LA-UR-14-28326 (Accepted Manuscript)

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To be published in: Radiochimica Acta ; Vol.103, p.577-585, August 2015

DOI to publisher's version: 10.1515/ract-2014-2362

Permalink to record: http://permalink.lanl.gov/object/view?what=info:lanl-repo/lareport/LA-UR-14-28326

Isolation of ^{163}Ho from Dysprosium Target Material by HPLC for Neutrino Mass Measurements

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Key Words: HPLC, ^{163}Ho, Lanthanide separation, Neutrino Mass, preparative HPLC

Abstract:

The rare earth isotope ^{163}Ho is of interest for neutrino mass measurements. This report describes the isolation of ^{163}Ho from a proton-irradiated dysprosium target and its purification. A Dy metal target was irradiated with 16 MeV energy protons for 10 hours. After target dissolution, ^{163}Ho was separated from the bulk Dy via cation-exchange high performance liquid chromatography using 70 mmol·dm^{-3} α-hydroxyisobutyric acid as the mobile phase. Subsequent purification of the collected Ho fraction was performed to remove the α-hydroxyisobutyrate chelating agent and to concentrate the Ho in a low ionic strength aqueous matrix. The final solution was characterized by MC-ICP-MS to determine the ^{163}Ho/^{165}Ho ratio, ^{163}Ho and the residual Dy content. The HPLC purification process resulted in a 99.9997% removal of Dy. The isolated Ho fraction contained 24.8±1.3 ng of ^{163}Ho corresponding to holmium recovery 72±3%.

Introduction:

Improving the precision of neutrino mass measurements is a current major challenge in modern particle and astrophysics. Electron capture spectroscopy (ECS) of the rare earth isotope ^{163}Ho, which has the lowest known Q-value, between 2.3 and 2.8 keV [1,2] of isotopes decaying via electron capture, is one method to conduct such measurement [3,4]. The low total decay energy maximizes the measurement's sensitivity to neutrino mass. Any

other radioisotope present in isolated ^{163}Ho sample, irrespective of the decay path, would have a deleterious effect on ^{163}Ho ECS spectra and must be minimized. Therefore, this experiment requires production of ^{163}Ho with extremely high radioisotopic and chemical purity at large scale, i.e., tens of nanograms to several micrograms for initial studies and likely milligrams for future experiments. Currently, there are no fully validated methods for production and isolation of ^{163}Ho at the purities and quantities required.

Engle et al. reviewed potential production methods to prepare ^{163}Ho for large-scale neutrino mass measurements, concluding that proton or neutron irradiations of dysprosium and erbium targets, respectively, can be used to produce the ^{163}Ho needed in sufficient quantity and radioisotopic purity for this application [5]. Reactor production of ^{163}Ho requires a highly enriched ^{162}Er target (abundance in natural Er is 0.139%), and while this method provides a high production rate, it suffers from the co-production of isotopic impurities, mainly ^{166m}Ho ($t_{1/2}$ = 1200 y, 100% β^-). The presence of significant amounts of ^{166m}Ho impurity in reactor-produced ^{163}Ho is expected to necessitate mass separation after holmium isolation to obtain ^{163}Ho of sufficient isotopic purity [6]. We chose to pursue proton irradiation of dysprosium in an effort to limit the coproduction of holmium isotopes. In our proof-of-concept work, a dysprosium metal target of natural isotopic composition was irradiated with 16 MeV protons using a commercial dual particle PETtrace cyclotron, producing 10^{14} - 10^{15} atoms primarily using the ^{164}Dy(p,2n)^{163}Ho nuclear reaction corresponding to tens to hundreds of nanograms of ^{163}Ho in 10 hours. A robust separation technique was therefore required to isolate these nanogram amounts of ^{163}Ho from tens to hundreds of milligrams of dysprosium target mass.

Isolation of individual elements of the lanthanide (rare earth) series is one of the greatest challenges in the separation of metal ions due to their chemical similarities and prevalent existence in the trivalent oxidation state. In the past, a number of techniques have been used to separate individual rare earth elements, and reviews of these techniques are available from the literature [7-9]. As early as in 1979, Qaim et al. reported scale up of radiolanthanide separation by HPLC to the semi-preparative scale [10]. Despite many publications on rare earth separations, only a few address the isolation of 10^{-9} – 10^{-6} grams of one lanthanide element from $\geq 10^{-3}$ grams of a neighboring member of the series, and fewer still focus on the Dy-Ho pair. Yasumi et al. reported on the separation of ^{163}Ho produced by the ^{164}Dy(p,2n)^{163}Ho reaction using enriched ^{164}Dy. Holmium was separated from the dissolved Dy target using cation exchange chromatography with α-hydroxyisobutyric acid (α-HIBA) as eluent. However, the mass of dysprosium loaded onto the column was not specified, and the chromatographic procedure took seven days to complete [11].

