## Technical Article

# Experimentation and Modeling of Electrodeposition of Rhenium-188 (<sup>188</sup>Re) on Medical 316L Stainless Steel Wires

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Electrodeposition experiments on stainless steel wires were performed in order to characterize the conditions for the codeposition of a radioactive isotope and cobalt. Adding the radioactive isotope Rhenium-188 (188 Re) enabled us to characterize some of the properties of the electrodeposited binary alloy layer without direct contact or destructive testing. The electrodeposition process was modeled and the formula derived for the case where the change of radioactivity concentration during the electroplating process can be neglected and for the case where concentration changes must be taken into account. Radioisotopes as markers also allow easy testing for homogeneous coating thickness and surface defects of the electrodeposited layer using autoradiography combined with image analysis. Our results will be directly applied to the preparation of radioactive <sup>188</sup>Re stents for lung cancer treatment. They might also be useful in the research and development of novel electroplating processes.

Lung cancer patients often have the tumor grow into the main bronchial airways and severely constrict breathing. Mostly inoperable, the only method of improving quality of life and extending survival times for lung cancer patients is to place a stent, which is a metallic or polymeric coil, in the stenosed area (Fig. 1).<sup>1</sup> We investigated ways of further improving the situation and attempting to

### Nuts & Bolts: What This Paper Means to You

This paper brings forth another emerging application for electroplating technology, in the medical field. Specifically, it deals with the codeposition of a radioactive isotope rhenium-188 with cobalt. The application is in the preparation of radioactive stents for lung cancer treatment. The amount of rhenium must be critically controlled, enough to do the job, but not too much. An indepth analysis of the theory behind the process is given for those wishing to go further.



Figure 1–View of a radioactive stent placed in the left main bronchus of a dog's airways during toxicity testing. The ramifications in the left bronchus are nicely visible.

get rid of the tumor cells by making the stents radioactive and thus locally irradiating the cancerous tissue. For this purpose, radioactive rhenium-188 (<sup>188</sup>Re) is electroplated together with cobalt onto stainless steel or nitinol stents in an automated fashion.<sup>2,3</sup>

A central issue in preparing radioactive stents is to make sure that the final implanted product is within 10% of the target radioactivity, thus ensuring an appropriate and legal radiation dose. Using a short-lived radioisotope like <sup>188</sup>Re with a half-life of 17 hr, this is especially important, because any delay of more than 3 hr will make the radio-

\* Corresponding author: Dr. Huixiong Zhang Department of Radiation Oncology The Cleveland Clinic Foundation Cleveland, OH 44195 Email: johnzhang\_oh@yahoo.com active implant worthless. We investigated and optimized the electroplating parameters using surgical-grade stainless steel wires, a low cost alternative to the expensive stents. Important parameters such as plating current density, wire surface area, electroplating time and radioactive solution concentration were investigated. In this work, we report ways of controlling the amounts of electrodeposited radioactivity. A major advantage of our system is that one component in the electrodeposited alloy, <sup>188</sup>Re, can be precisely analyzed by radioactivity measurements without touching or destroying the electrodeposited alloy layer.

### Experimental

All electroplating experiments were carried out with the automated electroplater developed by us and described in detail elsewhere.<sup>4,5</sup> The system is capable of controlling electroplating currents, plating times and can automatically change the plating solution and perform rinses. A user-friendly graphical interface developed with appropriate software<sup>\*\*</sup> controls a data acquisition board, <sup>\*\*\*</sup> which in turn performs a sequence of requested electroplating operations. The radioactive electroplating solution was prepared by mixing a 0.44M cobalt chloride solution buffered to pH 4.0 with boric acid (H<sub>3</sub>BO<sub>3</sub>) with the radioactive isotope <sup>188</sup>Re in the form of perthenate ReO<sub>4</sub><sup>-</sup> at a concentration of up to 74 MBq/mL. <sup>\*\*\*\*</sup> The radioactive β-emitter <sup>188</sup>Re was eluted daily from a <sup>188</sup>W/<sup>188</sup>Re-generator.<sup>6</sup>

The electroplating chamber used in this study was a 10-mL syringe with a diameter of about 0.8 cm (0.32 in) in which the anode made from platinum spirals along the wall and is protected from direct contact with the cathode (wires) by a layer of polyethylene mesh. In our later experiments for the preparation of radio-active stents, the chamber was chosen based on the stent size. In order to accommodate the largest stent (diameter = 16 mm; 0.63 in) a 60-mL syringe was needed. To plate objects other than stents, *e.g.*, metal foils, the shape of the plating chamber can be designed accordingly. We chose syringes because they are cheap, sterile, easy to obtain and their cylindrical shape fits perfectly with our purpose of electroplating wires and stents for clinical application.

