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BROOKHAVEN NATIONAL LABORATORY

MEMORANDUM

The Medical Research Center
Brookhaven National Laboratory
Upton, L. I., New York

DATE: 24 March 1971

TO: A. Harrison

FROM: E. P. Cronkite, M.D. E P Cronkite

SUBJECT: CIRC Numbers

The following CIRC #s are inactive. Except for completing old records, they should not be used for identifying patient activity until reactivation is formally approved.

Principal Investigator	CIRC #
Dr. Cronkite	3
	4
	20
	23
	35
	35A
Dr. Dahl	5
	6
	14
	25
Dr. Jesseph	1
Dr. Robertson	9
	10
	16
	28
Dr. Schiffer	22

EPC/ck
cc: CIRC Committee
Mr. Finn
Dr. Dahl

REPOSITORY Records Holding Area, Bldg. 494
COLLECTION Committee-Clinical Investigations and Uses of Radioisotopes
BOX No. 4
FOLDER CIRC #6

1179453

The Committee on Clinical Investigations and Uses of Radioisotopes hereby approves the program with the following title:

Whole Body Sodium Turnover Study

CIRC # 6 has been assigned to this program.

Walton W. Shreeve

Walton W. Shreeve, M.D., Ph.D., Chairman

E. P. Cronkite

Eugene P. Cronkite, M.D.

E. Schackow

Eckart Schackow, M.D.

M. H. Van Woert

Melvin H. Van Woert, M.D.

J. S. Robertson

James S. Robertson, M.D., Ph.D. (ex officio)

Date November 8, 1963

Place Medical Research Center
Brookhaven National Laboratory
Upton, New York

1179454

Resubmitted proposal of old Project # H-54

FORM FOR INITIATION OR REVIEW OF CLINICAL

INVESTIGATIVE PROGRAMS

(Submit original only to Department Chairman)

A. Title of the proposal: Whole Body Sodium Turnover Study

B. Sponsoring physician(s): Dr. L. K. Dahl

C. Responsible investigator(s): Drs. L. K. Dahl, L. C. Lax, and E. Schackow

D. Brief description of the study, including its general goals and purpose, and pertinent information on past studies: (Attach additional sheets if necessary.)

Previous studies by one of us (L.K.D.) have indicated that certain differences exist in the metabolism of sodium, between normotensive and hypertensive subjects.

The aim of this study, therefore, is to measure turnover of total exchangeable body sodium by estimation of biological half-life and to determine the mass of this sodium by the isotope dilution principle, in both hypertensive and normotensive human subjects.

E. Reasons why the investigation(s) are to be performed on human subjects.

Hypertension is a disease of humans beings and all hypotheses as to the role played by salt in hypertension must therefore, be tested in human subjects.

F. Type of patient in which the study is to be done (including approximate number of subjects, if known; special restrictions or requirements; method of obtaining consent; etc.):

Subjects with hypertensive cardiovascular disease and no secondary complications such as renal disease, and normotensive controls which are hospitalized for some other disease but not for hypertension (approximately 40 subjects per year). Subjects are to be placed on restricted salt diets and on varying salt intake regimens. Consent is obtained directly from the patient.

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Resubmitted propo l of old Project # H 54

SUPPLEMENTARY FORM FOR RADIOISOTOPE
ADMINISTRATION TO HUMAN BEINGS

A. Radioisotope

1. Species: (Radioisotope or labeled compound, eg. $Na^{24}Cl$ or 1-C^{14}- glucose)
Na^{22} Cl in HCl solution

2. Physical characteristics: (Physical half-life; decay scheme (or type, energy and relative frequency of major emissions)
Physical half-life = 2.6 years. See attached sheet for decay scheme.

3. Source: (BNL reactor, cyclotron, hot lab.), commercial supplier, etc.)
Accelerator produced - Nuclear Science and Engineering.

4. Preparation: (Target material, quantity, special problems)
Mg + d

5. Specific activity and isotopic purity of administered material:
> 99% radiochemically pure.

6. Radioassay and calibration procedures: (Include validation to be performed at BNL prior to use) Dilution to desired strength on arrival at Medical Res. Center and calibration on well counter #2, BNL #37172 in the Medical Research Center.