Dadachova et al. performed high performance liquid chromatographic (HPLC) separation of carrier-free ^{166}Ho from 0.2-3 mg ^{164}Dy formed from neutron irradiation of $^{164}Dy_2O_3$, using first the $^{164}Dy(n,\gamma)^{165}Dy$ reaction, whose product decays to stable ^{165}Ho, and subsequent neutron capture on this element, or $^{165}Ho(n,\gamma)^{166}Ho$ [12]. Aminex A5 cation exchange resin (13 μm particles) was found to be superior to Dowex AG 50W (37-74 μm particles) resin when α-HIBA was used as an eluent [12]. Later Lahiri et al. verified isolation of carrier-free ^{166}Ho and reported higher holmium end product purity [13]. Though Aminex resin provided good separation resolution for holmium from dysprosium, it is unsuitable for larger scale application due to limited availability and high cost.

Here we report the enhancement of the Ho-Dy separation resolution by HPLC using readily available AG50W-X8 cation-exchange resin with aqueous α-HIBA solutions as an eluent; optimized conditions were then applied to the isolation of ^{163}Ho from a proton irradiated dysprosium metal target. In this chromatographic system, holmium elutes first, prior to the bulk of dysprosium, enhancing the purification of desired ^{163}Ho and reducing the separation time. The main goals of this study were: (1) to optimize holmium separation from dysprosium, (2) scale up separation and isolate ^{163}Ho from tens of milligrams of irradiated Dy metal target, (3) develop a fast and efficient process for the α-HIBA removal from the collected holmium fraction and (4) to determine the amount of isolated ^{163}Ho in the final product. In this paper, we present the results of these experiments illustrating the feasibility of ^{163}Ho production using proton irradiated dysprosium and its isolation in high radioisotopic purity.

Experimental:

^{163}Ho production

A thin dysprosium foil was irradiated for 10 hours with an average proton current of 10 μA on the commercial dual particle (8 MeV deuteron, 16 MeV proton) negative ion, fixed-ion source, upright magnet 6-port PETtrace cyclotron (General Electric, Waukesha, WI) using a solid target designed and built in-house by Cyclotron group at the University of Wisconsin, Madison. The machine is retrofitted by a custom-dimensioned, aftermarket beamline (National Electrostatics Corporation, Middleton, WI) with quadrupole shaping and x/y-steering optical elements to focus beam into a 5 mm full width at half maximum strike area and afford access to ± 15° and ± 30° target positions. The measured proton energy at the target was approximately 16.1 ± 0.1 MeV. The foil was of 13.8 x 12.6 x 0.25 mm dimensions and had a measured mass of 377 ± 0.4 mg. The target was cooled via contact with a gold cold finger,

which was itself cooled by a direct water jet. After irradiation, the target showed distinct thermal discoloration in the location of the beam spot shown on the picture in Table 2, likely attributable to the relatively poor thermal conductivity (10.7 W m^{-1} K^{-1}) of dysprosium. Prior to irradiation, the dysprosium foil contained 250 ppm of stable holmium according to the supplier's certificate of analysis. A holmium concentration of 248.3 ppm ± 38.1 (2σ) in the un-irradiated foil was measured by MC-ICP-MS in our laboratory. The ^{163}Ho isolation was performed 19 months after the end of bombardment (EoB).

Materials and Chemicals

Alpha-hydroxyisobutyric acid (α-HIBA, 99%), 4-(2-pyridylazo)resorcinol monosodium salt hydrate, holmium nitrate pentahydrate (99.9%) and dysprosium nitrate hydrate (99.9%) (Sigma-Aldrich); ammonium hydroxide, nitric acid, hydrochloric acid, glacial acetic acid (Optima, Fisher Scientific) were used as received. Deionized water (specific resistance >18 MΩ-cm) was prepared from in-house deionized water by purification using Barnstead E-pure Ultrapure Water Purification Systems. A 0.25 mm thick dysprosium foil of natural isotopic composition and 99.9% chemical purity was acquired from Alfa Aesar. AG50W-X8 cation exchange resin, 200-400 mesh, 37-74 µm from BioRad Laboratories was used for all HPLC separations and the first step of the holmium fraction purification process. DGA branched resin (N,N,N',N'-tetrakis-2-ethylhexyldiglycolamide, 50-100 µm) from Eichrom Technologies was used for the final purification. Holmium standard 1000 mg.dm^{-3}, Claritas PPT Grade, for ICP-AES measurement was obtained from SPEX CertiPrep. Reagent preparation of the α-HIBA and the post column reagent 0.2 mmol.dm^{-3} 4-(2-pyridylazo)resorcinol (PAR), pH 10 followed a published method with the exception of substituting lithium hydroxide with ammonium hydroxide for α-HIBA pH adjustment [14].

