Production and Radiochemical Separation of ^{147}Gd

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The production of ^{147}Gd ($T_{1/2} = 38.1$ h) via the ^{147}Sm(^{3}He,3n)^{147}Gd and ^{144}Sm(α,n)^{147}Gd processes was investigated. A target system was constructed which allowed irradiation of the target material Sm$_2$O$_3$ with 15 µA beams of 36 MeV ^{3}He- or 27 MeV α-particles. A separation technique involving cementation with Na-amalgam followed by an ion exchange process was developed to separate the n.c.a. gadolinium from the bulk of Sm$_2$O$_3$ target material and from the n.c.a. europium isotopes. Experimental parameters such as sodium content in the amalgam, pH of the solution, Na$^+$ concentration in the solution etc., were optimised. The final purification of ^{147}Gd was done using a small glass column (3 mm $\varnothing$ × 120 mm) or an HPLC column (8 mm $\varnothing$ × 300 mm) filled with a cation exchanger. Using 97% enriched ^{147}Sm and the separation technique described here about 370–555 MBq (10–15 mCi) ^{147}Gd of high radionuclidic and chemical purity could be achieved. This corresponded to between 40 and 50% of the theoretical batch yield calculated from the excitation function of the ^{147}Sm(^{3}He,3n)^{147}Gd process. The chemical separation procedure developed also allowed an almost quantitative (> 90%) recovery of the enriched target material for cyclic use. © 1997 Elsevier Science Ltd. All rights reserved

Introduction

Several gadolinium complexes in macroscopic amounts are used in medical research as contrast agents for Magnetic Resonance Imaging (MRI) (cf. Lauffer, 1987; Atlas and Brasch, 1993). In order to study the biodistribution of those magnetopharmaceuticals *in vivo* experiments were done on animals using ^{153}Gd ($T_{1/2} = 241.6$ d) as a radionuclidic marker. Due to its long half-life, this radioisotope, however, cannot be used in humans. To study the detailed behaviour of MRI contrast agents, it would be meaningful to combine the techniques of MRI and Single Photon Emission Tomography (SPET) by using an appropriately labelled magnetopharmaceutical. The data obtained on the uptake kinetics would allow a better estimate of the diagnostic potential of new Gd-compounds in MRI. Of all the radioisotopes of gadolinium, ^{147}Gd seems to be the most suitable for SPET imaging: it has a half-life of 38.1 h and a strong γ-ray of 229 keV (61%).

For the production of ^{147}Gd, besides the spallation process, which has direct formation cross-sections of about 3 and 10 mb in irradiations of tantalum and terbium, respectively, with 660 MeV protons

(Rupp and Fenesch, 1970), and the ^{nat}Eu(p,xn) reactions at 100 MeV (Lebedev *et al.*, 1988), we recently evaluated two other promising reactions, namely ^{147}Sm(^{3}He,3n)^{147}Gd and ^{144}Sm(α,n)^{147}Gd, on enriched samarium isotopes (Denzler *et al.*, 1995). It could be shown that the ^{147}Sm(^{3}He,3n)-route constitutes the method of choice for the production of ^{147}Gd at a compact cyclotron, in spite of an estimated α-emitting ^{148}Gd ($T_{1/2} = 75$ a) impurity of < 0.003%, as compared to the irradiation of ^{144}Sm at α-particle energies of < 28 MeV. In order to obtain ^{147}Gd batch yields sufficient for SPET studies, development of a high current target and optimation of the separation procedure were mandatory.

A special feature of the present work was the presence of macro amounts of the samarium target material from which n.c.a. amounts of gadolinium and europium had to be separated. Such separations have been performed also in the past (cf. Qaim *et al.*, 1974; Qaim, 1976, 1984; Mel'nik *et al.*, 1995; Quinby *et al.*, 1988; Lebedev *et al.*, 1988). We have now developed a method which consists of an initial fast separation by amalgam extraction followed by a purification by means of cation exchange elution on two small Dowex 50 × 8 columns or via an HPLC column filled with Aminex A7.

