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LUCAS HEIGHTS RESEARCH LABORATORIES

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DECEMBER 1985

ISBN 0 642 59818 5

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ABSTRACT

High pressure liquid chromatography (HPLC) is used for the assay of nanogram quantities of technetium and to determine technetium in decayed pharmaceutical products, derived from three methods of manufacture.

These methods of manufacture give comparably low levels of technetium-99, at the time of collection of the solution. However, when the solutions are used to produce ready-to-inject technetium-99m, high levels of technetium-99 are present at the time of calibration, which is the day after the collection date. Where sensitive reagent kits are to be labelled, freshly collected solutions of technetium-99m should be used.

The HPLC assay is a valuable technique for the quality control of technetium-based radiopharmaceuticals, and for investigation of methods of manufacture of technetium-99m. Experimental studies confirmed the findings of previous workers.

National Library of Australia card number and ISBN 0 642 59818 5

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TECHNETIUM 99; RADIOPHARMACEUTICALS; HIGH PRESSURE; LIQUID COLUMN CHROMATOGRAPHY; PERTECHNETATES; SODIUM COMPOUNDS; ISOTOPE PRODUCTION; QUANTITATIVE CHEMICAL ANALYSIS; RADIOISOTOPE GENERATORS; DECAY

CONTENTS

1. INTRODUCTION

A sensitive quantitative assay of technetium was required to study solutions of sodium pertechnetate produced at the AAEC Research Establishment. The assay method was required for quality control and for the investigation of the suitability of the pertechnetate solutions for use in sensitive reagent kits.

A high pressure liquid chromatographic (HPLC) method was developed for estimating technetium in decayed pertechnetate solutions. The method was capable of detecting nanogram quantities of technetium, and proved to be a valuable method in quality control and in investigational studies.

2. LITERATURE REVIEW

In the past, little attention was paid to the significance of levels of technetium-99 in technetium-99m radiopharmaceuticals. Numerous reports received by the AAEC described the poor imaging quality with some reagent kits when they were labelled with ready-to-inject pertechnetate obtained by the methyl ethyl ketone (MEK) extraction process. Initially, it was thought that unknown organic compounds present in the MEK derived pertechnetate were the cause of the problem, especially where red blood cell (RBC) labelling and skeletal imaging studies were carried out.

Smith and Richards [1976] reported that the technetium-99m labelling of RBC kits containing 1 μg of stannous ion was adversely affected when more than 24 ng of technetium was added. They stated that this quantity was usually exceeded in ready-to-inject pertechnetate, because of the presence of technetium-99 due to radioactive decay. Porter *et al.* [1976] reported that 500 ng of technetium was the maximum amount that could be added to ^{99m}Tc-human serum albumin kits, and still retain a radiochemical purity above 90 per cent. Srivastava *et al.* [1977] reported reduced labelling efficiency with some commercial lung scanning agents, when the technetium levels exceeded certain values. Deutsch [1979] reported that the total concentration of pertechnetate (both as $^{99m}TcO_4^-$ and as $^{99}TcO_4^-$) determines the chemistry and kinetics of the conversion of pertechnetate in radiopharmaceuticals containing technetium-99m in the reduced state.

Domel [1981] studied RBC labelling by serial dilution of a technetium-99 standard solution. It was shown that labelling efficiencies began to decline at more than 25 ng of technetium per μg of stannous ion. This result agreed with that reported by Smith and Richards [1976]. Domel *et al.* [1982] and Mohammad [1982] carried out extensive studies on the effects of MEK derived pertechnetate on RBC labelling efficiency and found that the most likely cause of the problem was not the organics, but the relatively high concentrations of technetium-99 in the MEK derived pertechnetate used as a ready-to-inject solution in hospitals.

Moore [1983] examined the theoretical aspects of pertechnetate production. He reported that the technetium-99/technetium-99m ratio of a molybdenum trioxide target is about 13.5:1 after seven days' irradiation in a nuclear reactor, and concluded that, in the case of ready-to-inject pertechnetate solutions, the technetium-99/technetium-99m ratio increases rapidly between elution and use. Under poor production conditions, the ratio may increase to more than 600:1 by the time of use. Moore also stated that the technetium-99/technetium-99m ratio can increase to about 90:1 during the 90 hours that may elapse between the final stage of manufacture, and first elution in the hospital of a chromatographic generator. With frequent elutions, and with high elution efficiencies, the ratio will drop considerably.

