Accelerator-Based Production of the $^{99\text{m}}\text{Tc}$ - ^{186}Re Diagnostic-Therapeutic Pair using Metal Disulfide Targets (MoS_2 , WS_2 , OsS_2)

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Abstract

Novel, natural abundance metal disulfide targets were irradiated for 1 hour with a 10 μ A proton beam in a small, medical cyclotron. Osmium disulfide was synthesized by simple distillation and precipitation methods while MoS₂ and WS₂ were commercially available. The targets dissolved under mild conditions and were analyzed by γ -spectroscopy. Production rates and potential applications are discussed, including target recovery and recycling schemes for OsS₂ and WS₂.

Key Words: Metal disulfide targets; WS₂; OsS₂; MoS₂; high specific activity ¹⁸⁶Re; high specific activity ^{99m}Tc

1 INTRODUCTION

The use of radionuclides in medicine began in 1924 when George de Hevesy used ²¹⁰Pb and ²¹⁰Bi to study the metabolism of bismuth in rabbits thus establishing the tracer principle (Stoecklin 1995). Today, it has grown into an expansive medical modality with over 50 million nuclear medicine procedures performed every year. Diagnostic imaging accounts for about 90% of the nuclear medicine procedures performed with the remaining 10% being therapeutic applications. Of these diagnostic procedures, approximately 80% use a single isotope, ^{99m}Tc ($t_{1/2}$ =6.007 h; 140.5 keV γ ; 89% abundance) (“Radioisotopes in Medicine” 2015). The extensive use of ^{99m}Tc-based imaging agents makes their therapeutic rhenium analogues desirable. Rhenium-186 emits therapeutic β^- particles with an endpoint-energy of 1.07 MeV, allowing for a targeted tissue range of 3.6 mm. Additionally, its low abundance γ -ray emission of 137.2 keV (9.42%) allows for *in vivo* tracking of radiolabeled compounds and dosimetry calculations. With a long half-life of 3.72 days, synthesis and shipment of ¹⁸⁶Re-based radiopharmaceuticals are not geographically constrained. Together ^{99m}Tc and ¹⁸⁶Re would provide an excellent diagnostic/therapeutic pair.

Presently, there are some issues with the expanded use of ^{99m}Tc. The United States currently receives a substantial portion of its supply of fission-produced ⁹⁹Mo for ^{99m}Tc generators from reactors such as the Chalk River Facility in Canada; this facility is expected to cease routine production at the end of 2016 and close in 2018 (“Chalk River’s NRU Reactor” 2015). Though new suppliers are coming online to meet demand, this reliance on aging reactors highlights the importance of diversifying the supply chain to ensure it is reliable and robust. Several routes are under investigation to continue to meet the demand for ^{99m}Tc. Accelerator production (Khandaker 2007, Qaim 2014, Tárkányi “deuteron” 2012, Tárkányi “proton” 2012) of ^{99m}Tc utilizes primarily molybdenum metal, which is difficult to dissolve and regenerate (Targholizadeh 2010).

Generally, ¹⁸⁶Re is produced in a reactor via the ¹⁸⁵Re(n, γ) reaction resulting in low specific activity, which limits its therapeutic applications (Ehrardt 1997, Moustapha 2006). Production in an accelerator, such as the PETtrace at the University of Missouri Research Reactor Center (MURR), can theoretically provide a specific activity of 34,600 Ci/mmol⁻¹ Re, which represents a 62-fold increase over reactor-produced ¹⁸⁶Re. Previous studies on accelerator-based production of ¹⁸⁶Re primarily used tungsten targets (Moustapha 2006, Bonardi 2010, Lapi 2007, Fassbender 2013, Tárkányi 2007, Shigeta 1996, Tárkányi 2003), while osmium target studies are limited (Szelecsényi 2009). The use of osmium targets to produce

platinum and iridium radioisotopes has been reported (Hilgers 2005, Hilgers 2009, Hermanne 2015, Szelecsényi 2010), using either a thin electrodeposited layer of the metal or a thin metal foil. Production of clinically relevant quantities of ^{186}Re requires the use of thick, isotopically-enriched targets; the current target preparation methods do not meet this need.

Due to the brittle, dense nature of these metals (Mo, W, Os), the production of foils and pressed discs involves pressing and sintering metal powder to achieve a uniform, stable target; this method uses a large mass of material and special equipment, driving up the cost of target production and making reuse of the target more difficult. Thus, metal disulfides (MoS_2 , WS_2 , and OsS_2) were evaluated as novel, easy to use targets for the direct production of $^{99\text{m}}\text{Tc}$, the production of ^{99}Mo as a generator source, and the direct production of ^{186}Re as alternatives to electrodeposited metal targets or pressed metal discs. The method generates a target form suitable for producing thick pressed pellets, which can easily be irradiated and recovered for reuse.