HPLC separation optimization

Optimization of the holmium separation from dysprosium was performed by HPLC using an analytical-sized Omnifit glass separation column (Western Analytical) filled in the laboratory with cation exchange resin AG50W-X8. A resin bed of 6.6 mm x 32.5 cm was used for the analytical separations. The HPLC instrument consisted of an Alltech 627 pump for α-HIBA delivery, a Rheodyne 7000L injection valve with 2mL sample loop, a Dionex GP 50 pump for post column reagent delivery and a Dionex AD 25 absorbance detector connected using a mixing "T" (Sigma-Aldrich). The chromatograms were acquired using Chromeleon 6.6 software. The Ho and Dy were detected

by post-column derivatization with PAR (0.2 mmol.dm^{-3}, pH 10) followed by absorbance measurement of the resulting complexes at 530 nm [14]. This wavelength provided highest signal-to-noise ratio for holmium in-flow injection format when no separation column was connected. Prior to column filling, the resin was washed with deionized water three times and then equilibrated with the 100 mmol·dm^{-3} α-HIBA, pH 5.6, mobile phase for the initial experiment. The filled column was again equilibrated in the mobile phase prior to injection of lanthanides. Fresh α-HIBA was prepared daily, pH adjusted with ammonium hydroxide in the pH range 4.2 - 5.6, filtered through a 0.45 µm Nalgene cellulose nitrate filter and then degassed by sonication for 20 min immediately prior to use. Measurements of eluent pH were conducted using a Piccolo pH meter (Hanna Instruments) with an accuracy of ±0.01 pH units. Stable isotopes of the same elements as the radioactive target material were used throughout the optimization work. Stock lanthanide solutions were produced by dissolving the appropriate amount of each nitrate powder in 0.1 mol·dm^{-3} HNO_3 and filtering through a 0.2 µm (25 mm) Whatman GD/X Glass Microfiber syringe filter. Single injections of either 50 µg of holmium or 500 µg of dysprosium in 0.1 mol·dm^{-3} HNO_3 onto the column were performed to obtain information on the peak retention times and peak width for Ho-Dy resolution calculations. Separation resolution R_s values were calculated according to $R_s = (t_{R2} - t_{R1}) / ((0.5 * (w_1 + w_2))$, where t_{R1} and t_{R2} are retention times of peak 1 and 2 and w_1, w_2 are the widths of the two peaks at baseline [15]. The α-HIBA and PAR were delivered at flow rates of 2.3 and 0.5 mL/min respectively.

Semi-preparative HPLC

HPLC scale-up was performed using a semi-preparative 2.54 cm x 25 cm MODcol flanged stainless steel column. The separation column was filled with AG50W-X8 resin in 70 mmol·dm^{-3} α-HIBA, pH 4.6. The resin bed was packed by flowing the mobile phase through the column for 1 hour at 11 mL/min. Pressure application caused the resin bed to settle, therefore the separation column was opened and more resin added to top off the column. This procedure was repeated two more times until no further resin bed settling was observed. For the Ho-Dy separation, mobile phase α-HIBA was delivered at a flow rate of 10 mL/min. This flow rate exceeds the rating of the detector cell, thus an adjustable make-up flow splitter from Analytical Scientific Instruments was used with setting 1:10 to split the flow to the detector. The PAR reagent was delivered at 0.3 mL/min. The separation was performed in 70 mmol·dm^{-3} α-HIBA, pH 4.6 mobile phase.

^{163}Ho isolation from irradiated dysprosium foil

Irradiated foil digestion, radiochemical separation and sample purification were carried out in a radiological fume hood. In order to reduce the mass of Dy to be loaded on the HPLC column, autoradiography was used to identify the activated area of the foil. A series of excisions were performed, with the foil center and trimmings counted after each cut using γ-spectrometry using EG&G Ortec Model GMX-35200-S HPGe detector system as described in [16]. Gamma emitting isotopes identified in irradiated foil 19 month from EoB were ^{54}Mn, ^{56}Co, ^{57}Co, ^{88}Y, ^{143}Pm, ^{144}Pm,^{159}Dy and ^{160}Tb. The final reduced Dy target mass of 54.5 mg was dissolved in 1.5 mL of 9 mol·dm^{-3} HCl, which was accompanied by heat release and hydrogen evolution. A fine, black, undissolved residue remained; such residue was also observed by Yasumi et al. [11]. In this work, several transition metal impurities ^{48}Sc, ^{48}V, ^{51}Cr, ^{52}Mn, ^{54}Mn, ^{56}Co, ^{65}Zn were identified in the residue by γ-spectrometry and tantalum by x-ray spectroscopy [11]. The residue in this work was analyzed by Apollo 40 EDX (Silicon Drift Detector, 40 mm^2 area) on an FEI Scanning Electron Microscope. Tantalum was found as a major impurity in undissolved residue in the un-irradiated Dy starting material by SEM-EDX. No ^{159}Dy produced during irradiation was found in the residue after Dy foil dissolution using γ-spectrometry, which confirms complete dissolution of metallic lanthanides.

