18
60	5.3	1.2	1.9	2.2	0.56	0.54	0.31	0.13	0.14	0.12
120	6.2	2.3	2.0	2.4	0.62	0.69	0.52	0.17	0.17	0.15
180	5.4	1.8	2.6	2.3	0.68	0.68	0.42	0.12	0.17	0.13
240	4.8	2.6	2.4	3.0	0.62	0.33	0.34	0.14	0.08	0.12
360	4.4	3.8	3.5	2.2	0.79	0.22	0.19	0.20	0.04	0.14

TABLE 4. AVERAGE PERCENT (× 10^2) TOTAL DOSE/GRAM IN RABBIT TISSUES OF ^{69m}Zn

Sacrifice time after injection (hr)	Organ									
	Liver	Pancreas	Kidney	Spleen	Eye	Lung	Muscle	Fat	Intestine	Heart
2	0.13	0.14	0.12	0.104	0.12	0.049	0.008	0.006	0.134	0.025
4	0.14	0.10	0.076	0.058	0.004	0.035	0.007	0.004	0.062	0.028
8	0.13	0.03	0.10	0.082	0.005	0.035	0.007	0.005	0.112	0.043
12	0.10	0.12	0.10	0.088	0.003	0.039	0.006	0.005	0.097	0.046
16	0.08	0.075	0.067	0.52	0.002	0.018	0.003	0.002	0.070	0.031
20	0.04	0.039	0.031	0.023	0.005	0.022	0.004	0.003	0.045	0.019

of the zinc radionuclide found in prostate, pancreas and kidney were approximately one third of that measured in the liver (Table 3).

In the rabbit study the greatest accumulation of ^{69m}Zn per gram of tissue was found alternately in the pancreas, liver and intestines in the time intervals between 2 and 20 hr postinjection (Table 4).

In the rabbit study the greatest overall concentration of the zinc radionuclide in all time intervals was found in the pancreas and liver followed closely by kidney, spleen and intestines. Heart, lung and muscle showed lesser concentrations of the zinc radionuclide, while eye and fat showed the lowest concentration.

In dogs the zinc radionuclide was found to reach its peak concentration in the liver, spleen, retina, muscle and testes at approximately 120 min, the lung 150 min and kidney 180 min postinjection. The time of peak accumulation of the zinc radioisotope in the prostate, determined by *in vivo* monitoring, was found to occur 16 hr postinjection. The pancreatic concentration of the ^{69m}Zn in the dog study continued to increase beyond the 360 min studied. The rabbit study showed that the concentration of the zinc radioisotope in the pancreas peaked at 540 min postinjection. In general, the time for peak accumulation of the ^{69m}Zn in rabbits was found to be longer than that in dogs. Liver, lung and fat in the rabbit study reached peak concentrations at 300 min postinjection while spleen, heart and intestines showed peak concentrations at 420 min postinjection. Eye and muscle peak concentration times in the rabbit study were found to be the same as that in the dog study.

Radiation-absorbed tissue doses for man were estimated using the dog and rabbit study values. Radiation-absorbed dose for prostate was estimated to be approximately 4 rads, while liver ranged between 0.48 and 2.75 rads. In Table 5 a comparison is shown between the ^{69m}Zn radiation-absorbed tissue doses estimated for man and other radioisotopes used for organ scanning. The estimated beta-gamma absorbed tissue doses for man were found to be within the range of radiation-absorbed doses of other commonly used radionuclides. For example, 150 μCi of ^{198}Au will result in a radiation-absorbed dose to the liver of about 5.7 rads while the radiation-absorbed dose to the liver due to ^{69m}Zn is estimated to range between 0.48 and 2.75 rads.

Figure 2 shows a sequential *in vivo* gamma camera series of a dog's prostate taken 1, 2, 3, 15 and 21 hr following the injection of the zinc radioisotope. The scan at 15 hr postinjection shows a uniform distribution of the radioisotope within the gland. This prostate gland at autopsy was bilobate, hypertrophic and weighed 18 gm.

TABLE 5. COMPARISON OF ABSORBED DOSE FROM COMMONLY USED RADIONUCLIDES WITH ^{69m}Zn-Cl ABSORBED DOSE

Organ	Radiopharmaceutical	Administered dose	Absorbed dose (rads)	^{69m}Zn-Cl (500 μCi — 7 μCi/kg) Absorbed dose (rads)	
				Dogs	Rabbits
Prostate	^{69m}Zn Cl			4.27	—
Liver	^{99m}Tc-colloid*	2 mCi	0.66–0.72	2.75	0.48
	^{198}Au-colloid*	150 μCi	5.7		
	^{131}I-aggregated albumin*	500 μCi	0.300		
	^{75}Se-selenomethionine†	250 μCi	0.5		
	^{75}Se-selenomethionine‡	210 μCi	0.6		
	^{131}I-rose bengal*	150 μCi	0.25–0.50		
	^{131}I-macroaggregated HSA‖	300 μCi	0.397		
Pancreas	^{75}Se-selenomethionine†	250 μCi	0.06	0.58	0.29
Kidney	^{75}Se-selenomethionine‡	210 μCi	0.06		
	^{75}Se-selenomethionine†	250 μCi	14	1.64	0.20
Gonads	^{75}Se-selenomethionine†	250 μCi	2.5	0.02 (male)	—
	^{99m}Tc-colloid§	3 mCi	0.04 (male)		
	^{198}Au-colloid§	150 μCi	0.07 (female)		
			0.06 (male)		
			0.09 (female)		
Whole body	^{75}Se-selenomethionine†	250 μCi	2.2	0.15	
	^{131}I-macroaggregated HSA‖	300 μCi	0.103		
	^{131}I-albumin‖	375 μCi	0.04		
	^{198}Au-colloid*	150 μCi	0.35		
	^{131}I-aggregated albumin*	500 μCi	0.06		
	^{131}I-rose bengal*	150 μCi	0.05–0.15		
Lung	^{131}I-macroaggregated HSA‖	300 μCi	1.9	0.25	0.13
Blood	^{131}I-macroaggregated HSA‖	300 μCi	0.37–0.62	0.11	—
	^{131}I-albumin‖	375 μCi	2.00		
Spleen	^{99m}Tc-colloid§	3 mCi	0.48–1.3	0.09	0.42
	^{198}Au-colloid§	150 μCi	3.7–11.0		
Muscle				0.16	0.04
Heart					0.045
Intestine					0.71
Fat					0.014
Retina/eye				0.14	0.05

