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Thallium-201 for Medical Use*

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The purpose of this study is to develop various applications of thallium-201 for medical use, as shown in Figure 1.

(a) We expect ^{201}Tl to be an improved potassium analog because of its biological and physical properties.

(b) Unlike presently used renal agents which concentrate in the cortex, thallium preferentially concentrates in the renal medulla.

(c) We will also evaluate ^{201}Tl uptake in melanomas, as well as in other tumors, such as Dr. Charkes' work with ^{131}Cs and the work of the Cincinnati group with ^{129}Cs.

It was Dr. Paul Harper and his group who first suggested the use of radiothallium in nuclear medicine.

Let us next mention the physical properties of ^{201}Tl. As shown in Figure 2, ^{201}Tl decays by electron capture, mainly to the ground state of stable mercury-201. It emits Hg X-rays of 69-82 keV and photons of 135 and 167 keV in 10% total abundance.

We note that the photons of ^{201}Tl are detected with high efficiency and resolution in a low-energy collimator, gamma camera detection system.

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In fact, the ^{201}Tl photons are expected to give approximately the same number of counts/mCi as do ^{43}K and ^{129}Cs with their more abundant, higher energy photons. The highly abundant mercury X-rays of ^{201}Tl will give an image better in statistics, but worse in resolution than the gamma rays, using the Anger camera. Other future detection systems, such as solid-state detectors or multiwire chambers, may further enhance the usefulness of the Hg X-rays.

Thallium-201 then, has satisfactory imaging characteristics without excessive radiation dose, which has been calculated by Harper to be 0.24 Rads/mCi whole-body dose, and 1.5 Rads/mCi critical organ dose to the kidneys. This radiation dose is more favorable than ^{43}K or ^{129}Cs. We note that its 73-hour half-life gives this radiopharmaceutical a good shelf-life, which is not only generally convenient, but is invaluable for emergency use. An isotope with higher energy photons can also be used after the initial use of ^{201}Tl; for example, ^{81}Rb.

Figure 3 shows a normal heart imaged in a goat sacrificed 25 minutes post-intravenous injection. The dead goat simulates electrocardiogram gating of the camera; 530,000 counts of the Hg X-rays were collected, using the nuclear data selectronic camera and the parallel hole technetium collimator. There is no data enhancement in our scintiphotos.

Figure 4 is similar, using the 8-mm pinhole collimator, and collecting 378,000 counts.

From our data of counting in goats, adequate pictures could be obtained in a reasonable time in humans. For example, administering 3 mCi of activity,

using the technetium multihole converging collimator and ECG gating the camera, 300,000 X-ray counts could be collected in 5 minutes, or 100,000 gamma-ray counts in 19 minutes. Unlike smaller animals, and unlike potassium which it resembles in its initial rate of uptake, the myocardial uptake in goats decreases only slightly with time over the first few hours. This is in line with Harper's observation that the thallium activity remained in the myocardium even 18 hours later in the one patient they scanned with a mixture of thallium isotopes. Delayed scans may yield improved resolution and the ability to look for leakage of thallium from the myocardium over several days of observation for development of M. I.

Figure 5 indicates the organ uptake in %/g compared to the left ventricle in a normal goat 25 minutes postinjection.

Figure 6 shows the rapid clearance of the thallium activity from the blood.

Figure 7 shows the counts/g in an infarcted goat's heart, in agreement with histology, but not with visual observation.

We have also found a very inhomogeneous distribution of myocardial uptake in an old goat, but a much more homogeneous uptake in a young goat. The average standard deviation of uptake in %/g was $\pm$ 27% for the old goat, and only $\pm$ 10.6% for the young goat.

As is essential, our production method yields ^{201}Tl in high purity and specific activity. A natural thallium target is irradiated with 33-MeV protons to give the reaction $^{203}Tl(p,3n)^{201}Pb$, which then decays to ^{201}Tl. The production rate is 0.7 mCi/μAh, or higher with an enriched target.

As shown in Figure 8 the chemical purification is carried out in two stages: First the thallium target material is affixed to an ion-exchange column while complexed lead activity is eluted. After allowing the ^{201}Pb to decay for a day, lead activity is then separated from its thallium daughter by solvent extraction. We are doing our initial development work on the Brookhaven cyclotron, but if the clinical trials are successful, we hope, in the future, to evaluate its production capability in the BLIP Brookhaven Linac Isotope Producer using the $^{205}Tl(p,5n)$ reaction.

Figure 9 shows the excitation function for the production of ^{201}Pb, the parent of ^{201}Tl.