After centrifugation at 7000 rpm for 5 min, the supernatant was transferred into a new glass vial. The residue was washed twice in the centrifuge tube with 0.25 mL of 9 mol·dm^{-3} HCl to dissolve any residual lanthanides, followed by centrifugation and supernatant recovery. Combined supernatant was evaporated to dryness and re-dissolved in 1.3 mL of 0.1 mol·dm^{-3} HNO_3 which was injected into the equilibrated HPLC semi-preparative column with v. No detector or flow splitter was used. The holmium fraction was collected from 320-405 min following injection, with this time window identified from an equivalent cold mass test experiment as shown in Figure 4. The collected holmium fraction of 850 mL was acidified to 0.1 mol·dm^{-3} with concentrated HNO_3 and placed onto a 5 mL cation-exchange resin bed of AG50W-X8 (200-400 mesh) in 10 mL Poly-Prep chromatography columns from BioRad conditioned with 4 x 10 mL aliquots of 0.1 mol·dm^{-3} HNO_3. The acidified holmium fraction was loaded at 5 mL/min by vacuum application onto the chromatographic column attached to Büchner flask. The column was washed with 500 mL of 0.1 mol·dm^{-3} HNO_3 at 3 mL/min using vacuum. Holmium was eluted in 20 mL (8 x 2.5 mL aliquots) of 8 mol·dm^{-3} HNO_3. This eluate from the AG50W-X8 column was loaded onto a DGA resin, branched, of 1.2 mL column volume after column conditioning with 8 mol·dm^{-3} HNO_3 to remove residual α-HIBA. The DGA column

was washed with 40 mL (4 x 10 mL) of 8 mol·dm^{-3} HNO_3. Holmium was eluted with 5 mL in 0.5 mL increments of 0.01 mol·dm^{-3} HNO_3. The first 2 mL of eluate were discarded. Optimization of the holmium fraction processing was performed using ^{150}Eu tracer. Stable holmium solutions were used to evaluate recovery of the two step purification procedure. Holmium standards and holmium prior and after purification were measured using ICP-AES.

ICP-AES analysis

Inductively coupled plasma atomic emission spectroscopy (ICPE-9000 Multitype ICP Emission Spectrometer, Shimadzu Corp.) was used to measure holmium concentration prior to and after the two step purification to evaluate the holmium recovery in this process. A stable holmium spike of 14 µg was added into 850 mL of 70 mmol·dm^{-3} α-HIBA, pH 4.6, which was the expected volume of the Ho fraction after HPLC. The two-step extraction process was performed as described above. The concentration of holmium in the eluate after extraction chromatography with DGA was measured using ICP-AES and used to calculate the recovery from the final purification steps.

ICP-MS analysis

Samples of holmium and dysprosium were dissolved in 0.4 mol·dm^{-3} HNO_3 for measurement by multicollector inductively coupled plasma mass spectrometry (MC-ICP-MS). Analyses were conducted on a Thermo Neptune Plus operating in low-resolution mode with a Cetac Aridus II desolvating nebulizer. The instrument's sensitivity to Ho was 1.11 ± 0.04 volts per ppb and was determined from four Ho standards varying in concentration from 0.01 to 4 ppb. Masses 160 to 166 were measured in static mode on an array of Faraday detectors. One hundred cycles were collected for each sample with a 4 second integration time and a 3 second wait between cycles. Isotope ratios were internally corrected for machine-induced mass fractionation based on the measured $^{162/161}$Dy ratio in each sample using a linear correction law [17].

Results and Discussion:

HPLC separation optimization

In ion-exchange chromatography, the strength of ionic interaction between the oppositely charged ions or ionic groups in the sample molecule and the functional ligand of the stationary phase is governed by the concentration of the hydrated ions, the concentration of the complexing agent in the mobile phase and by the pH of the eluent matrix.

Positively charged lanthanide ions form complexes with α-HIBA which lowers the affinity of the lanthanide for the cation-exchange resin. Therefore, the effect of α-HIBA concentration and eluent pH on holmium and dysprosium retention was investigated in order to optimize Ho-Dy separation resolution. Initially, an analytical-sized chromatographic column was used to establish HPLC separation conditions. Holmium and dysprosium were detected by post-column derivatization with PAR followed by spectrophotometric detection [14]. First, the concentration of α-HIBA was varied from 100 to 60 mmol·dm^{-3} in 5-10 mmol·dm^{-3} increments at constant eluent pH = 5.6. At this pH, α-HIBA is largely deprotonated (pKa = 3.97). With decreasing α-HIBA concentration, holmium and dysprosium retention times and Ho-Dy separation resolution increased as shown in Figures 1A and 1B. Figure 1A displays an overlay of chromatograms when single injections of either 50 µg of holmium or 500 µg of dysprosium was acquired using α-HIBA of varying concentration. Holmium and dysprosium retention times as well as calculated Ho-Dy resolution as a function of α-HIBA concentration are shown in Figure 1B. Resolution for the Ho-Dy pair increased from 0.37 to 1.28 when α-HIBA concentration decreased from 100 to 60 mmol·dm^{-3}. At α-HIBA concentration below 65 mmol·dm^{-3} retention times of holmium and dysprosium increased significantly while resolution improves only marginally due to peak band broadening.