The quantitative determination of technetium-99 in a radiopharmaceutical is difficult when radiochemical methods are used. Technetium-99 is present in low concentrations, it has a low-energy beta emission (0.29 MeV), and other radionuclidic impurities may be present. Mohammad [1982] examined a number of samples of decayed AAEC ready-to-inject pertechnetate by scintillation counting. Technetium-99 levels in the range 500 to 9900 ng mL^{-1} were reported in samples obtained from the MEK extraction process.

Russell and Majerik [1979] compared the assay of pertechnetate in labelled radiopharmaceuticals using HPLC, thin layer chromatography and paper chromatography and found that HPLC indicated lower concentrations of pertechnetate than the other methods. Wong *et al.* [1981] showed that HPLC was a valuable method of quality control for labelled radiopharmaceuticals, including those labelled with technetium-99m. Zodda et al. [1982] developed an HPLC method for the quantitative determination of pertechnetate by ultraviolet detection.

Farrington and Miller [1983] obtained sharp HPLC peaks for pure samples of pertechnetate using the ion-pairing reagents 1-hexane sulphonic acid or 1-octyl sulphonic acid in a methanol/water mixture.

However, it was found that when decayed ready-to-inject pertechnetate samples were examined other impurities interfered.

Bonnyman [1983] described an HPLC assay of technetium in which tetrabutyl ammonium phosphate was used in a methanol/water solvent. This system was adopted in the present study to determine technetium levels by HPLC in AAEC-produced pertechnetate solutions.

The HPLC method used in this study was also used by Maddalena *et al.* [1983] to study the effects on RBC labelling of MEK extracted pertechnetate and pertechnetate from a large chromatographic generator-derived pertechnetate. The study showed that when the pertechnetate was eluted daily and used within a few hours, the RBC labelling was high irrespective of the source of the pertechnetate. However, when the pertechnetate was calibrated for use the following day, the technetium-99 level was great enough to interfere with the RBC labelling results, regardless of the source of the pertechnetate.

The study also illustrated that the RBC labelling technique could be a simple laboratory method of testing the suitability of technetium-99m solutions for use with sensitive reagent kits. It also showed that there was good agreement between RBC labelling and the quantitative results obtained with the HPLC assay. However, when fission-derived pertechnetate was examined the liquid scintillation technique gave results for levels of technetium-99 that were excessive, and not in agreement with the other two methods.

3. EXPERIMENTAL

A Waters model ALC/GPC 244 liquid chromatograph with a Waters model 6000A solvent delivery system was used. The HPLC had a Waters model 440 ultraviolet absorbance detector. A Waters C-18 radial PAK column was used with a Waters RCM-100 radial compression module. A Houston Instruments Omniscribe recorder was used with the system.

The solvent was a 40 per cent methanol/water mixture containing 0.005 *M* tetrabutyl ammonium phosphate (Waters PIC-A reagent). The solvent was delivered to the column at the rate of 0.5 mL min^{-1}, and the recorder chart speed was 1.7 mm min^{-1}. The retention time of technetium was 12 minutes. Scans were made at 254 nm, using a sensitivity of 0.01 AUFS.

Standards were made from ammonium (^{99}Tc) pertechnetate supplied by the Oak Ridge National Laboratory, Tennessee, USA. A 250 $\mu g\ mL^{-1}$ stock solution of technetium-99 was diluted to 10 $\mu g\ mL^{-1}$ of technetium-99m, and assayed by ultraviolet absorption spectroscopy using the method of Rulfs [1970]. A standard solution of 1 $\mu g\ mL^{-1}$ of technetium-99 was then prepared by dilution for use in the HPLC assay method. Figure 1 shows a typical standard curve. In all cases peak heights were measured. Figure 2 shows a trace taken with a decayed sample of MEK-extracted pertechnetate.

The decayed samples of pertechnetate that were assayed by the HPLC method were obtained from three methods of manufacture employed by the AAEC:

. a standard chromatographic generator,

. a large chromatographic generator, and

. the MEK extraction process.

Assays were carried out at room temperature, using 5 to 1000 μL of sample.

Standard chromatographic generators are loaded with up to 150 GBq of fission-produced molybdenum-99. These generators are manufactured weekly and despatched to hospitals throughout Australia. A generator from each batch is retained for quality control. The pertechnetate may be used for injection immediately after collection.