The 0.464-mm (0.018-in) diameter stainless steel wires<sup>†</sup> were clamped directly to a small, gold-coated test clip connected to the cathode and hung in the center of the plating chamber. The electroplating conditions were varied from current densities of 1.0 to 8.4 A/dm<sup>2</sup> (9.3 to 78.0 A/ft<sup>2</sup>) and plating times of 45 to 300 sec. Our electroplater supports currents up to 2 A with a resolution of 0.01 mA between 0.0 and 80 mA, and 0.5 mA between 80 and 2000 mA. All wires were of the same length  $\pm$  1 mm, and the current density could thus be calculated precisely. The activity of all solutions and the radioactive wires was measured in a calibrated ionization chamber.<sup>††</sup>

Autoradiography was performed by placing the electroplated samples directly on a radiation sensitive storage phosphor screen covered with a piece of polyvinyl chloride laboratory wrap to prevent any contamination. After 5 min (or less, depending on the amount of activity), the phosphor screen was analyzed in a phosphor imager.<sup>†††</sup>

### **Results and discussion**

### Influence of electroplating time

At constant electroplating current density and solution radioactivity concentration, the radioactivity deposited on the wires increased with electroplating time, as shown in Fig. 2.



Figure 2–Radioactivity deposited on a 30-mm (1.18-in) long stainless steel wire at a current density of 8.4 A/dm<sup>2</sup> (78.0 A/ft<sup>2</sup>) depends linearly on the electroplating time (R = 0.992). The electroplating solution concentration was 2.5 MBq/mL.

### Influence of electroplating current

In our experimental range [solution radioactivity concentration 2 to 50 MBq/mL; electroplating current density 2.0 to 12.0 A/dm<sup>2</sup> (18.6 to 111.5 A/ft<sup>2</sup>)], at constant radioactivity concentration in our targeted range, the radioactivity electrodeposited on the wires did not depend on the electroplating current density, as shown in Fig. 3. This result confirmed that the electrodeposition of the rhenium ions was under mass transfer control. With increasing current, more cobalt ions would be electrodeposited but the mass transfer resistance limited the rhenium-electrodeposition rate.



Figure 3—Radioactivity deposited on 30-mm (1.18-in) long 0.464-mm (0.018-in) diameter stainless steel wires. The radioactivity deposited after 60 sec of electroplating is almost independent of the current density (R = 0.93) in the experimental range. The electroplating solution concentration was 3.7 MBq/mL.

<sup>\*\*</sup> Visual Basic 6.0, Microsoft Corporation, Redwood, CA.

<sup>\*\*\*</sup> ADAC MF5500, IOtech Inc., Cleveland, OH.

<sup>\*\*\*\*</sup> The Becquerel (Bq) is the derived unit of radioactivity in the International System of Units (SI), equal to one disintegration or nuclear transformation/sec.

<sup>&</sup>lt;sup>†</sup> Ethicon DS-25, Ethicon, Inc., Div. of Johnson & Johnson, Somerville, NJ.

<sup>&</sup>lt;sup>††</sup> Radcal Dose Calibrator; Radcal Corp., Monrovia, CA.

<sup>&</sup>lt;sup>†††</sup> Cyclone Phosphor Imager, PerkinElmer, Boston, MA.

## Influence of solution radioactivity concentration on the radioactive electroplating efficiency factor

For our experimental <sup>188</sup>Re radioactivity concentration range of 2.0 to 44 MBq/mL and an electroplating current density of 8.4 A/dm<sup>2</sup> (78.0 A/ft<sup>2</sup>), the radioactive electroplating efficiency factor was nearly proportional to the solution radioactivity concentration C (in MBq/mL), as shown in Fig. 4. The experimentally-found radioactive electroplating efficiency factor *f* was 2.01 ×10<sup>-2</sup> × C  $-4.0 \times 10^{-2}$  MBq/coulomb with a good fit through the experimental values (R = 0.999). Our experimental results confirmed that the plated radioactivity was negligible when compared to the total radioactivity in solution. Mathematically, the fit indicated that rhenium electrodeposition took place under mass transfer control and can be described by Case 1 and Equation (2) in the Appendix. Case 1 can be used to control the electrodeposited radioactivity when the deposited amount is negligible (or considerably less than 5%) of the total available radioactivity in the plating solution.



