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LUCAS HEIGHTS RESEARCH LABORATORIES

TISCON, A BASIC COMPUTER PROGRAM FOR THE CALCULATION OF THE BIODISTRIBUTION OF RADIONUCLIDE-LABELLED DRUGS IN RATS AND MICE

by

D.J. MADDALENA

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ABSTRACT

Animal biodistribution studies on radionuclide-labelled drugs are labour-intensive and time-consuming. A method for rapidly carrying out these studies on rats and mice is presented. An interactive computer program, written in BASIC, is used to calculate parameters of interest, such as per cent injected dose (%ID),%ID per gram and target to non-target ratios. National Library of Australia card number and ISBN 0 642 59783 9

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MICE; RADIONUCLIDE KINETICS; RADIOPHARMACEUTICALS; RATS; T CODES

CONTENTS

1.	INTRODUCTION	1
2.	BIODISTRIBUTION METHOD	2
3.	THE COMPUTER PROGRAM 3.1 Input Data 3.2 Input Data Error Correction 3.3 Output Data	3 3 4 5
4.	METHOD OF CALCULATION	5
5.	CONCLUSIONS	8
6.	ACKNOWLEDGEMENTS	8
7.	REFERENCES	8
Арр Арр Арр	endix A TISCON data sheet endix B TISCON program endix C TISCON output data	11 12 15

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1. INTRODUCTION

Animal biodistribution studies are widely used in nuclear medicine to assess the tissue specificity of radionuclide-labelled drugs in the development of new radiopharmaceuticals [Risch et al. 1978]; in critical comparisons of radiopharmaceuticals from different manufacturers, or having different chemical characteristics that are directed to specific target tissues such as skeletal or tumour imaging agents [Hosain 1977; Glenn and 1979]: Colombetti and for the quality control of existing radiopharmaceuticals [Maddalena et al. 1977; US Pharmacopoeia 1980; Baker 1981].

Quantitative animal biodistribution studies involve the administration of a radionuclide-labelled drug to an animal. Most commonly, this is a small rodent such as the rat or mouse. After a prescribed time interval has elapsed, the animal is sacrificed for tissue samples which are then weighed and counted in a gamma counting device. The sample masses and counts, after correction for background and decay, are used to determine the biodistribution of the drug.

Such studies are often carried out on different formulations, each of which may be administered to three to six replicated animals per data point at different doses and over a number of time intervals. Each animal can be expected to yield from 20 to 30 tissue samples. Consequently, it is not uncommon to weigh and count from several hundred to several thousand samples from each experimental study. Without a reasonable degree of automation, the resultant sample and data manipulation can become rather tedious and prone to error.

At the AAEC Research Establishment, a Sartorius model 1219MP electronic balance facilitates sample weighing, and a Nuclear Data model 1185, 300-sample automatic gamma counter is used to automate sample counting. A computer program, TISCON, is used to carry out the data manipulation. With this system it is possible for two operators to carry out 1200 to 1500 routine animal biodistribution studies, involving the analysis of 30 000 to 40 000 tissue samples per annum.

2. BIODISTRIBUTION METHOD

The following method for biodistribution studies on rats and mice has been adopted at the AAEC Research Establishment. Each animal is lightly anaesthetised with diethyl ether and placed in a suitable restrainer. The test radiopharmaceutical solution is then intravenously injected into each animal using a glass microsyringe of suitable capacity (e.g. a Hamilton or SGE $100-\mu$ L syringe); the time of injection is recorded and the animal is placed in a metabolic cage for the collection of urine and faeces.

Where particulate suspensions are to be injected, a microsyringe cannot be used, since the fine bore of the needle can cause changes in the size distribution of the labelled particles. In such cases, a 1-mL disposable syringe fitted with a 23-25 gauge needle is used. The syringe is weighed accurately to 1 mg before and after injection, the difference between the two masses indicating the mass delivered.

Alternatively, the syringe can be counted before and after injection, the difference between the two counts being the activity delivered. However, this method can suffer from counting geometry problems.

When an injection is carried out, and there is doubt on whether the full dose was delivered into the vein, the animal is discarded and replaced by another. To verify the adequacy of injection, a section of the tail 2 cm below and 4 cm above the injection site is sampled.

A volume of the test solution equal to the dose administered to the animals is injected into a 10- or 25-mL volumetric flask, containing a small quantity of isotonic saline; the volume is then adjusted to full capacity with additional isotonic saline. Three 1-mL aliquots are transferred to sample counting containers for use as standards.

