Report: LURI 1975-03

LONG-LIVED RADIONUCLIDE-IMPURITIES IN ELUATES FROM MOLYBDENUM-TECHNETIUM GENERATORS AND THE ASSOCIATED ABSORBED DOSE TO THE PATIENT

Robert Finck
Sören Mattsson

April 1975

Radiation Physics Department
University of Lund
Lasarettet
S-221 85 LUND
Sweden

ABSTRACT

The activity-concentrations of several long-lived gamma-emitting radionuclides present in technetium generators and in eluates from these generators have been determined by means of Ge(Li) gamma-spectrometry. The principal contaminants of the eluates were: $^{192}Ir(T_{1/2} = 74.3\ d)$, ^{134}Cs (2.05 a), ^{131}I (8.05 d), $^{110}Ag^{m}$ (255 d), ^{103}Ru (39.5 d), ^{99}Mo (66.7 h) and ^{60}Co (5.26 a). The impurity-concentrations were found to vary considerably from generator to generator. Changes in the impurity-concentrations in eluates from the same generator have also been recorded during an elution-period of one week. In accord with their ability to be eluted from the generators, the long-lived radionuclide-impurities may be arranged in the following sequence $^{134}Cs > {}^{103}Ru \geq {}^{110}Ag^{m} > {}^{192}Ir > {}^{60}Co$.

INTRODUCTION

The radionuclide $^{99}Tc^m$ is at present one of the most commonly used radionuclides in nuclear medicine and research. It is the daughter-product of ^{99}Mo ($T_{1/2}$ = 67 h), which can be obtained either by irradiation of enriched ^{98}Mo with thermal neutrons or from fission of uranium. $^{99}Tc^m$ ($T_{1/2}$ = 6.05 h) decays to ^{99}Tc, which has a physical half-life of around $2 \cdot 10^5$ a. The hitherto most commonly used system for producing $^{99}Tc^m$ is the so called "generator" containing ^{99}Mo, from which the technetium can easily be separated. ^{99}Mo as molybdate is generally adsorbed on a column of Al_2O_3. Periodically, $^{99}Tc^mO_4^-$ is eluted with 0.9 % NaCl, while the ^{99}Mo-molybdate remains fixed on the sorbent. Together with $^{99}Tc^mO_4^-$ a number of different radioactive impurities may also be eluted [1-10]. The impurities, especially those with considerably long half-lives, are of great interest because of the associated absorbed dose to the patient, especially when high $^{99}Tc^m$-activities (10 mCi or more) are administered, as for example, for brain- and skeletal scintigraphy.

EXPERIMENTS

This investigation was performed with $^{99}Tc^m$-generators, used to produce $^{99}Tc^m$ in clinical routine at the University Hospital in Lund. Fourteen different generators manufactured by the Radiochemical Centre, Amersham, England, were studied. (Code: MCC.3, 400 mCi)

The generators were normally eluted once daily five times

a week, by means of 20 ml of isotonic saline. The daily eluted $^{99}Tc^{m}$-solution was split into four separate collection-vials, each containing 5 ml.

For twelve of the generators (I-XII), an additional 20 ml of eluates was taken for analysis before (Friday afternoon of week n-1) and after (Friday afternoon of week n) the routine elutions (week n).

For two generators (XIII-XIV), aliquots from the eluates used in clinical routine were taken.

The gamma-spectrometer, which was used for measurements of the impurities of the eluates and the columns, consisted of a 50 cm^3 Ge(Li)-detector and a 4096-channel pulse-height analyzer and provided an energy resolution (FWHM) of 2.9 keV at 1.332 MeV. The detector was housed in a lead cave with walls 10 cm thick, and placed in a low-background room.

The eluates were measured in the original vials, which were rigidly fixed close to the detector by means of a perspex sample-holder. Figure 1 shows a pulse-height distribution from an eluate recorded 10 days after elution. Determination of the detector's full-energy peak efficiency for different photon-energies was done from measurements on samples of the same geometry containing known amounts of ^{75}Se, $^{110}Ag^{m}$, ^{133}Ba and ^{182}Ta.

The counting-time used for measurements on the eluates was between 1000 and 5000 minutes. The $^{99}Tc^{m}$-activity of the eluates was measured immediately after elution by means of an ionization-chamber. This chamber was calibrated for

$^{99}Tc^{m}$ by means of comparative measurements with the Ge(Li) spectrometer mentioned earlier. After two to three months the generator-columns were taken out of their shields and measured at a distance of 30 cm from the front of the detector. Determinations of the counting-efficiency for various photon-energies were performed by means of point sources of known activity positioned at the same distance from the detector as the generator-columns. The counting-time for the generator-columns was 1000 minutes. Because of the long time-period between production and measurement of the generator-column, only radionuclides with a half-life greater than two weeks could be measured.
Evaluation of the recorded pulse-height distribution was carried out by means of the computer-programme SAMPO [11]. Decay-data for the different radionuclides were taken from standard handbooks [12,13].

