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Solid-phase extraction of ^{225}Ac using ion-imprinted resin and ^{243}Am as a radioactive tracer for internal dosimetry and incorporation measurements

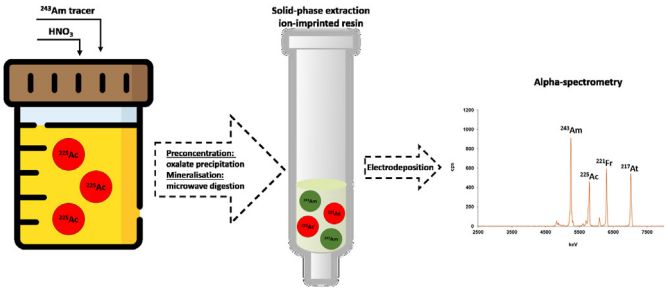
Ruslan Cusnir [a, b, *], Pascal Froidevaux [a], Pierre Carbonez [b], Marietta Straub [a, b]

[a] Institute of Radiation Physics, Lausanne University Hospital and University of Lausanne, Rue du Grand-Pré 1, CH-1007, Lausanne, Switzerland
[b] CERN, CH-1211, Geneva 23, Switzerland

HIGHLIGHTS

- ^{225}Ac and ^{243}Am extracted with equivalent recoveries using an ion-imprinted resin.
- Ion-imprinted resin was used to determine trace amounts of ^{225}Ac in urine.
- ^{243}Am was used as a yield tracer to measure ^{225}Ac with alpha spectrometry.
- A first method enabling incorporation measurements and internal dosimetry of ^{225}Ac.

GRAPHICAL ABSTRACT



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ABSTRACT

Actinium-225 is a highly radiotoxic alpha-emitting radionuclide, which is currently in the spotlight owing to its promising radiotherapeutic applications in nuclear medicine. Personnel involved in the production and handling of actinium-225 is exposed to a risk of accidental incorporation of this radionuclide. Radiological protection regulations require regular monitoring of incorporation and internal dosimetry assessment for workers manipulating open radioactive sources. Urine is often used as a biological sample for measuring the incorporation of actinides, however it requires a radiochemical separation with a certified metrological tracer to enable quantitative determination. There is no stable, nor sufficiently long-lived radioactive isotopes of actinium to provide a metrological yield tracer. In this article, we propose an application of an ion-imprinted polymer resin to extract actinium-225 from urine employing americium-243 as a radioactive tracer. The radiochemical separation was followed by a quantitative determination with alpha-spectrometry. Solid-phase extraction of both actinides from urine using ion-imprinted polymer resin resulted in good radiochemical yields: 57.7 ± 16.5% (n = 17) for actinium-225 and 62.8 ± 18.0% (n = 17) for americium-243. Equivalent recoveries showed that americium-243 is a suitable yield tracer for the determination of actinium-225 with an ion-imprinted polymer resin. Combined with a different measurement technique, this method can be applied for the separation of other isotopes of actinium, such as actinium-227.

* Corresponding author. Institute of Radiation Physics, Lausanne University Hospital and University of Lausanne, Rue du Grand-Pré 1, CH-1007 Lausanne, Switzerland.
E-mail address: ruslan.cusnir@chuv.ch (R. Cusnir).

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1. Introduction

^{225}Ac (actinium-225, $t_{1/2}$ = 9.9 days) is an artificial alpha-emitting radionuclide that has recently emerged as a promising agent for the targeted alpha therapy in nuclear medicine [1–3]. The decay chain of ^{225}Ac gives rise to a series of short-lived radionuclides, which rapidly reach secular equilibrium: alpha-emitting ^{221}Fr (francium-221, $t_{1/2}$ = 4.9 min), followed by alpha-emitting ^{217}At (astatine-217, $t_{1/2}$ = 32.3 ms), and beta-emitting ^{213}Bi (bismuth-213, $t_{1/2}$ = 45.6 min) which decays into ^{213}Po (polonium-213, $t_{1/2}$ = 4.3 μs), another alpha-emitter. Thus, each decay of ^{225}Ac results in 4 highly energetic alpha particles [4]. A small amount of ^{225}Ac is likely to deliver a large radiation dose in case of an internal exposure following an incorporation event [5,6]. The radiological protection regulations in Switzerland require regular monitoring of internal doses of workers with occupational exposure to open radioactive sources [7,8]. In addition, an accidental exposure event involving a potential incorporation of ^{225}Ac will require investigations in order to estimate the dose received by an individual. A whole-body counter could prove useful to estimate the internal exposure to radiation by detecting gamma-rays of ^{221}Fr (12% at 218 keV) and ^{213}Bi (26% at 440 keV) emitted from the body, however a very inhomogeneous distribution of ^{225}Ac in the body together with a high detection limit make such measurements rather challenging [9]. Bioassay samples such as urine are widely used to determine contamination by radionuclides, namely by actinides [10,11]. Urine is a suitable biological sample to work with. However, owing to a high content of mineral salts and organic products of nitrogen metabolism, the chemical separation of ^{225}Ac prior to measurement is indispensable.