7. Vehicle and route of administration:
Isotonic saline

8. Procedures for control of sterility and pyrogenicity: (Or note that commercially supplied isotopes are certified as ready for administration to human beings.) To be administered orally.

9. Extraneous effects, if pertinent: (Such as pharmacological or toxic actions of the parent compound or vehicle, etc.) None.

B. Radiation Dosage

1. Biological half-life or half-lives, including slow components:
See attached sheet.

2. Organ, cellular, or subcellular localization: (Should account for the effects of special drugs or agents on altering the natural distribution of the radioisotope)

a. Critical or "target" organ(s): No specific one.

b. Gonadal exposure: As for any other organ - see attached sheet.

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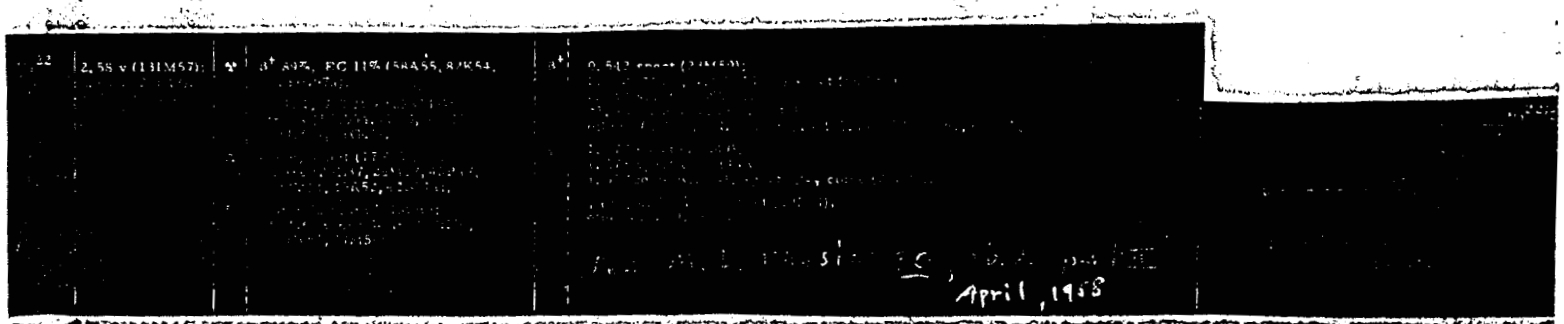
Supplementary Sheet No. 1

DECAY SCHEME OF NA^{22}

(See reference #4)



The patient will not be allowed to receive a cumulative dose that will average over 0.3 rad per week or 5.0 rad per year. Calculations for various biological half-lives, using different doses in a 70 Kg. individual have been made as follows: (See references 1, 2, 3, 4 as obtained from previous proposal of Project # H-54.)

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S lementary Sheet No. 2

Dose	Biological Half Life	Total Absorbed Dose in Rads
70 μc	10 days	1.19
70 μc	20 days	2.38
70 μc	30 days	3.57
70 μc	40 days	4.76
70 μc	50 days	5.95
70 μc	60 days	7.14
70 μc	2.6 years	113
50 μc	10 days	0.85
50 μc	20 days	1.70
50 μc	30 days	2.55
50 μc	40 days	3.40
50 μc	50 days	4.25
50 μc	60 days	5.10
50 μc	2.6 years	81
25 μc	10 days	0.43
25 μc	20 days	0.85
25 μc	30 days	1.27
25 μc	40 days	1.70
25 μc	50 days	2.12
25 μc	60 days	2.55
25 μc	2.6 years	41.
10 μc	10 days	0.17
10 μc	20 days	0.34
10 μc	30 days	0.51

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Supplementary Sheet No. 3

Dose	Biological Half Life	Total Absorbed Dose in Rads
10 μc	40 days	0.68
10 μc	50 days	0.85
10 μc	2.6 years	16.2
3 μc	10 days	0.05
3 μc	20 days	0.10
3 μc	30 days	0.15
3 μc	40 days	0.20
3 μc	50 days	0.26
3 μc	60 days	0.31
3 μc	2.6 years	4.9
1 μc	10 days	0.02
1 μc	20 days	0.04
1 μc	30 days	0.05
1 μc	40 days	0.07
1 μc	50 days	0.09
1 μc	60 days	0.11
1 μc	2.6 years	1.62