RESULTS AND DISCUSSION

The contents of twelve different gamma-emitting radionuclides in pre-clinical eluates, post-clinical eluates and generator-columns are given in Table 1 (Generators I-XII). Results from more detailed studies of the elution-pattern for the different radioactive impurities are given in Figures 2a-2e (Generators XIII and XIV).
Table 1 shows that ^{60}Co, ^{103}Ru, $^{110}Ag^{m}$, ^{131}I and ^{192}Ir are present in most of the eluates. As far as we know, it is the first time that the presence of ^{192}Ir has been detected in eluates from $^{99}Tc^{m}$-generators. The radionuclide ^{134}Cs

was found in eluates from three of the generators (IV, VII and XIV). It is important to note that the $^{110}Ag^{m}$- and ^{131}I-contents in some of the eluates are as high as of the order of 1-10 nCi/ml (mean-value for a 20 ml elution). The contents of radionuclide-impurities in the generator-columns refer to conditions after the post-clinical elution; the measurements were carried out two to three months after the last elution. In addition to the radionuclide-impurities found in the eluates, the radionuclides ^{54}Mn, ^{58}Co, ^{59}Fe, ^{65}Zn and ^{95}Zr-^{95}Nb were found in generator-columns V, VI and VII. The radionuclide ^{182}Ta was found in one generator-column (XII). The concentrations of these radionuclides in the eluates were below the minimum detectable concentrations, which were around 1 pCi/ml. This means that the eluted fractions of the generator-content per 100 ml of saline (1 week of normal operation) are: $^{54}Mn < 1$ %, $^{58}Co < 0.1$ %, $^{59}Fe < 0.1$ %, $^{65}Zn < 0.1$ %, $^{95}Zr < 0.01$ % and $^{182}Ta < 0.01$ %. The different radionuclide-impurities present in the eluates will now be discussed in detail:

^{60}Co: The contents of ^{60}Co in the columns were found to be up to 12 µCi, and a maximum of 6 nCi per 20 ml of saline was eluted during the pre-clinical elution. The elution-efficiency for most generators seems to be around 0.1 % per 100 ml of saline. Figure 2d shows that maximum concentrations can be reached in fractions 2 and 3 on the fourth day. This detailed study also shows that no significant amount of ^{60}Co was registrated in the first 5 ml on the first day (< 1 pCi/ml).

^{99}Mo: This radionuclide was not included in the table because of the limited data available. Most of the samples were measured such a long time after the delivery of the column that ^{99}Mo had decayed below the minimum detectable quantities. In the pre-clinical eluate of generator I, 9 nCi/ml was registered.

^{103}Ru: Typical concentration-values for ^{103}Ru in the eluates ranged between 10 and 100 pCi/ml of the pre- and post-clinical eluates. Because of the relatively/ short physical half-life (39.5 d), there is little data on the ^{103}Ru-contents of the columns. For columns III, VII and X, the eluted fraction of the ^{103}Ru present in the columns seems to be of the order of 10 % per 100 ml of the saline which flowed through the column. Column XI contained less than 1 nCi after the final elution. The pre-clinical elution gave 0.4 nCi per 20 ml of eluate, so the elution-efficiency seems to have been very high (≈100 %) in this case. Figure 2b shows a decrease of the ^{103}Ru-concentration by volume of eluate, which may indicate a high elution-efficiency also in this case.

^{110}Ag^{m}: Typical concentration-values for ^{110}Ag^{m} in the eluates ranged between 0.1 and 1 nCi/ml of the pre- and post-clinical eluates. The maximum value was 6 nCi/ml. The elution-efficiency seems to be around 10 % per 100 ml of saline. Figure 2e shows that the lowest ^{110}Ag^{m}-concentrations are obtained in the beginning of the elution-period (first day) and in the first 5 ml of eluate from each daily elution.

^{131}I: The ^{131}I-content in the eluates was found to be between 1 pCi/ml and 10 nCi/ml with a mean-value of around 0.2 nCi/ml. The average concentration of ^{131}I seems to be about 10 times lower in the post-clinical eluate than in the pre-clinical one. Due to the relatively long storage-time between elution and measurements of the columns, it has not been possible to study the ^{131}I-contents of the columns.

^{134}Cs: About 0.5 nCi (per 20 ml) was eluted during the pre-clinical elution of columns IV and VII. Less than 0.02 nCi (per 20 ml) was eluted during the last elution. This shows, together with the fact that less than 1 nCi of ^{134}Cs was present in the columns after the last elution, that this radionuclide-impurity is very easily eluted. The continuous washing-out of ^{134}Cs from the columns is also illustrated in Figure 2a. For each 25 ml of saline which flowed through the column, the ^{134}Cs-concentration in the eluate is reduced by one-half.