A committed effective dose E_{50} of 1 mSv is attained upon inhaling 154 Bq of ^{225}Ac, or upon ingesting 42 kBq of ^{225}Ac. The methodology for calculating these thresholds according to the Swiss Radiological Protection Ordinance is described in the Supplementary Information (SI). According to the ICRP biokinetic model for actinium, a major fraction of ^{225}Ac 24 h after an intake by ingestion or inhalation is found in the alimentary tract (≥50%), while urinary excretion is in the order of 0.1% and below [6]. The activity of ^{225}Ac sufficient to deliver 1 mSv committed effective dose is so low, that the urinary excretion results in concentrations in the order of mBq that have to be measured in a bioassay – not a trivial task for a chemist. For instance, 154 mBq of ^{225}Ac is equivalent to a specific mass of 7.17×10^{-17} g.

Radiometric techniques such as alpha spectrometry make possible the measurement of actinides at mBq levels. To enable accurate and quantitative determination of ^{225}Ac in urine with alpha spectrometry, an internal standard, also called a radiochemical yield tracer is needed in order to monitor the recovery during chemical separation steps. To the best of our knowledge, there is no alpha-emitting metrological tracer of Ac available because all of its alpha-emitting isotopes are short-lived. Current production methods for ^{225}Ac in accelerators involve the formation of 0.1–0.3% of the beta-emitting ^{227}Ac (actinium-227, $t_{1/2}$ = 21.8 years) impurity, which is even more restrictive in terms of radiation protection owing to its long half-life and high radiotoxicity [4,12,13]. A committed effective dose E_{50} of 1 mSv is attained upon inhaling 1.6 Bq of ^{227}Ac, or upon ingesting 910 Bq of ^{227}Ac, which follows the same biokinetic behaviour as ^{225}Ac [6]. Low-energy beta emissions (at 45 keV and 35.7 keV) challenge the direct determination of ^{227}Ac in bioassays, however its decay chain includes alpha emitters such as ^{227}Th (thorium-227, $t_{1/2}$ = 18.7 days) which may prove useful for alpha spectrometry measurements once in secular equilibrium.

The alpha-emitting radionuclide ^{243}Am (americium-243, $t_{1/2}$ = 7360 years) is a standardised metrological tracer used for the determination of americium isotopes in biological and environmental samples [14]. Solid-phase extraction (SPE) with ion-exchange resins is routinely used by radioanalytical chemists in the analysis of actinides by optimising the conditions of chemical separation [15]. Such steps as pre-conditioning the resin and adjusting the chemical composition of the analysed sample prior to extraction, as well as refining the composition of the eluent used to purify or release radionuclides enable to select optimal conditions for the extraction of a targeted radionuclide. Applications of ^{243}Am tracer for the determination of Cm (curium) isotopes are described in the literature, however slight differences in the chemical behaviour of Am^{3+} and Cm^{3+} require caution while carrying out chemical separations [16,17]. Being actinides with matching chemical properties, [^{243}Am]Am^{3+} and [^{225}Ac]Ac^{3+} may prove sufficiently similar to be extracted simultaneously for alpha spectrometry measurements. Ion-imprinted polymer (IIP) resin is a particular case of ion-exchange resin that consists of an organic co-polymer and a metal-binding ligand bearing a vinyl functional group [18,19]. Synthesis of IIP involves a step where the metal-binding organic ligand is arranged in the solution around the metal ion template occupying its coordination sphere, thus forming a complex. Once the polymerisation of the organic monomers is complete, the resulting co-polymer contains metal complexes, which are covalently bound within the polymer structure. Releasing metal ions with a strong mineral acid provides a polymer resin with structurally defined vacant cavities, available to selectively bind that metal again. An IIP resin synthesised by imprinting with Y^{3+} ion has been successfully used in our laboratory for determining radioactive ^{90}Sr(^{90}Y) in environmental and biological samples for a number of years, and it has been reported to effectively bind 3+ lanthanides [20–22]. This polymer has also been successfully used in the resin binding phase of DGT sampling devices for the measurement of bioavailable ^{241}Am in fresh and seawaters [23].

This study aimed at developing a solid-phase extraction method for determining ultra-trace ^{225}Ac in urine for internal dosimetry and incorporation measurements using ^{243}Am as a yield tracer. We tested the suitability of a synthetic polymer resin imprinted with Y^{3+} ion for the extraction of ^{225}Ac in the presence of ^{243}Am to enable quantitative determination with alpha spectrometry, providing a metrological traceability of the analytical results. A special focus was placed on ensuring equivalent radiochemical recoveries of ^{225}Ac and ^{243}Am. Finally, the developed method was applied to real urine samples spiked with ^{225}Ac to test the contamination measurement in case of a potential exposure of the personnel.

