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# An Osmium-191/Iridium-191m Radionuclide Generator Using An Oxalato Osmate Parent Complex

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A new osmium-191/iridium-191m ( $^{191}\text{Os}/^{191\text{m}}\text{Ir}$ ) radionuclide generator has been developed that offers high  $^{191\text{m}}\text{Ir}$  yield ( $>20\%/ml$ ) and low  $^{191}\text{Os}$  breakthrough ( $<5 \times 10^{-4}\%/ml$ ) when eluted with a solution of 0.001 M oxalic acid and 0.9% (normal) saline. This is the first  $^{191}\text{Os}/^{191\text{m}}\text{Ir}$  generator that combines the advantages of high  $^{191\text{m}}\text{Ir}$  yield, extremely low  $^{191}\text{Os}$  breakthrough, and an eluate that does not require buffering prior to injection. These improvements in performance were accomplished through use of the chelate *trans*-dioxobisoxalatoosmate(VI) as the parent complex on the generator. The clinical result of the combination of higher yield and lower breakthrough is a 100-fold decrease in the estimated patient radiation dose compared with the same study performed with technetium-99m ( $^{99\text{m}}\text{Tc}$ ), and the injectable eluate makes the generator easier to use. Acute and subacute toxicity studies performed on this generator eluate have shown no adverse effects attributable to the eluate.

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Ultrashort-lived radionuclides (i.e., those with physical half-lives of 5-30 sec) offer a number of advantages for angiocardigraphic studies including very low patient radiation dose, high photon flux, and the ability to perform repeated studies within a short period of time without interference from the background radiation of previous studies.

Although ultrashort-lived radionuclides offer many advantages in these applications, their very short half-lives also impose severe constraints on the generator systems that produce them. As a result of the short half-lives of these radiotracers, conventional dispensing and calibration are not possible. Instead, the radiopharmaceutical is produced by a generator system that is connected to a patient's intravenous line and the ultrashort-lived radionuclide is eluted directly into the patient's vein. The sterility and apyrogenicity requirements of these systems, as a result, are very strict. This mode of administration also imposes the additional limitations on the eluate that it be physiologically compatible (i.e.,

nontoxic, approximately isotonic, and near-neutral pH). The generator must also be able to deliver a sharp bolus (1-2 ml) of the radiotracer at high specific activity within a very short time ( $<2$  sec). Despite these severe constraints, generator systems have been developed for the production of several ultrashort-lived radionuclides, including mercury-195m/gold-195m ( $^{195\text{m}}\text{Hg}/^{195\text{m}}\text{Au}$ ), cadmium-109/silver-109m ( $^{109}\text{Cd}/^{109\text{m}}\text{Ag}$ ), and  $^{191}\text{Os}/^{191\text{m}}\text{Ir}$  (1).

Iridium-191m ( $T_{1/2} = 4.96$  sec) is the daughter of  $^{191}\text{Os}$  ( $T_{1/2} = 15.4$  d,  $\beta^-$ ) and decays by isomeric transition to stable  $^{191}\text{Ir}$  with emission of 129 keV gamma rays (26%) and 65 keV x-rays (56%), both of which may be imaged with Anger-type gamma scintillation cameras and multicrystal cameras. In addition, the x-rays may be imaged with the multiwire gamma camera (2).

The  $^{191}\text{Os}$  parent is produced by neutron irradiation of isotopically enriched  $^{190}\text{Os}$  ( $>96\%$ ) and the 15.4-day half-life of  $^{191}\text{Os}$  permits a useful generator shelf-life of at least 2 wk. The  $^{191}\text{Os}/^{191\text{m}}\text{Ir}$  generator, therefore, has the potential to be quite economical in the clinical setting.