^{192}Ir: In most eluates, the concentration values for ^{192}Ir ranged from 0.01 to 1 nCi/ml. The eluted fraction seems to be quite constant from generator to generator, about 2 % per 100 ml. Figure 2c shows nearly the same impurity-levels during the elution-week, except for an enhanced concentration in the first 5 ml of eluate on the first day.

The elution-efficiencies for various contaminants have been summarized in Table 2.

This table shows that the radionuclide-impurities which

are most easily eluted may be arranged in the following sequence: (elution-efficiency per 100 ml of saline is given in the brackets) ^{134}Cs(95 %) > ^{103}Ru(10-100 %) ≥ ≥ $^{110}Ag^{m}$(10 %) > ^{192}Ir(2 %).

α-emitting radionuclides

As a pilot-control, the eluate from one of the generators was also examined for α-emitting radionuclides.
50 ml of eluate was evaporated to a volume of 10 ml, which was then electroplated on a steel disc from a 1 M $(NH_4)_2SO_4$-solution. Measurements with a silicon surface barrier detector gave no significant rise of the background counting-rate in the 4-6 MeV energy-interval during a counting-time of 1000 minutes. This means that less than 0.02 α-particles per minute were emitted from the sample.

ESTIMATION OF THE ABSORBED DOSE TO PATIENTS FROM IMPURITIES IN GENERATOR-PRODUCED $^{99}Tc^{L}$

The radiation absorbed dose has been estimated for the situation when a patient has received 10 mCi of $^{99}Tc^{m}$ or 5 ml of eluate from the first fraction at the elution (which contains about 2 mCi of $^{99}Tc^{m}$). The maximum activities of administered long-lived radionuclides injected have been estimated to the following values: ^{60}Co- 3 nCi, ^{103}Ru- 4 nCi, $^{110}Ag^{m}$- 400 nCi, ^{131}I- 7 nCi, ^{134}Cs- 0.2 nCi and ^{192}Ir- 6 nCi. Typical values of the administered impurity-activities were taken as the mean content in 10 mCi of $^{99}Tc^{m}$ from fractions 2 and 3 on Monday to Friday:

^{60}Co- 0.2 nCi, ^{103}Ru- 0.1 nCi, $^{110}Ag^{m}$- 9 nCi, ^{131}I- 0.6 nCi, ^{134}Cs- 0.02 nCi and ^{192}Ir- 0.1 nCi.

The absorbed dose-constant Δ, mrad·kg·nCi^{-1}·a^{-1}, for the contaminants ^{60}Co, ^{103}Ru, $^{110}Ag^{m}$, ^{134}Cs and ^{192}Ir has been calculated using the MIRD-methods and -tables [14,15,16] for various organs. The physiological parameters were taken from ICRP [17]. The absorbed dose per activity-unit of $^{99}Tc^{m}$ and ^{131}I have been taken from COLOMBETTI et al. [18] and take into account the biological behaviour of these radionuclides, as reviewed by CÍFKA and VESELÝ [19].

The absorbed dose delivered to different organs in non-typical situations is given in Table 3.

The table shows that $^{110}Ag^{m}$ may give small but significant contributions to the absorbed dose in special organs such as bone, liver and kidneys.

It must, however, be pointed out that these dose-values are calculated for non-typical situations, and that normal impurity-concentrations may give rise to a radiation dose which is a factor of fifty lower than what is calculated for these non-typical situations.

CONCLUSION

The result of this work clearly shows that the radionuclide-impurities in generator-produced $^{99}Tc^{m}$-solutions vary considerably from generator to generator. It is also demonstrated that the concentrations of radionuclide-impurities vary as a function of the eluted volume. In accord with their ability to be eluted from the generators, the long-lived

radionuclide-impurities may be arranged in the following sequence: $^{134}Cs > {}^{103}Ru \geq {}^{110}Ag^{m} > {}^{192}Ir > {}^{60}Co$. It is in our opinion important to make routine quantitative measurements of the contents of different radionuclide-impurities in eluates from all molybdenum-technetium generators.

REFERENCES

1. SMITH E.M.
   J. Nucl. Med. 5, 871 (1964)

2. BATTIST L., SCHADT W.W. and ARRAS J.M.
   J. Nucl. Med. 11, 620 (1970)

3. BARRALL R.C., SMITH S.I., FINSTON R.A. and COLOMBETTI L.G.
   Impurities in $^{99}Tc^{m}$ used in medical diagnosis.
   Paper presented at Second International Symposium on Nuclear Medicine (May 11-14, 1971, Karlovy Vary, Czechoslovakia)

4. MUELLER TH. and STEINNES E.
   Scand. J. Clin. Lab. Invest 28, 213 (1971)

5. WOOD D.E. and BOWEN B.M.
   J. Nucl. Med. 12, 307 (1971)

6. MEINHOLD H., HERZBERG B., KAUL A. and ROEDLER H.D.
   Radioactive impurities of nuclide generators and estimation of resulting absorbed dose in man.
   In "New developments in radiopharmaceuticals and labelled compounds", IAEA, Vienna, 1973, pp. 39-52.