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Table 1. Isotopic composition of target materials used

Material	Isotopic composition (%)						
	^{144}Sm	^{147}Sm	^{148}Sm	^{149}Sm	^{150}Sm	^{152}Sm	^{154}Sm
^{144}Sm$_2$O$_3$	**86.6**	4.69	2.36	2.13	0.71	2.04	1.47
^{147}Sm$_2$O$_3$	0.10	**96.5**	2.1	0.5	0.2	0.4	0.2

Materials and Methods

Chemicals

All preliminary experiments were done using natural Sm$_2$O$_3$ as target material (Heraeus, Germany). The enriched isotopes ^{147}Sm and ^{144}Sm, commercially supplied as oxides by Chemotrade GmbH, were used as target materials in production runs. The isotopic compositions are given in Table 1. The chemical purity of the Sm$_2$O$_3$ was specified by the supplier to be > 99%. The resin Dowex 50 × 8 (200–400 mesh) was supplied by Sigma and Aminex A7 by BioRad. In the case of Dowex a sedimentation technique was used to obtain a fraction of mesh size about 400 which resulted in the necessary flow rate. α-hydroxyisobutyric acid (α-HIBA) was delivered by Fluka. All the other chemicals (NaCl, NaOAc, Hg, DTPA, NH$_4$OH) were of analytical grade and were supplied by Merck or Riedel de Haen. The HPLC separation was carried out using a high pressure pump Knauer 64 capable of providing a steady pressure of up to 400 bar and a maximum flow rate of 10 mL/min. A stainless steel column of 300 mm length and 8 mm dia was filled with about 25 g Aminex A7.

Thin layer chromatography was performed using a Merck F_{254} silica gel (SG) impregnated aluminium sheet and a solution of 10 g of NH$_4$OAc dissolved in 100 mL 50% (v/v) methanol as mobile phase. The pH of the latter was adjusted to 7 with 1 M NaOH.

Irradiations

Irradiation of ^{nat}Sm$_2$O$_3$ or enriched ^{144,147}Sm$_2$O$_3$ target was done for 4–8 h with a 15 μA beam of 36 MeV ^{3}He- or 27 MeV α-particles at the Jülich compact cyclotron CV28. The longer-lived ^{153}Gd was produced at the research reactor DIDO by activation of ^{nat}Gd$_2$O$_3$ for 10 days with thermal neutrons at a flux density of 10^{14} n cm^{-2} s^{-1}. ^{147}Eu ($T_{1/2}$ = 24.6 d, E_γ = 197 keV), ^{149}Gd ($T_{1/2}$ = 9.5 d, E_γ = 150, 298 keV), ^{153}Gd ($T_{1/2}$ = 241.6 d, E_γ = 97, 103 keV) and ^{153}Sm ($T_{1/2}$ = 46.8 h, E_γ = 104 keV) were used as radioactive markers in some experiments. They were all produced via cyclotron or reactor irradiations.

Measurement of radioactivity

The radioactivity was determined by γ-ray spectrometry using either a Ge(Li) or a HPGe detector coupled to an Ortec (Spectrum ACE) 4 K MCA plug-in card. The card was connected to an IBM-compatible PC-AT. The peak area analysis was done using GammaVision$^®$ 2.0 software. In some cases the activity was measured simply using a scintillation counter (Canberra Packard Auto Gamma Counter 5000).

Preparation of sodium amalgam

Sodium amalgam was prepared by electrolysis of a 20% solution of NaOH, with mercury as cathode and a 25 cm^2 Pt-foil as anode (10 V, 10 A, 6–8 h). It was washed with water and ethanol and stored under a layer of ethanol. The amount of sodium in the amalgam was determined by decomposition of 1 mL of the amalgam with 1 mL of 4 M HCl, followed by a titration with 0.1 M NaOH.

Preparation of target material

The target for irradiation was prepared by pressing 100–200 mg of Sm$_2$O$_3$ to a pellet at 10 tonnes/cm^2. All possible moisture was removed by sintering the pellet at 1000°C for several hours to avoid damage during the irradiation.