In 1956, Campbell and Nelson reported the chromatographic separation of osmium and iridium using a Dowex-1 column and 6 N HCl as the eluent (3). This

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system was subsequently modified by Yano and Anger (4,5) who attempted to evaluate regional pulmonary blood flow by continuous infusion of  $^{191m}\text{Ir}$ . In 1977, further improvements were made in the generator (6, 7); and the new design generator was used to demonstrate the feasibility of first-pass radionuclide angiocardiology with  $^{191m}\text{Ir}$  in monkeys (8). The first  $^{191}\text{Os}/^{191m}\text{Ir}$  generator suitable for first-pass radionuclide angiographic investigations in human subjects was reported in 1980 (9,10). This generator was used to demonstrate the feasibility of  $^{191m}\text{Ir}$  radionuclide angiocardiology for the detection and quantitation of left-to-right shunts and the measurement of ventricular ejection fraction in pediatric and adult patients (11,12). More recently, this generator was also used to demonstrate that  $^{191m}\text{Ir}$  radionuclide angiocardiology could be used routinely for the measurement of right and left ventricular ejection fraction in adults (13,14). The development of an  $^{191}\text{Os}/^{191m}\text{Ir}$  generator that uses charcoal as an adsorbant for the  $^{191}\text{Os}$  parent has also been reported recently (15) and this generator is currently being used in human studies in Europe. The properties of these generators are summarized in Table 1.

As can be seen from Table 1, each of these generators uses as the parent a chloroosmate complex, either hexachloroosmate(IV) or *trans*-dioxotetrachloroosmate(VI). In each case it can also be noted that the  $^{191m}\text{Ir}$  yield is quite modest and the eluent used with the generator is acidic, hypertonic, or both. The eluates of these generators, because they are not physiologically compatible, must be either buffered or diluted before injection, complicating clinical use of the generator.

In an attempt to avoid these limitations we have investigated generators based on osmium complexes other than hexachloroosmate(IV) and *trans*-dioxotetrachloroosmate(VI). We have previously reported the development of an  $^{191}\text{Os}/^{191m}\text{Ir}$  generator using the malonate complex *trans*-dioxobismalonatoosmate(VI), which has a significantly higher  $^{191m}\text{Ir}$  yield than earlier designs (16). We report herein the properties of a new

$^{191}\text{Os}/^{191m}\text{Ir}$  generator based on the chemically similar *trans*-dioxobisoxalatoosmate(VI) complex.

## MATERIALS AND METHODS

### Production of Osmium-191

Osmium-191 was produced by neutron irradiation of isotopically enriched (>95%)  $^{190}\text{Os}$  metal in either the Oak Ridge National Laboratory High Flux Isotope Reactor (HFIR) or the Brookhaven National Laboratory High Flux Beam Reactor. The details of the production of this isotope have been previously reported (17). A typical irradiation at the HFIR for 3 days at  $\sim 2.5 \times 10^{15}$  n-cm $^{-2}$ -s $^{-1}$  produced 250 mCi of  $^{191}\text{Os}$ /mg of  $^{190}\text{Os}$ .

The isotope was supplied as a solution of potassium perosmate(VIII),  $\text{K}_2[\text{OsO}_4(\text{OH})_2]$ , in 0.4 N KOH.

### Preparation of the Oxalate Complex

Radioactive potassium perosmate solution containing the desired amount of activity was added to 3.7 ml of nonradioactive perosmate solution (0.074 mM) to which 0.1 g (1.8 mmoles) KOH had been previously added. Ethanol (35 ml) was then added to reduce perosmate(VIII) to osmate(VI). The resulting suspension was centrifuged and the excess ethanol decanted from the purple precipitate of potassium osmate(VI),  $\text{K}_2[\text{OsO}_2(\text{OH})_4]$ . The precipitate was washed once with ethanol (35 ml) and dried under a stream of argon or nitrogen. The resulting powder was dissolved in 10 ml 0.1 N KOH and 10 ml of 0.5 M oxalic acid rapidly added. On addition of oxalic acid, the purple color of the osmate(VI) complex was immediately replaced by the golden-brown color of *trans*-dioxobisoxalatoosmate(VI),  $\text{K}_2[\text{OsO}_2(\text{ox})_2]$  (19). The electronic spectrum of this complex is identical to that reported by Preetz and Schulz (19).