The large chromatographic generator was introduced to supply ready-to-inject pertechnetate, when it was thought that organic compounds present in MEK extracted pertechnetate interfered in the labelling of sensitive kits. The generators are loaded with 1 to 7 TBq of fission-produced molybdenum-99. Up to 24 hours may elapse between the elution time and the calibration time of ready-to-inject pertechnetate solution prepared by this method.

The MEK extraction plant is loaded with up to 18.5 TBq of non-fission-produced molybdenum-99. The technetium-99m is used as a source of ready-to-inject pertechnetate. Up to 24 hours may elapse between the extraction time and the calibration time.

4. RESULTS

The HPLC method was used to determine the levels of technetium in decayed eluates from pertechnetate produced by the three methods. Similarly, determinations were made on decayed ready-to-inject solutions, which were made by dilution of eluates obtained from the three methods of manufacture.

Since the levels of technetium-99m were measured at elution, the levels of technetium-99 at elution time and at calibration time could be determined by difference, using the value for total technetium obtained by the HPLC assay.

The total level of technetium per millilitre has little significance when comparing pertechnetate solutions produced by three processes because each method used varying loadings of molybdenum-99, and the eluates had varying volumes and concentrations of technetium. For comparison, the ratio of technetium-99/technetium-99m was calculated, and the values compared with the theoretical results computed by the method of Hetherington [1984]. Comparative results were also calculated, from experimental data, for the levels of technetium-99 present at calibration in a 1 GBq solution of technetium-99m.

4.1 Standard Chromatographic Generator

Table 1 lists results of the HPLC assays for technetium obtained on a series of elutions from a standard chromatographic generator. In all cases, the elution efficiencies were greater than 97 per cent. The data in table 2 are derived from HPLC assays carried out on a series of first elutions of chromatographic generators. These results are of importance because they indicate how well the generator has been washed free of decayed technetium during the manufacturing process.

4.2 Large Chromatographic Generator

Table 3 contains data derived from the HPLC assay of technetium found in a series of elutions from a production generator. Table 4 lists the data derived from the technetium assays of a series of first elutions of large chromatographic generators.

The data in table 5 are derived from ready-to-inject pertechnetate solutions. At calibration (0900 h) the products contained approximately 2 GBq mL^{-1} of technetium-99m. The calculated technetium-99/technetium-99m values were computed from data obtained from the series of generator elutions, taking into account growth time, elution efficiency and decay times.

4.3 MEK Extraction Process

In the MEK extraction process it is customary to discard the first, or first and second extractions. Table 6 lists the data obtained from the HPLC assay of technetium in a series of MEK extractions. Table 7 gives data for a series of first extractions of pertechnetate for radiopharmaceutical use, and table 8 the data obtained from ready-to-inject solutions, made by diluting the extracts obtained from the MEK extraction process.

The results shown in table 9 are from ready-to-inject pertechnetate which was obtained by diluting extracts from the MEK process after the growth time of the technetium-99m was restricted to between four and six hours. This procedure has now been adopted as standard practice at Lucas Heights. The pertechnetate obtained by allowing the technetium-99m to grow overnight is used to make labelled radiopharmaceuticals.

5. DISCUSSION

Deutsch et al. [1982] reported values for moles total technetium/mCi technetium-99m obtained by a HPLC technique that were about 35% consistently higher than the predicted value for eluates from chromatographic generators.

In this study the HPLC assay gave technetium-99/technetium-99m values that were in good agreement with the calculated values when a series of elutions for both the standard and large chromatographic generators were examined. These results demonstrate that this type of assay separates technetium from other interfering substances. Some of the values shown for technetium in table 1 are higher than those encountered under hospital conditions, where the generator is eluted more frequently. However, as reported by Bonnyman [1983] and Moore [1983], the level of technetium-99 is high in the first eluates because of the long period between manufacture and elution. In the case of generators produced at Lucas Heights, this time may exceed 72 h; imported generators may also have a longer growth period than 72 h.