Cyclotron targetry

From the excitation functions of the ^{147}Sm(^{3}He,3n), and ^{144}Sm(α,n) processes reported earlier (Denzler et al., 1995) it was concluded that the maximum energies of 36 MeV ^{3}He and 27 MeV α-particles available at the compact cyclotron CV28 need to be fully utilized for production purposes. Thus, a front covering foil or a front cooling of the target material could not be tolerated. Furthermore, in order to achieve sufficient yields, a high particle flux was mandatory. Both these constraints demanded the construction of a specially cooled target system. ^{144,147}Sm were used in the form of oxides, therefore the two commonly utilized targets at Jülich, i.e. the 4π cooled (Michael et al., 1981) and the 2π cooled (Blessing et al., 1982) systems, could not be used advantageously. We modified the 2π water cooled system (cf. Figure 1). The modified target is now made of copper and guarantees a good cooling from the back and the sides of the Sm$_2$O$_3$ pellet. A ring of a Cu–Al foil (Al side facing the target) was placed in front of the pellet to give it mechanical stability. With this arrangement the target could be irradiated with ^{3}He- or α-particles at 15 μA for 8 h which resulted in
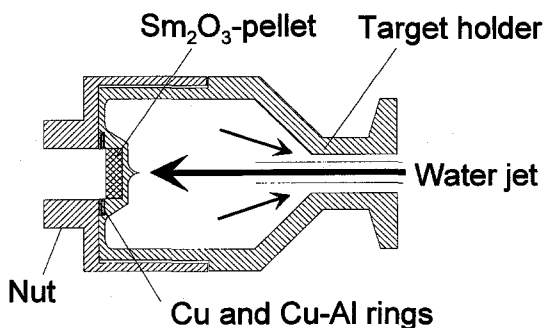

Fig. 1. Improved water cooled target system for irradiation of samarium oxide pellet which is cooled from the back as well from the sides.

a ^{147}Gd yield of about 1 or 0.5 GBq, respectively. The loss of ^{144,147}Sm$_2$O$_3$ during the irradiation was below 5%. After the irradiation the pellet could be easily removed by opening the target with a special wrench.

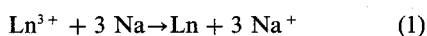### Recovery of the enriched target material

^{144,147}Sm can be recovered from the sodium amalgam by a simple extraction with 2 M HCl. In acidic medium the sodium amalgam is destroyed and the samarium is released as SmCl$_3$. Some mercury (I) chlorides, if formed, are removed by centrifugation. The samarium is then precipitated as oxalate at pH ~1 and is converted to the oxide by heating at 1000°C for several hours during which the residual mercury traces are removed. The recovery of samarium is nearly quantitative. The small amount of samarium adhering to the ion exchange column can be easily removed by elution with 0.5 M α-HIB (pH = 5). After destruction of the complex with HClO$_4$ or HNO$_3$, samarium was precipitated as oxalate. This removal is also nearly quantitative so that a total of > 90% of the ^{144,147}Sm$_2$O$_3$ target material could be recovered.
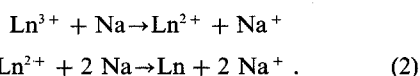
Results and Discussion

### Cementation of samarium and europium by sodium amalgam

The separation of different lanthanides with Na-amalgam was first described by Marsh (1942, 1943) and further experiments were done later by Barret et al. (1962), Novgorodov et al. (1966; Novgorodov and Khalkin, 1968), Lebedev et al. (1988) and Mel'nik et al. (1995). The method was optimised in the present work to separate n.c.a. gadolinium from n.c.a. europium and macroscopic amounts of samarium. Reductive separation of the lanthanides (Ln) with Na-amalgam could be described via the following reactions (Barret et al., 1962; Hickling and Salt, 1942; Mel'nik et al., 1995):

$$Ln^{3+} + 3\ Na \rightarrow Ln + 3\ Na^+ \qquad (1)$$

or

$$Ln^{3+} + Na \rightarrow Ln^{2+} + Na^+$$
$$Ln^{2+} + 2\ Na \rightarrow Ln + 2\ Na^+ . \qquad (2)$$

Besides these reactions, there could be a direct reaction of the sodium with hydrogen ions in the solution and a possible oxidation of the lanthanides, followed by a back extraction.