2 EXPERIMENTAL

2.1 Materials

All reagents, tungsten metal, tungsten trioxide, and sodium hydrosulfide were purchased from Fisher Scientific (Pittsburgh, PA). Molybdenum disulfide, sodium tungstate, tungsten disulfide, and osmium metal powder were purchased from Alfa Aesar (Ward Hill, MA). Poly prep columns (0.8 cm ID; 10 mL reservoir) were purchased from Bio-Rad (Hercules, CA). Aluminum metal backings and thick beam degraders were prepared on-site to designed specifications using 6061 grade aluminum purchased from McMaster-Carr (Elmhurst, IL). Commercial food-grade aluminum foil was purchased from a local market. Araldite 2011 epoxy adhesive was purchased from Freeman Supply (Avon, Ohio). All reagents and materials were used as received without further purification. All water used was purified on-site (deionized water fed into a Millipore system to $> 18 \text{ M}\Omega\cdot\text{cm}$).

2.2 Irradiation and Counting Facilities

Neutron irradiations were performed using the MURR, which is a 10 MW light-water moderated, flux-trap design reactor with a neutron flux up to $4.5\cdot 10^{14} \text{ n}\cdot\text{cm}^{-2}\cdot\text{s}^{-1}$. All proton irradiations were performed using a General Electric (GE) PETtrace 800 cyclotron with dual particle capabilities with energies up to 16.5 MeV for protons and 8.5 MeV for deuterons and currents up to 80 microamps. The beam was collimated to a 10 mm diameter aperture for all irradiations. Radiochemical assays were performed by γ -ray spectrometry using a Canberra Model GC2018S HPGe detector system (60.5 mm diameter, 30.5 mm length, 5 mm space to the window). The detector FWHM at 1.33 MeV was 1.8 keV. Spectral analyses were performed with a Canberra Model 9600 multichannel analyzer.

2.3 Synthesis and Characterization of Osmium Disulfide

Osmium metal (~100 mg) was dissolved in a 25 mL impinger using 10-15 mL of 12% NaOCl with gentle heating (45° C) to oxidize the osmium to osmium tetroxide, OsO_4 (**Figure 1**). **Caution!** *Do not perform osmium distillation outside of a hood or glove box. The potential release of osmium tetroxide can pose a significant health risk to the operator* (National Academic Press 2005). Once the sample was fully dissolved, the temperature was increased to 90° C to distill osmium tetroxide under argon gas flow.

Osmium was captured as potassium perosmate, $K_2[OsO_4(OH)_2]$, in a second impinger containing 5-10 mL of a 25% w/v KOH solution; a dark red solution that appears black when highly concentrated is formed. Distillation was complete when the red NaOCl solution becomes colorless. The potassium perosmate solution was transferred to a centrifuge tube and an additional 5-10 mL of 25% w/v KOH was added to ensure the sample was highly basic. Sodium hydrosulfide (5-10 mL of 10% w/v) was then added to the potassium perosmate solution; osmium disulfide precipitated immediately as a black solid. Osmium disulfide was serially washed with several 25-30 mL aliquots of water and acetone by agitating the sample, centrifuging to separate precipitate and supernatant, and decanting the supernatant. Osmium disulfide was then annealed at 575° C for three hours in a tube furnace and allowed to slowly cool to room temperature over three hours; all high temperature work was performed under argon gas flow to prevent osmium interactions with atmospheric oxygen. Osmium disulfide was characterized by Raman spectrometry, powder x-ray diffraction, and elemental sulfur analysis. Raman spectroscopy was performed using an Action SpectroPro 500i spectragraph with a Princeton L-N₂ cooled Si detector, a 532 nm laser light source from Coherent Compass powered to 850 μ W, and a collection time of 150 seconds. Powder x-ray diffraction was performed using a Bruker D8 Discover with a general area detector diffraction (GADD) system, using Cu-K alpha (1.5418 Å) x-rays and a collection time of 100 seconds. Elemental sulfur analysis was performed by Atlantic Microlab, Inc. (Norcross, Ga); Elem. Anal. Calc'd (Found) for OsS_2 : S, 25.2% (25.12%).

Figure 1. Osmium Distillation Setup

2.4 Target Preparation and Irradiation

Each target material (OsS_2 , WS_2 , or MoS_2) was dried overnight in an oven heated to 100° C to remove any moisture within the material and then transferred to a desiccator (placed under vacuum) to cool prior to pressing. The desired mass of the material was weighed directly into an aluminum backing, and pressed three times at incrementally increased pressure with a hydraulic press up to a final pressure of 13.8 MPa to ensure a smooth, evenly-distributed pellet. After pressing, the target was sealed in the backing using 16 μ m thick aluminum foil, which was held by epoxy over the face of the target. The epoxy was allowed to cure for a minimum of 15 hours per the manufacturer's specifications.