2. Materials and methods

2.1. Reagents and materials

All reagents used were of analytical grade from Merck, Sigma-Aldrich and Fluka (Switzerland). Deionised water (<0.05 μS) was produced using UltraPure system (Evoqua Technologies). ^{229}Th(^{225}Ac) and ^{243}Am tracer solutions were obtained from the Metrology Group of the Institute of Radiation Physics with traceability to the Isotope Products Laboratories, Burbank, USA (^{243}Am, cat. no. 7243-1U, source no. 499-50) or AEA Technology Nuclear Science, Harwell, UK (^{229}Th, batch n_ 90/229/13, TPP10030). Y-imprinted polymer resin was synthesised as described by Froidevaux et al. [22].

2.2. Instruments

Alpha spectrometry counting was carried out on PIPS detector (450 mm^2) in an Alpha Analyst spectrometer with Apex Alpha

software (Canberra, France). Energy calibration of PIPS detectors was carried out using a multi-alpha source containing ^{242}Pu, ^{243}Am, and ^{244}Cm.

2.3. Solid-phase extraction of ^{225}Ac and ^{243}Am

To test the suitability of Y-imprinted resin to quantitatively extract ^{225}Ac and ^{243}Am, tracer experiments were first carried out using a small column. A column (ø = 9 mm, length = 33 mm) was loaded with 300 mg of Y-imprinted resin in a slurry of $H_2O(H^+)$ at pH 3 containing 10% of ethanol to improve wetting. The column of approximately 1 mL bed volume was conditioned with 10 mL of $H_2O(H^+)$ at pH 3. Next, 1 mL of ^{243}Am tracer (25.0 ± 0.6 mBq mL^{-1} in 1 M HCl) and 1 mL of ^{229}Th tracer (49.2 ± 1.2 mBq mL^{-1} in 2 M HNO_3, providing ^{225}Ac in equilibrium as an *in situ* generator) diluted with H_2O to 10 mL and the pH was adjusted at 3 by titrating with NaOH. The sample was then loaded on column at 1 mL min^{-1} flow rate, followed by a wash with 10 mL of $H_2O(H^+)$ at pH 3. To obtain the elution profile of ^{225}Ac and ^{243}Am as a function of pH in an additional experiment, the column was washed with 10 mL of $H_2O(H^+)$ at pH 2. To elute ^{225}Ac and ^{243}Am, the column was washed with 10 mL of 1 M HCl. The column was regenerated by washing with 10 mL of 0.1 M oxalic acid adjusted at pH 4 by addition of NaOH, followed by 30 mL of $H_2O(H^+)$ at pH 3. Oxalate wash enables the removal of any residual cations assuring no interference from previous experiments.

After the preliminary experiments, larger columns of Y-imprinted resin were prepared to test the equivalence of ^{225}Ac and ^{243}Am extraction. Three columns (ø = 13 mm, length = 68 mm) containing 2 g of resin in 5 mL bed volume were used in parallel, and the experiment was reproduced twice.

To demonstrate that extraction of ^{225}Ac and ^{243}Am on Y-imprinted resin was determined by the effect of ion imprinting with Y^{3+}, a batch of polymer resin was synthesised according to the same protocol, but without the addition of Y^{3+} [22]. Identical tracer experiments as above with ^{243}Am and ^{229}Th(^{225}Ac) were carried out on a small column containing 300 mg of this resin providing 1 mL bed volume.

Direct electrodeposition was carried out with 9.8 mBq of ^{229}Th(^{225}Ac) and 25 mBq of ^{243}Am tracers in triplicate (n = 3 technical replicates) in three separate experiments (n = 3 experimental replicates) to determine the yield of electrodeposition of ^{225}Ac and ^{243}Am tracers.

2.4. Urine sample preparation

Pre-concentration of actinides in urine was tested by co-precipitation with calcium phosphates or with calcium oxalates. 500 mL urine was used for each single analysis, and each experiment was carried out in triplicate. Each urine sample was acidified by addition of 10% of concentrated HNO_3. Urine was spiked with 49.2 ± 1.2 mBq of ^{229}Th(^{225}Ac), providing ^{225}Ac in secular equilibrium, and 25.0 ± 0.6 mBq of ^{243}Am as the yield tracer. Samples covered with a watch glass were heated at near boiling for 2–3 h upon stirring to break down organic molecules. Once urine was clarified, heating was stopped and 100 mg of Ca^{2+} was added. To precipitate calcium oxalate, 3 g of oxalic acid dihydrate was added and the pH adjusted between 1.5 and 2 by addition of 32% NaOH solution. To precipitate calcium phosphate, 2 mL of concentrated H_3PO_4 was added, and pH adjusted between 8 and 9 by addition of 32% NaOH solution. The precipitate was left to develop in coarse grains for 30 min at 70 °C upon stirring, then let to settle by gravity overnight. After decantation, the precipitates were transferred to Teflon® vessels and centrifuged at 3000 rpm. Next, the precipitates were solubilised with 5 mL concentrated HNO_3 in the presence of 1 mL of 30% H_2O_2 and submitted to microwave-assisted digestion under pressure at 180 °C for 20 min (MLS Ultraclave IV). Cleared solutions were transferred to glass beakers and diluted with H_2O to 100 mL. The pH of the samples was adjusted to 3 by titrating with NaOH solution, and the final sample volume was adjusted to 120 mL by addition of acidified $H_2O(H^+)$ at pH 3.