Furthermore, the influence of mobile phase pH on the separation of holmium and dysprosium was explored by performing the separation using eluate pHs of 5.6, 4.6 and 4.2 at constant α-HIBA concentration of 70 mmol·dm^{-3}. With decreasing pH from 5.6 to 4.6, holmium and dysprosium retention times increased and their resolution increased as summarized in Table 1. However, with further decrease of pH to 4.2, the retention time of holmium more than tripled, resulting in severe peak band broadening. The chromatogram for dysprosium was not acquired due to the expected unreasonably long run time and therefore Ho-Dy resolution was not calculated at pH 4.2. The highest Ho-Dy resolution and shortest separation time was achieved in 70 mmol·dm^{-3} α-HIBA of pH 4.6; hence this composition of mobile phase was selected as the optimum for holmium separation from bulk of dysprosium.

Semi-preparative HPLC and ^{163}Ho isolation

Scale-up of the separation was performed to accommodate the large mass of the dysprosium target material. A typical chromatogram of separation of 500 µg of holmium from 112 mg dysprosium, chosen as representative masses from irradiation, acquired in 70 mmol·dm^{-3} α-HIBA, pH 4.6 using a 2.5 cm x 25 cm sized semi-preparative

HPLC column is shown in Figure 2. The entire chromatogram was collected to demonstrate the difference in Ho and Dy mass loaded onto the chromatographic column. During dysprosium elution, α-HIBA concentration was raised three times to 0.1, 0.2 and finally to 0.4 mol·dm^{-3}, pH 5.6 to accelerate the elution of dysprosium from the column, causing a distortion of Dy peak shape and the appearance of several spikes in the chromatogram during Dy elution.

The effect of variation in the dysprosium mass loaded onto the semi-preparative separation column was also studied. Comparison of chromatograms acquired when 112 or 280 mg of Dy were loaded on the column under otherwise identical conditions (e.g., Ho concentration and separation parameters) is displayed in Figure 3. At the higher mass of 280 mg, holmium is no longer resolved from the dysprosium peak. This experiment motivated the reduction of the 377 mg dysprosium target mass prior to undertaking chromatographic separation of the irradiated target. Dysprosium target mass reduction provided two major improvements (1) improved Ho-Dy separation resolution and thus higher purity of isolated Ho fraction and (2) reduced amount of stable ^{165}Ho impurity in the final product since a small amount of ^{165}Ho is present as an impurity in dysprosium target material. A reduced Dy mass allows for the use of only one HPLC separation using the semi-preparative column, without further scale up or employment of two consecutive HPLC separations to achieve the desired resolution of Ho from Dy.

Autoradiography was performed to identify the activated area of the foil for excision. Table 2 shows the effect of dysprosium target mass reduction on expected amount of ^{165}Ho impurity in Dy material, produced amount of ^{163}Ho calculated using actual target dimensions and irradiation parameters and the repository of excitation functions from the TALYS/TENDL as well as predicted ^{165}Ho/^{163}Ho ratio in isolated ^{163}Ho product [18]. Initial target mass reduction when only the edges of the dysprosium foil were trimmed off resulted in 33% Dy mass reduction and no loss of ^{163}Ho, as evaluated by gamma spectrometry using ^{159}Dy ($t_{1/2}$ 144 d, EC, γ) coproduced during irradiation. As indicated in Figure 3, reduced Dy mass of 253 mg would not provide complete holmium separation from bulk of Dy and would necessitate second separation step to obtain product with better Dy decontamination. Therefore, in order to further improve Ho-Dy resolution and also to reduce the ^{165}Ho/^{163}Ho ratio, only the center of the beam spot of the irradiated target was isolated. This second mass reduction brought the Dy mass down to 54.5 mg with an associated loss of the 43% of total activity, i.e. also ^{163}Ho, evaluated by gamma spectrometry of ^{159}Dy in the target beam spot and trimmings. Lower Dy mass of 54.5 mg afforded better holmium resolution from dysprosium as shown in Figure 4 and significant reduction of the ^{165}Ho/^{163}Ho ratio in the final product; see Table 2, justifying the loss of ^{163}Ho.

The chromatogram in Figure 4 was obtained when an identical mass of 54.5 mg of un-irradiated dysprosium foil from the same batch and lot as the irradiated foil was dissolved, and the resulting solution separated using the semi-preparative column with 70 mM α-HIBA, pH 4.6 eluate. The holmium peak in the chromatogram is entirely from the holmium impurity in the dysprosium metal (250 ppm corresponds to 13.6 µg Ho in 54.5 mg Dy), no holmium was added. Based on this data, the Ho fraction, shown by vertical lines on the chromatogram in Figure 4, was identified to be collected during the separation of the dissolved irradiated Dy target material.