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Supplementary Sheet No. 4

For a person, given an initial concentration of 1 μc Na^{22}/kg body weight, the absorbed radiation dose received at a point at the center of the trunk, when the isotope can be assumed uniformly distributed over the whole body, can be calculated as (references 1, 2, 3):

	β-dose rate (millirad/hr)	λ - dose rate (millirad/hr)	Combined dose rate (millirad/hr)
Na^{22} 1 μc/kg	0.40	3.05	3.45

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REFERENCES

1. Marinelli, L.D., et al. Rev. Mod. Phys. 19: 25, 1947.

2. Hine, G.J., and Brownell, G.L. (Eds). (1956). Radiation Dosimetry, New York, Academic Press.

3. Mayneord, W.V., and Sinclair, W.K. The Dosimetry of Artificial Radioactive Isotopes. Advances in Biological and Medical Physics, 3: (1953), New York, Academic Press.

4. Hollander, J.M. et al. Rev. Mod. Phys. 25: 469, 1953.

1179461

BROOKHAVEN NATIONAL LABORATORY

MEMORANDUM

DATE: June 22, 1959

TO: Committee for the Use of Isotopes in Humans.

FROM: L.K. Dahl, M.D. and W.H.Gordon, Jr., M.D.

SUBJECT: Appendix to Use of Na^{22} as a tracer in hospitalized patients.

H-54

Preparation of material:

The material will be administered either intravenously or orally. The material to be administered I.V. will be sterilized by autoclaving and placed in a carrier solution of glucose in water or saline, depending on the nature of the particular experiment. This will be free from pyrogens.

The Na^{22} will be calibrated (by aliquot) in the form actually injected.

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BROOKHAVEN NATIONAL LABORATORY

MEMORANDUM

DATE: June 15, 1959

TO: Committee for the Use of Isotopes in Humans.

FROM: L. K. Dahl, M.D., and LKD.
W. H. Gordon, Jr., M.D. WHG

SUBJECT:
Use of Na^{22} as a tracer in hospitalized patients.

H-54

Request is made for authorization for the use of Na^{22} in tracer quantities in selected hospitalized patients. For the most part, these patients will be over 45 years of age, and should the isotope be considered for administration to individuals of younger age, it would be only in persons known to have diseases which will result in a sharply limited life span.

This isotope will be used in conjunction with long term studies and research on hypertension where the shorter-lived Na^{24} cannot be used without prohibitive radiation dosage being given.

It is proposed to administer the isotope orally and intravenously; for some studies the whole-body counter will be used, and for others urine, stool, blood, and possibly other tissues will be collected.

While Na^{22} has a physical half-life of 2.6 years, the biological half-life has been shown to depend on the sodium intake and sodium balance of the individual (1); the excretion of Na^{22} can be hastened readily by a high intake of sodium (2), a fact confirmed in our own laboratory on rats (3). Estimates

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of the biological half-life of Na^{22} in humans, range from 10 - 26 days (4,5) but our own evidence from rats with Na^{22} (3) and humans using Na^{24} suggests that on a low sodium diet (100 mgm/day) the biological half-life would be longer, and on a high sodium diet (4 - 8 gm/day, i.e. 10 - 20 gm as NaCl) it would be much shorter than these stated ranges. In any event, in the adult individual, excluding pregnancy and situations where mineralization of bone is occurring, there is no evidence of permanent retention of Na^{22} (5). In view of our capacity to vary the biological half-life of this isotope at will, no problems are anticipated in the use of Na^{22} at the dose levels proposed.