Five minutes before completion of the test period post injection, the animal is stimulated to urinate and defaecate, then transferred to a container loaded with diethyl ether for sacrifice. After sacrifice, each animal is weighed and tissue samples of similar size (0.5-2 g) are taken, transferred to pre-weighed counting containers and weighed. A sample data sheet is shown in Appendix A. If sample counting containers are pre-weighed and pre-sorted into groups of the same mass, the balance can be tared for a group container mass, and hence eliminate the need to subtract individual sample container masses at a later date.

The urine is washed from the sides of the metabolic cage and, after total urine mass has been determined, a 1-mL aliquot is transferred to a sample counting container. All samples are counted in an automatic gamma scintillation counter. The three standards are counted at the front of the line and then transferred to the rear to be counted again. The standards are corrected for decay to give a mean standard count per unit time, calculated back to the start of each group of animal tissue samples (i.e. zero time). At this stage, data are ready to be entered into the TISCON program.

3. THE COMPUTER PROGRAM

The TISCON (TISsue CONcentration) program was first written in FORTRAN [Maddalena 1973] then rewritten [Wood 1975] in ACL, an AAEC developed interactive language [Sanger 1971]. The present interactive version has been written in the Digital Systems Corporation's version of [BASIC [DEC 1976] and is run on a PDP11/45 computer. A Microsoft BASIC version of the program is in preparation.

The program is fully prompted, and can be used by students with minimal prior experience. A listing is given in Appendix B.

3.1 Input Data

The following input data are required:

- (a) Initial Data.
 - (i) Animal species (rat or mouse).
 - (ii) Option to add extra tissue sample types. Nineteen tissue types are given, extras can be simply added if required at this stage.

(iii) Option to correct tissue sample counts for decay. This option enables a series of tissue sample counts to be corrected for decay back to time zero when the counting period plus sample handling periods are constant between samples, as is the case for a series of samples counted in an automatic multisample gamma scintillation counter.

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- (iv) Experimental details title, names, dates, etc.
- (v) Numbers of animals (N).
- (vi) Option to determine net sample mass. This option is useful if there is a need for the program to calculate the net sample mass by subtracting the sample container mass from the combined masses of the sample plus sample container.
- (b) Sample Data.
 - Body mass for each rat (g); body mass and carcass mass for each mouse (g).
 - (ii) Standard for each rat or mouse (counts per unit time). This refers to the activity of the injected dose or the dose remaining in the animal corrected to time zero.
 - (iii) Information on sample mass, organ mass and sample counts. This gives the name of the tissue sample and requires sample mass (g), organ mass (g) and sample counts for each rat or mouse (counts per unit time).

3.2 Input Data Error Correction

(a) Correction of Initial Data. After initial data are entered, the option is given either to accept and continue or to re-enter initial data.

(b) Correction of Sample Data. If an incorrect entry is made for a tissue, the program will step backwards to the incorrect tissue for correction, by entering a negative number in lieu of the next sample mass.

(c) Extensive Correction of Sample Data. If a number of incorrect entries are made for the rat or mouse, it may be easier to re-enter all relevant data. This option is given after all the tissues for each animal have been entered.

3.3 Output Data

The TISCON program produces the following output:

- (i) All the input information.
- (ii) The sample counts and counts per organ corrected for decay.
- (iii) The percentage injected dose (% ID) per gram, and tissue-tomuscle, tissue-to-blood and tissue-to-liver ratios for the group of animals.
- (iv) The mean and standard deviations of the % ID, % ID per gram, and tissue-to-muscle and tissue-to-blood ratios.

An example of the program output is given in Appendix C.

4. METHOD OF CALCULATION

The results of biodistribution studies can be expressed in a variety of ways; however, the method most frequently employed is as follows [Risch et al. 1978; Glenn and Colombetti 1979]:

- . Activity of each tissue is expressed as percentage dome per tissue.
- Activity concentration of each tissue is expressed as percentage dose per gram of tissue.
- . Target to non-target ratios are estimated.

The percentage dose per tissue is an estimate of the quantity of the radionuclide-labelled drug localised in the tissue at a prescribed time. It can be based on either the activity of the dose at the time of injection (%

ID) or the activity remaining in the animal at the time of sacrifice (percentage dose remaining (% DR)). The former measurement usually includes excreta (urine, faeces) data whereas the latter does not. Hence

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$$\%ID = \frac{C2 \times W2 \times 100}{W1 \times S}$$

where C2 is the decay corrected sample count per unit time, S is the count per unit time of an external standard of suitable geometry corrected for decay, W1 is the sample mass (g) and W2 is the organ mass (g).

It should be noted that the organ mass of the muscle, skin, bone and blood cannot be conveniently measured; in such cases, a factor based on the body mass of the animal is used.