Figure 10 gives a chemical analysis of our entire product, showing its suitability for clinical use. For quality assurance of the product, we use a spot test to detect carrier thallium, sensitive to 3 μg/ml.

Figure 11 shows the germanium-lithium spectrum of the product, the main peaks being the X-rays and photons of ^{201}Tl. Radioisotopic purity is ≥99% as shown in Figure 12.

We also check the product radiochemical purity for the chemical state of the ^{201}Tl. The product is at neutral pH, isotonic, and pyrogen free.

In conclusion, we feel that thallium-201 merits evaluation for medical use.

Potential Applications of ^{201}Tl

a) Myocardial visualization & functional analysis

b) Kidney studies

c) Tumor diagnosis

Figure 1

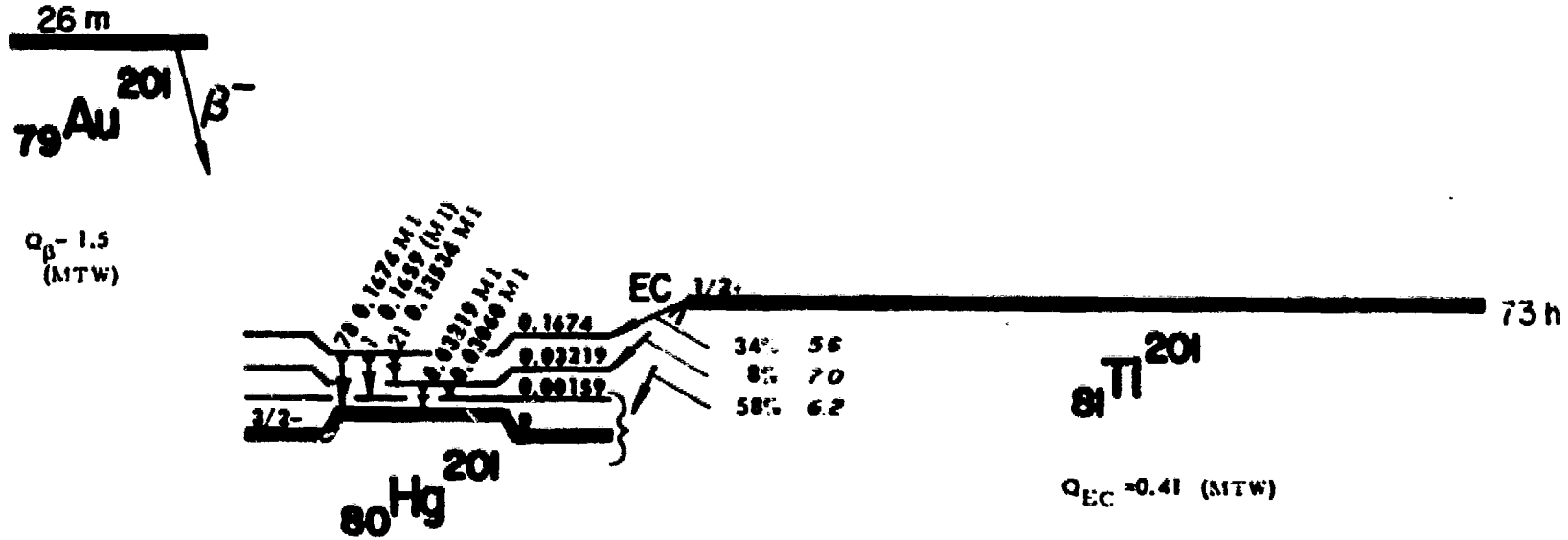

26 m
79Au201
β−
Qβ− 1.5
(MTW)
EC
1/2+
73 h
0.1674
0.03219
0.00159
34%
8%
58%
5.6
7.0
6.2
3/2−
80Hg201
81Tl201
QEC =0.41 (MTW)

