A MODIFIED ^{125}I PLASMA VOLUME PROCEDURE

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FOREWORD

This report was prepared in the Internal Medicine Branch under task No. 775502. The work was accomplished between May and July 1969. The report was submitted for publication on 22 July 1969.

A Packard series 5000 Auto-Gamma spectrometer was used to measure the ^{125}I activity.

This report has been reviewed and is approved.

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ABSTRACT

Reducing the radiation exposure dose from radioisotope procedures is a constant requirement of the radioisotope laboratory. A modified RISA-^{125}I plasma volume procedure has now been developed which, without sacrificing accuracy, reduces the exposure dose by a factor of 10. Curves are also presented which permit selection of a minimum plasma sample or a minimum dose of RISA-^{125}I, with short or long counting times.

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I. INTRODUCTION

The reduction of radiation dose to patients is a matter of continual interest and importance for the radioisotope laboratory. The results of an examination of a standard ferrokinetics procedure, in which the exposure dose was reduced by a factor of 10, have been presented previously (1). In the current report we have used a similar approach (2) to analyze our present method for performing RISA-^{125}I plasma volume determinations (RISA-^{125}I is radioiodinated human serum albumin in a saline solution). In addition to determining the minimum exposure dose, we have also studied the minimum sized possible blood samples.

In a recent report, we examined the problem of performing repeated total body water determinations with tritium within a restricted period of time (3). Because plasma volume determinations can likewise be determined repeatedly within such a restricted period, we have also studied this problem in relation to RISA-^{125}I plasma volumes.

II. MATERIALS

The RISA-^{125}I solution is sterile and suitable for human injection. The concentration of activity is 10 μc./ml., and the activity used per plasma volume determination was either 5 μc. or 0.5 μc. The RISA-^{125}I activity was measured by means of a gamma spectrometer system.

The total body exposure dose from RISA-^{125}I was calculated through the formula:

$$D\gamma = 0.0346 \times \tau \times \bar{g} \times T\tfrac{1}{2}_{(effective)} \times \mu c./gm.$$

in which

$\tau = 0.6$

$\bar{g} = 126$ and

$T\tfrac{1}{2}_{(effective)} = 13$ days.

The value of grams was calculated on the basis of a 70-kg. man (standard man), thus making the value equal to 70,000 gm. The dose was calculated for amounts of RISA-^{125}I activity ranging from 0.1 to 100 μc. The values calculated are listed in table I.

III. METHOD

The standard procedure for the plasma volume determination involves the following seven steps. (a) The patient takes, orally, 10 drops of Lugol's solution (iodine, potassium iodide, and water) to block the uptake of RISA-^{125}I by the thyroid. This solution is usually taken 24 hr. before the determination is made. (b) The injection and standard doses are prepared. (c) Accordingly, 10 μc. of RISA-^{125}I are mixed with saline to a total volume of 6.0 ml.—of which 3 ml. are used in the injection dose, and 3 ml. in the standard dose. (d) Next the standard dose is prepared. The 3 ml. of the solution (5 μc.) of RISA-^{125}I are diluted to 1 liter with isotonic saline plus 0.5 ml. of human serum albumin. (e) The injection dose, containing 5 μc. of RISA-^{125}I solution, is injected into the patient. (f) Then, 10 to 20 min. after injection, 5 ml. of the whole blood are withdrawn in heparin. The blood is centrifuged and 2 ml. of plasma are collected

TABLE I

Change in exposure with increasing amount of ^{125}I

RISA-^{125}I (μc.)	Total body exposure (mrad)
0.1	0.05
0.5	0.25
1.0	0.5
2.0	1.0
3.0	1.5
4.0	2.0
5.0	2.5
6.0	3.0
7.0	3.5
8.0	4.0
9.0	4.5
10.0	5.0
20.0	10.0
30.0	15.0
40.0	20.0
50.0	25.0
100.0	50.0

for measurement. (g) Finally, the ^{125}I activity is measured in the 2 ml. of the plasma sample and of the standard solution, respectively, and the plasma volume is calculated. To reduce the statistical error of radioactive measurement to 1%, both the sample and standard activities are measured over a period of time sufficient for the accumulation of 10,000 counts.