At the AAEC Research Establishment the following factors are used for the rat (where B is the body mass (g)):

organ	mass	(muscle)	=	0.45 x B
organ	mass	(skin)	=	0.20 x B
organ	mass	(bone)	=	0.12 x B
organ	mass	(blood)	=	0.07 x B

These factors are based on results from the dissection of 20 pathogen-free Australian Albino Wistar (AAW) rats (10 male, 10 female), fasted overnight and with body weights between 200 and 300 g. Results are similar to those found for such tissues in other strains of rats [Schümichen et al. 1977; Altman and Dittmer 1964].

For fasted, pathogen-free Balb C mice with body weights between 20 and 30 g, the factors we use are based upon the carcass mass, which is defined as the body mass less the visceral organs, i.e. liver, spleen, kidneys, gastrointestinal tract, reproductive organs, heart and lungs. This was found to give a more reproducible estimator. The factors are as follows (where E is the carcass mass (g)):

organ mass	s (muscle)	=	0.54 x E
organ mass	s (skin)	=	0.25 x E
organ mas	s (bone)	=	0.15 x E
organ mas	s (blood)	=	0.065 x B

It is noted that organ mass (blood) is normally expressed as a factor of body weight.

It should be remembered that the use of factors to determine the organ masses gives an estimate that is accurate to approximately \pm 15 per cent. The alternative to the estimation of organ masses is to count the whole carcass and report the results as % ID in the carcass. This method, however, gives no idea of the amount of injected dose localised within the muscle, skin or bone compartments.

Calculations of the % DR are based on the amount of dose left in the whole body of the animal at the time of sacrifice. After correction for decay and geometry, the whole body counts are used as the standard count. Hence

$$\% DR = \frac{C2 \times W2 \times 100}{W1 \times S1}$$

where S1 are the counts per unit time of animal whole body corrected for decay and geometry.

The percentage dose per gram of tissue is a measure of the activity concentration found in the tissue at the time interval post administration. Hence

which reduces to

% ID/g (tissue) =
$$\frac{C2 \times 100}{W1 \times S}$$

The target to non-target ratios give a relative measure of the concentration in the target tissue compared to other non-target tissues. High target to non-target ratios are desirable in external scintigraphic imaging studies [Glenn and Colombetti 1979].

Target to non-target ratio = $\frac{\% \text{ ID/g of target tissue}}{\% \text{ ID/g of non-target tissue}}$

Tissue-to-blood and tissue-to-muscle ratios are often quoted where radionuclide-labelled compounds are expected to localise in implanted tumours, whereas liver-to-lung and liver-to-spleen ratios are popular in studies on radionuclide-labelled particulate suspensions. When tissue samples are counted in an automatic counting machine, the counting period and the time between samples, that is the time taken for the machine to move a sample from the counting well and replace it with the next, can be accurately determined. Knowing these periods makes it possible to correct all samples for decay to either the start or end of the series. Hence

1

$$N_0 = N_t \times e \frac{\ell n 2 \times t \times N}{3600 \times H}$$

where N_0 is the decay corrected counts per unit time, N_t is the uncorrected counts per unit time, N is the sample number, t is the time between samples (s), and H is the isotope half-life (h).

5. CONCLUSIONS

The TISCON program and associated methods have been developed in an attempt to minimise the time and effort required for biodistribution studies on rats and mice with minimal loss of accuracy.

The structure and options available within the program should enable it to accommodate variations in biological technique with minimal changes to the program itself.

6. ACKNOWLEDGEMENTS

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APPENDIX A TISCON DATA SHEET

ANIMAL NO.	
I.D. NO.	
BODY MASS	
CARCASS MASS	
STD. COUNT	

TISSUE	Mass Sample	Mass Tube	Counts	Mass Sample	Mass [*] Tube	Counts
LIVER						
SPLEEN						
KIDNEY						
MUSCLE						
SKIN						
BONE						
LUNGS						
HEART						
BLOOD						
URINE						
BLADDER						
STOM						
GUT 1						
GUT 2						
GUT 3						
CAECUM						
RECTUM						
				[