Bonnyman [1983] reported values of 3.5 to 46 ng of ^{99}Tc per mCi of ^{99m}Tc for first eluates from ten standard generators, which were normally eluted 72 h after manufacture. This is equivalent to 95 to 1243 ng of ^{99}Tc per GBq of ^{99m}Tc. The results for first eluates from standard generators (table 2) gave 12 to 91 ng of ^{99}Tc per GBq of ^{99m}Tc and are of a lower order than those of Bonnyman. His higher value represents an imported generator that was delayed in delivery, and most of the generators listed in table 2 had short growth times of from 17 to 22 hours. The technetium-99/technetium-99m values for first eluates were, in some cases, higher than the calculated values. This may indicate that further washing is required.

At elution, the large chromatographic generator gave similar results to those obtained with the standard generator. However, because the stock pertechnetate from the large chromatographic generator is used for ready-to-inject pertechnetate, which must be transported throughout Australia, the technetium-99/technetium-99m values increase considerably before the product is used.

Bonnyman [1983] reported that in 36 samples of ready-to-inject pertechnetate the levels were 3.4 to 51 ng of ^{99}Tc per mCi of ^{99m}Tc (92 to 1378 ng of ^{99}Tc per GBq of ^{99m}Tc) 12 to 18 h after preparation. From the values given in tables 3 to 5 for eluates from the large chromatographic generator, a range of 19 to 520 ng of ^{99}Tc per GBq of ^{99m}Tc was found. These products had decay times in the range 4 to 25 h from elution to the time of calibration.

The overall efficiency of the MEK technetium-99m extraction process used at Lucas Heights is not known. A number of factors diminish the yield of technetium-99m during the process. After examining data in tables 6 and 7 by computer it was assumed that the efficiency of the process was variable, and that it was much lower than the elution efficiency of the chromatographic generator system. Because of these factors no attempt was made to calculate theoretical technetium-99/technetium 99m values.

Tables 6 to 9 give the results obtained from the HPLC technetium assay of pertechnetate extracts, or dilutions of extracts from the MEK process. These solutions contained 62 to 1758 ng of ^{99}Tc per GBq of ^{99m}Tc where the decay times to calibration were 12 to 25 h. These results are in agreement with the values of 92 to 1378 ng of ^{99}Tc per GBq of ^{99m}Tc for decay times of 12 to 18 hours found for AAEC ready-to-inject pertechnetate solutions by Bonnyman [1983].

Bonnyman [1983] recommended that MEK systems should be 'fully' eluted each day to minimise build-up of ^{99}Tc in the system. He concluded that if this was done it should be possible to maintain ^{99}Tc levels below 10 ng per mCi of ^{99m}Tc for pertechnetate prepared 18 to 24 h before calibration. The system at Lucas Heights is that the MEK generator is extracted each morning, and the extract used for ready-to-inject labelled radiopharmaceuticals. After a growth time of 4 to 6 h, another extraction is made, and the solution obtained used for ready-to-inject pertechnetate. Table 9 gives data obtained from the HPLC assay of technetium in decayed samples of ready-to-inject pertechnetate obtained by the new production method. All samples were below the 10 ng of ^{99}Tc per mCi of ^{99m}Tc (270 ng of ^{99}Tc per GBq of ^{99m}Tc) except the first usable extraction.

6. CONCLUSIONS

The HPLC method for the determination of technetium in decayed samples of pertechnetate gave technetium-99/technetium-99m values that were in agreement with calculated values. Values for technetium-99/technetium-99m in solutions of pertechnetate from the three AAEC methods of manufacture were, in general, in the range of values recorded by Bonnyman [1983].

It was demonstrated that changes in the manufacturing process for the MEK extraction method led to more consistent and lower technetium-99/technetium-99m values. It is evident that the necessity to prepare ready-to-inject pertechnetate long before the calibration time will be a limiting factor in the use of the product, with some sensitive reagent kits. However, ready-to-inject solutions will continue to be a valuable source of technetium-99m for direct injection, for labelling ready-to-inject radiopharmaceuticals and for use with more stable reagent kits. The assay of technetium by the HPLC method is not only a valuable experimental tool, but is also suitable for quantitative quality control purposes. It has the advantage that it can be used with both active and inactive solutions.

7. ACKNOWLEDGEMENTS

The author wishes to acknowledge the valuable technical advice and assistance given by Mr R. Miller. Thanks are due to Mr R. Jones for art work, to Dr P. Moore for helpful suggestions on the preparation of

the report and also to Mr R.E. Boyd who arranged that the study form part of an IAEA research agreement.