Figure 2

^{201}THALLIUM

NO. 9 GOAT ••• STILL HEART IN SITU ••• CONTROL

369 μCi 5/25/73 378 K X RAYS

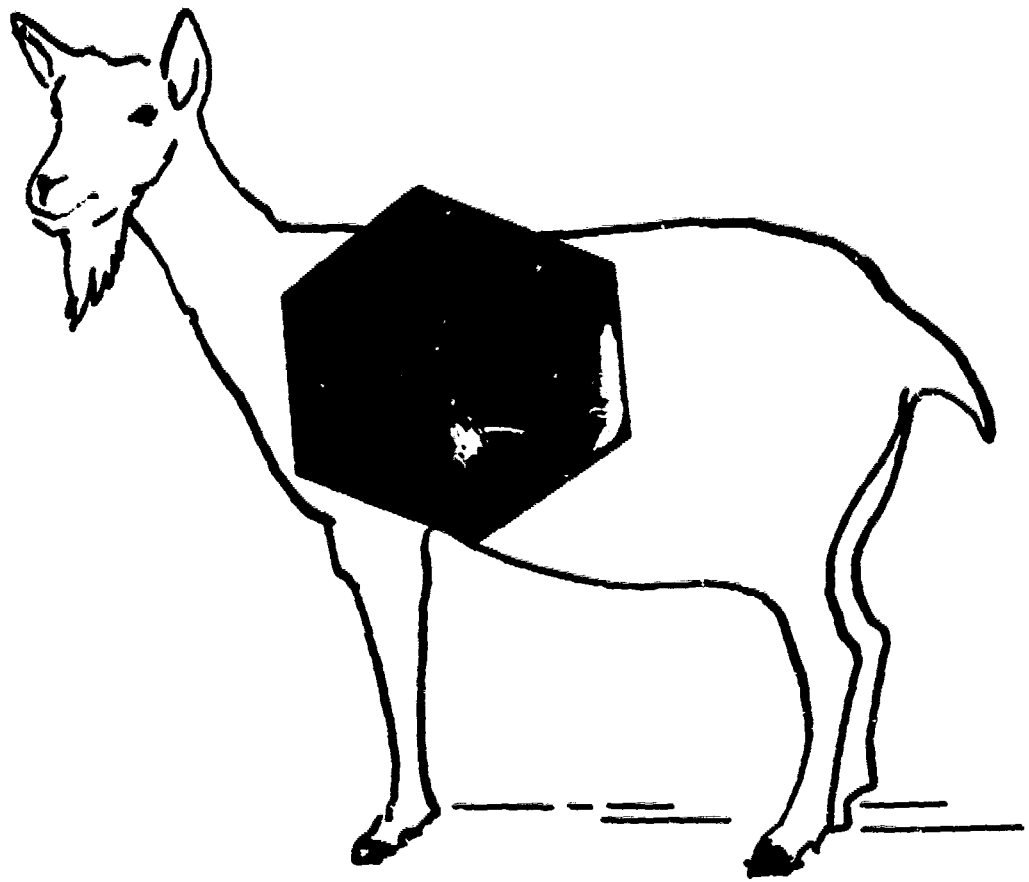


Figure 3

^{201}THALLIUM