APPENDIX B

TISCON PROGRAM

1 REM TISCON VERSION 1.0 2 REM BY D.J.MADDALENA, ISOTOFE DIVISION, AAEC, NOV. 1982. 3 REM FROGRAM FOR THE CALCULATION OF THE BIODISTRIBUTION 4 REM OF RADIOPHARMACEUTICALS IN RATS AND MICE 5 REM 100 PRINT:PRINT TAB(24); "TISCON 1.0":PRINT:PRINT 110 FRINT TAB(10); "RADIOPHARMACEUTICAL DISTRIBUTION STUDY" 120 PRINT TAB(9);STRING\$(40,42):PRINT:PRINT 130 DIM W1(25),W2(25),C1(25),C2(25),C3(25) 140 DIM D1(6,25),D2(6,25),R1(6,25),R2(6,25),R3(6,25),M(5,2) 145 REM FOR >6 ANIMALS OR >25 SAMPLES INCREASE DIM 150 S\$="LIVER SPLEEN KIDNEY MUSCLE SKIN BONE LUNGS HEART BLOOD 160 S\$=S\$+*UR+BLADTOT.GUTSTOMACHGUT 1 GUT 2 GUT 3 CAEC.1 CAEC.2 RECTUM * 170 S\$=S\$+*FEMUR TAIL ":N1=INT((LEN(S\$)+1)/7) 190 REM INPUT INITIAL DATA 200 INFUT"TYPE OF ANIMAL (RAT/MOUSE)";A\$ 210 R=0:IF LEFT(A\$,1)="M" OR LEFT(A\$,1)="m" THEN R=1 220 PRINT: INPUT DO YOU WISH TO ADD EXTRA TISSUE TYPES ;A\$ 230 IF LEFT(A\$,1)="N" DR LEFT(A\$,1)="n" THEN 300 240 INPUT*HOW MANY EXTRA TISSUE TYPES (MAX.=DIM-20)*;51 250 FOR I=1 TO S1 260 PRINT*NAME OF TISSUE NO, "\$I\$" (MAX, 7 CHR)= "\$:INPUT A\$ 270 IF LEN(A\$)>7 THEN 260 280 IF LEN(A\$)<7 THEN A\$=A\$+STRING\$((7-LEN(A\$)),32) 290 S\$=S\$+A\$;NEYT I:N1=N1+S1 300 PRINT:PRINT"FOR DECAY CORRECTION OF SAMPLES ENTER ISOTOPE HALF LIFE(HRS)" FOR NO DECAY CORRECTION ENTER ZERO"; : INFUT H 310 PRINT:PRINT* 320 IF H=0 THEN H=1:P=0:GDTD 340 330 PRINT: INPUT "ENTER PERIOD RETWEEN SAMPLES (SEC)";P 340 PRINT: INPUT'ENTER EXPERIMENT DETAILS "\$L\$:PRINT 350 INPUT NUMBER OF ANIMALS= "\$N:PRINT 355 REM ENTER ANIMAL DATA 360 FOR I=1 TO N 370 PRINT"ENTER RESULTS OF ANIMAL NO. ";I;PRINT:PRINT 380 INPUT'ANIMAL BODY MASS= ";B(I):PRINT 390 IF R=1 THEN INPUT MOUSE CARCASS MASS= ";E:PRINT 400 INPUT'STANDARD COUNTS= "\$S:PRINT 410 INPUT DD YOU WISH TO FIND NETT SAMPLE MASS (Y/N)";A\$:PRINT 420 IF LEFT(A\$,1)="Y" OR LEFT(A\$,1)="y" THEN S9=1 ELSE S9=0 430 INFUT DO YOU WISH TO CORRECT INITIAL DATA FOR THIS ANIMAL (Y/N)*;A\$ 440 IF LEFT(A\$,1)="Y" OR LEFT(A\$,1)="y" THEN 380 450 FRINT: PRINT 500 K=1:GOTO 520 505 REM STEP BACKWARDS 510 IF W1(J)>-J THEN K=J+INT(W1(J)) ELSE K=J-1 520 IF K<1 THEN K=1 530 FOR J=K TO N1: A\$=MID(S\$, J*7-6,7) 540 IF AS="UR+BLAD" THEN AS="URINE 550 IF As="TOT.GUT" THEN As="BLADDER" 560 PRINT A\$;;IF S9=0 THEN PRINT TAB(19);"SAMPLE MASS= ";:INPUTW1(J):GOTO 600 570 INFUT" SAMPLE+CONTAINER MASS= ";W3 575 IF W3=0 THEN 840 580 IF W3<0 THEN W1(J)=W3:GOT0 510 590 INPUT* CONTAINER MASS= ";W4:W1(J)=W3-W4 600 IF W1(J)=0 THEN 840

Ready

(Continued)

