PRODUCTION OF TUNGSTEN-188 AND OSMIUM-194 IN A NUCLEAR REACTOR FOR NEW CLINICAL GENERATORS

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ABSTRACT

Rhenium-188 and iridium-194 are potential candidates for radioimmunotherapy with monoclonal antibodies directed against tumor-associated antigens. Both nuclei are short-lived and decay by high energy ß⁻ emission. In addition, both nuclei emit γ-rays with energy suitable for imaging. An important characteristic is availability of ^{188}Re and ^{194}Ir from decay of reactor-produced parents (^{188}W and ^{194}Os, respectively) in convenient generator systems. The ^{188}W and ^{194}Os are produced by double neutron capture of ^{186}W and ^{192}Os, respectively. The large scale production yields of ^{188}W in several nuclear reactors will be presented. We also report a new measurement for the cross-section of ^{193}Os(n,γ)^{194}Os reaction and discuss the feasibility of producing sufficient quantities of ^{194}Os.

Key words: Radionuclide Generator, ^{188}W/^{188}Re, ^{194}Os/^{194}Ir, Nuclear Reaction Cross-section, Nuclear Reactor

INTRODUCTION

We are currently developing the ^{188}W($t_{1/2}$=70 d)/^{188}Re($t_{1/2}$=17 h)[1-6] and ^{194}Os($t_{1/2}$=6.0 y)/^{194}Ir($t_{1/2}$=20 h)[6,7] biomedical generator systems. The ^{188}Re and ^{194}Ir daughters both decay by emission of high energy ß⁻ particles ($E_ß^{max}$ = 1.89 and 2.24 MeV, respectively) and are potential candidates for therapy.[7-9] The decay of ^{188}Re follows with emission of a predominant 155 KeV γ-ray with moderate intensity (15.8%) which can be efficiently detected with gamma cameras for *in vivo* biodistribution and kinetic studies. The decay of ^{194}Ir follows with emission of a 328 KeV γ-ray (13.0%) which is also within the detection range of gamma cameras. In addition to the emission of an abundant high-energy particle, an appropriate physical half-life and stable daughter, both nuclei have suitable characteristics for protein labeling through bifunctional chelates. Rhenium-188 is of special interest since it is an analogue of Tc and recent advances in the chemistry of Tc for biomedical applications of ^{99m}Tc could in principal be extended to Re.

The ^{188}W and ^{194}Os parent nuclei are produced in a fission nuclear reactor with double neutron capture on ^{186}W and ^{192}Os, respectively, according to the schemes shown in Figure 1a&b. In the case of ^{188}W, we report here large scale production yield of ^{188}W from ORNL-HFIR, BNL-HFBR, MURR and FFTF reactors[#] and compare the theoretical and experimental data. For ^{194}Os production, the thermal neutron capture cross-section of primary reaction, ^{192}Os(n,γ), is well known and is used extensively for neutron activation analysis of Os, however, the reported cross-section for the second reaction, ^{193}Os(n,γ), differs significantly.[10-14] An attempt has been made to resolve this discrepancy and our results are presented in this report.

EXPERIMENTAL

Tungsten-188: Typically, 50 mg of enriched ^{186}W as WO_3 (95% enrichment) was encapsulated in a quartz ampule and irradiated for a period of 21 days (one reactor cycle) in the hydraulic tube of the ORNL-HFIR. Neutron fluxes and other irradiation conditions for various reactors are given in Table 1. After irradiation, the target was generally allowed to decay for a period of 10 days to reduce the ^{187}W activity to a level comparable to that of ^{188}W activity. Subsequently, the quartz ampule was crushed, WO_3 was dissolved in 1.0 M KOH[4] and a small aliquot (~10 µL) was taken for assay.

Osmium-194: An ^{192}Os target (27.1 mg with 99.3% enrichment) encapsulated in a quart ampule was irradiated for one cycle (24 d) at position "Modified V-16" together with 2.0 and 5.5 mg of high purity Fe as flux monitors. The induced radioactivities in the ampules were measured directly without chemical separation. However, due to high levels of radioactivity, it was necessary to allow the samples to decay for a period of about 6 months before the first measurement.

Radioactivity Measurements: A calibrated 50-cm^3 high-purity Ge detector (EG&G ORTEC, Oak Ridge, TN) coupled to a AccuSpec PC-based multichannel analyzer (Nuclear Data/Canberra Inc., Meriden, CT) was used for radioactivity measurements. The activity of ^{187}W and ^{188}W were quantitated by measurement of the intensity of their predominate γ-rays at 685.5 keV (31.6%) and 155.0 (15.4%)[14] keV (from ^{188}Re daughter), respectively. For the determination of ^{194}Os, the 328.4 (13.0%) keV γ-ray (from ^{194}Ir) was

$^{192}Os(n,\gamma)^{193}Os$ reaction and discuss the feasibility of producing sufficient quantities of ^{193}Os.

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#HFIR: High Flux Isotope Reactor, Oak Ridge Nat. Lab.
HFBR: High Flux Beam Reactor, Brookhaven Nat. Lab.
MURR: Missouri University Research Reactor
FFTF: Fast Flux Test Facility, Westinghouse Hanford Co.