$$2\ Na + 2\ H^+ \rightarrow 2\ Na^+ + H_2\uparrow \qquad (3)$$
$$2\ Ln + 6\ H^+ \rightarrow 2\ Ln^{3+} + 3\ H_2\uparrow . \qquad (4)$$
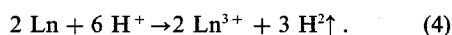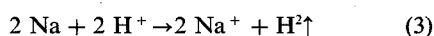
The redox potentials of the three lanthanides relative to hydrogen potential are shown in Table 2. A comparison of the polarographic (cf. Noddack and Bruhl, 1937; Puroshottam and Ragbava Rao, 1955)

Table 2. Redox potentials of Sm, Eu and Gd relative to the hydrogen potential (Ionova et al., 1990; Herman and Rairden, 1976)

Element	$E_{III\ II}$ (−V)	$E_{III\ 0}$ (−V)
Sm	1.55	2.29
Eu	0.30	2.00
Gd	2.85	2.27

and other data (cf. Pearce, 1935; Klemm and Bommer, 1937; Herman and Rairden, 1976; Ionova et al., 1990; Rizkalla, 1993) indicated the possibility of Sm and Eu forming bivalent states and thereby reacting according to Eqns (1) and (2). The transfer of the 5d electron to a 4f orbital results in the relatively stable Eu^{2+} with its f^7-configuration, and a possible Sm^{2+} with an f^6-configuration. This allows the preparation of dichlorides of these lanthanides in solution (Rossmanith, 1979; Kamenskaya et al., 1979). In the case of Gd, however, a stable bivalent state is unknown. The polarographic data also revealed that especially Eu but also Sm followed a two step reduction from + 3 to + 2 and finally to the metal. The detailed mechanism of the reductive cementation of the lanthanide with amalgam is electrochemically not very well understood. In order to achieve an effective separation, however, the main experimental parameters are the pH of the solution, the Na$^+$ concentration affecting the potential of the sodium amalgam and the reaction time.

Cementation studies were carried out in a separatory funnel equipped with an electric stirrer. The irradiated target material (for example, 100 mg Sm$_2$O$_3$) was dissolved in 20 mL concentrated HCl and evaporated to dryness. 25 mL of an aqueous sodium chloride solution and 1.36 g (0.1 M) sodium acetate (NaAc·3H$_2$O, used as buffer) were added to the SmCl$_3$ residue. Preliminary experiments with ^{153}Sm had shown that samarium and europium react under these conditions with nearly the same extraction results. The target solution, 0.1–1 mL conc. HCl and 5 mL of the sodium amalgam were then placed together in a separatory funnel and stirred for 1–10 min. Thereafter the amalgam was separated from the solution; the latter was measured γ-spectrometrically to determine the amount of extracted Eu (Sm).

Influence of pH and sodium content in the amalgam

Experiments were done with sodium contents of 0–0.5% in the amalgam. The lower Na contents were achieved by diluting the previously prepared amalgam with mercury. The percentage of sodium in each individual solution was determined by titration. The pH of the SmCl$_3$ solution was adjusted with concentrated HCl. Experiments were done as a function of pH and sodium content. Figure 2 shows the correlation between the pH and sodium content. A pH value of 2–3 (adding ~0.7 mL conc. HCl) and a sodium content of 0.4% appear to constitute the optimum conditions. At lower pH, the amalgam
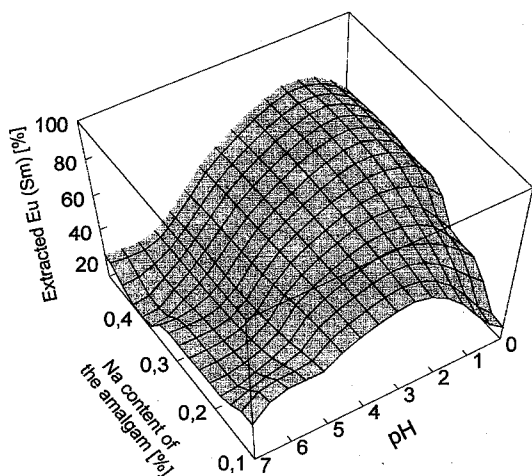
Fig. 2. Influence of pH and Na content of amalgam on extraction of n.c.a. europium from macroamounts of samarium.
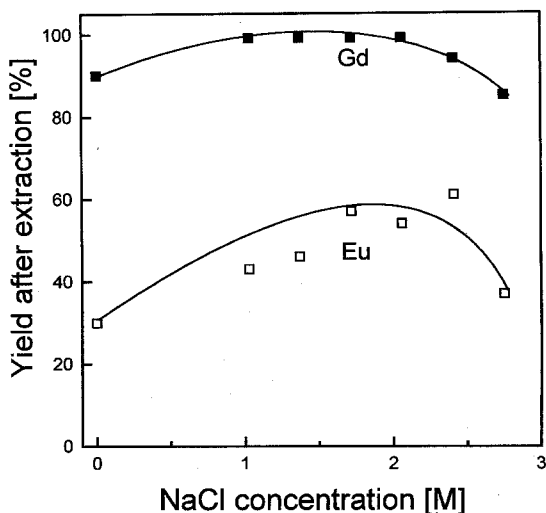