NO. 9 GOAT ••• STILL HEART IN SITU ••• CONTROL
369 μCi 5/25/73 530 K X RAYS
PIN-HOLE

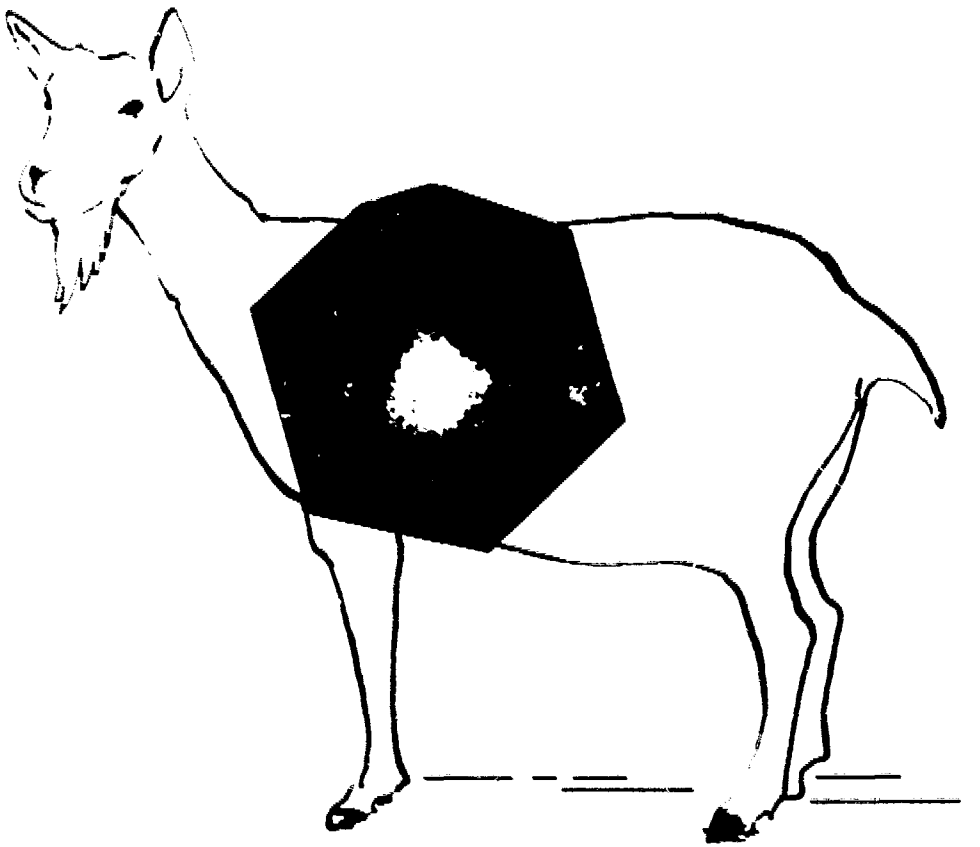
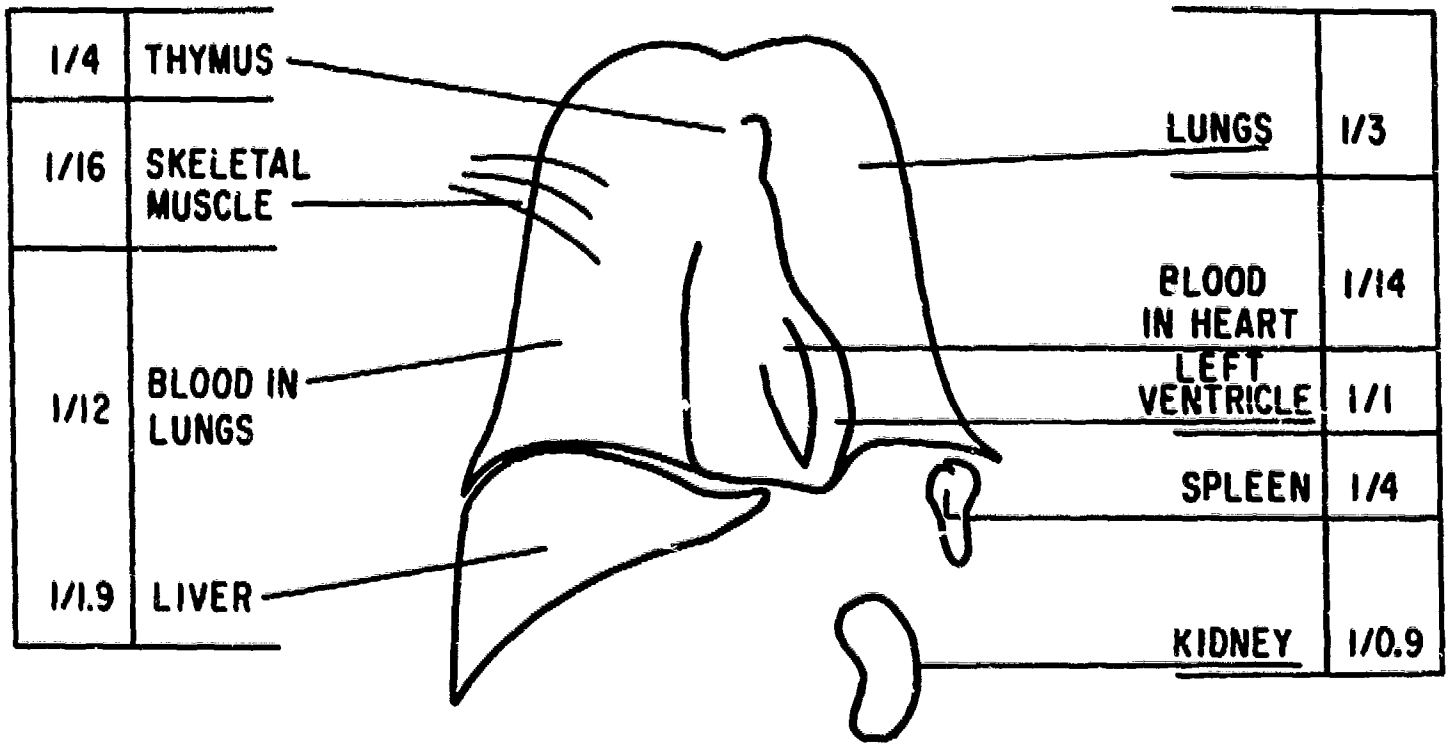