Figure 4—Electroplating efficiency depends linearly on the radioactivity concentration (R = 0.999). The current density was kept constant at 8.4 A/dm<sup>2</sup> (78.0 A/ft<sup>2</sup>). The stainless steel wires were 450 mm (17.7 in) long and had a diameter of 0.464 mm (0.018 in).

## Situation where the concentration in solution changes during the plating process

The high cost of the to-be electroplated materials, their low availability, poor solubility or, for our targeted application, radiation safety aspects, might require that the amount of material to be deposited from the solution be as high as possible within a reproducible range. Also, by extending the electroplating times, the amounts of radioactivity deposited will be non-negligible and could exceed 5% of the radioactivity in the total plating solution. This is Case 2 described in the Appendix. In Fig. 5, we compared the experimentally determined <sup>188</sup>Re deposition to the values expected from Case 1, or more exactly, the process described in Equation (2) from the Appendix to the process described in equation (9). Equation (9) better predicts radioactivity deposition over longer times when compared to Equation (2). We were able to predict the electrodeposited radioactivity within 10% when the target radioactivity was less than 12.5 % of the total radioactivity in solution. Further improvements on the prediction are expected by stirring the electroplating solution. This was not done in the current work because of the small size of the electroplating chamber [0.8cm (0.32-in) diameter], thus probably violating the assumption that radioactivity was evenly distributed in solution. The radioactivity concentration in the solution close to the wire surface was therefore probably lower than the concentration further from the wire



Figure 5–Comparison of predicted and measured radioactivity on stainless steel wires. The electroplating solution concentration was 3.05 MBq/mL. The wires used were 450 mm (17.7 in) long and had a diameter of 0.142 mm (0.006 in).

surface. This might explain why the deviation between our model in Equation (9) and the experimental results increased with larger targeted radioactivity amounts.

### Homogeneity of the electrodeposited layer

Using radioactive isotopes, it was possible to measure the radioactivity distribution on the electrodeposited alloy layer simply by placing the radioactive material on a radiosensitive film and then developing or scanning the resulting picture, followed by image analysis (Fig. 6).



Figure 6-Homogeneity testing of the radioactive coating by autoradiography. The electroplated right wire clearly contains two defects (arrows) in the radioactive coating. These defects were confirmed by electron microscopy.

### Conclusions

As a preliminary study for the preparation of radioactive stents, we electroplated a Co/188Re alloy on stainless steel surgical wires. The use of the radioactive element <sup>188</sup>Re allowed us to differentiate efficiently and precisely the two elements (cobalt and rhenium) in the electrodeposited alloy layer. It was found that during the process, the electrodeposition of the rhenium ions was under mass transfer control. After accounting for concentration changes in the radioactive solution during the electroplating process, we were able to control the radioactivity electrodeposition in a reliable and repeatable way. A more general use of radioactive electroplating would be its use for the characterization of the amount of an electroplated species and the investigation of its homogeneous distribution using a radioactive tracer substance. Radioactive electroplating thus would not only be clinically useful in radiation therapy of cancer, but also could facilitate a quick way of checking how homogeneously coated a plated surface is. Using short-lived radioisotopes such as the clinically used 99mTc or the described 188Re would render the materials and solutions non-radioactive within a short time (2 to 7 days).

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### **Appendix: Data Analysis and Derivations**

During the electroplating process, ions of radioactive isotope (<sup>188</sup>Re) are deposited on the cathode surface (target wire). The radioactivity concentration of the solution and the rate of radioactivity deposition will therefore change during the process as a result of the change in solution concentration. In the following we will analyze two cases. In the first case, the amount of radioactivity electrodeposited onto the cathode surface is negligible compared to the total amount of radioactivity electrodeposited onto the cathode surface is negligible compared to the total amount of radioactivity electrodeposited onto the cathode surface is larger than 5% of the total amount of radioactivity in the plating chamber and must be taken into account.