### Preparation of the Generator

The generator was constructed from a machined Lucite tube equipped with low dead volume high performance liquid chromatography fittings as previously described (9) with the following exceptions: (1) the anion exchange resin (AG MP-1)\* was converted to the oxalate form prior to being loaded into the column; and (2) a second, "scavenger," column was not required. The solution of the oxalate complex was loaded

TABLE 1  
Performance of  $^{191}\text{Os}/^{191m}\text{Ir}$  Generators\*

Systems	Yield	Breakthrough	Eluent
$[\text{OsCl}_6]^{2-}/\text{Ag1-x8}^\dagger$	10%/3 ml	0.1%	16%–18% NaCl
$[\text{OsCl}_6]^{2-}/\text{AG1-x4}^\ddagger$	4.5%/ml	$2 \times 10^{-2}\%$	8.7% NaCl/pH 2.2
$[\text{OsO}_2\text{Cl}_4]^{2-}/\text{AG MP-1}^\S$	10%/ml	$5 \times 10^{-3}\%$	0.9% NaCl/pH 1.0
$[\text{OsCl}_6]^{2-}/\text{charcoal}^\P$	18%/2 ml	$3 \times 10^{-4}\%$	0.9% NaCl/ 0.025% KI/pH 2.0

\* Yield and breakthrough are expressed as percentage of  $^{191}\text{Os}$  activity in the column.

† Ref. 4.

‡ Ref. 6.

§ Ref. 9.

¶ Ref. 15.

onto the column using a syringe and allowed to equilibrate on the resin overnight.

#### Measurement of Yield and Breakthrough

The  $^{191\text{m}}\text{Ir}$  yield of the system was measured by elution of the generator directly into a polystyrene centrifuge tube placed in the counting chamber of a dose calibrator. The maximum reading obtained was then corrected for decay of  $^{191\text{m}}\text{Ir}$  during instrument response to the maximum reading. This method has the advantage of allowing rapid measurement of generator yield and breakthrough of these generators in the clinical setting. Osmium-191 breakthrough was determined (after decay of  $^{191\text{m}}\text{Ir}$ ) using a dose calibrator for generators containing more than 250 mCi  $^{191}\text{Os}$  or a multichannel analyzer equipped with a NaI(Tl) well-counter for generators with less activity. Iridium-191 yield and  $^{191}\text{Os}$  breakthrough are expressed as a percentage of total  $^{191}\text{Os}$  activity on the generator.

#### Evaluation of the Eluent

The  $^{191\text{m}}\text{Ir}$  yield and  $^{191}\text{Os}$  breakthrough of the system were measured between pH 2 and 8, and as a function of oxalic acid concentration between 0.001 and 0.075M and sodium chloride concentration between 0.10 and 0.75M. The goal was the development of an eluent as physiologically compatible as possible, consistent with high  $^{191\text{m}}\text{Ir}$  yield and low  $^{191}\text{Os}$  breakthrough.

#### Animal Studies

Determination of the biodistribution of the  $^{191}\text{Os}$  breakthrough products of the oxalate generator was complicated by the very low breakthrough of the generator. For example, a 100-mCi oxalate generator with a breakthrough of  $3 \times 10^{-4}\%$  would produce only 0.3  $\mu\text{Ci}$  of  $^{191}\text{Os}/\text{ml}$ , too low a specific activity with which to conduct a biodistribution study. To circumvent this difficulty, a generator was prepared with higher than normal  $^{191}\text{Os}$  breakthrough and the eluate of this generator was used for the biodistribution studies.

The distribution of the  $^{191}\text{Os}$  breakthrough products was determined in male CD-1 mice at time points ranging from 1 to 28 days. Animals were injected via the tail vein with 0.2 mL of generator eluate containing  $\sim 0.5 \mu\text{Ci}$   $^{191}\text{Os}$ . The animals were then killed by ether overdose, and selected organs were excised, weighed, and counted in a NaI(Tl) well counter. The percent injected dose per organ and the percent injected dose per gram of tissue were then calculated by comparison of these values with an appropriate standard. Determination of the biodistribution of  $^{191\text{m}}\text{Ir}$  is precluded by its extremely short half-life. Absorbed dose estimates were made using the MIRD technique (20).