* Wagner, H. N. Jr.: *Principles of Nuclear Medicine,* W. B. Saunders Co., Philadelphia, 1968, p. 608.
† Wagner, H. N. Jr.: *Principles of Nuclear Medicine,* W. B. Saunders Co., Philadelphia, 1968, p. 621.
‡ Croll, M. and Brady, L. W.: *Recent Advances in Nuclear Medicine,* Appleton-Century-Croft, New York, 1966, p. 83.
‖ Wagner, H. N. Jr.: *Principles of Nuclear Medicine,* W. B. Saunders Co., Philadelphia, 1968, p. 778.
§ Croll, M. and Brady, L. W.: *Recent Advances in Nuclear Medicine,* Appleton-Century-Croft, New York, 1966, p. 107.

SUMMARY

In summary, zinc chloride in the form of radioactive ^{69m}Zn-chloride when injected into mature male dogs and female rabbits was found to concentrate most in the liver and less in the prostate, pancreas and kidney. The ^{69m}Zn beta-gamma absorbed doses of the target organs studied were found to be within the acceptable ranges of other commonly used radioisotopes. Satisfactory gamma-camera scans of the prostate were obtained. The possibility of morphological evaluation of the prostate by scanning is especially promising.

ACKNOWLEDGMENT

The authors wish to acknowledge the American Cancer Society, Miss Pierette Wise, and Mrs. Katherine Boddie for their assistance in this study.

REFERENCES

1. PRASAD, AS: *Zinc Metabolism,* Charles C Thomas, Springfield, 1966

2. SHELINE GE, CHAIKOFF IL, JONES HB et al: Studies on the metabolism of zinc with the aid of its radioactive isotope. I. The excretion of administered zinc in urine and feces. *J Biol Chem* 149: 139–156, 1943

3. PROUT GR, SIERP M, WHITMORE WF: Radioactive zinc in the prostate, some factors influencing concentrations in dogs and men. *JAMA* 169: 1703–1710, 1959

4. MESCHAN I, QUINN JL, WITCOFSKI RL, et al: Utilization of radioactive zinc and manganese in an effort to visualize pancreas. *Radiology* 73: 62–68, 1959

5. JOHNSTON GS, WADE JC, MURPHY GF, et al: Prostate scintiscanning. *J Nucl Med* 9: 328, 1968

6. STROMINGER D, HOLLANDER JM, SEABORG GT: Table of Isotopes. In *Radiological Health Handbook,* Division of Radiological Health, U.S. Department of Health, Education and Welfare, Washington, D.C., 1960, p. 255

7. LOEVINGER R: *Radiation Dosimetry,* vol. III, Attix, FH and Rochlin E, eds., Academic Press, New York, 1969, pp. 51–90

8. LOEVINGER R, BERMAN M: A scheme for absorbed dose calculations for biologically-distributed radionuclides. *J Nucl Med Suppl. No. 1,* 7, 1968

9. SMITH EM, BROWNELL GL, ELLETT, WH: *Principles of Nuclear Medicine,* Wagner HN, ed., W. B. Saunders Company, Philadelphia, 1968, p. 756

10. SMITH EM, BROWNELL GL, ELLETT WH: *Principles of Nuclear Medicine,* Wagner HN, ed., W. B. Saunders Company, Philadelphia, 1968, p. 769

THE SOCIETY OF NUCLEAR MEDICINE 18th ANNUAL MEETING

June 28–July 2, 1971 **Biltmore Hotel** **Los Angeles**

SECOND CALL FOR SCIENTIFIC EXHIBITS

The Scientific Exhibits Committee announces that abstracts of exhibits are now being reviewed for the 18th Annual Meeting. Abstracts of exhibits, large or small, are welcomed from members, non-members and organizations. Exhibits supporting scientific papers to be presented are encouraged. Illuminators similar to those used by RSNA will be available.

Abstract format: Abstracts must be submitted on a special abstract form for scientific exhibits which is available from The Society of Nuclear Medicine, 211 E. 43rd St., New York, N.Y. 10017.

Scientific Exhibit Awards. The Society is pleased to announce the presentation of Gold Medal, Silver Medal, Bronze Medal and Honorable Mention awards for the most outstanding scientific exhibits. These are judged on the basis of scientific merit, originality, display format and appearance.

Abstract deadline: Send abstracts on or before April 1, 1971 to:

A. EVERETTE JAMES, JR., M.D.
The Johns Hopkins Medical Institutions
Department of Radiological Sciences
615 North Wolfe Street
Baltimore, Maryland 21205