The final fraction containing ^{163}Ho collected from HPLC separation was purified to remove undesirable α-HIBA complexing agent and to concentrate holmium into a small volume for incorporation into microcalorimeter sensors for electron capture spectroscopy. The 850 mL of holmium fraction was acidified and sorbed onto a 5 mL AG50W-X8 cation exchange column. Application of vacuum during the loading step significantly reduced the loading time of the large fraction volume, which contained over 6 g of α-HIBA. No lanthanide breakthrough was observed during loading at high flow rates of up to 10 mL/min when tested with ^{150}Eu as a lanthanide tracer. Thorough washing of the column was performed with a total of 500 mL of 0.1 mol·dm^{-3} HNO_3 to remove α-HIBA. Upon evaporation of the last five 10 mL-aliquots of collected column washes, decreasing amounts of α-HIBA were observed, visible as residues in the evaporation vial. After these washes, holmium was eluted with 20 mL of 8 mol·dm^{-3} HNO_3. Dadachova et al. reports of an α-HIBA-free product using a similar procedure. However, we found α-HIBA in the last 10 mL aliquot of the wash as a visible residue. Therefore, a final purification using a column with a resin of branched DGA was employed to remove remaining traces of α-HIBA. More efficient washing of α-HIBA is achieved with this resin because a higher concentration of HNO_3 can be used than on the AG50W-X8 column without eluting holmium, which helps to completely dissociate the α-HIBA-lanthanide complex. The eluate from the AG50W-X8 column was loaded onto a 1.2 mL column with DGA resin, branched, and the column was washed with 4 x 10 mL of 8 mmol·dm^{-3} HNO_3. Holmium was eluted with 5 mL of 0.01 M HNO_3. Recovery efficiency of the two-step purification was evaluated using 14 µg of stable Ho added into a volume identical to the volume of eluent (850 cm^3 of 70 mmol·dm^{-3} α-HIBA, pH 4.6). The dysprosium target material contained 250 ppm of stable holmium, thus 14 µg of stable Ho was used as a test since this amount was expected as an impurity in the 54.5 mg of dysprosium target as shown in Table 2. Holmium recovery from the two step purification process was calculated at 81.8 ± 0.6% based on a Ho concentration determined by ICP-AES.

Isolated ^{163}Ho analysis by MC-ICP-MS

After HPLC separation and ^{163}Ho fraction purification, MC-ICP-MS was performed to assay the final product. Due to the isobaric interference of ^{163}Dy on ^{163}Ho, all stable Dy isotopes and the isotope ratios $^{160/161}$Dy, $^{162/161}$Dy, and $^{164/161}$Dy were measured in standard solutions, un-irradiated dysprosium target material and in the final sample to account for the ^{163}Dy contribution to the measured 163 signal. Isotope ratios measured in the standards and dysprosium foil were consistent with natural Dy isotope ratios. An elevated 163/161 ratio was found in the isolated holmium fraction. A high 163/161 ratio could be explained either by an elevated 163 signal, or a lower 161 signal. Given that the other isotope ratios normalized to ^{161}Dy ($^{160/161}$Dy, $^{162/161}$Dy, $^{164/161}$Dy) did not deviate from natural, this deviation is caused by an increased signal at mass 163 and was attributed to ^{163}Ho. The amount of ^{163}Ho isolated from the proton irradiated dysprosium target was 24.8 ± 1.3 ng, which corresponds to more than 400 Bq. This material is expected to provide enough ^{163}Ho material to prepare electron capture detectors with embedded ^{163}Ho. The amount of dysprosium in the isolated ^{163}Ho sample was only 401 ± 15 ng, corresponding to a removal of 99.9997% of the Dy amount (54.5 mg) injected for HPLC separation, and a Dy decontamination factor of $1.3 \cdot 10^5$. Table 3 summarizes quantitative information on the purified holmium product together with initial dysprosium material specifications. Since ^{163}Ho decays by pure electron capture, it is unmeasurable in the irradiated dysprosium target. Therefore, stable holmium, ^{165}Ho, which was present as an impurity in dysprosium foil, was used to evaluate the recovery of the overall holmium isolation process. The whole separation and purification process resulted in 72.2 ± 2.9% holmium recovery, calculated from stable holmium content (250 ppm Ho according to certificate of analysis). The holmium content in the un-irradiated Dy foil measured by MC-ICP-MS in our laboratory was 248.3±38.1 ppm. Lower holmium recovery could be due to (1) losses during the purification process after HPLC separation (81.8 ± 0.6% Ho recovery) and (2) due to sacrificing part of the holmium fraction per Figure 4 to improve decontamination of the product from dysprosium.