Stopping Range in Matter-2008 (SRIM-2008) software (Ziegler 2010) was used to calculate theoretical proton stopping power for each of the targets and degraders to determine the projectile entry energy and exit energy within each target. The targets were irradiated with protons of the desired energy for a total of 10 μ Ah. High vacuum was used on the target face while the back side of the target was water cooled to dissipate heat from the charged particle beam. The following irradiations were performed:

- (1) A proton energy range of 14.5 – 16 MeV was used for the direct production of ^{99m}Tc via the $^{100}\text{Mo}(p, 2n)$ reaction to minimize the production of $^{96g+m}\text{Tc}$ as unwanted impurities at lower energies.
- (2) Two distinct entry energies (11 and 14 MeV) were evaluated with the WS_2 targets for the production of ^{186}Re via the $^{186}\text{W}(p, n)$ reaction. The irradiation at 11 MeV was used to evaluate the production rate near the optimal energy of ~ 10 MeV, while the irradiation at 14 MeV was used to determine the production of ^{186}Re over a wider energy range to increase overall yield.
- (3) The optimal proton energies for the $^{189}\text{Os}(p, \alpha)$ and the $^{192}\text{Os}(p, \alpha 3n)$ reactions to produce ^{186}Re are both approximately 24 MeV. The PETtrace is only capable of a maximum energy of 16 MeV, therefore, a proton energy of 16 MeV was used to evaluate ^{186}Re production.

Radiochemical assays for $^{181,182,182m,183,184,186}\text{Re}$, $^{186,187,188,189,190}\text{Ir}$, and $^{94,95,95m,96,99m}\text{Tc}$ were performed by γ -ray spectrometry.

2.5 MoS_2 Target Dissolution and Activation Product Analysis

For the development of the dissolution method, ~ 100 mg of MoS_2 was added to 10 mL of 30% H_2O_2 ; gentle heating was used to initiate the dissolution, which was then self-sustaining. The samples were centrifuged to isolate any undissolved MoS_2 ; the supernatant containing the dissolved molybdate (MoO_4^-) was transferred to a clean vial, and the vials containing the undissolved MoS_2 were dried overnight in a vacuum oven. The mass of undissolved MoS_2 was quantified the next day once the vials had thermally cooled.

For the irradiated targets, a sample of known mass of the irradiated MoS_2 was dissolved in 30% H_2O_2 with gentle heating (50°C) to initiate the dissolution. Once the reaction was complete, any remaining undissolved target material was not removed; rather the sample was agitated prior to analysis to generate a homogeneous suspension and analyzed by gamma spectroscopy using an HPGe detector to quantify and qualify activation products.

2.6 WS_2 Target Dissolution and Activation Product Analysis

Following cyclotron irradiation of the WS_2 target material, the aluminum foil was mechanically removed from the target backing and the irradiated WS_2 transferred to a clean high density polyethylene (HDPE) vial. Ten milliliters of 30% H_2O_2 were added to the vial, which was then gently heated (60°C) with stirring to dissolve the WS_2 . When fully dissolved, the entire sample was analyzed by gamma spectroscopy using a high purity germanium (HPGe) detector to qualify and quantify the produced radioisotopes.

2.7 OsS₂ Target Dissolution and Activation Product Analysis

The irradiated OsS₂ material was mechanically separated from the target body and transferred to the reaction flask of a distillation setup (**Figure 1**). The OsS₂ was then dissolved in 5-10 mL of 12% NaOCl with gentle heating (45° C) within the distillation setup. Only minimal OsO₄ distillation was observed at this point, but this reaction was performed in the distillation setup for safety purposes. Following dissolution, 5 M NaOH (2-3 mL) was added to the solution to increase the pH to ≥ 14 . A small aliquot of this solution was used to determine activation products generated and their relative abundances. Extraction of perrhenate was achieved using 10 mL of methyl ethyl ketone (MEK); the aqueous layer turned black upon agitation generating heat. The two phases were collected in separate scintillation vials. Additional impurities were removed from the rhenium product by extraction of the initial MEK layer with an additional 10 mL of 1 M NaOH. Similarly, additional rhenium was recovered from the first aqueous layer by extraction with an additional 10 mL aliquot of MEK. All aliquots were collected in separate HDPE vials. Both MEK layers were then passed through a MEK-conditioned, acidic alumina column (0.8 cm ID; 1 mL bed volume) to further purify the isolated rhenium product. Ir and Os impurities were retained on the alumina while the perrhenate passed through and was collected. All samples were analyzed by γ -spectroscopy using an HPGe detector to identify and quantify the activation products produced.