Acute toxicity studies were conducted using CD-1 female mice. The animals were divided into three groups and injected via the tail vein with: (a) generator eluate equal to ten times the expected dose to a 12.5-kg child; (b) generator eluate equal to 100 times the dose to a 12.5-kg child; or (c) normal saline (as a control). On Days 1, 5, and 7 postinjection, randomly selected animals were used for the collection of blood and urine samples. On Day 7, all remaining animals were killed, blood samples were obtained by cardiac puncture, and the animals were examined for gross pathologic changes.

Subacute toxicity studies were also performed using CD-1 female mice. The animals were divided into three groups and injected on each of 11 consecutive days with: (a) generator

eluate equal to five times the expected dose to a 12.5-kg child; (b) generator eluate equal to 50 times the expected dose to a 12.5-kg child; or (c) normal saline (as a control). On Day 12, the animals were killed and ten animals randomly selected from each group were prepared for histopathologic examination. In addition, blood and urine samples were collected before the initial injection and at Days 1, 7, and 11 after the initial injection.

## RESULTS

The  $^{191\text{m}}\text{Ir}$  yield of the generator was found to be independent of eluent pH within the range 2–8. A decrease in  $^{191}\text{Os}$  breakthrough was observed, however, at pH 4. The higher breakthrough observed at pH 2 was presumably a result of the higher ionic strength of the pH 2 solution, whereas, the higher breakthrough at pH 6 and 8 may be attributed to hydrolysis of the parent oxalato osmate complex. This latter possibility is consistent with observations of the electronic spectrum of the *trans*-dioxobisoxalatoosmate(VI) complex where marked changes were observed above pH 5. The  $^{191\text{m}}\text{Ir}$  yield of the generator was found to increase at higher sodium chloride concentrations. However, this advantage was offset by a larger increase in  $^{191}\text{Os}$  breakthrough. At constant sodium chloride concentration (0.154M), changes in oxalic acid concentration had little effect on either  $^{191\text{m}}\text{Ir}$  yield or  $^{191}\text{Os}$  breakthrough except in the absence of oxalic acid where the breakthrough more than doubled, presumably due to hydrolysis of the parent complex either because of the higher (neutral) pH of the isotonic saline solution and/or the absence of excess ligand.

On the basis of these observations a solution of 0.001 M oxalic acid/0.154 M (0.9%) saline was chosen as the eluent for the generator. The pH of this solution was found to be 3.5, a result that offers a balance between the increased breakthrough of  $^{191}\text{Os}$  at low pH due to the higher ionic strength and increased breakthrough of  $^{191}\text{Os}$  at higher pH due to hydrolysis of the oxalato osmate complex. A significant advantage of this result is that the solution is approximately isotonic. This eluent provides an initial  $^{191\text{m}}\text{Ir}$  yield of 30%/ml and  $^{191}\text{Os}$  breakthrough of  $3 \times 10^{-4}\%/ \text{ml}$ .

A wide range of anion exchange materials was evaluated for use in the oxalate generator including organic resins, inorganic exchangers (e.g., alumina, tin oxide, etc.) and activated charcoal. None of these materials were found to be superior to AG MP-1. Although an inorganic exchanger would be preferred in this application because of the inherently superior resistance of these materials to ionizing radiation, previous studies in our laboratory have found no evidence of degradation of the AG MP-1 resin at column loadings of up to 1 Ci of  $^{191}\text{Os}$  (9).

The yield and breakthrough of the generator were

also measured as a function of elution volume and generator age. As stated above, a 1-ml bolus elution of this system results in an initial  $^{191m}\text{Ir}$  yield of 30% with  $^{191}\text{Os}$  breakthrough of  $3 \times 10^{-4}\%$ . The  $^{191m}\text{Ir}$  yield is approximately twice that of the chloro (9) or charcoal generators (15), while the  $^{191}\text{Os}$  breakthrough is less than one-tenth that of the chloro generator and equivalent to that of the charcoal design.