Conclusions:

Separation of 24.8 ± 1.3 ng of ^{163}Ho and 9.82 ± 0.40 μg of ^{165}Ho from a dysprosium target of rather large mass (54.5 mg) was accomplished using semi-preparative HPLC with a cation-exchange resin and 70 mmol.dm^{-3} α-HIBA, pH 4.6 as an eluent. A one-step HPLC purification process followed by α-HIBA removal and holmium

preconcentration resulted in 99.9997% removal of bulk dysprosium. MC-ICP-MS, was used to determine Ho and Dy in the final isolated fraction. The analysis revealed that sufficient amount of ^{163}Ho, over 400 Bq, was isolated for detector development for neutrino mass determination using electron capture spectroscopy. No ^{166m}Ho was found in the isolated product using γ-ray spectrometry, indicating that ^{163}Ho obtained via proton irradiation of dysprosium provides superior radioisotopic purity compared to the product obtained via neutron irradiation of ^{162}Er [6]. A 72.2± 2.9 % holmium recovery was achieved for the overall dissolution, separation and purification process, calculated from stable holmium content in irradiated Dy target material. An 81.8 ± 0.6% recovery of holmium from the two step purification process after HPLC separation was achieved. The developed HPLC method can be readily scaled up to accommodate up to several grams of dysprosium target mass using a larger preparative column. Similar separation conditions can be extended to other neighboring lanthanide pairs after adjustment of eluent concentration and/or pH as indicated in [19]. One possible example of using this method would be the isolation of other lanthanide isotopes from irradiated rare earth targets for the measurement of neutron capture cross-sections; many of these are either still unknown or poorly investigated. Future efforts of our team will be directed towards the acquisition and irradiation of a high purity dysprosium target with minimal content of stable holmium, the improvement of the Ho-Dy separation resolution by reducing resin bead size and their distribution by sieving, and towards further scale-up to accommodate dysprosium target masses of several grams.

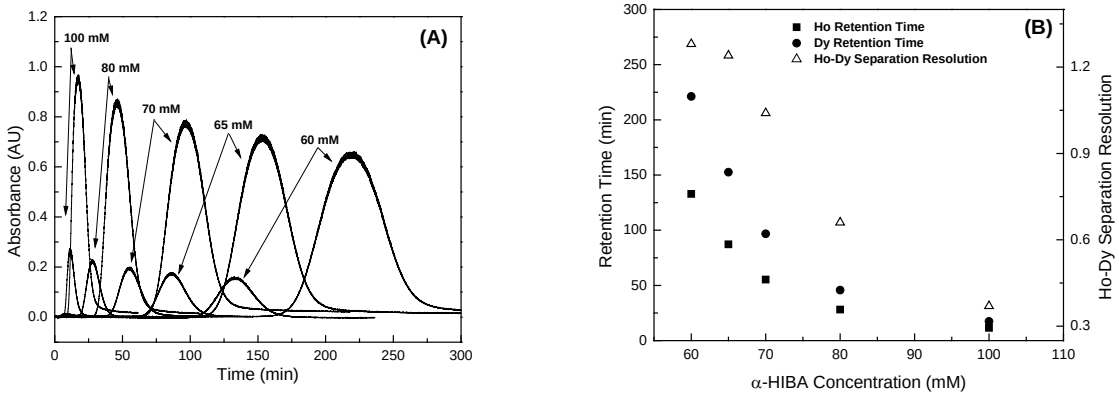

Fig. 1. (A) Overlay of chromatograms acquired after single injections of 50 µg of holmium (small peaks) and 500 µg dysprosium (large peaks) in varying concentration of α-HIBA of a constant pH of 5.6, column size 32.5 x 0.66 cm with AG50W-X8, α-HIBA flow rate 2.3 mL/min, post column reagent 0.2 mmol.dm^{-3} PAR, pH 10 and flow rate 0.5 mL/min, detection at 530

nm, 2 mL sample volume. (B) Holmium and dysprosium retention times (left vertical axis) and Ho-Dy separation resolution (right vertical axis) as a function of α-HIBA concentration at constant pH 5.6.

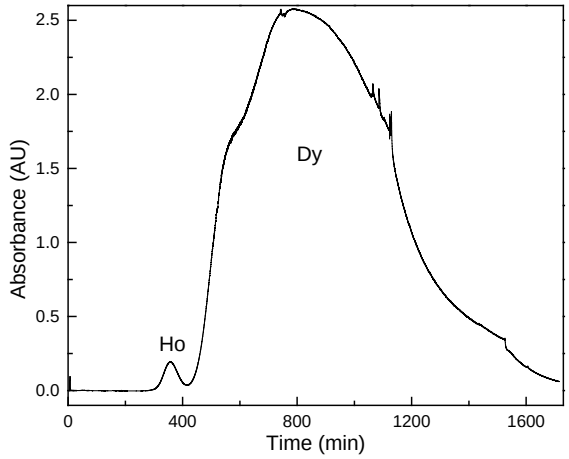

Fig. 2. Chromatogram of separation of 500 μg of holmium from 112 mg dysprosium in 70 mM α-HIBA, pH 4.6 using a semi-preparative HPLC column sized 25 cm x 2.5 cm with AG50W-X8, α-HIBA flow rate 10 mL/min, flow splitter 1:10, post column reagent 0.2 mmol.dm^{-3} PAR, pH 10 and flow rate 0.3 mL/min, detection at 530 nm, 2 mL sample volume. Note near baseline resolution of Ho peak, also in Figure 3, solid line.