Figure 4

^{201} THALLIUM HEART VISUALIZATION
GOAT No. 9 AGE 6 YEARS



RATIOS OF CONTIGUOUS ORGAN / LV
25 min INJ ⟷ SACRIFICE

Figure 5

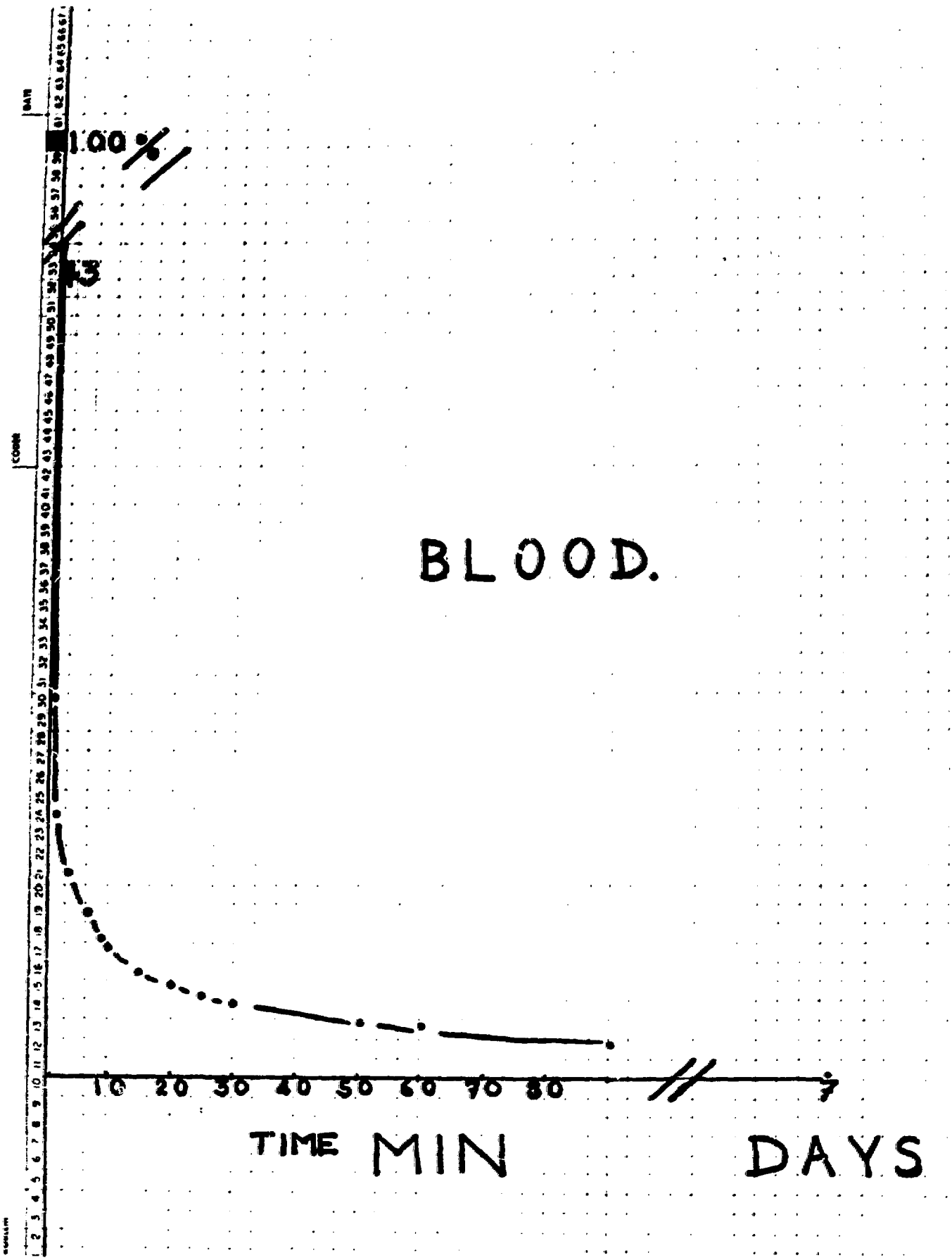


Figure 6

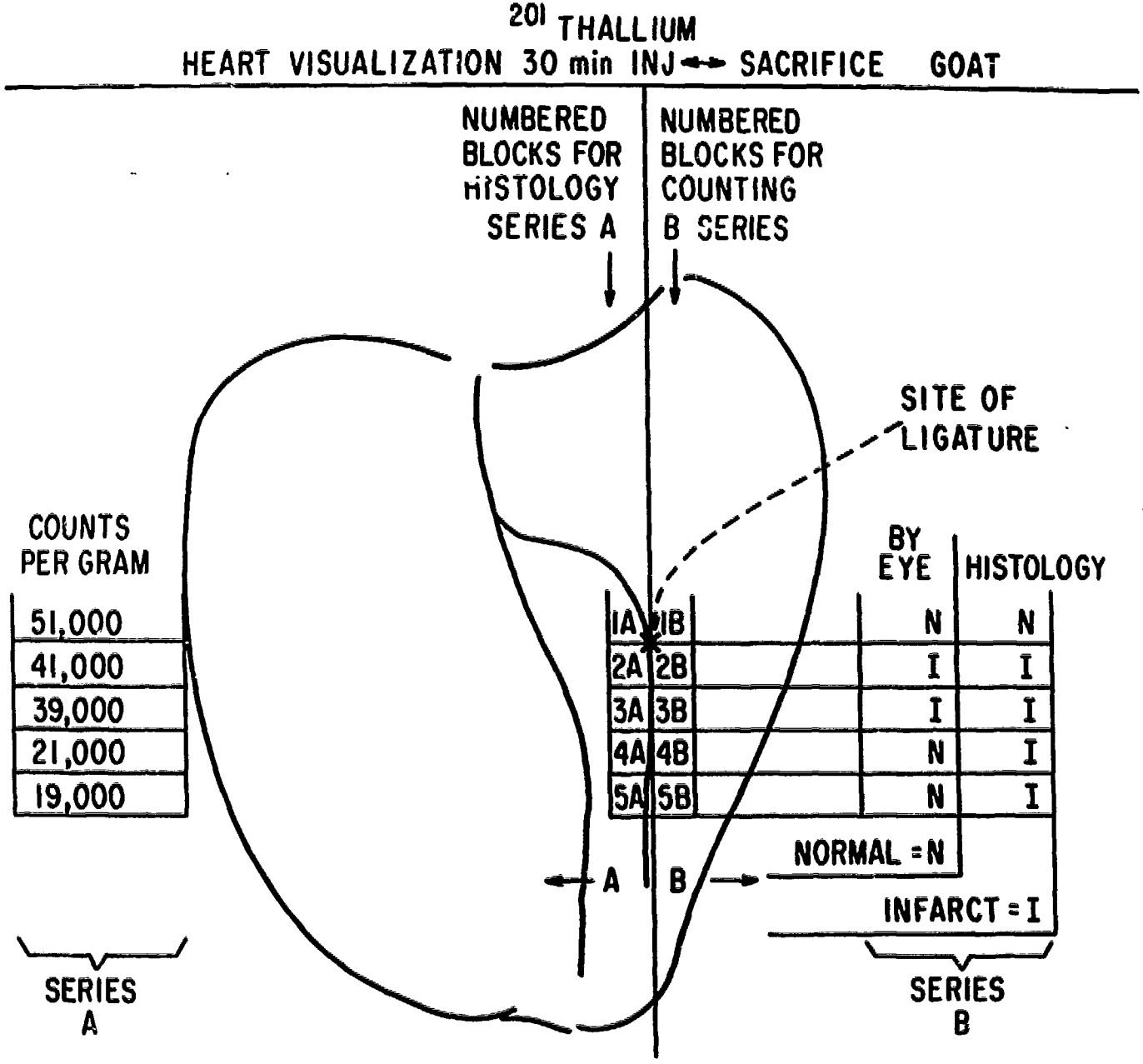
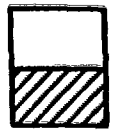

201 THALLIUM
HEART VISUALIZATION 30 min INJ ↔ SACRIFICE GOAT
NUMBERED BLOCKS FOR HISTOLOGY SERIES A
NUMBERED BLOCKS FOR COUNTING B SERIES
SITE OF LIGATURE
COUNTS PER GRAM
51,000
41,000
39,000
21,000
19,000
SERIES A
1A 1B
2A 2B
3A 3B
4A 4B
5A 5B
BY EYE
HISTOLOGY
N N
I I
I I
N I
N I
A
B
NORMAL = N
INFARCT = I
SERIES B

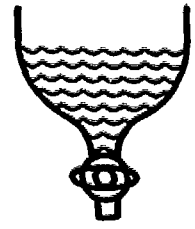
Figure 7

CHEMICAL SEPARATION

(1)