To test advanced oxidation of the organic matter in some experiments, 20 mg of Mohr's salt $(HN_4)_2Fe(SO_4)_2 \cdot 6H_2O$ and 20 mL of 30% H_2O_2 was added to urine twice at 1 h interval to initiate the Fenton reaction. When the Fenton reaction was employed to oxidise the organic matter, 100 mg of ascorbic acid was added to the samples after microwave digestion prior to adjusting to pH 3 in order to reduce Fe (III) to Fe (II).

2.5. Solid-phase extraction of ^{225}Ac and ^{243}Am from urine

Columns for solid-phase extraction of [^{225}Ac]Ac^{3+} were prepared by loading a slurry of Y-imprinted polymer resin in H_2O containing 10% of ethanol to improve wetting. Each column (ø = 13 mm, length = 68 mm) contained 2 g of Y-imprinted resin providing approximately 5 mL bed volume. Columns were pre-conditioned with 60 mL of $H_2O(H^+)$ at pH 3. The sample solutions at pH 3 were loaded on columns at 1 mL min^{-1} flow rate. The columns were washed with 60–90 mL of $H_2O(H^+)$ at pH 3, followed by elution with 30–60 mL of 1 M HCl. Regeneration of columns was carried out by washing with 30 mL of 0.1 M oxalic acid adjusted to pH 4 by addition of NaOH, followed by 60 mL of $H_2O(H^+)$ at pH 3. In one experiment employing Fenton reaction for urine pre-treatment, the columns were washed with 60 mL of 10 mM ascorbic acid at pH 3 to test iron removal prior to eluting the actinides.

2.6. Electrodeposition and determination of actinides

The fractions from columns loading, washing and elution were evaporated to dryness. Electrodeposition of the actinides was carried out with sulphate buffer, according to Bajo et al. [24]. Briefly, 0.6 mL of 1 M $NaHSO_4$ and 0.4 mL of concentrated H_2SO_4 was added to each sample and evaporated to dryness, gradually increasing the temperature on hot plate. Once the evolution of white fumes had ceased, the temperature of the hot plate was ramped up to the maximum (~300 °C) and the samples were calcined to dryness, resulting in a white residue. After cooling down, the residue was dissolved in 4.2 mL H_2O and transferred to electrodeposition cell equipped with a platinum wire anode and a stainless-steel disc cathode. Beakers were rinsed with 5.2 mL of 1 M Na_2SO_4 that was added to the cell. Finally, 0.6 mL of 1 M $NaHSO_4$ was added directly to the cell, resulting in a pH close to 1.9. Electrodeposition was carried out for 1 h 15 min at constant current of 1.2 A, resulting in approximately 10 V. 1 min before the end of electrodeposition, 1 mL of 32% NH_4OH was added to the cell to avoid re-dissolution of the actinides once the current is interrupted. Stainless steel discs were removed, carefully rinsed with 1% NH_4OH, H_2O, and ethanol, and then annealed on a hot plate. Samples were measured by alpha spectrometry.

To calculate the activity of ^{225}Ac, counts from ^{217}At were used because ^{217}At peak is free from isotopic interferences and ^{217}At activity is at secular equilibrium with ^{225}Ac activity. The activity of ^{225}Ac was decay corrected for the time of counting and for the time elapsed from the moment of radiochemical separation. Samples (n = 3) for alpha spectrometry from one experiment with urine were first counted shortly after radiochemical separation of ^{225}Ac and ^{243}Am and stored for 100 days (10 half-lives of ^{225}Ac) to allow for ^{225}Ac decay. After 100 days, these samples were recounted to demonstrate the decay of ^{225}Ac and its progenies in the absence of precursors (*e.g.* ^{229}Th).

3. Results and discussion

3.1. Electrodeposition of ^{225}Ac and ^{243}Am

Electrodeposition of actinides for alpha spectrometry is often carried out in a sulphate buffer [24]. The reduction potential for Ac^{3+} is −2.21 V, and is −2.07 V for Am^{3+} vs standard hydrogen electrode [25]. To verify that the analyte ^{225}Ac and the tracer ^{243}Am were electrodeposited identically, we carried out direct electrodeposition of 9.8 mBq of ^{225}Ac with 25 mBq of ^{243}Am for 1 h (n = 6) or 1.5 h (n = 3). Average yield of electrodeposition (n = 9) was 100.6 ± 1.8% for ^{225}Ac and 95.4 ± 3.0% for ^{243}Am (Table 1) with no difference for the duration of electrodeposition. These values are compatible with the 2% uncertainties ($k = 2$) determined on the initial tracer activities. Direct electrodeposition of ^{225}Ac and ^{243}Am in sulphate buffer showed that no fractionation occurred and that both actinides were electrodeposited quantitatively.