7. BOYD R.E.
   Recent developments in generators of technetium-99m.
   In "New developments in radiopharmaceuticals and labelled compounds", IAEA, Vienna, 1973, pp. 3-26.

8. CONSTANT R., FALLAIS C., CHARLIER R. and BIEVELEZ P.
Le générateur ^{99m}Tc. Contrôle de pureté et contrôle de production.
In "New developments in radiopharmaceuticals and labelled compounds", IAEA, Vienna, 1973, pp. 27-38.

9. BILLINGHURST M.W., GROOTEHEDDE M. and PALSER R.
J. Nucl. Med. 15, 266 (1974)

10. BRINER W.H. and HARRIS C.C.
J. Nucl. Med. 15, 466 (1974)

11. ROUTTI J.T. and PRUSSIN S.G.
Nucl. Instrum. Meth. 72, 125 (1969)

12. LEDERER C.M., HOLLANDER J.M. and PERLMAN I.
Table of isotopes, 6th ed.
(J.Wiley & Sons Ltd., New York)

13. WAKAT M.A.
Nuclear Data Tables Sec. A 8, 445 (1971)

14. BROWNELL G.L., ELLETT W.H. and REDDY A.R.
MIRD/J. Nucl. Med. Suppl. No. 1, p. 27 (1968)

15. SNYDER W.S., FORD M.R., WARNER G.G. and FISHER H.L. Jr.
MIRD/J. Nucl. Med. Suppl. No. 3, p. 5 (1969)

16. DILLMAN L.T.
Private communication
Ohio Wesleyan University, Delaware, Ohio 43015, U.S.A.

17. INTERNATIONAL COMMISSION ON RADIOLOGICAL PROTECTION (ICRP)
Publication 2, Pergamon Press, London (1959)

18. COLOMBETTI L.G., HUSAK V. and DVORAK V.
Int. J. Appl. Rad. Isotopes 25, 35, (1974)

19. CÍFKA J. and VESELÝ P.
Review of biological behaviour of pertechnetate-^{99m}Tc in some organs and calculation of radiation doses to these organs from ^{99m}Tc and its possible radionuclidic impurities.
Nuclear Research Institute of the Czechoslovak Academy of Science
Report ÚJV 2696 D, September 1971

TABLE 1

Radionuclide impurities in $^{99}Tc^{m}$-columns and eluates.

Radionuclide impurity in eluate and column after elution		Generator nr											
		I	II	III	IV	V	VI	VII	VIII	IX	X	XI	XII
^{54}Mn	initial eluate	-	-	-	-	-	-	-	-	-	-	-	-
	final eluate	-	-	-	-	-	-	-	-	#	#	#	#
	column	-	#	-	-	5	5	5	-	#	-	-	-
^{58}Co	initial eluate	-	-	-	-	-	-	-	-	-	-	-	-
	final eluate	-	-	-	-	-	-	-	-	#	#	#	#
	column	-	#	-	-	6	6	6	-	#	-	-	-
^{59}Fe	initial eluate	-	-	-	-	-	-	-	-	-	-	-	-
	final eluate	-	-	-	-	-	-	-	-	#	#	#	#
	column	-	#	-	-	6	6	6	-	#	-	-	-
^{60}Co	initial eluate	-	-	-	2	1	-	1	2	1	1	3	-
	final eluate	-	-	-	2	1	-	1	2	#	#	#	#
	column	4	#	4	8	6	6	6	8	#	4	7	7
^{65}Zn	initial eluate	-	-	-	-	-	-	-	-	-	-	-	-
	final eluate	-	-	-	-	-	-	-	-	#	#	#	#
	column	-	#	-	-	6	6	6	-	#	-	-	-
^{95}Zr	initial eluate	-	-	-	-	-	-	-	-	-	-	-	-
	final eluate	-	-	-	-	-	-	-	-	#	#	#	#
	column	-	#	-	-	7	7	7	-	#	-	-	-
^{103}Ru	initial eluate	2	2	2	2	2	2	3	2	2	3	2	-
	final eluate	2	2	1	1	1	1	2	1	#	#	#	#
	column	#	#	5	#	#	#	6	#	#	5	-	#
$^{110}Ag^{m}$	initial eluate	2	3	4	3	3	3	3	-	3	3	3	4
	final eluate	2	2	2	3	2	3	2	2	#	#	#	#
	column	6	#	5	6	5	6	5	6	#	5	6	7
^{131}I	initial eluate	3	3	#	4	2	#	#	2	3	3	2	#
	final eluate	2	2	2	1	2	#	3	3	#	#	#	#
	column	#	#	#	#	#	#	#	#	#	#	#	#
^{134}Cs	initial eluate	-	-	-	2	-	-	2	-	-	-	-	-
	final eluate	-	-	-	-	-	-	-	-	#	#	#	#
	column	-	#	-	-	-	-	-	-	#	-	-	-
^{182}Ta	initial eluate	-	-	-	-	-	-	-	-	-	-	-	-
	final eluate	-	-	-	-	-	-	-	-	#	#	#	#
	column	-	#	-	-	-	-	-	-	#	-	-	7
^{192}Ir	initial eluate	3	3	3	3	3	3	3	2	3	3	2	-
	final eluate	2	2	2	2	2	2	2	1	#	#	#	#
	column	6	#	6	6	6	6	6	6	#	6	5	5