610 IF W1(J)<0 THEN 510 620 IF R=1 AND J<>10 THEN 650 630 IF J=1 OR J=10 THEN PRINT TAB(19);"ORGAN MASS= ";:INPUT W2(J):GOTO 650 ORGAN MASS= 0" 640 FRINT' SAMPLE CTS- "#C1(J) 650 INPUT* 660 IF R=0 THEN 750 **390 REM CALCULATE ORGAN MASSES** 700 IF As="MUSCLE "THEN W2(J)=E*.54:G010 820 "THEN W2(J)=E*+25:GOTO 820 710 IF A\$="SKIN 720 IF A\$="BONE *THEN W2(J)=E*.15:G0T0 820 730 IF A\$="BLOOD "THEN W2(J)=B(I)*.065:60T0 820 740 GOTO 800 750 IF A\$="MUSCLE "THEN W2(J)=B(T)*,45:GOTO 820 760 IF A\$="SKIN "THEN W2(J)=B(I)*,20:GOTO 820 "THEN W2(J)=B(I)*,125:GOTO 820 770 IF A\$="BONE 780 IF A\$="BLOOD "THEN W2(J)=B(I)*.07:00T0 820 790 IF AS="LIVER "THEN 820 "THEN 820 800 IF As="URINE 810 W2(J)=W1(J) 815 REM DECAY CORRECTION 820 C2(J)=C1(J)*EXP(0.0001925*P*J/H):C3(J)=(C2(J)/W1(J))*W2(J) 825 REM CALCULATE %INJ DOSE,% PER GRAM 830 D1(I,J)=C3(J)*100/S:D2(I,J)=D1(I,J)/W2(J);GOTO 850 840 C2(J)=0:C3(J)=0:D1(I,J)=0:D2(I,J)=0 850 IF AS="MUSCLE "THEN T1=D2(I,J) 860 IF A\$="BLOOD "THEN T2=D2(1,J) 870 IF AS="LIVER "THEN T3=D2(I,J) 880 FRINT:NEXT J 895 REM CALCULATE TOT, GUT, URINE + BLADDER 900 IF R=1 THEN GOTO 970 910 C3(10)=C3(10)+C3(11) 920 W1(11)=0:C3(11)=0:FOR L=13 T018 930 C3(11)=C3(11)+C3(L):W1(11)=W1(11)+W1(L):NEXT L 940 W2(11)=W1(11):C2(11)=C3(11):C1(11)=C2(11) 950 IF W2(11)=0 THEN W2(11)=1 960 D1(T,11)=C3(11)*100/S:D2(T,11)=D1(T,11)/W2(11) 970 GOSUB 1000:NEXT I:GOTO 2000 995 REM PRINT INPUT DATA 1000 PRINT DO YOU WISH TO RE-ENTER DATA FOR THIS ANIMAL (Y/N)* 1010 INFUT" ■ IF NOT THEN START A NEW PAGE IF NECESSARY"\$A\$ 1020 IF LEFT(A\$,1)="Y" OR LEFT(A\$,1)=""" THEN 370 1030 PRINT: PRINT: PRINT L&: PRINT 1040 IF R=0 THEN As=" RAT" ELSE As=" MOUSE" 1050 FRINT RESULTS OF ";A\$;" BIODISTRIBUTION NO.";I 1060 PRINT STRING\$(35,42) 1070 LET Z\$≕"\ N BODY MASS= ###.# STANDARD CTS.= #########." 1080 PRINT USING Z\$,A\$,B(I),S 1090 IF R=1 THEN PRINT" CARCASS MASS = ";E 1100 FRINT: FRINT: FRINT 1110 PRINT"TISSUE SAMPLE WT ORGAN WT SAMPLE CTS DK COR CTS CTS/ORGAN" ***** 谢谢你都非举辞。" 1120 Z\$="\ 非常、津井 書書朱 . 治 ****** 1130 FOR L=1 TO N1:IF W1(L)=0 THEN 1160 1140 A\$=MID(S\$,L*7-6,7) 1150 PRINT USING Z\$,A\$,W1(L),W2(L),C1(L),C2(L),C3(L) 1160 NEXT L :FRINT:FRINT 1170 FRINT TISSUE ZINJ DOSE % PER GRAM TIS/MUS TIS/LIV" TIS/BLOOD 1180 Z\$="∖ 1 ** ** 赤条 • 华林华 **** *** *** *** 1190 REM CALCULATE TISSUE RATIOS 1200 FOR L=1 TO N1