3.2. Tracer experiments

The results displayed in Fig. 1-A show that ^{225}Ac and ^{243}Am were both quantitatively extracted at pH 3 with Y-imprinted resin, providing equivalent recoveries: 84.5 ± 6.5% for ^{225}Ac and 81.6 ± 6.2% for ^{243}Am. Although ^{225}Ac and ^{243}Am are both actinide elements in +III oxidation state, their chemical properties slightly differ, challenging the application of ^{243}Am as a proxy yield tracer for ^{225}Ac. Ionic radius of Ac^{3+} with coordination number VI is 1.12 Å, slightly larger than the 0.98 Å value of Am^{3+} with the same coordination number. The resin used for the solid-phase extraction was imprinted with Y^{3+}, which has an ionic radius of 1.02 Å at a coordination number of VIII, making it a closer match for Am^{3+} than for Ac^{3+}. Experiments carried out in identical conditions using the inert resin (Fig. 1-B) showed that only ^{243}Am was nearly quantitatively (80.9 ± 10.9%, n = 4) extracted at pH 3, while ^{225}Ac quantitatively passed through the column from the feed solution at pH 3. These results demonstrate that imprinting with Y^{3+} cation during the resin synthesis is essential for the structural arrangement of dipicolinic ligands that bind Ac^{3+} and Am^{3+} in a coordinating environment of a predefined size and structure. Although stable macrocyclic complexes of Ac^{3+} containing picolinic ligands are known, it is likely that in the absence of ion imprinting, the polymer formed without a predefined structure cannot accommodate Ac^{3+} - the largest cation in the periodic table [26–28]. Smaller ionic radius of Am^{3+} enabled its binding to dipicolinic ligands incorporated randomly within the inert resin [29].

The optimal extraction capacity of Y-imprinted resin towards 3+ cations is achieved in the pH range of 2–3 [20–22]. The elution profile of ^{225}Ac and ^{243}Am as a function of pH (Fig. 2) showed that both ^{225}Ac and ^{243}Am were effectively extracted on a 1 mL column at pH 3, however they behaved differently at pH 2. A large fraction of ^{225}Ac (72.8 ± 11.4%, n = 2) was lost from the column upon washing at pH 2, while the loss of ^{243}Am at the same pH was only 0.7 ± 0.2% (n = 2). These results show that pH is an important parameter defining the coordination of ^{225}Ac and ^{243}Am by dipicolinic ligands. Therefore, to ensure quantitative extraction of ^{225}Ac in the presence of ^{243}Am with Y-imprinted resin, the pH of the feed solution must be maintained at 3 ± 0.1. We did not investigate the effect of higher pH, however it is reasonable to assume that at higher pH such processes as hydrolysis and precipitation of ^{225}Ac and ^{243}Am would complicate the extraction even further. Therefore, all further samples in our experiments with ^{225}Ac and ^{243}Am were adjusted to pH between pH 3 and 3.1 prior to solid-phase extraction.

Experiments on larger columns with 2 g of Y-imprinted resin providing 5 mL bed volume at pH 3 showed reproducible and equivalent extraction of ^{225}Ac and ^{243}Am with good recovery yields in the range 60–70% (Table 2). Overall recovery for ^{225}Ac was 68.4 ± 15.5% (n = 6) and 72.7 ± 15.2% (n = 6) for ^{243}Am. Discrepancies observed between different experimental replicates were attributed to uncertainties of B-type, for instance the stacking of the column or the presence of very fine particles of resin in the elution solution, which might prevent quantitative electrodeposition. Nevertheless, these experiments enabled us to consider Y-imprinted resin suitable for further studies with real urine samples.

Table 1
Yield of electrodeposition of ^{225}Ac and ^{243}Am. Uncertainty for each measurement was calculated by a quadratic summation of relative uncertainties on sample volume, tracer activity, and number of counts determined with alpha spectrometry. SD is one standard deviation.

Yield, %	^{225}Ac	^{243}Am
[a]I	99.9 ± 7.1	99.4 ± 5.1
	101.3 ± 7.2	95.2 ± 4.9
	101.0 ± 7.2	98.1 ± 5.0
[a]II	102.6 ± 7.3	94.4 ± 4.9
	99.8 ± 7.1	95.6 ± 4.9
	96.7 ± 7.0	89.8 ± 4.7
[b]III	101.4 ± 6.7	98.4 ± 4.4
	102.6 ± 6.8	94.1 ± 4.2
	100.3 ± 6.7	93.6 ± 4.2
Mean ± SD (n = 9)	100.6 ± 1.8	95.4 ± 3.0

[a] Electrodeposition carried out for 1 h.
[b] Electrodeposition carried out for 1.5 h.