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RESULTS AND DISCUSSION

The experimental yields of ^{188}W from four reactors (HFIR, HFBR, MURR, and FFTF) and

available maximum neutron fluxes are given in Table 1. The large-scale production yield of ^{188}W at EOB from the HFIR hydraulic tube at 80 MW power and for one cycle irradiation (~ 21 d) at a thermal neutron flux of 2×10^{15} $n.s^{-1}cm^{-2}$ is 4 mCi/mg of ^{186}W which is lower than the theoretical value by almost a factor of five. However, for a one day irradiation at the HFBR the yield of ^{188}W is lower than the theoretical value by a factor of two. The extent of discrepancy between the theoretical and experimental values cannot be totally attributed to the neutron self-shielding in the target material since the effect was found to be insignificant in the HFBR experiment in which two targets of 5 and 8 mg were irradiated together and the induced activities of ^{188}W were found to vary within 2% (Table 1). The higher yield of ^{188}W from the HFBR versus HFIR, in spite of lower thermal neutron flux, is indicative of some contribution from resonance neutron absorptions in the epithermal region. The neutron flux spectrum is harder in the HFBR core. The low yield of 0.3 mCi/mg at MURR reflects the lower neutron flux. As indicated in Table 1, the yield of ^{187}W at EOB is about 850 times higher than ^{188}W for a 21-d irradiation in the HFIR.

Relative to the cross-section of 1.28 mb for $^{58}Fe(n,\gamma)^{59}Fe$ flux monitoring reaction, a cross-section of ~ 250 b was calculated for the $^{193}Os[n,\gamma]^{194}Os$ reaction. A summary of the reported cross-section for this reaction is given in Table 2. Based on our data 12 mCi of ^{194}Os can be produced by irradiating 25 mg of enriched ^{192}Os for 60 d at HFIR ($\phi_n = 2 \times 10^{15}$ $n.cm^{-2}s^{-1}$) and the production of ^{194}Os at the HFIR is currently being explored.

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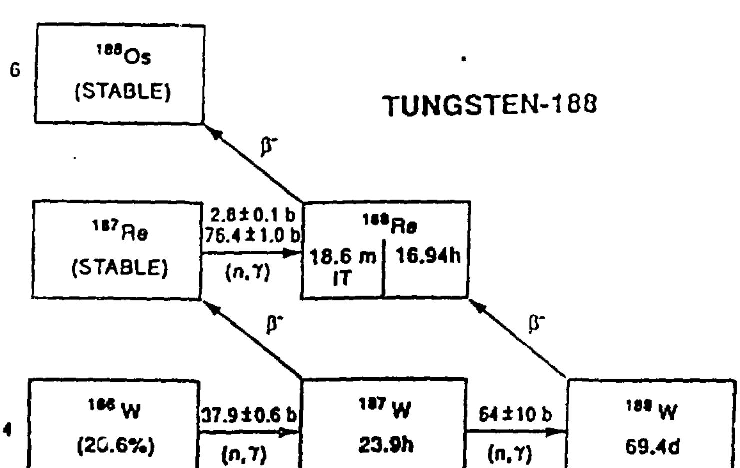