In general two ranges of dosage level are planned for our studies. For the most part doses of 0.5 to 3 μc will be used for the whole body counter work; occasionally it is possible that 25 - 70 μc may be administered for studies not involving the whole body counter. Since the addition of increments of NaCl to the diets of our rats has decreased the biological half-life of Na^{22} to about one day, it is anticipated that the larger amounts of Na^{22} in humans can be eliminated as rapidly by similar means. In any event, however, the patient will not be allowed to receive a cumulative dose that will average over 0.3 rad per week or 5.0 rad per year. Calculations for various biological half-lives, using different doses in a 70 Kg. individual have been made as follows: (4, 6, 7, 8, 9):

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Na^{22} Characteristics (References (10,11)

	Half Life	Radiation	Maximum Energy, MEV
$_{11}Na^{22}$	2.60 year	β_1^+ ($\sim$100%)	0.542
		β_2^+ ($<$0.1%)	$\sim$1.8
		γ (after β_1^+)	1.277

DECAY SCHEME

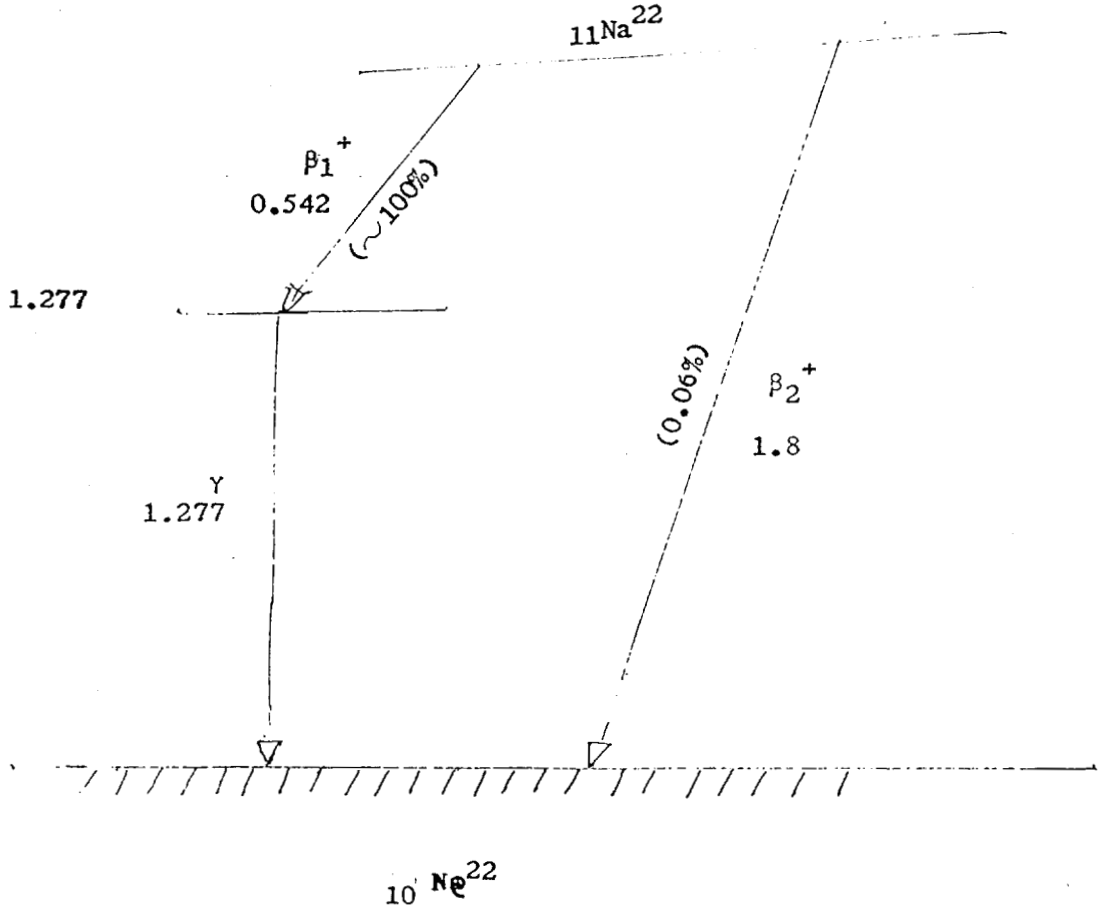

DIAGRAM #1

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Dose	Biological Half Life	Total Absorbed Dose in Rads
70 μc	10 days	1.19
70 μc	20 days	2.38
70 μc	30 days	3.57
70 μc	40 days	4.76
70 μc	50 days	5.95
70 μc	60 days	7.14
70 μc	2.6 years	113
50 μc	10 days	0.85
50 μc	20 days	1.70
50 μc	30 days	2.55
50 μc	40 days	3.40
50 μc	50 days	4.25
50 μc	60 days	5.10
50 μc	2.6 years	81
25 μc	10 days	0.43
25 μc	20 days	0.85
25 μc	30 days	1.27
25 μc	40 days	1.70
25 μc	50 days	2.12

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Dose	Biological Half Life	Total Absorved Dose in Rads
25 μc	60 days	2.55
25 μc	2.6 years=	41
10 μc	10 days	0.17
10 μc	20 days	0.51
10 μc	30 days	0.51
10 μc	40 days	0.68
10 μc	50 days	0.85
10 μc	2.6 years	16.2
3 μc	10 days	0.05
3 μc	20 days	0.10
3 μc	30 days	0.15
3 μc	40 days	0.20
3 μc	50 days	0.26
3 μc	60 days	0.31
3 μc	2.6 years	4.9
1 μc	10 days	0.02
1 μc	20 days	0.04
1 μc	30 days	0.05
1 μc	40 days	0.07

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Dose	Biological Half Life	Total Absorbed Dose in Rads
1 μc	50 days	0.09
1 μc	60 days	0.11
1 μc	2.6 years	1.62