Fig. 3. Influence of NaCl concentration on n.c.a europium and gadolinium extraction into Na-amalgam (0.4% sodium in the Na-amalgam, pH 4.5, 5 min stirring). The solid lines are eye-guides

starts decomposing, therefore a higher Na content is needed. On the other hand, in a sligthly neutral medium the lanthanides begin to precipitate as hydroxides which prevents their transfer to the amalgam.

Influence of NaCl concentration

From the Nernst equation it is understood that an increasing Na^+ concentration would lead to a decreasing electrochemical potential of the sodium amalgam. Novgorodov *et al.* (1966) and Novgorodov and Khalkin (1968) found a 2 M NaCl concentration to be optimum for the separation of samarium and europium from gadolinium. In the present work experiments were performed with sodium chloride concentration in the solution ranging between 0–2.7 M. For optimised parameters, i.e. for pH and sodium content in the amalgam given above, the effect observed was small. To make the general effect best visible we instead chose a pH of 4.5, which resulted in a bad Eu and Sm cementation (Fig. 3). In contrast to the earlier publications which showed this effect only for Gd (cf. Novgorodov *et al.*, 1966; Novgorodov and Khalkin, 1968) we found that a high NaCl concentration reduced the cementation of both Gd and Eu. Consequently, the optimum condition of 1–2 M NaCl decreases the extraction of Gd by less than 2%, but the Eu extraction could be optimised by varying the other conditions (pH, sodium content).

The results are in good agreement with the literature data (cf. Barret *et al.*, 1962; Marsh, 1942, 1943; Mel'nik *et al.*, 1995; Novgorodov *et al.*, 1966; Novgorodov and Khalkin, 1968) and show that the degree of cementation is inversely proportional to the redox potential $E_{Ln(III)/Ln(0)}$ but in the case of Eu and possibly Sm, directly proportional to the stability of the divalent state (Mel'nik *et al.*, 1995).

Influence of reaction time

Further experiments were done to establish the optimum time of stirring. As shown in Fig. 4 there is practically no change in the separation yield after 5 min of reaction time. This indicates that the rate determining step is the reduction of Eu (Sm) to the bivalent state, as reported also by Malan and Münzel (1966). About 5 min are necessary for this relatively slow process. It was found unnecessary to perform more than two individual separations: in repeated separations even a deterioration of the separation of gadolinium was observed.
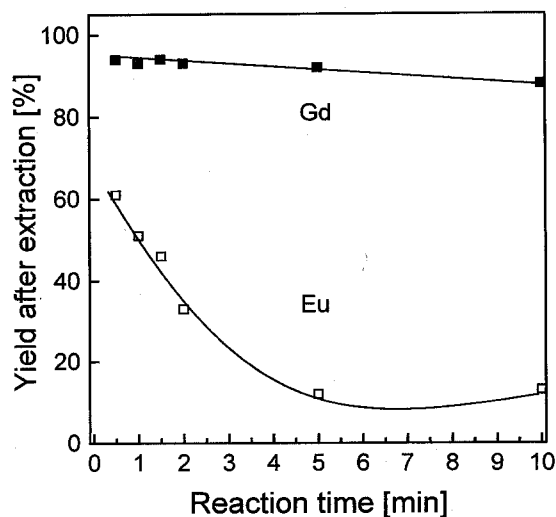