2.8 Further Optimization of OsS₂ Target Purification Method

To profile the osmium separation, an osmium radiotracer was prepared. Osmium metal (10 mg) was neutron irradiated in the reactor to produce Os-191 ($t_{1/2} = 15.4$ d; $\gamma = 129.4$ keV (26.5%)) as a radiotracer. Once irradiated, osmium metal was converted to OsS₂ as previously described. The reactor-irradiated Os was added to a cyclotron-irradiated target and the dissolution method performed as described with one exception; rather than purifying the MEK aliquots with an alumina column, various (alumina, silica, and cation exchange) sep-paks were evaluated to determine the chromatographic material that most effectively separated osmium and iridium impurities from the rhenium product. For each chromatographic material, a 3 mL aliquot of the first MEK extract was passed through the sep-pak followed by 7 mL of fresh methanol to wash the column and recover any remaining rhenium. The entire sample was collected into a single HDPE vial and counted by gamma spectroscopy using an HPGe.

3 RESULTS AND DISCUSSION

Several methods have been reported for the production of ^{99m}Tc and ¹⁸⁶Re, with most utilizing metal targets. This requires additional processing and the separated enriched metal target materials are difficult to regenerate. To develop easy to process and reusable target forms, metal disulfide (MoS₂, WS₂, and OsS₂) targets were evaluated for cyclotron-based production of ^{99m}Tc and ¹⁸⁶Re. Targets were irradiated and separation methods were developed to isolate the ¹⁸⁶Re product and recover the target material.

3.1 OsS₂ Synthesis and Characterization

Osmium disulfide (OsS₂) is not available commercially and was successfully synthesized in high yield (93 ± 13 %; $n = 3$) by reacting potassium perosmate with sodium hydrosulfide under basic conditions. Some losses were observed during the transfer of material during the synthesis, washing, and annealing.

Static interaction with the walls of the tube furnace resulted in additional sample loss. The overall yield (93%) is still considered quite high, with the final product a dark grey – black powder.

Raman spectroscopic analysis of the OsS_2 showed an intense peak at $\sim 354\text{ cm}^{-1}$ and a weak peak at $\sim 393\text{ cm}^{-1}$ (**Figure 2**), which is consistent with the literature (Müller 1991). No spectral data above 500 cm^{-1} was reported by Müller, but a weak peak near 900 cm^{-1} was noted. This peak may be associated with Os – S bonding. OsS_4 formation has been described in the literature (Liang 2009) and could be an impurity during the production of OsS_2 , however the elemental analysis results are not consistent with this. Assuming some similarities between their structural properties, the Raman spectra of OsS_4 and OsO_4 may be similar. The Raman spectrum for OsO_4 shows sharp peaks at 335 and 965 cm^{-1} and a weak, broad peak at 954 cm^{-1} ; the weak peak near 900 cm^{-1} could be similar for Os-S bonding (Woodward 1956). The experimental spectrum is shown in Figure 2 and has been normalized to the intensity of the 354 cm^{-1} peak.

Figure 2. Raman spectrum of an annealed OsS_2 sample.

Powder x-ray diffraction analysis of OsS_2 prior to annealing showed it was amorphous. Annealing the sample reorganized the solid on slow cooling to room temperature. The dryness of the argon gas was critical; any water present during the annealing process was potentially trapped in the crystal lattice, which created outgassing issues during sample irradiation. To prevent this, the argon was passed through a Drierite column prior to entering the tube furnace. Anhydrous, crystalline OsS_2 forms a face-centered cubic structure (Stingl 1992). A sample of the annealed material was analyzed by powder x-ray diffraction (**Figure 3**) and matched the literature spectrum well in the ICDD-PDF database (OsS_2 : 65-3324) using Bruker's EVA software; the experimental unit cell dimension ($a = 5.627\text{ Å}$) also closely matched the literature value ($a = 5.619\text{ Å}$) (Stingl 1992).

Figure 3. Crystal diffraction spectrum of annealed OsS₂ with comparison to literature peaks (from the ICDD-PDF database).

A sample of the annealed osmium disulfide was sent for elemental sulfur analysis and found to contain 25.12% sulfur, very close to the calculated value of 25.2%. The combined Raman, XRD, and elemental analysis results indicated the OsS₂ was ready for use in target irradiations.

3.2 Target Preparation

Tungsten metal, tungsten trioxide, and osmium metal formed brittle, chalky pellets even at high pressure (41.4 MPa), while the metal disulfides (MoS₂, WS₂, and OsS₂) formed smooth, firmly-packed pellets (**Figure 4**) at a significantly lower pressure (13.8 MPa). The best method for preparing the pressed pellet targets was to directly press the target material into the backing; material loss can occur in the pellet die and while transferring from the pellet die to the backing. Additionally, transferring pellets often resulted in air gaps between the pressed pellet and the wall of the aluminum backing, and resulted in expansion on heating causing the aluminum foil to separate from the target face during irradiation.

(a)

(b)

(c)

Figure 4. Representative thick pressed discs of MoS₂ (a), WS₂ (b), and OsS₂ (c) to demonstrate the compressibility of these materials. Thinner targets were used during the irradiations.