Ready

```
1210 IF D1(I,L)=0 THEN 1280
1220 IF T1=0 THEN R1(I,L)=0 ELSE R1(I,L)=D2(I,L)/T1
1230 IF T2=0 THEN R2(I,L)=0 ELSE R2(I,L)=D2(I,L)/T2
1240 IF T3=0 THEN R3(I,L)=0 ELSE R3(I,L)=D2(I,L)/T3
1260 As=MID(Ss,L*7-6,7)
1270 PRINT USING Z$,A$,D1(I,L),D2(I,L),R1(I,L),R2(I,L),R3(I,L)
1280 NEXT L:PRINT:PRINT:PRINT:PRINT
1290 INPUT*START A NEW PAGE IF REQUIRED";A$
1300 RETURN
2000 IF N<2 THEN GOTO 2390
2010 PRINT:PRINT:PRINT:PRINT L$:PRINT
2020 IF R=0 THEN A$=" RATS" ELSE A$=" MICE"
2030 FRINT MEANS AND STU DEVS. FOR "$N$A$
2040 FRINT STRING$(33,42):FRINT
2050 FRINT TISSUE
                     ZINJ
                              SD
                                      7./G
                                               SD
                                                        T/M
                                                                 SD
                                                                        T/B
                                                                               STI *
2060 Z$≈"∖
                 \mathbf{N}
                    **.** **.** **.***
                                          *******
2100 REM CALCULATE MEANS & STD DEVS
2110 FOR J=1 TO N1
2120 IF D1(I+J)=0 THEN 2320
2130 K=1:FOR I=1 TO N
2140 W1(I)=D1(I,J):NEXT I
2150 GOSUB 2500
2160 K=2:FOR I=1 TO N
2170 W1(I)=D2(I,J):NEXT I
2180 GOSUB 2500
2190 K=3:FOR I=1 TO N
2200 W1(I)=R1(I,J):NEXT I
2210 GOSUB 2500
2220 K=4:FOR I=1 TO N
2230 W1(I)=R2(I,J):NEXT I
2240 GOSUB 2500
2300 As=MID(Ss,J*7-6,7)
2310 PRINT USING Z$;A$;M(1,1);M(1,2);M(2,1);M(2,2);M(3,1);M(3,2);M(4,1);M(4,2)
2320 NEXT J
2330 GOTO 2400
2390 PRINT MEANS & STD DEVS, CANNOT BE FOUND FOR ONE ANIMAL"
2400 PRINT:PRINT:PRINT DO YOU WISH TO CONTINUE (Y/N) ?"
2410 PRINT: INPUT "IF YES THEN START A NEW PAGE"; A$
2420 IF LEFT(A$,1)="Y" OR LEFT(A$,1)="s" THEN 10
2430 GO TO 3000
2490 REM SUBROUTINE 2500 MEANS & STD DEVS WITH ZERO JUMP
2500 M1=0:M2=0:N3=0:FDR L=1 TO N
2510 IF W1(L)=0 THEN 2530
2520 M1=M1+W1(L):M2=M2+W1(L)^2:N3=N3+1
2530 NEXT L:IF N3<2 THEN M(K,2)=-1:GOTO 2550
2540 M(K,2)=SQR((M2-((M1^2)/N3))/(N3-1)):REM STD DEV.
2550 M(K,1)=M1/N3:RETURN: REM MEAN
3000 END
```

Ready

APPENDIX C

TISCON OUTPUT DATA

TYPE OF ANIMAL (RAT/MOUSE)? rat

DO YOU WISH TO ADD EXTRA TISSUE TYPES? wes HOW MANY EXTRA TISSUE TYPES ? 2 NAME OF TISSUE NO. 1 (MAX. 7 CHR)= ? femur1 NAME OF TISSUE NO. 2 (MAX. 7 CHR)= ? femur2

FOR DECAY CORRECTION OF SAMPLES ENTER ISOTOPE HALF LIFE(HRS)

FOR NO DECAY CORRECTION ENTER ZERO? 6.02

ENTER PERIOD BETWEEN SAMPLES (SEC)? 37.5

ENTER EXPERIMENT DETAILS? To99m Purophosphate

NUMBER OF ANIMALS= ? 1

ENTER RESULTS OF ANIMAL NO. 1

ANIMAL BODY MASS= ? 243.2

STANDARD COUNTS= ? 1489086

DO YOU WISH TO FIND NETT SAMPLE MASS (Y/N)? n

DO YOU WISH TO CORRECT INITIAL DATA FOR THIS ANIMAL (Y/N)? n

LIVER	SAMPLE MASS= ? 1.75 DRGAN MASS= ? 10.7
	SAMPLE CTS= ? 19624
SPLEEN	SAMPLE MASS= ? .84
	ORGAN MASS= 0
	SAMPLE CTS= ? 2878
KIDNEY	SAMPLE MASS≔ ? ₊94
	ORGAN MASS= 0
	SAMPLE CTS= 7 10678
MUSCLE	SAMPLE MASS= ? 2.09
	ORGAN MASS= 0
	SAMPLE CTS= 7 686
SKIN	SAMPLE MASS= ? 0
BONE	SAMPLE MASS= ? O
LUNGS	SAMPLE MASS= ?