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TABLE 1
HPLC ASSAY OF ELUATES FROM A STANDARD CHROMATOGRAPHIC GENERATOR

Eluate No.*	Growth Time (h)	HPLC Tc ($ng\ mL^{-1}$)	^{99m}Tc at Elution ($ng\ mL^{-1}$)	^{99}Tc at Elution ($ng\ mL^{-1}$)	$^{99}Tc/^{99m}Tc$ at Elution from HPLC	$^{99}Tc/^{99m}Tc$ Calculated Value	^{99}Tc in Standard Product containing 1 GBq ^{99m}Tc at Calibration ($ng\ mL^{-1}$)
1	20	63	20.6	42.4	2.1	2.0	11
2	72	123	11.3	111.7	9.9	11.9	51
3	48	48	6.7	41.3	6.2	6.5	32
4	48	28	3.8	24.2	6.4	6.5	33
5	96	28	1.4	26.6	19.0	19.5	98
6	72	15	1.0	14.0	14.0	13.2	72

* Generator No 299-2A. Calibration is at elution time. Elution efficiency >97%.

TABLE 2
HPLC ASSAYS OF FIRST ELUATES FROM STANDARD CHROMATOGRAPHIC GENERATORS

Generator No.	Growth Time (h)	HPLC Tc ($ng\ mL^{-1}$)	^{99m}Tc at Elution ($ng\ mL^{-1}$)	^{99}Tc at Elution ($ng\ mL^{-1}$)	$^{99}Tc/^{99m}Tc$ at Elution from HPLC	$^{99}Tc/^{99m}Tc$ Computed Value	^{99}Tc in Standard Product containing 1 GBq ^{99m}Tc at Calibration ($ng\ mL^{-1}$)
299-2A	20	63	21	42	2.0	2.0	10
301-3A	20	70	16	54	3.4	2.0	17
301-4A	20	63	16	47	2.9	2.0	15
302-2A	20	70	19	51	2.7	2.0	14
304-3A	19	57	17	40	2.4	1.9	12
305-1A	21	80	20	60	3.0	2.2	16
305-2A	22	63	13	50	3.8	2.3	20
305-3A	93	187	10	177	17.7	17.9	91

Calibration is at elution time. Elution efficiency >90%

TABLE 3
HPLC ASSAY OF ELUATES FROM LARGE CHROMATOGRAPHIC GENERATOR

Eluate No.*	Growth Time (h)	Generator Efficiency (%)	HPLC Tc (ng mL^{-1})	^{99m}Tc at Elution (ng mL^{-1})	^{99}Tc at Elution (ng mL^{-1})	^{99}Tc/^{99m}Tc at Elution		Decay Time at Calibration (h)	^{99m}Tc at Calibration (ng mL^{-1})	^{99}Tc at Calibration (ng mL^{-1})	^{99}Tc/^{99m}Tc at Calibration		^{99}Tc in Standard Product Containing 1 GBq ^{99m}Tc at Calibration (ng mL^{-1})
						HPLC	Calc.				HPLC	Calc.	
1	21	100	1650	641	1009	1.6	2.2	24	40	1610	40.3	49.1	207
2	30	70	1500	349	1151	3.3	3.4	19	39	1461	37.5	38.1	193
3	7	85	720	213	507	2.4	2.4	12	54	666	12.3	13.2	64
4	19	80	1100	343	845	2.2	2.3	18	43	1057	24.6	24.7	127
5	7	89	400	170	230	1.4	1.4	11	48	352	7.3	7.7	38
6	19	85	752	222	530	2.4	2.1	15	40	712	17.8	17.2	92
7	8	85	280	137	143	1.0	1.3	7	61	219	3.6	4.3	19

*Generator No 306. Calibration is at 0900 h.

TABLE 4
HPLC ASSAY OF FIRST ELUATES FROM LARGE CHROMATOGAPHIC GENERATOR

Generator No.*	Growth Time (h)	HPLC Tc (ng mL^{-1})	^{99m}Tc at Elution (ng mL^{-1})	^{99}Tc at Elution (ng mL^{-1})	^{99}Tc/^{99m}Tc at Elution		Decay Time at Calibration (h)	^{99m}Tc at Calibration (ng mL^{-1})	^{99}Tc at Calibration (ng mL^{-1})	^{99}Tc/^{99m}Tc at Calibration		^{99}Tc in Standard Product Containing 1 GBq ^{99m}Tc at Calibration (ng mL^{-1})
					HPLC	Calc.				HPLC	Calc.	
306-01	21	1650	641	1009	1.6	2.2	24	40	1610	40.3	49.1	207
308-01	2	363	184	179	1.0	0.3	20	19	344	18.1	11.8	93
309-01	8	185	50	135	2.7	0.8	14	10	175	17.5	7.8	90
315-01	22	5100	880	4220	4.8	2.3	25	50	5050	101.0	57.5	520
316-01	22	4150	735	3415	4.6	2.3	25	43	4107	95.5	57.5	492