Column code

- = < 1 nCi
4 = 1 - 10 nCi
5 = 10 - 100 nCi
6 = 0.1 - 1 μCi
7 = 1 - 10 μCi
8 = 10 - 100 μCi
9 = 0.1 - 1 mCi

Eluate code

- = < 1 pCi/ml
1 = 1 - 10 pCi/ml
2 = 10 - 100 pCi/ml
3 = 0.1 - 1 nCi/ml
4 = 1 - 10 nCi/ml
5 = 10 - 100 nCi/ml
6 = 0.1 - 1 μCi/ml
7 = 1 - 10 μCi/ml
8 = 10 - 100 μCi/ml
9 = 0.1 - 1 mCi/ml

= Not measured

TABLE 2

Elution-efficiency for different radionuclides in molybdenum-technetium-generators.

Radionuclide	Elution-efficiency per 100 ml of saline
^{54}Mn	< 1 %
^{58}Co	< 0.1 %
^{59}Fe	< 0.1 %
^{60}Co	0.1 %
^{65}Zn	< 0.1 %
^{95}Zr	< 0.01 %
^{103}Ru	10 - 100 %
$^{110}Ag^{m}$	10 %
^{134}Cs	95 %
^{182}Ta	< 0.01 %
^{192}Ir	2 %

TABLE 3

Maximal injected activity of radionuclide-impurities in $^{99}Tc^{m}$-eluates and estimated absorbed dose in various organs. The absorbed dose from $^{99}Tc^{m}$ is given as a comparison.

Radio-nuclide	Total injected activity	Organ	Absorbed dose, mrad
$^{99}Tc^{m}$	2 mCi of first eluted volume	whole body	26
		liver	48
		kidneys	62
		thyroid	920 x)
^{103}Ru	4 nCi	whole body	0.004
		bone	0.02
		kidneys	0.12
^{131}I	7 nCi	whole body	0.01
		thyroid	15 x)
^{134}Cs	0.2 nCi	whole body	0.01
^{192}Ir	6 nCi	whole body	0.04
		liver	0.4
		kidneys	0.5
		spleen	0.5
$^{99}Tc^{m}$	10 mCi of elution peak volume	whole body	130
		liver	240
		kidneys	310
		thyroid	4600 x)
^{60}Co	3 nCi	whole body	0.05
$^{110}Ag^{m}$	400 nCi	whole body	2
		bone	5
		liver	15
		kidneys	15
^{131}I	7 nCi	whole body	0.01
		thyroid	15 x)

x) assuming that the thyroid gland is not blocked.

FIGURE-CAPTIONS

Figure 1. Pulse-height distribution from a $^{99}Tc^{m}O_4^-$-eluate recorded by means of a 50 cm^3 Ge(Li)-detector seven days after elution. The counting-time was 2000 minutes.

Figure 2a. ^{134}Cs-content (nCi/ml) in different eluate-fractions during a week (generator IV).

Figure 2b. ^{103}Ru-content (nCi/ml) in different eluate-fractions during a week (generator XIII).

Figure 2c. ^{192}Ir-content (nCi/ml) in different eluate-fractions during a week (generator XIII).

Figure 2d. ^{60}Co-content (nCi/ml) in different eluate-fractions during a week (generator XIII).

Figure 2e. $^{110}Ag^{m}$-content (nCi/ml) in different eluate-fractions during a week (generator XIII).