3.3 MoS₂ Target Irradiations

Pressed ^{nat}MoS₂ targets were irradiated with 16 MeV protons for a total of 10 μ Ah and analyzed for activation products by HPGe (**Table 1**).

Table 1. Activities of identified technetium isotopes at the end of bombardment, 102.3 mg ^{nat}MoS₂ target, 77.1 mg·cm⁻², 16 MeV protons, 10 μ Ah.

Isotope	t _{1/2}	Gamma Energy (Intensity)	Primary Production Route(s)	Activity at EOB
^{99m} Tc	6.0067 h	140.5 (89%)	¹⁰⁰ Mo(p, 2n)	1059 μ Ci
⁹⁶ Tc	4.3 d	849 (98%), 812.7 (82%)	⁹⁶ Mo(p, n), ⁹⁷ Mo(p, 2n)	391 μ Ci
⁹⁵ Tc	20.0 h	766 (93.8%)	⁹⁵ Mo(p, n), ⁹⁶ Mo(p, 2n)	1485 μ Ci
^{95m} Tc	61 d	204 (63.2%)	⁹⁵ Mo(p, n), ⁹⁶ Mo(p, 2n)	11.2 μ Ci
⁹⁴ Tc	4.88 h	703 (99.6%)	⁹⁴ Mo(p, n), ⁹⁵ Mo(p, 2n)	1573 μ Ci

The proton irradiation was used to demonstrate the direct production of ^{99m}Tc via the ¹⁰⁰Mo(p, 2n)^{99m}Tc reaction using a small, medical cyclotron and evaluate the MoS₂ target material. As illustrated in **Table 1**, several isotopes of technetium were produced using a natural molybdenum target. Molybdenum has seven naturally occurring isotopes, all with significant abundances (9.25 – 24.13%). In an actual production scenario, an enriched ¹⁰⁰MoS₂ would be used to increase the production yield of ^{99m}Tc and minimize or eliminate the production of the other technetium isotopes. Molybdenum-100 is only 9.63% abundant, thus an enriched target could provide a 10-fold increase in ^{99m}Tc compared to a natural abundance target. An enriched target with similar dimensions to the one used in this irradiation could yield 1.06 mCi/ μ Ah of ^{99m}Tc.

Table 2. Comparison of theoretical and experimental production rates for the ^{nat}MoS₂ target irradiated at MURR.

Isotope	Production Rate (μ Ci· μ Ah ⁻¹ ·g ⁻¹)		Percentage of Theoretical Production
	Theoretical	Experimental	
^{99m} Tc	790	1059	134
⁹⁶ Tc	220	391	178
⁹⁵ Tc	1180	1485	126
^{95m} Tc	7.3	11.2	153
⁹⁴ Tc	2199	1573	71.5

The production rates observed experimentally were compared to the experimental production rates calculated using data from Lebeda 2010 (Lebeda 2010) (**Table 2**), and the production rates are biased slightly high for all isotopes produced except ⁹⁴Tc. This systematic bias suggests the beam current on the target was likely higher than expected. This irradiation demonstrated a suitable rate for the direct production of ^{99m}Tc. The significant production rates for ^{94,95m,96}Tc indicate the necessity for an enriched ¹⁰⁰Mo target.

3.4 MoS₂ Dissolution

The dissolution of molybdenum disulfide was evaluated in various organic and aqueous media, with no dissolution in acetone, ethanol, hexane, or 6 M HNO₃. Only the strong oxidizing agent, 30% H₂O₂, showed signs of dissolution with slow effervescence at the MoS₂-H₂O₂ interface. Molybdenum disulfide is hydrophobic and remained suspended on top of the aqueous solutions until oxidation was initiated by gentle heating (50° C), and then was self-sustaining (exothermic) according to the following reaction (Shigegaki 1988):

A small quantity of a dark colored precipitate was observed following reaction completion, likely molybdenum dioxide generated by the following competing reaction (Shigegaki 1988):

Molybdenum dioxide is violet in color, and appeared black in solution; hot sulfuric acid is required for its dissolution.

The 30% hydrogen peroxide dissolution of MoS₂ was further evaluated alone, and under acidic or basic conditions with gentle heating to initiate the reaction. The basic peroxide solution reacted more vigorously, effervescing significantly more than the other solutions. The production of MoO₂ was observed in each sample. The mass of MoO₂ and the percentage of molybdenum not dissolved were determined. The best overall dissolution of MoS₂ was observed using 30% H₂O₂ with ~92.4% recovered, while the acidic and basic peroxide showed only 81.6% and 80.2% recoveries, respectively.