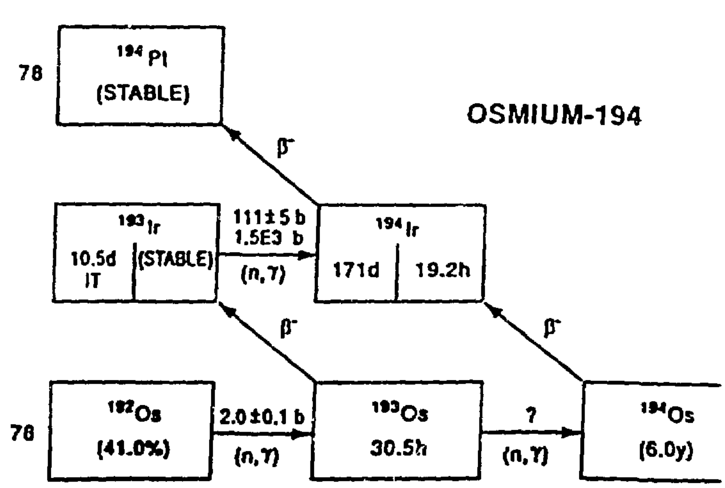

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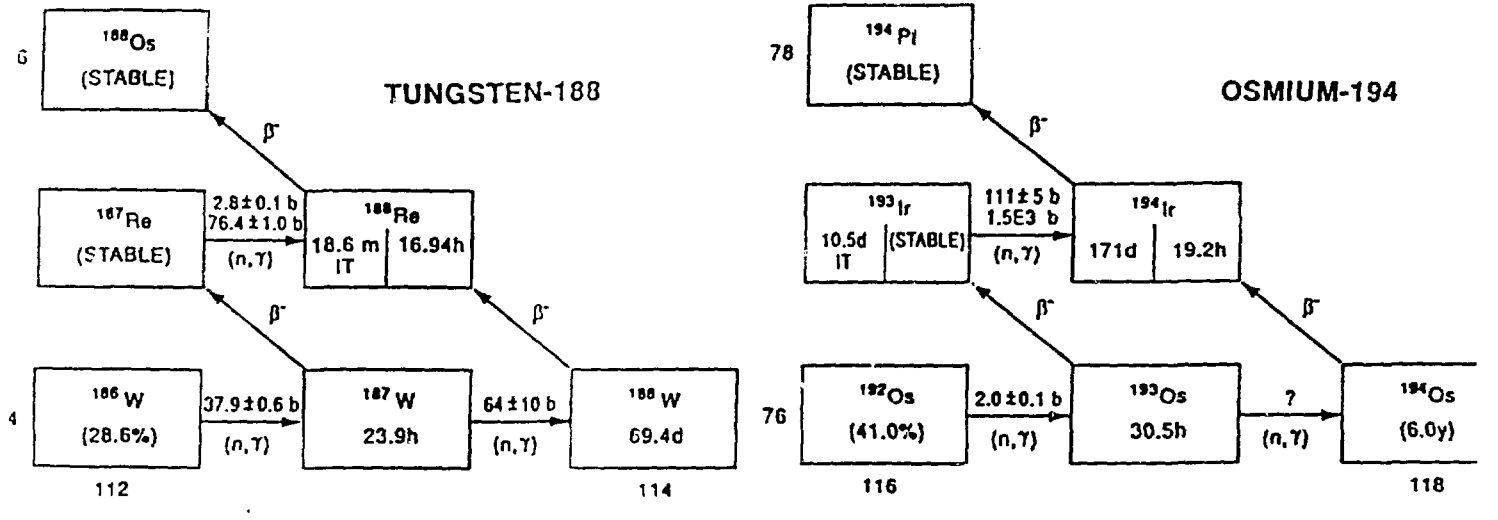

Figure 1a&b. Production Schemes of ^{188}W and ^{194}Os in a Nuclear Reactor

Table 1. **Production of Tungsten-188**

Reactor/ Irradiation position	Power MW	Neutron Flux, $n.s^{-1}.cm^{-2}$ Thermal (2200 ms^{-1})	Fast (> 1 MeV)	Target mass, g as WO_3 (Enrichment, %)	Irradiation Period	Yield, mCi/mg at EOB ^{187}W	^{188}W
HFIR-ORNL							
HT position #5	100	$2.5x10^{15}$	$1 x 10^{15}$	10.3 (97.3)	21 d	NM	4.49
" #5	80	$2 x 10^{15}$	$8 x 10^{14}$	49.2 (96.07)	19.5 d	NM	3.94
" #3	80	$2 x 10^{15}$	$8 x 10^{14}$	50.2 (96.07)	21.1 d	$3.25x10^{-3}$	3.88
" #5	80	$2 x 10^{15}$	$8 x 10^{14}$	50.2 (96.07)	~40 d [b]	NM	6.22
HFBR-BNL							
V-14(core-edge)	60	$8.25x10^{14}$	$9.0x10^{13}$	4.97 (97.06)	24.0 h	8.8	$2.62x10^{-2}$
				8.03 (97.06)	24.0 h	NM	$2.57x10^{-2}$
MURR							
Flux Trap	5	$4.5x10^{14}$	?	92.1 (96.07)	63.4 d	NM	~ 0.3
FFTF-Hanford							
	291	(1-2)x10 [a]	-	14.0 (96.07)	10 d[c]	-	$3.89x10^{-2}$
				12.7 (96.07)	10 d	-	$3.81x10^{-2}$

[a]Epithermal flux, [b]Several short and a 3-d shut down, [c] See reference 17
EOB = End of Bombardment, HT = Hydraulic Tube, NM = not measured

Table 2. Thermal Neutron Capture Cross-section of ^{193}Os

Reactor/ Irradiation position	Thermal Neutron Flux, (2200 ms^{-1}) $n.s^{-1}cm^{-2}$	Target mass, g as Os metal (Enrichment, %)	Irradiation Period	Effective Cross-section, b	References
-					
HFBR-BNL	$4.5x10^{14}$ *	27.1 (99.3)	24 d	240#	this work
ORNL-Graphite	~ $1x10^{12}$	-	-	200	Lindner (1951)[10]
MTR	$3x10^{14}$	50	150 d	8	Williams (1964)[11]
?	?	?	?	1540	Mughabghab (1973)[12]
ILL/GAMS1-3	$8x10^{14}$	84 (99.1)	on-line	38±10	Casten (1978)[13]

*Measured #Relative to the cross-section of 1.28 mb for $^{58}Fe(n,\gamma)^{59}Fe$ flux monitoring reaction

14. Coursey B. M., Calhoun J. M., Cessna J., Hoppes

16. Neutron Cross Sections, (Mughabghab, S. F., Divadeenam M., and Holden N. E.), Vol. 1,

" #5	80	2 x 10^{13}	8 x 10^{1}	50.2 (96.07)	~40 d	NM	
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