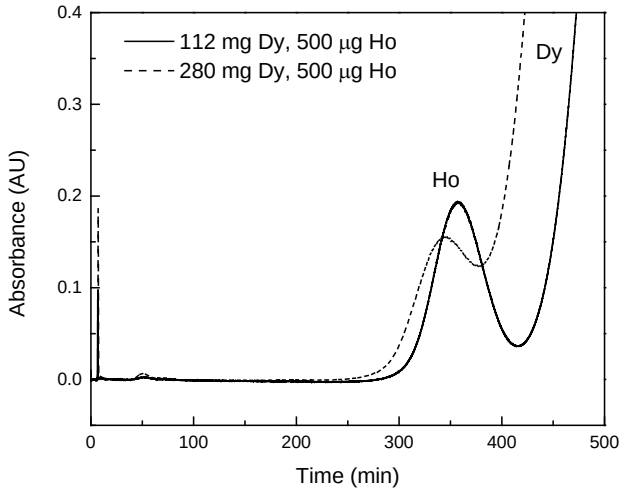

Fig. 3. Chromatogram of 500 µg holmium separation from 112 mg (solid) and 280 mg (dashed) dysprosium loaded onto semi-preparative HPLC column. Other separation conditions identical as in Fig. 2.

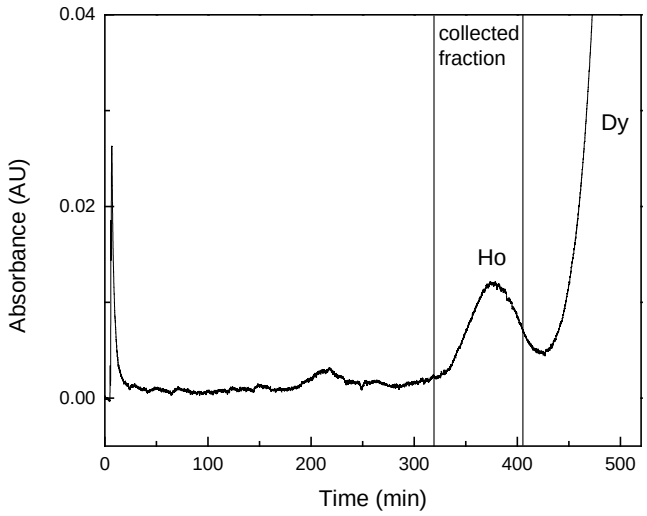

Fig. 4. Chromatogram of holmium (impurity in Dy) separation from 54.5 mg of un-irradiated dysprosium. Vertical lines identify the time of holmium fraction collection used for Ho separation form the irradiated Dy target. Separation conditions identical to those shown in Figure 2.

Eluent pH	Ho retention time (min)	Dy retention time (min)	Ho-Dy resolution
5.6	55.3	96.7	1.04
4.6	114	202	1.34
4.2	397	-	-

Table 1. Effect of eluent pH at a constant α-HIBA concentration of 70 mmol.dm^{-3} on Ho and Dy retention times and Ho-Dy separation resolution.

	Dy (mg)	^{165}Ho (µg)	Predicted ^{163}Ho (ng) †	Predicted ^{165}Ho/^{163}Ho ratio
Whole Dy target 	377	94.3	27-270 (10^{14}-10^{15} atoms)	3500-350
Dy mass reduction 1 	253	63.3	27-270	2300-230
Dy mass reduction 2 	54.5	13.6	15-154 (43% reduction)	880-88

Table 2. Effect of dysprosium target mass reduction on the Dy mass, amount of ^{165}Ho impurity in Dy material, predicted amount of ^{163}Ho and ^{165}Ho/^{163}Ho ratio. † ^{163}Ho content calculated using actual target dimensions and irradiation parameters and the repository of excitation functions from the TALYS/TENDL.

	Prior to separation	Isolated ^{163}Ho fraction
Dysprosium	54.5 mg	401 ± 15 ng
^{163}Ho	15.4 - 154 ng†	24.8 ± 1.3 ng
^{165}Ho	13.6 µg	9.82 ± 0.40 µg
^{165}Ho/^{163}Ho ratio	880 - 88‡	397 ± 15

Table 3. Summary of Dy and Ho concentrations in the dysprosium target before and after irradiation and HPLC separation and purification. † ^{163}Ho content in 54.5 mg Dy foil, calculated using actual target dimensions and irradiation parameters and the repository of excitation functions from the TALYS/TENDL. ‡ ^{165}Ho/^{163}Ho ratio calculated based on expected ^{163}Ho content in 54.5 mg Dy foil.

Acknowledgements: The authors would like to thank Los Alamos National Laboratory LDRD support, 20130679ER. The research described in this paper was also funded by the United States Department of Energy, Office of Science via funding from the Isotope Development and Production for Research and Applications subprogram in the Office of Nuclear Physics. The authors would like to acknowledge help of Nina Weisse-Bernstein for acquisition of the SEM-EDX data. Dr. Michael Fassbender is thanked for helpful discussions and suggestions.

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