3.5 WS₂ Target Irradiations

Cross sections for the ^{nat}W(p,x)¹⁸⁶Re reaction have been reported in the literature (Bonardi 2010, Lapi 2007, Tárkányi 2007, Shigeta 1996). There is some discrepancy on the absolute value of the cross section but there is agreement that the optimal cross section is observed at ~10 MeV. SRIM calculations were performed to determine the entry and exit energies for the experimental targets. The energy ranges selected are a good representation of potential irradiation parameters for production. With the intent of transitioning to an enriched target, both 11 MeV and 14 MeV protons were investigated to determine the radionuclidic impurities produced using ^{nat}W at different energies and to determine a cumulative yield for ¹⁸⁶Re production over a broad energy range.

Pressed ^{nat}WS₂ targets were irradiated with protons at 11 or 14 MeV for 10 μAh, and analyzed for Re radioisotopes. The 16 MeV proton beam from the GE PETtrace was degraded using aluminum degraders placed in front of the target. For a natural abundance target, 11 MeV is better due to its larger production cross section. At this proton energy, ¹⁸⁶Re was produced in microcurie quantities and the relative amounts of radioisotopic contaminants of Re were lower (**Table 3**). The irradiation performed using 14 MeV protons had a production rate of ¹⁸⁶Re close to a quarter of the rate observed with the 11 MeV

irradiation and the relative production of $^{181,182,182m,183}\text{Re}$ were all increased; this highlights the necessity of using an enriched ^{186}W target for yield and purity.

Table 3. Activities of identified rhenium isotopes at the end of bombardment of (a) 581 mg $^{\text{nat}}\text{WS}_2$ target, 437.8 mg·cm⁻², 11 MeV protons, 10 µAh and (b) 139 mg $^{\text{nat}}\text{WS}_2$ target, 104.7 mg·cm⁻², 14 MeV protons, 10 µAh.

Isotope	$t_{1/2}$	Gamma Energy (Intensity)	Activity at 11 MeV	Activity at 14 MeV
^{181}Re	20 h	366 (56%)	0.00 µCi	13.6 µCi
^{182}Re	12.7 h	169 (11.4%), 1121 (22.1%)	19.9 µCi	17.3 µCi
^{182m}Re	2.67 d	1121 (32%)	144.3 µCi	103.0 µCi
^{183}Re	70 d	162 (23.3%)	1.7 µCi	1.56 µCi
^{184}Re	38 d	793 (37.7%)	6.38 µCi	1.44 µCi
^{186}Re	3.718 d	137 (9.47%)	21.9 µCi	5.24 µCi

The production rate observed experimentally was compared to the theoretical production rate calculated using data from Tarkanyi et al. (Tárkányi 2007) (**Table 4**). At 11 MeV, the production rate for ^{186}Re (and ^{182}Re) was biased slightly lower than those for many of the others. Ambiguity in the absolute value of the cross section for this reaction in the literature suggests it may be overestimated for the $^{186}\text{W}(p, n)^{186}\text{Re}$ reaction in this energy range. Assuming the lowest cross-section was correct (Lapi 2007), the ^{186}Re production rate would increase to 75% of the theoretical production rate. The observed, experimental production rate for ^{186}Re was significantly closer to the theoretical value at 14 MeV than at 11 MeV. The literature values for the $^{186}\text{W}(p, n)^{186}\text{Re}$ reaction are in close agreement at this energy as the cross section values begin to plateau at higher energies. The target thickness can still be optimized to increase the production rate.

Table 4. Comparison of literature and experimental production rates for the $^{\text{nat}}\text{WS}_2$ target irradiated at (left) 11 MeV and (right) 14 MeV using the MURR PETtrace.

Isotope	Production Rate at 11 MeV (µCi·µAh ⁻¹ ·g ⁻¹)		Percentage of Theoretical Production	Production Rate at 14 MeV (µCi·µAh ⁻¹ ·g ⁻¹)		Percentage of Theoretical Production
	Calc.	Expt.		Calc.	Expt.	
^{181}Re	0.00	0.00	-	106.90	2.34	2.21
^{182}Re	18.29	3.43	18.73	27.64	2.98	10.77
^{182m}Re	40.76	24.84	60.93	33.87	17.73	52.33
^{183}Re	0.82	0.29	35.86	1.27	0.27	21.11
^{184}Re	2.16	1.10	50.80	0.22	0.25	114.29
^{186}Re	24.85	3.77	15.17	2.93	0.90	30.82

Enriched ^{186}W should result in a ^{186}Re production rate nearly 4-fold higher than observed for $^{\text{nat}}\text{W}$ with significant reduction of radioisotopic impurities of Re (**Table 5**). Using enriched ^{186}W , the primary radioisotopic impurity would be ^{182m}Re (2.67 d half-life), whose cross section is significant at this proton energy; a substantial amount will be co-produced. However, the activity produced would still be > 99% ^{186}Re .

Table 5. Comparison of natural abundance tungsten to enriched ^{186}W and the resultant effect to rhenium isotope production rates.