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For a person, given an initial concentration of 1 μc Na^{22}/kg body weight, the absorbed radiation dose received at a point at the center of the trunk, when the isotope can be assumed uniformly distributed over the whole body, can be calculated as (references 3, 7, 8, 9):

	β-dose rate (millirad/hr)	λ - dose rate (millirad/hr)	Combined dose rate (millirad/hr)
Na^{22} 1 μc/kg	0.40	3.05	3.45

It is requested therefore, that permission be given to administer Na^{22} to selected individuals in amounts and under conditions as noted in the foregoing.

Request approved.

Elmer E. Stickley, Ph.D.

Walton W. Shreeve, M.D., Ph.D.

Donald C. Borg, M.D.

Gerald F. McGinniss, M.D.

James S. Robertson, M.D., Ph.D.
Ex-officio

Lee E. Farr, M.D. Ex-officio

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REFERENCES

1. Martin, M. Mencer and Walker, G. Studies with Na^{22} - an Assessment of Sodium Balance and Distribution. Metabolism, 6: 466, September 1957.

2. Martin, M. Mencer, Walker, G. and Chapman, M. Sodium Balance Studied with ^{22}Na and an External Counter for Measuring Whole-Body Radioactivity. The Lancet , March 30, 1957, pp.653-656.

3. Dahl, L.K., and Gordon, W.H., Jr. Biological Half-life of Na^{22} in Rats. Unpublished data of experiments done at Brookhaven National Laboratory.

4. Veall, N. and Vetter, H. Radioisotope Techniques in Clinical Research and Diagnosis, Butterworth & Co. (Publishers) Ltd. (1958).

5. Veall, N., Fisher, H.J., Brown, J.C.M., Bradley, J.E.S., An Improved Method for Clinical Studies of Total Exchangeable Sdoium, Lancet, i: 419, (1955).

6. Bertinchamps, A.J., and Cotzias, G.C. Dosimetry of Radioisotopes. Science, 128: No. 3330, 988-990, Oct. 24, 1958.

7. Marinelli, L.D., et al. Rev. Mod. Phys. 19: 25, 1947.

8. Hine, G.J., & Brownell, G.L. (Eds). (1956) Radiation Dosimetry, New York, Academic Press.

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References (Continued)

9. Mayneord, W. V., and Sinclair, W.K. The Dosimetry of Artificial Radioactive Isotopes. Advances in Biological and Medical Physics, 3: (1953), New York, Academic Press.

10. Hollander, J.M. et al. Rev. Mod. Phys. 25: 469, 1953.

11. National Bureau of Standards. Circ. 499, with Supp. 1, 2, & 3.

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