3.3. Urine sample treatment

Pre-concentration of trace actinides for analytical purposes is often carried out by co-precipitation with alkaline earth phosphates or oxalates [30]. Co-precipitation with calcium phosphates takes advantage of calcium and phosphate present naturally in the analysed urine matrix. However, in our lab, addition of 50–100 mg of Ca^{2+} per sample to ensure thorough and quantitative transfer of precipitate is common practice. Precipitation of calcium phosphates occurs in neutral and basic medium at pH 7–8. In these conditions, actinides are trapped within the matrix of calcium phosphates precipitate. However, the solubility of calcium phosphate is significantly lower ($K_{sp} = 10^{-33}$) than the solubility of calcium oxalate ($K_{sp} = 10^{-8}$). This may become an issue during the later step of solid phase extraction on Y-imprinted columns carried out at pH 3. The pre-concentration of ^{225}Ac and ^{243}Am in urine with calcium phosphate yielded varied and irreproducible results in our experiments and was abandoned in favour of oxalate precipitation. Calcium oxalate precipitates already at pH 1 to 2, co-precipitating quantitatively ^{225}Ac and ^{243}Am [31]. Other common metal ions, namely Fe^{3+}, which occur naturally in urine matrix, do not precipitate with oxalates in these conditions. Fe^{3+} is also extracted by Y-imprinted resin and it is essential to avoid Fe^{3+} interference for quantitative extraction of ^{225}Ac and ^{243}Am [20]. Furthermore, microwave-assisted digestion ashed quantitatively the oxalate precipitate to CO_2, resulting in clear acidic solutions containing Ca^{2+} and the actinides, which after dilution and adjustment of pH are ready for the SPE.

Urine is a convenient biological specimen widely used for monitoring the incorporation of radionuclides owing to the ease of sampling and laboratory processing. However, urinary excretion rate of ^{225}Ac is rather low – in the range of 10^{-3}-10^{-4} for a 24 h sample, in function of the incorporation mode and chemical form of ^{225}Ac. In addition, urine samples require a complex work-up and pre-concentration prior to radioanalytical measurements [32]. Organic nitrogen in the form of urea and creatinine is the main concern for sample preparation, as the urea is known to complex some trace metals [33,34]. Acid digestion of urine prior to pre-

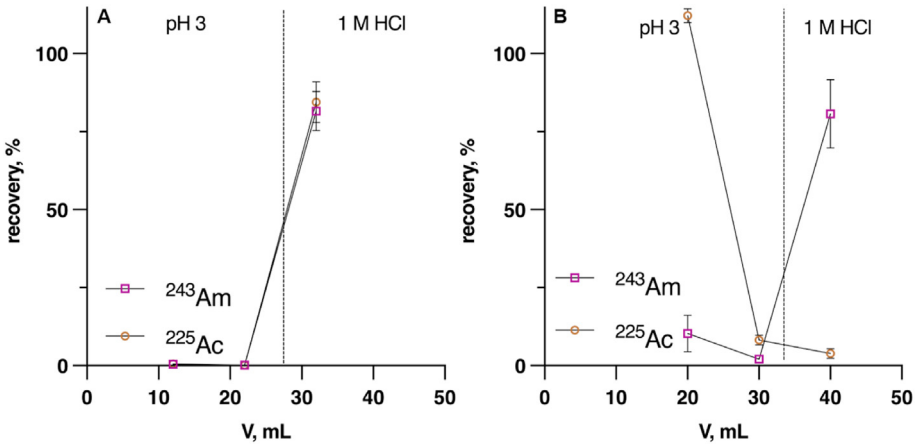

Fig. 1. (A and B). Extraction of ^{225}Ac and ^{243}Am with Y-imprinted (A) and inert (B) resin. ^{229}Th(^{225}Ac) at pH 3 loaded on a column of Y-imprinted resin (n = 1) and on a column of inert resin (n = 4) and washed with $H_2O(H^+)$ at pH 3. Uncertainty for each measurement was calculated by a quadratic summation of relative uncertainties on sample weight, tracer activity, and number of counts determined with alpha spectrometry.

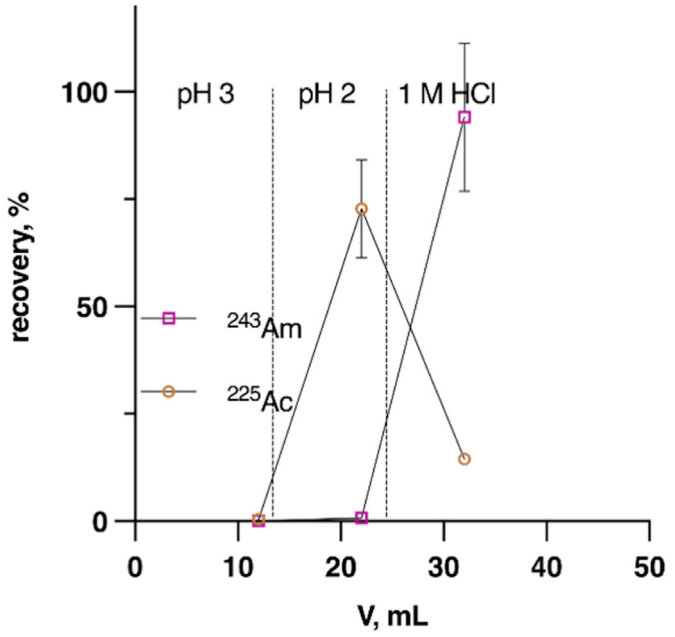

Fig. 2. Elution profile of ^{225}Ac and ^{243}Am on Y-imprinted resin. ^{229}Th(^{225}Ac) at pH 3 loaded on a column of Y-imprinted resin (n = 2), and washed consecutively with $H_2O(H^+)$ at pH 3 and at pH 2. Uncertainty was calculated for each measurement by a quadratic summation of relative uncertainties on sample weight, tracer activity, and number of counts determined with alpha spectrometry.