The yield of this generator is not constant, however, but decreases slowly with time from an initial value of  $\sim 30\%/ml$  to  $\sim 16\%/ml$  after 15 days (Table 2). Even at this lower value, however, the yield for a 1-ml elution is greater than that of the chloro generator and approximately the same as that obtained from the charcoal generator with a 2-ml elution volume. After 2 wk, a 2-ml elution of the oxalate generator gives an  $^{191m}\text{Ir}$  yield of  $\sim 25\%$ . The breakthrough tends to decrease slightly through this period from  $4\text{--}5 \times 10^{-4}\%$  to  $\sim 2 \times 10^{-4}\%$ .

The decreasing yield of the generator over time is presumably due to radiolysis of the parent oxalatoosmate complex. A similar result was observed for the generator prepared using the malonato complex (16). Although photolytic decomposition was not reported by Preetz and Schultz for the oxalato complex (19), this explanation is reasonable in view of the chemical similarity of the malonato and oxalato complexes and the extremely high photon flux present in the generator (as gamma rays and x-rays). This hypothesis is also supported by the observation that the rate of decrease of  $^{191m}\text{Ir}$  yield with time is a function of total  $^{191}\text{Os}$  activity in the column; those columns containing lower amounts of  $^{191}\text{Os}$  did not show as rapid a decrease in  $^{191m}\text{Ir}$  yield.

The toxicity study on the eluate of the oxalate generator revealed no changes in blood or urine attributable to injection of the eluate, and histopathologic examination of the carcasses, likewise, revealed no anatomic changes due to injection of the eluate.

The results of the biodistribution study (Table 3) were used to estimate the radiation dose to a patient resulting from a single radionuclide angiogram (Table 4). These data clearly show the superior dosimetry characteristics of the eluate of the oxalate generator in comparison with the eluate of the chloro generator and the current standard procedure using  $^{99m}\text{Tc}$ .

The more favorable dosimetry characteristics of the oxalate generator eluate are partly attributable to more rapid clearance of the  $^{191}\text{Os}$  breakthrough products from the body but, to a greater extent, to the much lower breakthrough and higher yield of the new generator. A difference in the clearance rate of the breakthrough products is not an unexpected result, because the use of a different chemical form of the osmium parent would be expected to lead to different chemical forms of osmium in the generator eluate, which in turn, would behave differently in vivo (16).

**TABLE 2**  
 $^{191m}\text{Ir}$  Yield and  $^{191}\text{Os}$  Breakthrough of a Typical Oxalate Generator versus Time\*

Day	Yield (%)	Breakthrough (%)
1	32	$3.8 \times 10^{-4}$
2	23	$2.3 \times 10^{-4}$
3	23	$1.4 \times 10^{-4}$
4	20	$1.3 \times 10^{-4}$
5	19	$1.3 \times 10^{-4}$
6	19	$1.3 \times 10^{-4}$
7	18	$1.2 \times 10^{-4}$
8	18	$2.0 \times 10^{-4}$
9	17	$1.3 \times 10^{-4}$
10	17	$9.7 \times 10^{-5}$
11	17	$9.4 \times 10^{-5}$
12	16	$1.0 \times 10^{-4}$
13	16	$1.2 \times 10^{-4}$
14	16	$1.3 \times 10^{-4}$
15	16	$1.2 \times 10^{-4}$

\* Total  $^{191}\text{Os}$  activity on column 4.5 mCi on Day 1, elution volume 1 ml. Yield and breakthrough expressed as percent of total  $^{191}\text{Os}$  activity on the generator.

The contribution of  $^{192}\text{Ir}$  ( $T_{1/2} = 74.3$  days) to the estimated dose has not been included because it is assumed that this impurity will be removed either by prewashing of the column (21) or distillation of the starting material to remove nonosmium impurities (22). Implementation of either of these procedures is particularly important in view of the unfavorable dosimetric characteristics of  $^{192}\text{Ir}$  and the resulting contribution of  $^{192}\text{Ir}$  to the absorbed radiation dose (23). Prewashing of the column has been found to be an effective method of removing  $^{192}\text{Ir}$  in earlier designs of the  $^{191}\text{Os}/^{191m}\text{Ir}$  generator (11).