(Continued)

	0
HEART	SAMPLE MASS= ? 0
BLOOD	SAMPLE MASS= ? 1,12 ORGAN MASS= 0 SAMPLE CTS= ? 1603
URINE	SAMPLE MASS= ? 28.1 ORGAN MASS= ? 28.1 SAMPLE CTS= ? 22651
BLADDER URINE	SAMPLE MASS= ? -1 SAMPLE MASS= ? 1.15 ORGAN MASS= ? 28.1 SAMPLE CTS= ? 22651
BLADDER	SAMPLE MASS= ? 11.0 ORGAN MASS= 0 SAMPLE CTS= ? 0
STOMACH BLADDER	SAMFLE MASS= ? -1 SAMFLE MASS= ? 1.0 ORGAN MASS= 0 SAMFLE CTS= ? 69395
STOMACH	SAMPLE MASS= ? 0
GUT 1	SAMFLE MASS= ? 0
GUT 2	SAMPLE MASS= ? 0
GUT 3	SAMPLE MASS= ? 0
CAEC.1	SAMPLE MASS= ? 0
CAEC.2	SAMPLE MASS= ? 0
RECTUM	SAMPLE MASS= ? O
FEMUR	SAMPLE MASS= ? O
TAIL	SAMPLE MASS= ? 1.0 ORGAN MASS= 0 SAMPLE CTS= ? 14804
femur1	SAMPLE MASS= ? .54 ORGAN MASS= 0 SAMPLE CTS= ? 19320
femur2	SAMPLE MASS= ? .53 ORGAN MASS= 0 SAMPLE CTS= ? 20186

DO YOU WISH TO RE-ENTER DATA FOR THIS ANIMAL (Y/N) IF NOT THEN START A NEW PAGE IF NECESSARY?

Tc99m Pyrophosphate

TISSUE	SAMPLE WT	ORGAN WT	SAMPLE CI	IS DK COR C'	TS CTS/ORGAN
LIVER	1.75	10.7	19624	4. 19648	3. 120131.
SFLEEN	0.84	0.8	2878	3. 2885	5. 2885.
KIDNEY	0.94	0.9	10678	3. 10710	6, 10716,
MUSCLE	2.09	109.4	686	5 . 68'	7, 36094,
BLOOD	1.12	17.0	1603	3. 1620	0, 24630,
UR+BLAD	1.15	28.1	22651	L. 2292/	4. 630465.
TAIL	1+00	1.0	14804	4. 1516	3. 15163.
femur1	0.54	0.5	1932(), 1981;	3, 19813,
femur2	0.53	0.5	20186	5. 20726	6. 20726.
TISSUE	XINJ DOSE	% PER GRAM	TIS/MUS	TIS/BLOOD	TIS/LIV
LIVER	8.07	0.754	34.0	7.76	1.00
SFLEEN	0.19	0.231	10.4	2.37	0.31
KIDNEY	0.72	0.766	34+6	7.88	1.02
MUSCLE	2.42	0.022	10	0.23	0.03
BFOOD	1.65	0.097	4.4	1.00	0.13
UR+BLAD	37+62	1.339	60+4	13,78	1.78
TAIL	1.02	1.018	46.0	10,48	1.35
femuri	1+33	2.464	111.2	25,36	3.27
femur2	1.39	2.626	118.6	27,03	3,48

START A NEW PAGE IF REQUIRED? MEANS & STD DEVS, CANNOT BE FOUND FOR ONE ANIMAL

DO YOU WISH TO CONTINUE (Y/N) ?

IF YES THEN START A NEW PAGE? no

Reads

TYPE OF ANIMAL (RAT/MOUSE)? mouse

DO YOU WISH TO ADD EXTRA TISSUE TYPES? yes HOW MANY EXTRA TISSUE TYPES ? 1 NAME OF TISSUE NO, 1 (MAX, 7 CHR)= ? swab

FOR DECAY CORRECTION OF SAMPLES ENTER ISOTOPE HALF LIFE(HRS)