The standard count rate is multiplied by 1,000 to obtain the total activity injected. When the total activity injected is divided by the activity found, the plasma volume is determined. Thus,

$$\text{Plasma volume} = \frac{\text{standard (c.p.m./2 ml.} \times \text{1,000)}}{\text{sample (c.p.m./2 ml.)}}$$

IV. RESULTS

In the previous report on the measurement of blood volumes with RISA-^{125}I, a 5 μc. dose was used (2). This dose was sufficient to give a counting rate of about 5,000 c.p.m. per 2 ml. of plasma. A rate of 10,000 counts per 2 min. is thus obtained. If this counting rate is held constant and the microcurie dose or plasma sample size varies, a curve of sample size vs. microcurie dose is produced. A point on the curve represents a combination of sample size and microcurie dose which will give 5,000 c.p.m. (fig. 1).

If a 5 μc. dose will produce 5,000 c.p.m./2 ml. plasma sample, then, proportionately, a 0.2 μc. dose should produce 200 c.p.m./2 ml. plasma sample. Since the spectrometer background at the ^{125}I settings is about 100 c.p.m., 200 c.p.m. represents a 2:1 sample-to-background ratio. In our studies with the tritiated water procedure for total body water measurement, a ratio of 2:1 was found to be the minimum which would give reproducible results (3). Therefore, the 200 c.p.m. counting rate should be the minimum which could be used to measure plasma volume reproducibly.

Since 200 c.p.m. is considered the minimal counting rate, this value can be held constant and the microcurie dose or plasma sample size can be varied. Varying the dose or sample size produces a minimal curve whose every

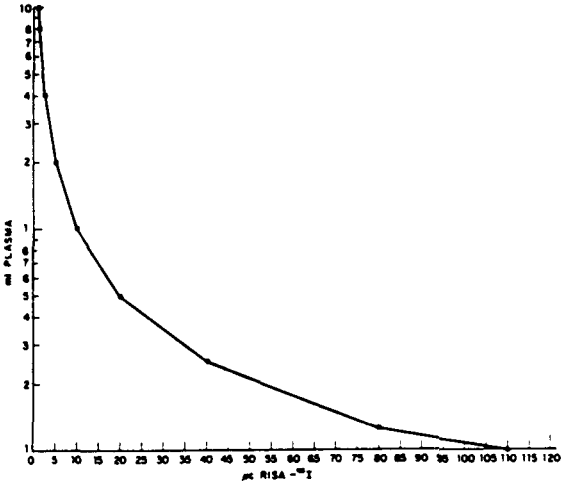

FIGURE 1

This plasma sample size vs. microcuries of RISA-^{125}I will produce a sample counting rate of 5,000 c.p.m.

point represents a combination of factors producing a rate of 200 c.p.m. (fig. 2). Selection of a dose and sample size from this curve should provide conditions for accurate measurement of the plasma volume.

To test the validity of this curve, a dose-sample size set was chosen from a curve slightly above the minimal curve (fig. 2), with a constant count rate of 500 c.p.m. The dose was 0.5 μc. and the sample size was 2 ml. The plasma volume of four subjects was determined by the use of both the standard dose of 5 μc. and the lower dose of 0.5 μc. (table II). Examination of table II shows that the percent difference between the mean plasma volumes is about 1%. This value is close to the statistical error of counting (1%). If the plasma volume is to be repeated many times, within a limited time, other considerations can produce an increased error. For reproducible measurements to be obtained, a 2:1 sample-to-background counting ratio must be possible. The background is the product of the percent clearance per day of the previous ^{125}I dose from the bloodstream, and of the radioactive decay rate of ^{125}I. The product of these two factors must equal 50% before a 2:1 counting ratio is obtainable.

The first step in determining the minimal time-interval between determinations is the calculation of the percent clearance. Five normal male subjects were studied. An injection of 5 μc. of RISA-^{125}I was given on day 0. Samples of 2 ml. of whole blood were collected at time-intervals of: 1, 2, 4, 6, 8, 10, 14, 21, and 28 days after day 0. The activity of all samples was measured and recorded. The decline in activity with time is a product of both the percent clearance and the radioactive decay. In order to present the percent clearance separately from the radioactive decay, all values were first corrected for decay back to day 0. Dividing the resulting values by the day 0 value produced the percent clearance per day. When this value is multiplied by the factor of radioactive decay for each day from day 0, the actual clearance factor per day is produced. If an initial sample count rate of about 5,000 c.p.m. is assumed, the sample-to-background counting ratio per day can be calculated. These values are all summarized in table III.