Isotope	Natural Abundance of Target Nuclide	Enriched Target Material	Effective Change
^{180}W	0.12 %	0.01 %	1/12 x original
^{182}W	26.50 %	0.01 %	1/2650 x original
^{183}W	14.31 %	0.01 %	1/1431 x original
^{184}W	30.64 %	0.1 %	1/306 x original
^{186}W	28.43 %	99.9 %	3.5 x original

Once the production method is optimized, enriched ^{186}W will be irradiated; the cost of the enriched target material requires its recovery and reuse. The separation method outlined in Gott et al. (Gott 2014) results in tungsten recovery as the tungstate ion (WO_4^{2-}) in a 1 M NaOH solution. Acidification of this solution resulted in quantitative recovery of tungsten as tungstic acid. A modified method of one outlined by Ramakrishna Matte et al. (Ramakrishna Matte 2010) was used to make and recycle tungsten disulfide. The method involves heating a mixture of tungstic acid and thiourea to generate tungsten disulfide, providing a quick efficient method to recycle the target material. The proposed Re production cycle for WS_2 is illustrated in **Figure 5**. Combining the percent recoveries from each step, it is possible that 89% of the target material can be recovered from each run based on recovery yields from an unirradiated target.

Figure 5. Proposed “Full Circle” Re production process using WS_2 .

3.2 OsS₂ Target Irradiation

Pressed ^{nat}OsS₂ targets were irradiated for 1 hour with a 10 μ A current of 16 MeV protons, which is lower than the 24 MeV optimal reaction energy, but is the maximum proton energy achieved on our GE PETtrace. Under these irradiation conditions, Re radioisotopes were produced in nanocurie quantities while iridium radioisotopes were produced in microcurie quantities (**Table 6**). No detectable quantities of osmium radioisotopes were observed.

Table 6. Identified iridium and rhenium radioisotopes produced from an ^{nat}OsS₂ target (46 mg; 34.7 mg·cm⁻²) with their half-lives, utilized gamma energies, and produced activities at the end of bombardment.

Isotope	t _{1/2}	Gamma Energy (Intensity)	Activity (All aliquots)
¹⁸⁶ Ir	16.64 h	137 (23%), 297 (8.6%)	3.00 μ Ci
¹⁸⁷ Ir	10.5 h	912 (4.3%)	143. μ Ci
¹⁸⁸ Ir	1.72 d	155 (30%), 1210 (6.9%)	10.0 μ Ci
¹⁸⁹ Ir	13.2 d	245 (6%)	9.00 μ Ci
¹⁹⁰ Ir	11.8 d	187 (52%)	1.34 μ Ci
¹⁸⁶ Re	3.718 d	137 (9.47%)	2.20 nCi
¹⁸⁸ Re	17.004 h	155 (15.61%)	0.78 nCi
¹⁸⁹ Re	24 h	216 (5.5%)	6.58 nCi

The production rate observed experimentally was compared to the theoretical production rate calculated using data from the TENDL-2014 database (**Table 7**). For several radionuclides including the one of interest, ¹⁸⁶Re, only a small fraction of the expected radioactivity was produced. A few radionuclides including ^{187,189,190}Ir and ¹⁸⁸Re more closely matched their theoretical production rates. Interestingly, ¹⁸⁹Re was produced from the ¹⁹²Os(p, α)¹⁸⁹Re reaction, and with higher activity than the ¹⁸⁶Re under these irradiation conditions. The ¹⁸⁹Re is another potentially useful theranostic Re isotope (24.3 h; 1.009 MeV β^- ; 216 (5.5%) keV γ). Interestingly, a significant quantity of ¹⁸⁶Ir was produced when the theoretical data from TENDL-2014 suggested that the cross section would be zero at 16 MeV.

Table 7. Comparison of theoretical and experimental production rates for the ^{nat}OsS₂ target irradiated at MURR.

Isotope	Production Rate (μ Ci· μ Ah ⁻¹ ·g ⁻¹)		Percentage of Theoretical Produced
	Theoretical	Experimental	
¹⁸⁶ Ir	0.00	6.45	-
¹⁸⁷ Ir	755.62	307.47	40.69
¹⁸⁸ Ir	267.11	21.50	8.05
¹⁸⁹ Ir	57.23	19.35	33.82
¹⁹⁰ Ir	3.47	2.88	83.14
¹⁸⁶ Re	0.16	0.005	3.01
¹⁸⁸ Re	0.008	0.002	20.12
¹⁸⁹ Re	0.38	0.014	3.72