Table 2
Radiochemical yield of ^{243}Am and ^{225}Ac extracted with Y-imprinted resin. Uncertainty for each measurement was calculated by a quadratic summation of relative uncertainties on sample weight, tracer activity, and number of counts determined with alpha spectrometry. SD is one standard deviation.

Recovery, %	I	II	III	Mean ± SD (n = 3)
^{243}Am	47.9 ± 4.8	66.2 ± 4.3	99.5 ± 3.8	71.2 ± 26.2
^{225}Ac	40.8 ± 4.8	58.2 ± 4.3	87.2 ± 3.8	62.1 ± 23.4
^{243}Am	76.6 ± 3.8	73.4 ± 3.8	72.7 ± 3.8	74.2 ± 6.8
^{225}Ac	80.7 ± 3.1	76.2 ± 3.2	67.3 ± 3.2	74.2 ± 2.1

concentration of actinides is usually sufficient to break down the bulk of organic components. In addition to the acid digestion of

Table 3
Radiochemical yield of ^{243}Am and ^{225}Ac extracted from urine with Y-imprinted resin. Uncertainty was calculated for each measurement by a quadratic summation of relative uncertainties on sample weight, tracer activity, and number of counts determined with alpha spectrometry. SD is one standard deviation.

Recovery, %	I	II	III	Mean ± SD (n = 3)
^{243}Am	44.5 ± 1.7	67.5 ± 2.3	70.6 ± 2.4	60.9 ± 14.3
^{225}Ac	53.0 ± 2.0	68.6 ± 2.4	66.6 ± 2.3	62.7 ± 8.5
^{243}Am	*7.2 ± 0.6*	45.91 ± 1.92	55.69 ± 2.16	36.3 ± 25.6
^{225}Ac	*7.2 ± 0.6*	43.04 ± 1.81	53.39 ± 2.08	34.5 ± 24.3
^{243}Am	60.4 ± 2.4	62.9 ± 2.5	29.5 ± 1.3	50.9 ± 18.6
^{225}Ac	53.8 ± 2.2	58.1 ± 2.3	26.7 ± 1.2	46.2 ± 17.0
^{243}Am	44.8 ± 2.2	47.2 ± 2.4	78.1 ± 3.4	56.7 ± 18.6
^{225}Ac	39.9 ± 2.0	38.7 ± 1.9	57.7 ± 2.5	45.4 ± 10.6
^{243}Am	75.5 ± 2.6	83.5 ± 2.8	84.2 ± 2.8	81.1 ± 4.9
^{225}Ac	71.5 ± 2.5	73.0 ± 2.5	73.7 ± 2.5	72.7 ± 1.1
^{243}Am	80.8 ± 3.2	91.28 ± 3.50	45.36 ± 2.16	72.5 ± 24.1
^{225}Ac	78.4 ± 3.1	86.02 ± 3.34	38.63 ± 1.85	67.7 ± 25.5

urine, in this work we used microwave-assisted digestion of precipitate in concentrated HNO_3 in the presence of H_2O_2 which enabled further advanced decomposition of any remaining organic molecules [35]. Microwave-assisted digestion provided clear acidic solutions, which were ready for solid-phase extraction of ^{225}Ac and ^{243}Am after dilution and adjustment of pH.

The Fenton reaction enabled apparent rapid oxidation of the organic matter present in urine. After 2 h of reaction time, the urine samples appeared completely clear and colourless. However, the presence of Fe^{3+} is undesired because Y-imprinted resin also effectively binds Fe^{3+}. Addition of 100–150 mg of ascorbic acid per sample prior to SPE to reduce Fe^{3+} to Fe^{2+} was likely not sufficient to eliminate this interference because the experiments yielded scattered and irreproducible recoveries for both ^{225}Ac and ^{243}Am. Therefore, the Fenton reaction was deemed not suitable for the sample preparation for the SPE with Y-imprinted resin.