Fig. 4. Influence of reaction time on the extraction of n.c.a. Gd from n.c.a. Eu and macroscopic amounts of Sm-target material into Na-amalgam. The solid lines are eye-guides
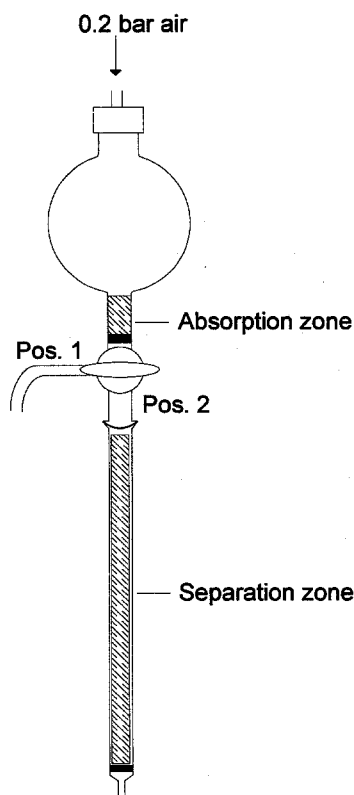
0.2 bar air

Fig. 5. Low pressure small glass column used for separation of Gd, Eu and Sm via cation exchange chromatography. Upper part: absorption zone; lower part: separation zone.

In summary, the optimum conditions for this separation technique consist of two extractions, each with a reaction time of 5 min at pH 2–3, ~1 M NaCl and a Na content of 0.4% in the amalgam. Under these conditions > 95% of europium and samarium are removed, the loss of gadolinium activity being < 10%.

Purification via cation exchange chromatography

Following the first separation from the bulk of samarium, the n.c.a. Gd and Eu were precipitated as hydroxides with the remaining samarium (1–5 mg) by addition of NH$_4$OH. After centrifugation the hydroxides were dissolved in 0.1 M HCl and centrifuged again to remove the possible mercury compounds (Hg$_x$Cl$_y$). This solution was then used for the final separation of ^{147}Gd via the the the well-known cation exchange chromatography (cf. Karol, 1973; Qaim *et al.*, 1974; Dadachowa *et al.*, 1994; Maoliang *et al.*, 1988; Choppin *et al.*, 1956). Since > 95% of the target material had been removed, the dimensions of the column were based on the remaining small amount (< 5 mg) of Sm^{3+}. A standard cation exchange system utilizing a small glass column was compared with an HPLC column method for routine use.

Separation using a small glass column

The column constructed is shown in Fig. 5. The small upper part (3 mm $\varnothing$ × 15 mm, Dowex 50 × 8, NH$_4^+$-form) constituted the absorption zone, where the lanthanides were localized at the start of the separation. The removal of non- or weakly-absorbed impurities could be done without affecting the main column (3 mm $\varnothing$ × 120 mm, Dowex 50 × 8, NH$_4^+$-form). The latter was reserved for use only during the final separation. All the separations were done at room temperature.

After closing the stopcock, the 0.1 M HCl lanthanide solution was transferred onto the top of the resin. A few minutes later the stopcock was opened to position 1 and the resin washed with a few mL of 0.1 M HCl, H$_2$O and 0.075 M α-HIB (NH$_4^+$-form, pH = 4.7). This removed all the disturbing cations (such as sodium) and possible iron impurities. Subsequently the stopcock was turned to position 2 and the elution done with 0.16 M α-HIB (NH$_4^+$-form, pH = 4.7) to separate gadolinium from europium and samarium (pressure of 0.2 bar and a flow rate of 0.1 mL/min). Fractions were collected in 0.2 mL volumes and analysed via γ-ray spectrometry.The time required for the complete separation amounted to 70 min and Gd could be collected after 30 min within a total volume of 2 mL, but with appreciable amounts of Eu (Fig. 6).