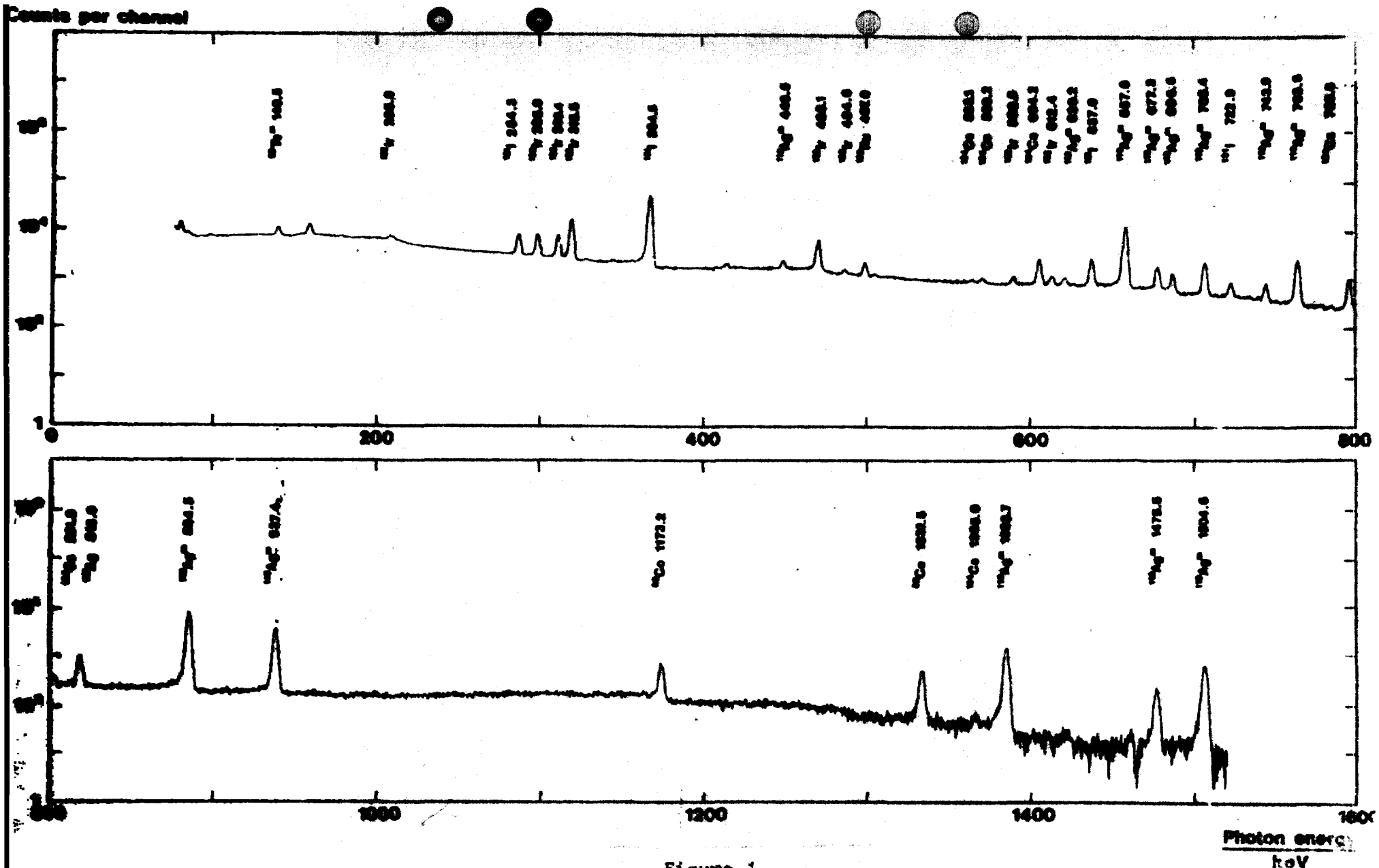
Counts per channel
200
400
600
800
1000
1200
1400
Photon energy
keV

Figure 1.

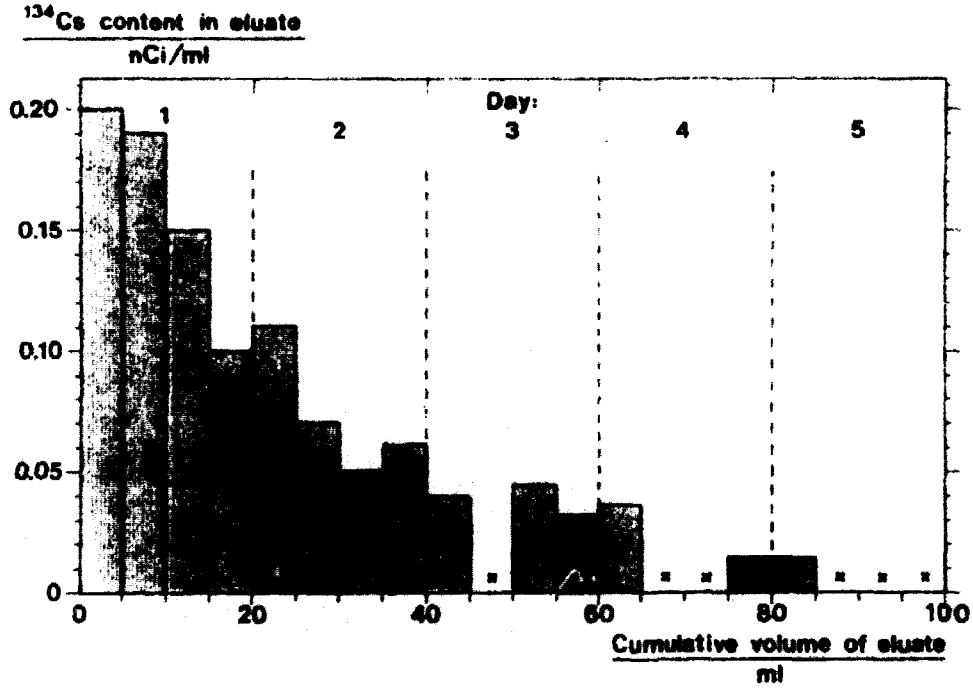

Figure 2a.