## DISCUSSION

These results demonstrate the importance of the chemical form of the parent radionuclide in the development of a generator system. In this case, the use of a nonchloro osmium complex has led to the development of the first  $^{191}\text{Os}/^{191m}\text{Ir}$  generator with a directly injectable eluent. The more physiologic pH of the eluate of the oxalate, compared with the chloro and charcoal systems, simplifies clinical use of the generator because buffering of the eluate is not required before injection (Fig. 1). The  $^{191m}\text{Ir}$  yield of this generator is significantly higher than that of other  $^{191}\text{Os}/^{191m}\text{Ir}$  generator designs and, although the yield decreases slowly with time, it remains higher than that of other  $^{191}\text{Os}/^{191m}\text{Ir}$  generators throughout the life of the generator. The  $^{191}\text{Os}$  breakthrough of the generator remains extremely low throughout the entire period.

The ability of the oxalate generator to produce high specific activity  $^{191m}\text{Ir}$  makes it suitable for radionuclide

**TABLE 3**  
Biodistribution of <sup>191</sup>Os Breakthrough Products (Percent Injected Dose/Organ)\*

Organ	Time (post injection)										
	15 min	30 min	1 hr	4 hr	1 day	2 days	3 days	1 wk	2 wk	3 wk	
Blood	6.6 (1.6)	4.4 (2.0)	7.6 (0.4)	6.7 (1.7)	2.0 (0.6)	1.7 (0.3)	0.43 (0.08)	0.15 (0.03)	0.16 (0.06)	0.05 (0.03)	
Bone	24 (4)	20 (4)	22 (3)	38 (10)	31 (2)	24 (1)	23 (5)	24 (1)	20 (4)	20 (3)	
Fur/skin/fat	18 (3)	12 (5)	14 (2)	14 (7)	11 (1)	10 (1)	7.2 (2.2)	6.2 (0.9)	4.0 (0.4)	3.5 (1.1)	
Muscle	12 (3)	8 (3)	10 (1)	9.8 (2.3)	5.9 (2.0)	5.3 (1.4)	3.1 (0.6)	2.7 (0.3)	1.9 (0.5)	1.3 (0.4)	
Heart	0.23 (0.09)	0.16 (0.07)	0.22 (0.04)	0.18 (0.04)	0.10 (0.02)	0.08 (0.01)	0.05 (0.02)	0.04 (0.01)	0.03 (0.01)	0.02 (0.00)	
Liver	10 (3)	13 (3)	8.2 (0.4)	8.9 (1.9)	7.6 (0.6)	6.7 (0.3)	5.3 (0.6)	4.4 (0.2)	3.6 (0.7)	2.3 (0.3)	
Spleen	0.22 (0.06)	0.25 (0.10)	0.43 (0.14)	0.47 (0.12)	0.66 (0.05)	0.71 (0.09)	0.41 (0.05)	0.44 (0.03)	0.43 (0.05)	0.34 (0.04)	
Lungs	4.4 (0.8)	3.8 (1.2)	2.2 (0.3)	1.7 (0.3)	0.69 (0.04)	0.48 (0.05)	0.34 (0.05)	0.27 (0.03)	0.20 (0.05)	0.12 (0.01)	
Brain	0.09 (0.01)	0.06 (0.02)	0.08 (0.01)	0.06 (0.01)	0.03 (0.01)	0.03 (0.01)	0.02 (0.01)	0.01 (0.01)	0.01 (0.01)	0.01 (0.01)	
Stomach	0.41 (0.09)	0.28 (0.14)	0.33 (0.05)	0.27 (0.09)	0.21 (0.03)	0.19 (0.12)	0.08 (0.02)	0.07 (0.01)	0.05 (0.01)	0.04 (0.01)	
Intestine	3.0 (0.6)	2.6 (1.2)	2.6 (0.2)	3.1 (3.0)	1.5 (0.4)	0.94 (0.13)	0.52 (0.10)	0.34 (0.04)	0.24 (0.07)	0.16 (0.03)	
Kidney	6.7 (2.2)	6.6 (1.8)	5.0 (1.5)	5.4 (3.0)	3.4 (0.4)	1.7 (0.4)	1.5 (0.3)	1.2 (0.3)	0.65 (0.17)	0.35 (0.07)	

\* Estimated s.d. in parentheses.