Calibration is at 0900 h. Elution efficiency >97%.

TABLE 5
HPLC ASSAY OF READY-TO-INJECT PERTECHNETATE FROM LARGE CHROMATOGRAPHIC GENERATOR

Eluate No.*	Growth Time (h)	Generator Efficiency (%)	HPLC Tc (ng mL^{-1})	^{99m}Tc at Elution (ng mL^{-1})	^{99}Tc at Elution (ng mL^{-1}	$^{99}Tc/^{99m}Tc$ at Elution		Decay Time at Calibration (h)	^{99m}Tcat Calibration (ng mL^{-1})	^{99}Tc at Calibration (ng mL^{-1})	$^{99}Tc/^{99m}Tc$ at Calibration		^{99}Tc in Standard Product Containing 1 GBq ^{99m}Tc at Calibration (ng mL^{-1})
						HPLC	Calc.				HPLC	Calc.	
1	23	100	520	174	346	2.1	2.4	24	11	509	46.3	53.2	238
2	24	70	653	174	479	2.8	2.6	24	11	642	58.4	55.3	301
3	30	83	385	89	296	3.3	4.7	19	10	375	37.5	50.2	193
5	19	71	200	62	138	2.2	2.3	15	11	189	17.2	17.7	89
10	9	85	55	16	39	2.4	1.4	4	10	45	4.5	2.9	23

*Generator No.290. Approximately 2GBq ^{99m}Tc at Calibration 0900 h.

TABLE 6
HPLC ASSAY OF EXTRACTS FROM THE MEK EXTRACTION PROCESS

Extraction No.*	Growth Time (h)	HPLC Tc at Extraction (ng mL^{-1})	^{99m}Tc at Extraction (ng mL^{-1})	^{99}Tc at Extraction (ng mL^{-1})	$^{99}Tc/^{99m}Tc$ at Extraction	Decay Time to Calibration (h)	^{99m}Tc at Calibration (ng.mL^{-1})	^{99}Tc at Calibration (ng mL^{-1})	$^{99}Tc/^{99m}Tc$ at Calibration	^{99}Tc in Standard Product containing 1 GBq ^{99m}Tc at Calibration (ng mL^{-1})
3	19	3800	804	2996	3.7	23	57	3743	65.7	338
5	23	2450	756	1694	2.2	24	48	2402	50.0	258
6	12	2500	768	1732	2.3	12	193	2307	12.0	62
7	60	4800	428	4372	10.2	24	27	4773	176.8	910
9	5	900	186	714	3.8	18	23	877	38.1	196

*Generator 537. Calibration at 0900 h.

TABLE 7

HPLC ASSAY OF FIRST EXTRACTS FOR RADIOPHARMACEUTICAL USE FROM MEK EXTRACTION PROCESS

Generator No.*	Growth Time (h)	HPLC Tc at Extraction (ng mL^{-1})	^{99m}Tc at Extraction (ng mL^{-1})	^{99}Tc at Extraction (ng mL^{-1})	^{99}Tc/^{99m}Tc at Extraction	Decay Time to Calibration (h)	^{99m}Tc at Calibration (ng mL^{-1})	^{99}Tc at Calibration (ng mL^{-1})	^{99}Tc/^{99m}Tc at Calibration	^{99}Tc in Standard Product containing 1 GBq ^{99m}Tc at Calibration (ng mL^{-1})
512-03	24	1620	171	1449	8.5	24	11	1609	146.3	753
535-03	6	1400	364	1036	2.8	12	92	1308	14.2	73
537-03	19	3800	804	2996	3.7	23	57	3743	65.7	338
538-03	17	7700	870	6830	7.9	24	55	7645	139.0	716
539-03	17	6300	742	5558	7.5	25	42	6258	149.0	767
541-02	45	17800	829	16971	20.5	24	52	17748	341.3	1758

*Calibration at 0900 h.