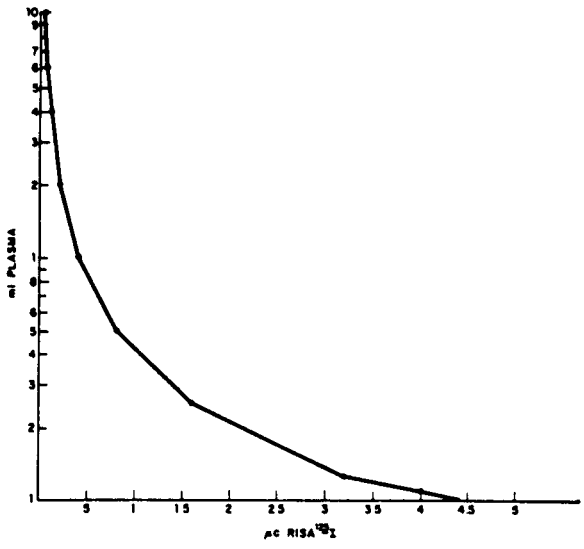

FIGURE 2

A minimal sample counting rate of 200 c.p.m. is produced by this plasma sample size vs. microcuries of RISA-^{125}I.

TABLE II

Comparison of plasma volume determinations

Subject	Injection dose		
	0.5 μc.	5 μc.	Difference
		ml./kg.	
1	53.27	53.00	0.27
2	51.22	50.05	1.17
3	51.42	50.82	0.60
4	48.84	48.20	0.64
$\overline{X}$	51.18	50.51	0.67

The minimum time-interval to reach a 2:1 counting ratio is 4 days. However, since the RISA-^{125}I clearance curve is not linear, 50%

TABLE III

Sample-to-background counting ratios with increasing clearance

Days post-injection	Percent clearance	Percent decay	Sample: background ratio
1	65	98.9	1.6:1
2	56	97.7	1.8:1
4	51	95.7	2.1:1
6	43	93.3	2.5:1
8	38	91.2	2.9:1
10	35	89.1	3.1:1
14	27	85.1	4.0:1
21	20	78.5	6.4:1
28	15	72.4	9.2:1

of the activity is cleared only during the *first 4 days* (not every 4 days). Therefore repetition at a constant dose cannot occur more than three times at the 4-day time-interval without decreasing the ratio below 2:1. By trial and error testing, 14 days was found to be a time-interval at which repeated determinations (with a constant dose) could be made. The initial ratio is 4:1; and the ratio decreases to 2:1 with repetition, but will not decrease below this level. The 14-day interval is selected as the minimal time-interval at which plasma volume determinations can be reproducibly repeated for an indefinite time with a constant dose of RISA-^{125}I.

V. DISCUSSION

We have presented an approach to selecting a dose and sample size which will not only minimize the exposure dose to the patient but also allow accurate determination of the plasma volume. Shown in figure 1 is a single curve which will allow selection of a set of factors, depending on whether the microcurie dose or the sample size is to be minimized. The use of this procedure (fig. 1) also makes possible short counting times, because of the counting rate of 5,000 c.p.m.

If a patient is subject to several isotopic procedures or if counting times are not an important consideration, the factors provided in figure 2 will greatly reduce the exposure dose. If counting times of 50 min. are too long, the exposure dose can be reduced considerably by use of doses between 0.2 μc. and 1 μc. Our study has shown that the exposure can be reduced by a factor of 10—from 2.5 mrad (for a 5 μc. dose) to 0.25 mrad (for a 0.5 μc. dose)—and reproducible results can still be obtained. This exposure is probably close to the minimum dose; however, if the factors in figure 2 and a large sample size are used, the exposure dose can easily be reduced to less than 0.1 mrad.

Repeated determinations at these lower dose levels make possible many plasma volume procedures which have the same total exposure dose as a single plasma volume measurement with the standard 5 μc. dose. To perform these repeated determinations with a constant dose, a time-interval of 14 days between tests is a minimum. If shorter periods of time are required, gradually increasing doses (beginning with low doses) can be used. The limit on this approach occurs when the next highest millicurie dose would subject the patient to a total radiation dose which would be unacceptably high.

The method presented here—for determining the respective minimum for dosage, sample size, and interval between tests—can also be applied to other procedures using radioisotopes. Similar studies of some of these technics are now underway and will be presented in future reports.

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