3.3 Osmium Target Dissolution and Separation

Osmium disulfide dissolves in 12% NaOCl though a significant difference in dissolution rate is noted between the hydrated and anhydrous forms of osmium disulfide. The hydrated form readily dissolves in NaOCl or HNO₃, while the anhydrous form only very slowly dissolves under either set of conditions, even with heating. Liquid-liquid extraction into MEK quickly isolated rhenium from greater than 98% of the iridium isotopes produced (**Table 8**). It is important to allow sufficient time (2-3 minutes) after mixing for the layers to properly separate. Additionally, draining the aqueous layer from the separatory funnel must be performed at a slow flow rate (1-2 mL / minute) to prevent beading on the glass, and loss to the organic phase. Since perrhenate is quickly extracted into the first organic phase, the second organic extraction may be unnecessary and should be treated separately to prevent the reincorporation of iridium impurities. Additionally, the first organic layer should be washed with an additional aliquot of 1 M NaOH as a significant portion of iridium was extracted by the second aqueous wash. This could eliminate the need for a column purification step. The acidic alumina column used to purify the combined organic phases was not effective in removing the iridium impurities. The results discussed in Section 3.4 indicate it may be more appropriate to use a cation exchanger rather than acidic alumina.

Table 8. Percentage of rhenium and iridium isotopes found in aqueous and organic layers, and on the alumina column using the OsS₂ sample quantified in Table 6.

Layer	Rhenium Isotopes	Iridium Isotopes
Aqueous 1	0%	83.32%
Aqueous 2	0%	14.51%
Organic 1	100%	0.04%
Organic 2	0%	2.06%
Acidic Alumina	0%	0.08%

3.4 Optimization of the Purification Method

A small sample of osmium metal was irradiated in the reactor to produce an osmium radiotracer according to the $^{190}\text{Os}(n, \gamma)^{191}\text{Os}$ reaction. The reactor-irradiated osmium sample was dissolved and distilled as described; $\geq 99.9\%$ of the osmium was removed from the NaOCl solution during the distillation. The osmium metal was then converted to the disulfide by the described method and combined with the cyclotron-irradiated osmium disulfide sample for processing. During the extraction process, the aqueous layer turned black upon agitation generating heat. Osmium in oxidation state +8 is a potent oxidizer, and may have catalyzed or facilitated a reaction with MEK under these basic conditions. Reduction of Os(VIII) could generate the insoluble black OsO₂. Sedimentation may allow some of this precipitate to transfer to the organic phase. Yet greater than 89% of the osmium was separated from the rhenium during the MEK extraction. The majority of the transferred osmium was in the second MEK extract. The first MEK layer was divided into aliquots and passed through acidic alumina, silica, and cation exchange sep-paks to further purify the rhenium product. Alumina and silica removed $\sim 83\%$ of the residual osmium transferred with the rhenium while the cation exchanger removed $\sim 95\%$. A cation exchange sep-pak will be utilized in future studies as a secondary clean-up step. The results of this study indicate it is necessary to distill the bulk of the osmium (as OsO₄) from the irradiated sample prior to the MEK extraction to better purify the final Re product. The nearly quantitative removal of osmium during

distillation ensures a high purity rhenium product while simultaneously recovering osmium for reuse in further production of OsS_2 . The proposed Re production cycle using OsS_2 is illustrated in Figure 6.

Combining the percent recoveries from each step, it is possible that 88% of the target material can be recovered from each run.

Figure 6. Proposed “Full Circle” Re production process using OsS_2 .

4 Conclusions

New MoS_2 , WS_2 , and OsS_2 targets were developed for the production of $^{99\text{m}}\text{Tc}$ and ^{186}Re . The results demonstrate the potential use of MoS_2 to directly produce $^{99\text{m}}\text{Tc}$ via proton bombardment at a small, medical cyclotron. The production of ^{186}Re via proton irradiation of WS_2 demonstrated the potential of this production route. Although the proton energies at a small, medical cyclotron are not ideal, the production of ^{186}Re from an OsS_2 target was achieved. The number of technetium and rhenium radioisotopes produced highlights the need for enriched target materials to minimize the co-production of unwanted side-products. The thermal conductivities for the disulfide targets are significantly lower than for their metal analogues and maximum applied currents that can safely be applied will need to be determined. The disulfide targets will require extensive cooling for proper heat dissipation. The metal disulfides are viable target materials, dissolving under mild conditions, and readily recovered for reuse (88-93% recoveries based on natural metal disulfide targets). These targets may be useful for production

via longer, lower-current irradiations with proper cooling. Recycling the metal disulfide targets is significantly easier than regenerating the metal targets of Mo, W and Os.

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Figure Captions

Figure 1. Osmium Distillation Setup

Figure 2. Raman spectrum of an annealed OsS₂ sample.

Figure 3. Crystal diffraction spectrum of annealed OsS₂ with comparison to literature peaks (from the ICDD-PDF database).

Figure 4. Representative thick pressed discs of MoS₂ (a), WS₂ (b), and OsS₂ (c) to demonstrate the compressibility of these materials. Thinner targets were used during the irradiations.

Figure 5. Proposed “Full Circle” Re production process using WS₂.

Figure 6. Proposed “Full Circle” Re production process using OsS₂.