TABLE 8

HPLC ASSAY OF READY-TO-INJECT PERTECHNETATE FROM THE MEK EXTRACTION PROCESS

Extraction No.*	Growth Time (h)	HPLC Tc at Extraction (ng mL^{-1})	^{99m}Tc at Extraction (ng mL^{-1})	^{99}Tc at Elution (ng mL^{-1})	^{99}Tc/^{99m}Tc at Extraction	Decay Time to Calibration (h)	^{99m}Tc at Calibration (ng mL^{-1})	^{99}Tc at Calibration (ng mL^{-1})	^{99}Tc/^{99m}Tc at Calibration	^{99}Tc in Standard Product containing 1 GBq ^{99m}Tc at Calibration (ng mL^{-1})
2	3	460	95	365	3.8	19	11	449	40.8	210
4	24	1300	179	1121	6.3	24	11	1289	117.2	604
6	5	440	99	341	3.4	19	11	429	39.0	201
9	25	600	168	432	2.6	24	10	590	59.0	304
12	5	840	113	727	6.4	20	11	829	75.4	388

*Generator No.510. Approximately 2GBq mL^{-1} ^{99m}Tc at Calibration (0900 h).

TABLE 9

HPLC ASSAY OF READY-TO-INJECT PERTECHNETATE FROM MEK EXTRACTION PROCESS (SHORT GROWTH TIME)

Extraction No.*	Growth Time (h)	HPLC Tc at Extraction (ng mL^{-1})	^{99m}Tc at Extraction (ng mL^{-1})	^{99}Tc at Extraction (ng mL^{-1})	^{99}Tc/^{99m}Tc at Extraction	Decay Time to Calibration (h)	^{99m}Tc at Calibration (ng mL^{-1})	^{99}Tc at Calibration (ng mL^{-1})	^{99}Tc/^{99m}Tc at Calibration	^{99}Tc in Standard Product containing 1 GBq ^{99m}Tc at Calibration (ng mL^{-1})
2	4	800	98	702	7.2	19	11	789	71.7	369
4	5	495	100	395	4.0	20	10	485	48.5	250
6	5	450	100	350	3.5	20	10	440	44.0	227
8	6	455	98	357	3.6	19	11	444	40.4	208
9	5	310	55	255	4.6	14	11	299	27.2	140

*Generator No.560. Approximately 2 GBq mL^{-1} ^{99m}Tc at Calibration (0900 h).