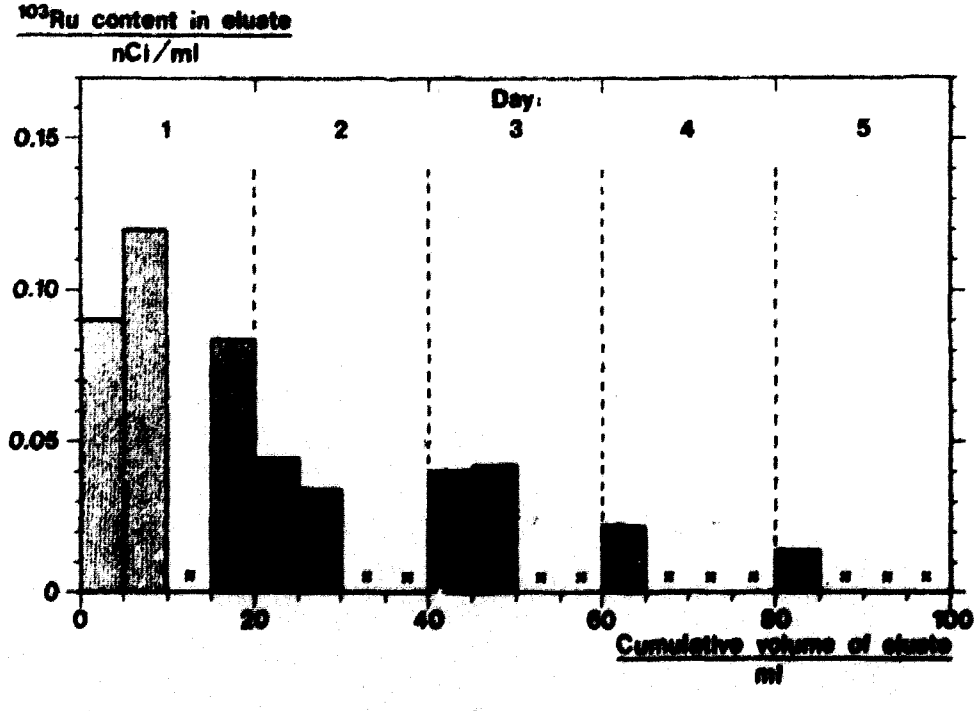

Figure 2b.

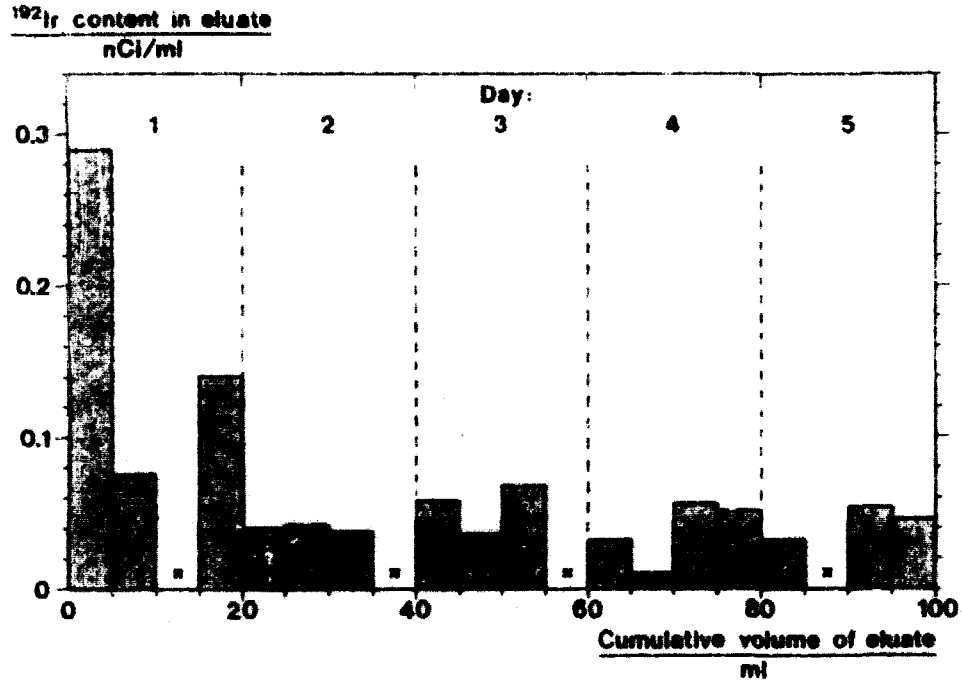

Figure 2c.