3.4. Solid-phase extraction of ^{225}Ac and ^{243}Am from urine

To enable quantitative determination of ^{225}Ac in urine of people potentially contaminated or continuously exposed to this

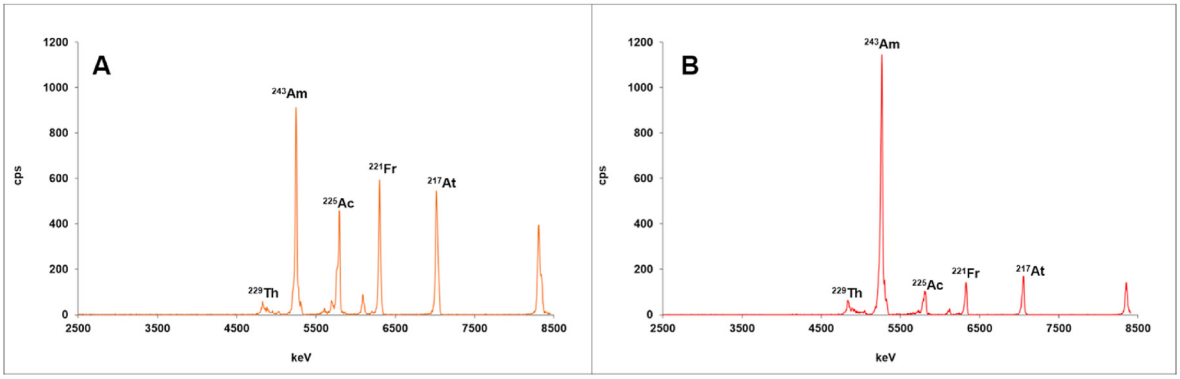

Fig. 3. (A and B). Alpha spectrum of ^{225}Ac and ^{243}Am extracted from urine with Y-imprinted resin. Spectrum A obtained by counting the sample shortly after radiochemical separation, spectrum B obtained by repeated counting of the same sample after 100 days to allow for ^{225}Ac decay.

radionuclide, a certified metrological tracer is required to monitor the chemical recovery of the analyte [36]. All isotopes of Ac are radioactive and short-lived, with exception of ^{227}Ac that has a half-life of 21.8 years. To the best of our knowledge, there is no certified Ac tracer available for radioanalytical separation of ^{225}Ac. In this study we proposed to use ^{243}Am, an actinide with reasonably similar chemical properties, as a proxy yield tracer for the determination of ^{225}Ac. The results in Table 3 showed that the extraction of ^{225}Ac and ^{243}Am from urine using Y-imprinted resin was reproducible with a satisfactory overall yield above 60%. Recoveries of ^{225}Ac and ^{243}Am were equivalent within the uncertainty of the measurement, demonstrating that ^{243}Am can be used as a yield tracer for the determination of ^{225}Ac using Y-imprinted resin. One may notice the variation of radiochemical yield between different experimental replicates, *e.g.* 7.2 ± 0.6% for ^{225}Ac and 7.2 ± 0.6% for ^{243}Am in one experiment against 78.4 ± 3.1 for ^{225}Ac and 80.8 ± 3.2 for ^{243}Am in a different experiment. This variability was attributed to the uncertainty of type B related to the manipulation of the sample and to the inability to control some steps, such as the electrodeposition of the final sample highly sensitive to adventitious contaminations with common metals (*e.g.* Fe^{3+}).

A representative alpha spectrum of a urine sample shown in Fig. 3 (A and B) substantiates our assumption that ^{225}Ac was extracted with Y-imprinted resin in the presence of ^{243}Am. Fig. 3, A shows ^{243}Am tracer peak, and ^{225}Ac peak in equilibrium with its decay products – ^{221}Fr and ^{217}At – measured shortly after radiochemical separation. After the electrodeposited ^{225}Ac was allowed to decay for 10 half-lives (Fig. 3, B), only ^{243}Am tracer peak remained unchanged owing to its long half-life. Small residual peaks of ^{225}Ac and its decay products ^{221}Fr and ^{217}At were attributed to the equilibrium with residual ^{229}Th, which was used in our experiments as an *in-situ* generator of ^{225}Ac. Small fraction of approximately 5% of ^{229}Th impurity systematically broke through the Y-imprinted resin in our experiments.

4. Conclusion

In this study, we developed a new method for radiochemical separation of ^{225}Ac in urine for incorporation measurements and internal dosimetry using ^{243}Am as a metrological tracer. This was made possible by employing Y-imprinted polymer resin that earlier has demonstrated good outcomes with ^{90}Y, Am^{3+} and the lanthanides. The advantage of radiochemical separation of ^{225}Ac in urine with ^{243}Am tracer consists in very low (mBq) concentrations of ^{225}Ac that can be measured in urine with alpha spectrometry. To the best of our knowledge, this is the first method enabling incorporation measurements of ^{225}Ac in urine samples. Such incorporation measurements will allow to comply with the Swiss legal requirements in terms of internal dose monitoring and ensure that the committed effective dose E_{50} limit of 1 mSv is respected for workers that handle ^{225}Ac. The capability of Y-imprinted resin to effectively extract ^{225}Ac and ^{243}Am as demonstrated in our experiments can be applied to the study of other isotopes of actinium, *e.g.* ^{227}Ac which is used as an environmental tracer in ocean research.

CRediT authorship contribution statement

Ruslan Cusnir: Conceptualization, Methodology, experimental, Writing – original draft. **Pascal Froidevaux:** Methodology, Writing – review & editing. **Pierre Carbonez:** problem statement, Funding acquisition, Writing – review & editing. **Marietta Straub:** Funding acquisition, Writing – review & editing.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.aca.2021.339421.

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