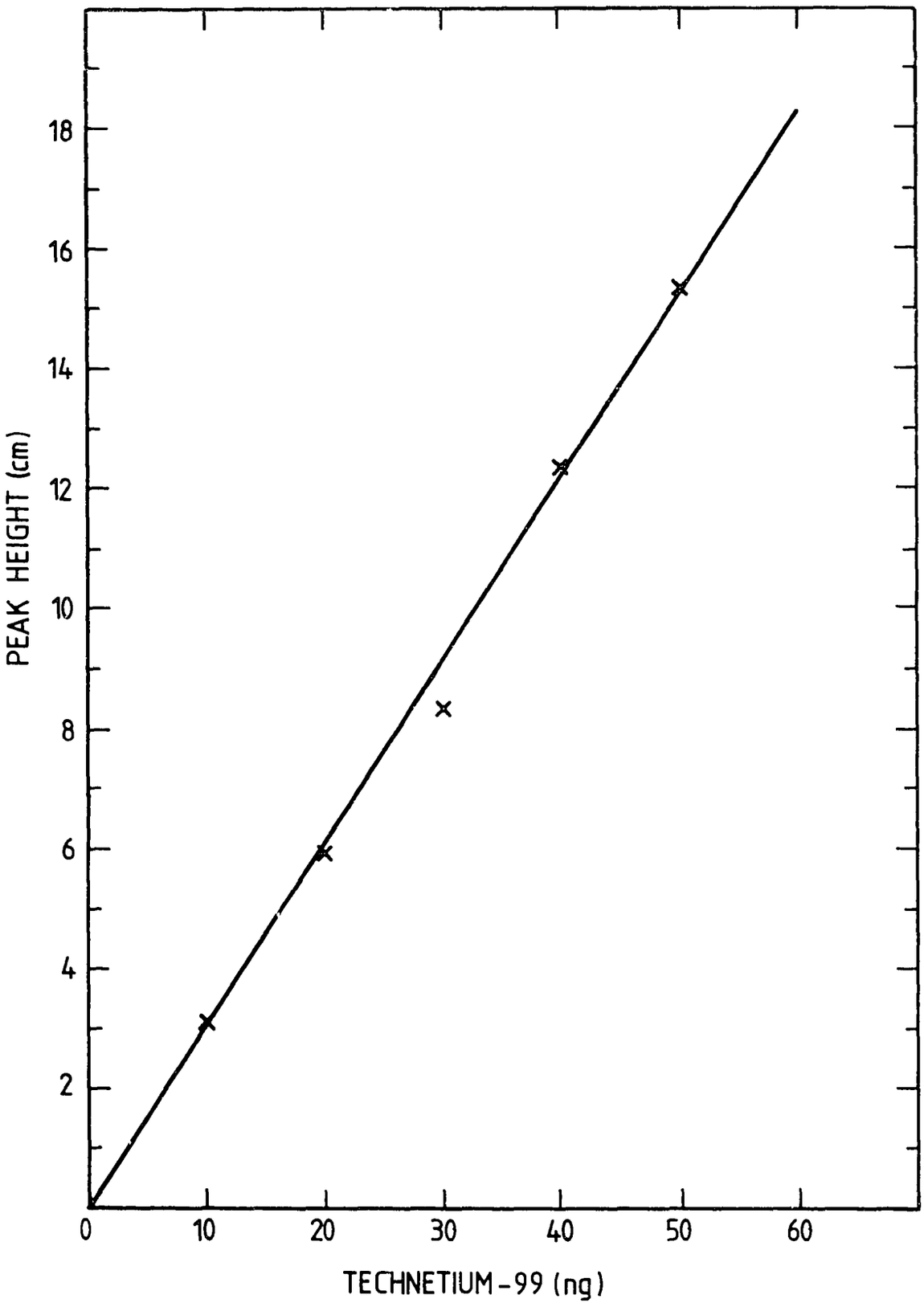

Figure 1 Standard curve HPLC assay technetium-99 at 254 nm

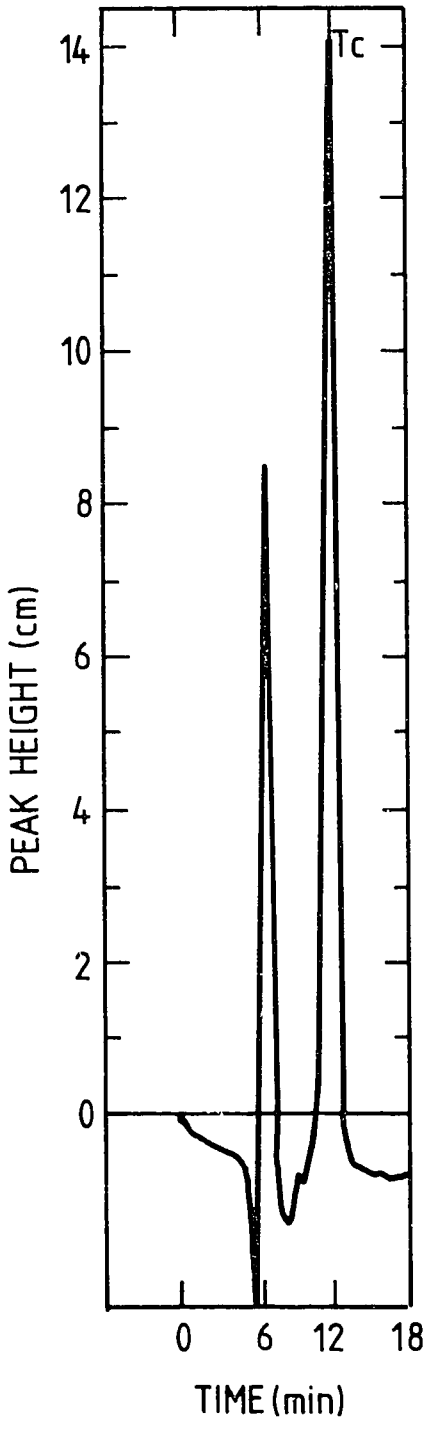

Figure 2 Chromatogram MEK extracted pertechnetate