FOR NO DECAY CORRECTION ENTER ZERO? O

ENTER EXPERIMENT DETAILS? Gallium -67 1Hr p/i

NUMBER OF ANIMALS= ? 1

ENTER RESULTS OF ANIMAL NO. 1

ANIMAL BODY MASS= ? 26.3

MOUSE CARCASS MASS= ? 19.2

STANDARD COUNTS= ? 104786

DD YOU WISH TO FIND NETT SAMPLE MASS (Y/N)? yes

DO YOU WISH TO CORRECT INITIAL DATA FOR THIS ANIMAL (Y/N)? no

LIVER SAMPLE+CONTAINER MASS= ? 5.184 CONTAINER MASS= ? 3.645 SAMPLE CTS= ? 5727

- SPLEEN SAMPLE+CONTAINER MASS= ? 3.744 CONTAINER MASS= ? 3.646 SAMPLE CTS= ? 338
- KIDNEY SAMPLE+CONTAINER MASS= ? 4.097 CONTAINER MASS= ? 3.645 SAMPLE CTS= ? 3004
- MUSCLE SAMPLE+CONTAINER MASS= ? 4.113 CONTAINER MASS= ? 3.643 SAMPLE CTS= ? 1394

SKIN SAMPLE+CONTAINER MASS= ? 0

BONE SAMPLE+CONTAINER MASS= ? 6\3.681 CONTAINER MASS= ? 3.645 SAMPLE CTS= ? 268

LUNGS SAMPLE+CONTAINER MASS= ?

18

HEART SAMPLE+CONTAINER MASS= ? 0 SAMPLE+CONTAINER MASS= ? 4.330 BLOOD CONTAINER MASS= ? 3.644 SAMPLE CTS= ? 11297 HEINE SAMPLE+CONTAINER MASS= ? 0 BLADDER SAMPLE+CONTAINER MASS= ? 4.927 CONTAINER MASS= ? 3.646 SAMPLE CTS= ? 9036 STOMACH SAMPLE+CONTAINER MASS= ? 0 SAMPLE+CONTAINER MASS= 7 6,602 GUT 1 CONTAINER MASS= ? 3.645 SAMPLE CTS= ? 10464 GUT 2 SAMPLE+CONTAINER MASS= ? 0 GUT 3 SAMPLE+CONTAINER MASS= ? 0 SAMPLE+CONTAINER MASS= ? 0 CAEC.1 SAMPLE+CONTAINER MASS= ? 0 CAEC+2 RECTUM SAMPLE+CONTAINER MASS= ? 0 SAMPLE+CONTAINER MASS= ? 0 FEMUR SAMPLE+CONTAINER MASS= ? 4.192 TAIL CONTAINER MASS= 7 3.645 SAMPLE CTS= ? 2307 SAMPLE+CONTAINER MASS= ? 4 swab CONTAINER MASS= ? 3 SAMPLE CTS= 7 611

DO YOU WISH TO RE-ENTER DATA FOR THIS ANIMAL (Y/N) IF NOT THEN START A NEW PAGE IF NECESSARY?

19

Gallium −67 1Hr p/i

TISSUE	SAMPLE WT	ORGAN WT	SAMPLE CTS	B DK COR CT	S CTS/ORGAN
LIVER	1.54	1.5	5727+	5727	. 5727.
SFLEEN	0.10	0.1	338.	338	. 338.
KIDNEY	0.45	0.5	3004.	3004	. 3004.
MUSCLE	0+47	10.4	1394.	1394	. 30751.
BONE	0.04	2.9	268.	268	. 21440.
BLOOD	0.69	1.7	11297.	11297	. 28152.
TOT.GUT	1.28	1.3	9036.	9036	• 9036•
GUT 1	2.96	3.0	10464.	10464	. 10464.
TAIL	0.55	0.5	2307.	2307	. 2307.
swab	1.00	1.0	611.	. 611	• 611.
TISSUE	XINJ DOSE :	% PER GRAM	TIS/MUS	TIS/BLOOD	TIS/LIV
LIVER	5.47	3.551	1.3	0.23	1.00
SEL FEN	0.32	3,291	1.2	0.21	0.93

SFLEEN	0.32	3,291	1.2	0.21	0.93
KIDNEY	2.87	6+342	2.2	0.40	1.79
MUSCLE	29.35	2.830	1.0	0.18	0.80
BONE	20.46	7.104	2.5	0.45	2.00
BLOOD	26.87	15.716	5.6	1.00	4.43
TOT.GUT	8.62	6.732	2.4	0+43	1.90
GUT 1	9,99	3,377	1.2	0.21	0,95
TAIL	2.20	4.025	1.4	0.26	1.13
swab	0.58	0.583	0.2	0.04	0.16

START A NEW PAGE IF REQUIRED? MEANS & STD DEVS, CANNOT BE FOUND FOR ONE ANIMAL

DO YOU WISH TO CONTINUE (Y/N) ? IF YES THEN START A NEW PAGE? DO

Ready