**TABLE 4**  
Whole-Body Radiation Absorbed Dose

System	Absorbed dose	
	Per study	Per mCi
<sup>191m</sup> Ir (oxalate) <sup>†</sup>	2.2 mR	0.018 mR
<sup>191m</sup> Ir (charcoal) <sup>†</sup>	2.6 mR	0.021 mR
<sup>191m</sup> Ir (chloro) <sup>‡</sup>	63.0 mR	0.51 mR
<sup>99m</sup> Tc <sup>§</sup>	240.0 mR	12.00 mR

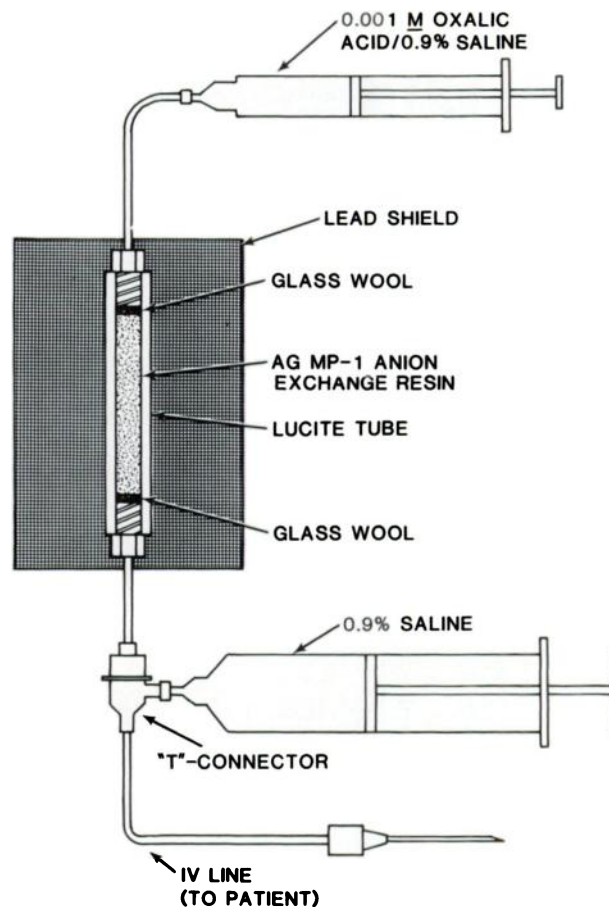
<sup>†</sup> Total <sup>191</sup>Os activity in column 500 mCi; <sup>191m</sup>Ir yield 25%; <sup>191</sup>Os breakthrough  $5 \times 10^{-4}\%$ ; 1 ml bolus.

<sup>‡</sup> Data from Ref. 15, adjusted for 125 mCi bolus.

<sup>§</sup> Total <sup>191</sup>Os activity in column 750 mCi; <sup>191m</sup>Ir yield 10%; <sup>191</sup>Os breakthrough  $5 \times 10^{-3}\%$ ; 1 ml bolus (9).

<sup>¶</sup> 20-mCi <sup>99m</sup>Tc as pertechnetate.

angiocardiographic applications where small bolus volumes are required (e.g., for small children). In adults, the higher <sup>191m</sup>Ir yield of this generator design offsets loss of <sup>191m</sup>Ir due to decay during pulmonary transit. In both cases, the dosimetry characteristics of <sup>191m</sup>Ir are clearly superior to those of <sup>99m</sup>Tc for first-pass radionuclide angiography. A series of clinical studies using the oxalate generator recently has been undertaken in



**FIGURE 1**  
Schematic drawing of oxalate generator.

order to more fully explore potential clinical applications of  $^{191\text{m}}\text{Ir}$  angiocardigraphy.

Having demonstrated the importance of the chemical form of the osmium parent to the development of a useful radionuclide generator, we are continuing the evaluation of other osmium complexes that might offer higher  $^{191\text{m}}\text{Ir}$  yield without the limitation of photolytic decomposition of the complex.

## NOTES

\* Bio-Rad, Rockville Center, NY.

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