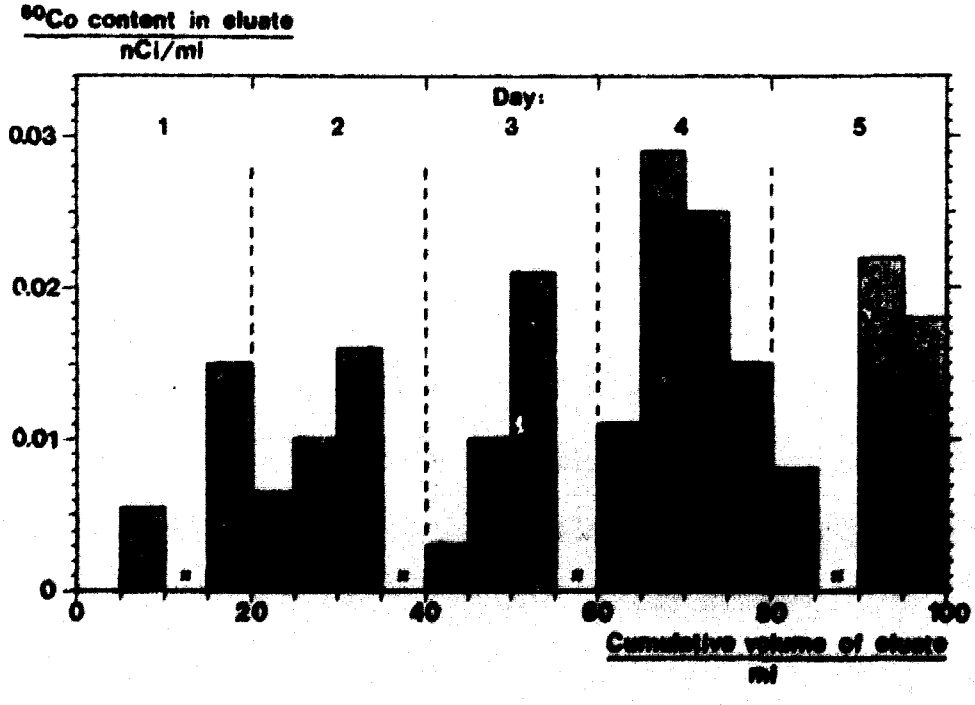

Figure 2d.

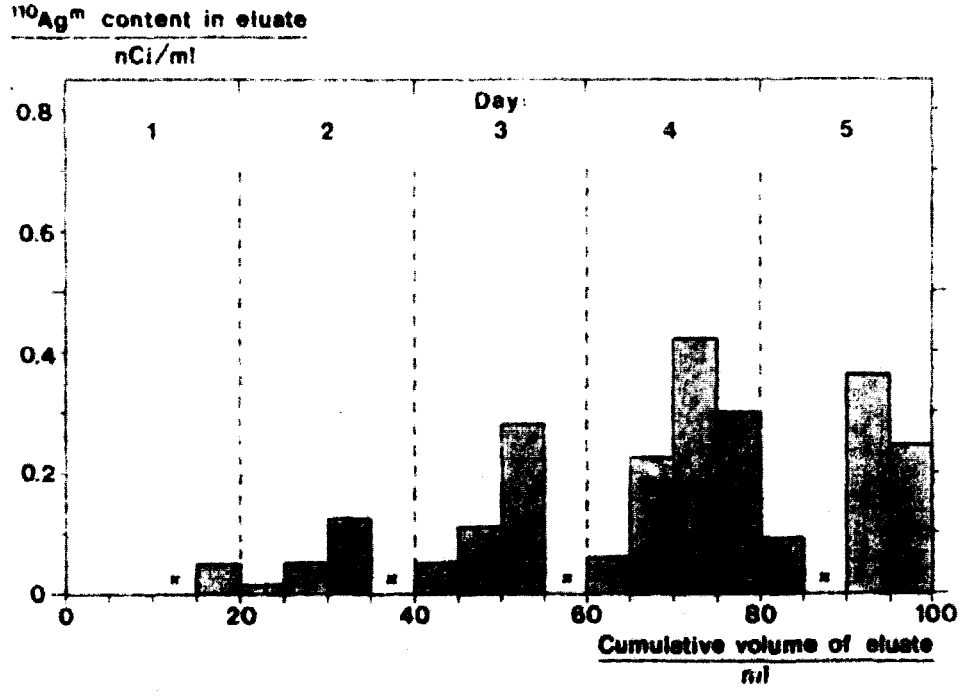
$^{110}Ag^{m}$ content in eluate
nCi/ml
Day
1
2
3
4
5
0.8
0.6
0.4
0.2
0
0
20
40
60
80
100
Cumulative volume of eluate
ml

Figure 2e.