Separation using an HPLC column

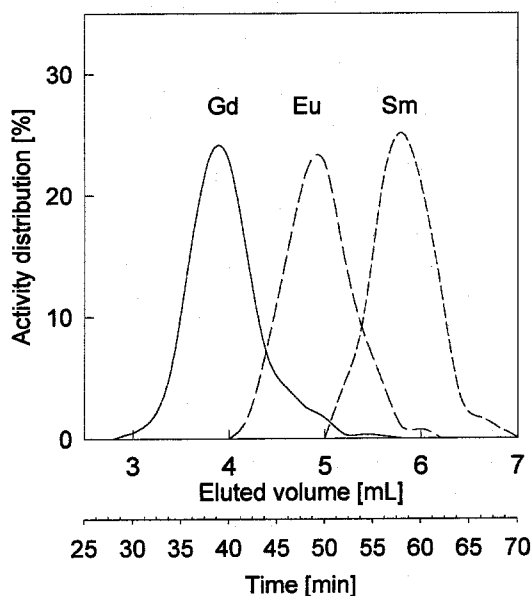For routine separation of lanthanides the use of an HPLC system is advantageous (cf. Campbell, 1973,

Fig. 6. Elution profiles of Gd, Eu and Sm in cation exchange chromatography using the glass column system (Dowex 50 × 8; elution with 0.16 M α-HIB, pH = 4.7; flow rate 0.1 mL/min).
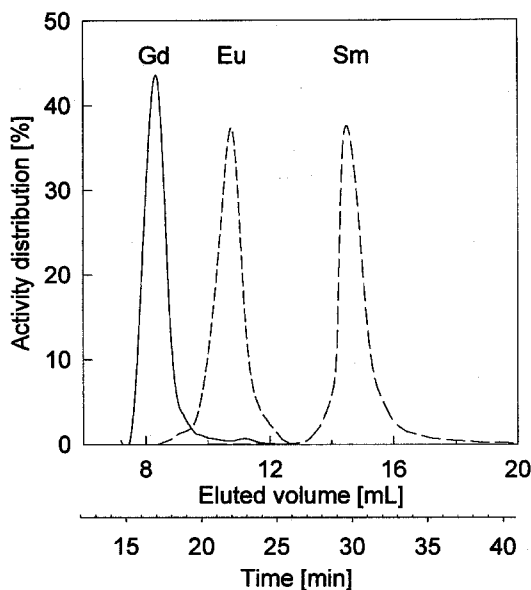
Fig. 7. Elution profiles of Gd, Eu and Sm in cation exchange chromatography obtained using the HPLC column system (8 mm $\varnothing \times 300$ mm, Aminex A7; elution with 0.25 M, α-HIB pH = 4.7; flow rate 0.5 mL/min). To detect the samarium peak, [153]Sm was added as radioactive tracer.

1976; Specht *et al.*, 1976; Qaim *et al.*, 1979; Qaim, 1976, 1984; Dadachowa *et al.*, 1994). We used a stainless steel tube column (8 mm $\varnothing \times 300$ mm) filled with AMINEX A7 cation exchange resin (cf. Schädel *et al.*, 1977; Elchuk and Cassidy, 1979). The spherical form and the small particle size of 9 ± 2 μm resulted in high column efficiencies. After washing with distilled water and diluted HCl the column was eluted at room temperature with the α-HIB until the pH of the eluate was constant. Schädel *et al.* (1977) used 0.5 M α-HIB at a pH of 3.7. We used 0.25 M α-HIB at a pH of 4.7. According to the log K_i of 3.79 for α-HIB (H$^+$ as ion) this would result in the same effective concentration of 0.22 M butyrate with the advantage of higher insusceptibility against changes in pH than using a concentration at a pH close to the pK_i of the ligand.

The 0.1 M HCl lanthanide solution was brought to a pH of 4–5 with NH$_4$OH. The volume of the solution should depend on the size of the injection loop. In our case a loop of 500 μL was large enough for a solution containing 3–5 mg Sm^{3+} carrier. The samples were loaded directly on the top of the column with a sample injecting device and elution was done immediately thereafter at a flow rate of 0.5 mL/min. The eluted samples were collected with a fraction collector in 0.4 mL portions and were analyzed via γ-ray spectrometry.

The time required for the complete separation amounted to 35 min and Gd could be collected after 15 min within a total volume of 2 mL (Fig. 7). The contamination from Eu was much smaller than in the case of a conventional glass column. The macro-

scopic samarium is eluted after Gd and Eu with some tailing of the peak. This, however, did not affect the sharp Gd elution.