Pb-201 DECAYS TO Tl-201



ION-EXCHANGE COLUMN. THALLIUM TARGET MATERIAL STICKS ON COLUMN, & ^{201}Pb & ^{203}Pb ARE ELUTED

SOLVENT EXTRACTION. ^{201}Tl EXTRACTED FROM LEAD RADIOISOTOPES

Figure 8

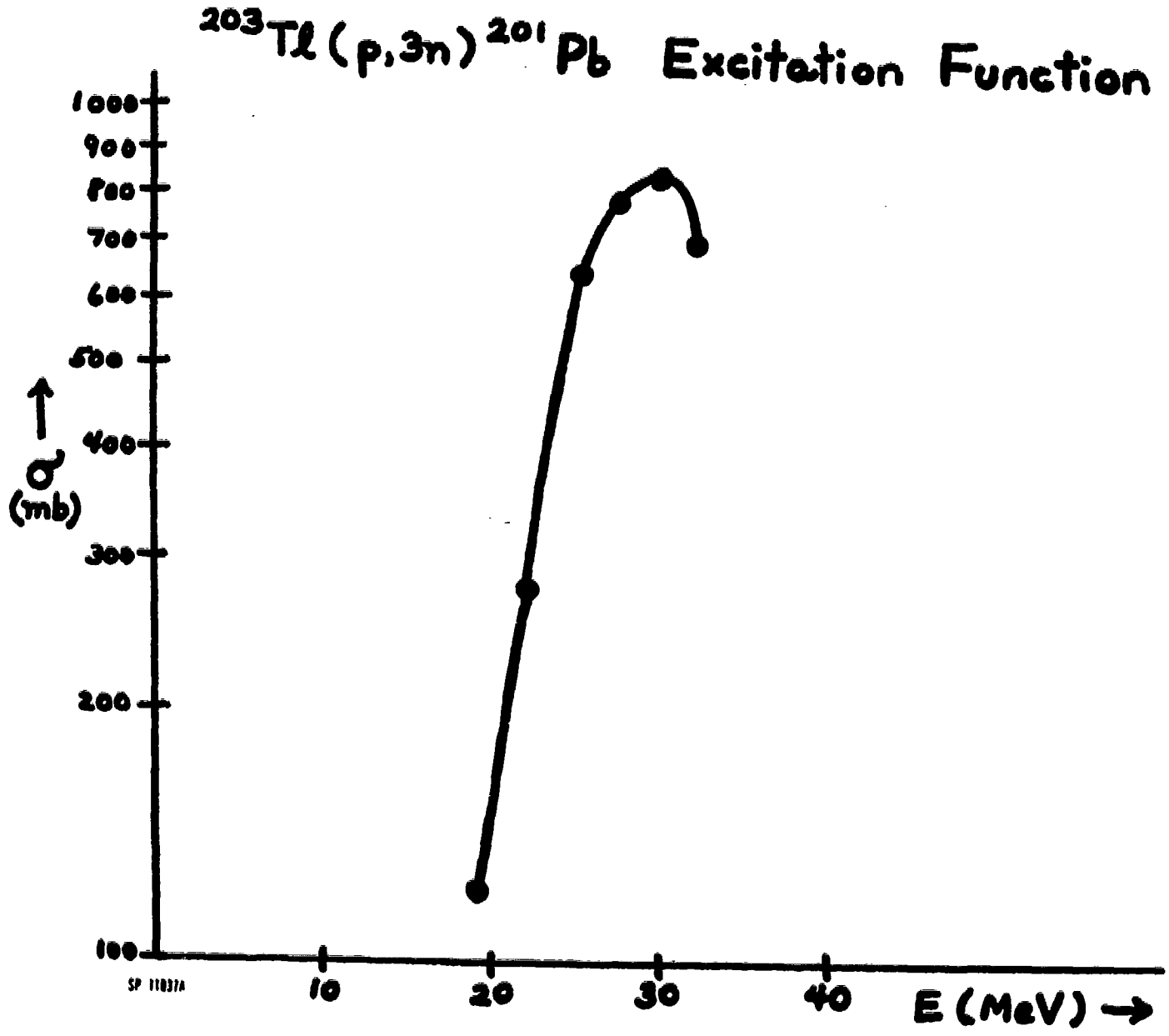

$^{203}Tl(p,3n)^{201}Pb$ Excitation Function
1000
900
800
700
600
500
400
300
200
100
σ (mb)
SP 11037A
10
20
30
40
E (MeV) →

Figure 9

Chemical Analysis of the Thallium-201 Product

Element	Quantity	Element	Quantity
Tl	<0.7 μg	Cu	7 μg
Mg	70 μg	Fe	7 μg
Al	70 μg	Ni	7 μg
Ca	56 μg	V	7 μg
Pb	21 μg	Cr	0.21 μg
Si	21 μg	Ti	0.35 μg