Purification of [147]Gd

To remove α-HIB a fast final purification on a second small column (3 mm $\varnothing \times 120$ mm, Dowex 50×8, NH$_4^+$-form) was done. The separated Gd fraction was acidified by adding a few drops of 65% HNO$_3$ to reach the concentrations of 0.2 M HNO$_3$. It was then transferred to the resin. After washing with 1 mL 0.5 M HNO$_3$, 7 M HNO$_3$ was used as eluent to obtain a pure n.c.a. Gd fraction in about 1 mL of solution (cf. Molnar *et al.*, 1967; Molnar and Lebedev, 1969).

Substitution of the final column separation of [147]Gd with direct chelate synthesis

Since the basic aim of this work was to produce [147]Gd for the clinical evaluation of different gadolinium chelates such as Gd-DTPA (Tweedle *et al.*, 1991), the final column purification step was modified to incorporate a direct production of the chelate on the column. The gadolinium fraction obtained after the elution with α-HIB was acidified with a few drops of 65% HNO$_3$ and transferred to another cation exchange column of the same type (3 mm $\varnothing \times 120$ mm, Dowex 50×8, NH$_4^+$-form). After washing with water, elution was done with 0.05 M DTPA (Diethylentriaminepentaacetic Acid), which was buffered to pH 6.0 with NH$_4$OH (Hale and Hammer, 1972). Gd-DTPA could be eluted as the first fraction within 20 drops. The fraction was collected and checked for radiochemical purity. This was done by a thin layer chromatography method, as described by Tweedle *et al.* (1991) and Meares *et al.* (1984). 200 μL of 0.1 M phosphate buffer, pH 7, was mixed with 100 μL of the eluted Gd-DTPA for 10 min at room temperature. About 10 μL of the mixture was transferred to the ITLC-SG. The chromatogram was developed and removed when the solvent front had migrated to 10 cm. The strip was cut into 10 pieces and measured for activity. As known from a blank experiment with [153]GdCl$_3$, unchelated Gd remains at the origin as GdPO$_4$, the remaining strips contained the gadolinium complex ($R_f = 0.8$, tailing as far down as $R_f = 0.6$). In this experiment a radiochemical purity of $> 98\%$ [147]Gd-DTPA was achieved.

Conclusion

It is possible to use both the [147]Sm(^{3}He,3n) and [144]Sm(α,n) processes for the production of [147]Gd. A high current target capable of withstanding 15 μA beam currents of ^{3}He or α-particles was constructed which allowed the production of sufficient quantities of [147]Gd for medical applications (about 1 GBq using the ^{3}He induced reaction). A two step procedure was developed to separate large amounts of the target

material Sm from n.c.a. isotopes of Eu and Gd. The first step consisted of an amalgam method to separate the bulk target material from the n.c.a. Gd-isotopes. The optimum conditions for this separation were: two extractions, each with a 5 min reaction time, pH 2–3, ~1 M NaCl, Na content in amalgam of 0.4%. More than 95% of europium and samarium are removed, the loss of the gadolinium activity being < 10%.

The second step of separation entailed the well-known cation exchange technique on a small glass column or in combination with HPLC, using α-HIB (0.25 M, pH = 4.7) as an eluent. Finally, either a purification with 7 M HNO$_3$ or direct chelate synthesis with DTPA was done. Compared to the separation via the low pressure glass column, the HPLC technique gives more reproducible results with sharper peaks and better separation factors in shorter times. For single experiments, however, the standard glass column system could still be the method of choice, since under optimum conditions the quality could be nearly the same.

The radiochemical separation process developed provides radiochemically pure ^{147}Gd with an overall separation yield of 60–70% within 4–5 h, without any detectable Sm or Eu contamination. This would result in 370–555 MBq (10–15 mCi) batch yield, which, combined with the high radionuclidic purity of ^{147}Gd (for example ^{146}Gd < 3%, ^{149}Gd < 0.3% and ^{148}Gd < 0.005% for the ^{3}He induced reaction on ^{147}Sm) should allow an *in vivo* evaluation of the pharmacokinetics of Gd-magnetopharmaceuticals in patients.

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