Figure 10

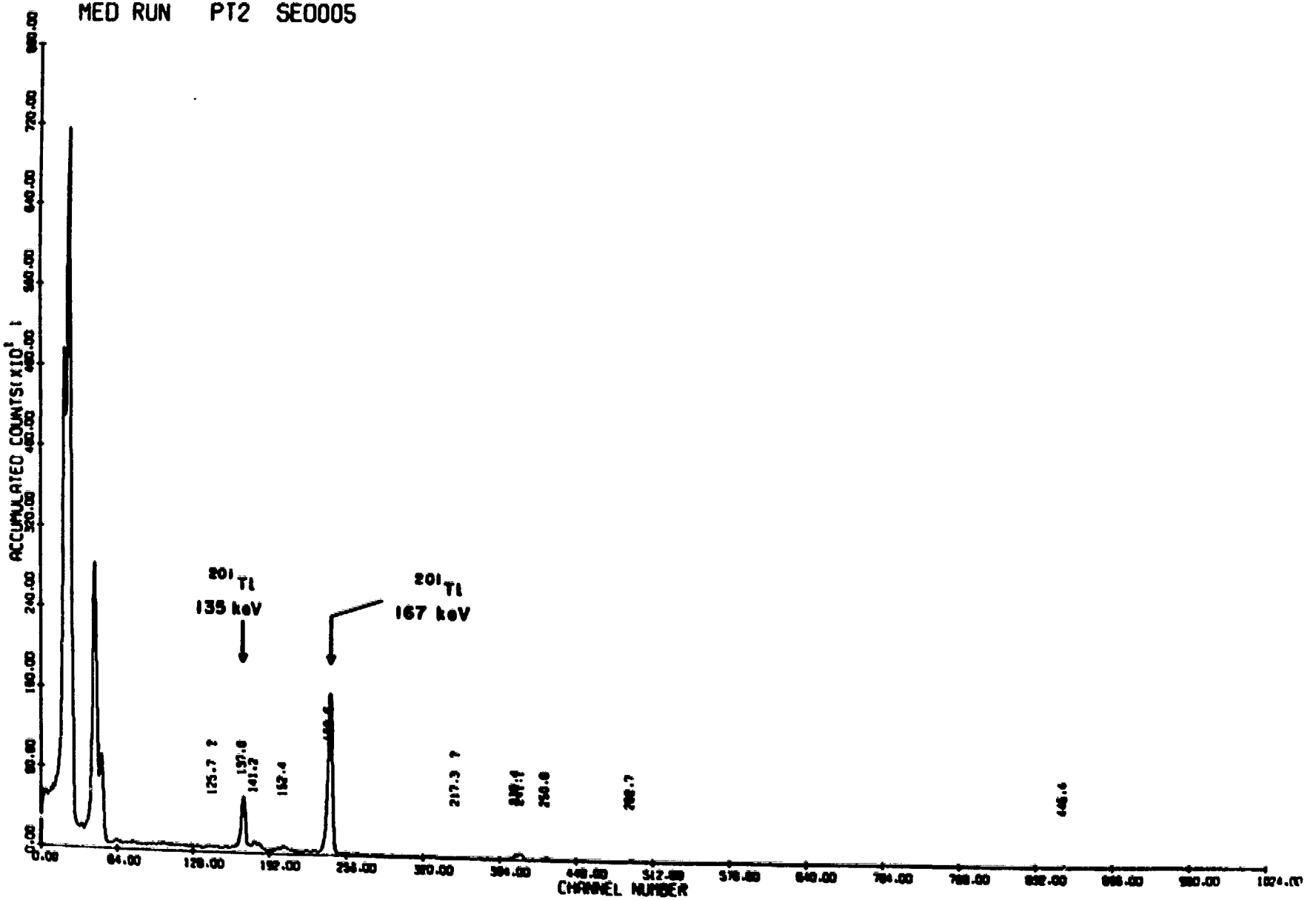

MED RUN PT2 SE0005
ACCUMULATED COUNTS(X10)
201 Tl
135 keV
201 Tl
167 keV
CHANNEL NUMBER

Figure 11

Radioisotopic Analysis of Thallium-201 Product

Isotope	$t_{1/2}$	At time of preparation, %	18 hrs later, %	73 hrs later, %	146 hrs later, %
Tl-199	7.4 hr	0.79	0.15	0.0015	-
Pb-203	52 hr	0.099	0.09	0.075	0.056
Pb-201	9.4 hr	0.031	0.0098	0.0003	-
Tl-200	26 hr	0.021	0.015	0.006	0.0017
Tl-202	12.2 d	0.070	0.079	0.12	0.20

Figure 12