#### *Case 1*: Change of radioactivity concentration during the electroplating process can be neglected.

The radioactive electroplating efficiency factor f (in MBg/ coulomb) can be determined at constant current density by directly dividing the electrodeposited radioactivity on the cathode by the amount of electricity used. The following analysis is valid for a constant electroplating current density. The perrhenate ( $\text{ReO}_4^-$ ) concentration for the radioactive electroplating solution with 2 to 50 MBq of <sup>188</sup>Re per mL is lower than 10<sup>-7</sup>M, which is much lower than the cobalt concentration of 0.44M. The electrodeposition of rhenium is thus most likely under mass transfer control, in which both the diffusivity of the perrhenate and the average distance for the perrhenate to travel from the bulk liquid phase to the stainless steel surface is constant over the entire perrhenate concentration range. The rhenium deposition rate is thus expected to be proportional to the bulk liquid phase radioactivity concentration. However, this perrhenate concentration must exceed a threshold before the radioactive rhenium is electrodeposited. With this in mind, the radioactivity electrodeposition efficiency factor f can be expressed generally as:

$$f = aC - b \tag{1}$$

where a and b are positive constants and C is the radioactivity concentration of the solution in (MBq/mL). Without considering the radioactivity concentration change during the electroplating process, the radioactivity amount R electrodeposited on the wire is:

$$R = \int_{0}^{t} Ifdt = Itf_{0} = ItA$$
<sup>(2)</sup>

with

$$\mathbf{A} = f_0 = aC_0 - b \tag{3}$$

where  $C_0$  is the radioactivity concentration at the beginning of the radioactive electroplating process and  $f_0$  is the radioactive electroplating efficiency factor based on the initial radioactivity concentration.

*Case 2:* Change of radioactivity concentration during the electroplating process cannot be neglected and must be taken into account

When more than 5% of the radioactivity needs to be deposited, the radioactivity concentration of the radioactive electroplating solution will change dramatically during the electroplating process, as will the radioactive electroplating efficiency factor. The continued use of Equation (3), which does not consider the radioactivity concentration during the radioactive electroplating process, will thus cause significant errors between predicted and deposited amounts. To prevent these errors, the concentration is taken into account and described in the following paragraphs as Case 2.

The radioactivity concentration C changes as a function of time and the initial radioactivity concentration  $C_0$  during the electroplating process:

$$C = \frac{C_0 V - \int_0^t If dt}{V} = C_0 - \frac{I \int_0^t f dt}{V}$$
(4)

where V is the volume of the radioactive solution and I is the electroplating current. Equation (4) is based on the assumption that the radioactivity is always homogeneously distributed throughout the total electroplating solvent volume. By substituting equation (4) into Equation (1) we get Equation (5), which describes the relation between the radioactive electroplating factor and the electroplating time.

$$f = aC - b = a \left( C_0 - \frac{I \int_0^t f dt}{V} \right) - b = (aC_0 - b) - \frac{aI}{V} \int_0^t f dt = A + B \int_0^t f dt$$

where,

$$A = aC_0 - b$$
$$B = -\frac{aI}{V}$$

and the boundary condition at t = 0 is

$$f = aC_0 - b = A \tag{6}$$

By differentiating equation (5) with time we get

$$\frac{df}{dt} = Bf \Rightarrow \frac{df}{f} = Bdt \Rightarrow f = Ze^{Bt}$$
<sup>(7)</sup>

In equation (7), Z is a constant and has a value equal to A based on the boundary equation in equation (5). The electroplating efficiency factor can therefore be described as

$$f = Ae^{Bt} \tag{8}$$

Using the general Equation (1) from Case 1 and taking into account the change of radioactivity concentration, R becomes

$$R = \int_{0}^{t} Ifdt = I \int_{0}^{t} A e^{Bt} dt = I A \frac{1}{B} e^{Bt} \Big|_{0}^{t} = I A \frac{1}{B} (e^{Bt} - 1)$$
<sup>(9)</sup>

where

$$e^{Bt} = 1 + bt + \frac{1}{2!}(Bt)^2 + \frac{1}{3!}(Bt)^3 + \dots$$
<sup>(10)</sup>

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University, Cleveland OH, all in Chemical Engineering. Dr. Zhang's research interests include the use of therapeutic radioisotopes for cancer therapy, medical physics, chemical and biomedical engineering, instrumentation, image processing, surface science and mass transfer. Substituting Equation (10) into Equation (9) gives

$$R = IA\left(t + \frac{1}{B}\left(\frac{1}{2!}(Bt)^2 + \frac{1}{3!}(Bt)^3 + ...\right)\right)$$
(11)

The absolute value for Bt is in the range of 0.01 to 0.1 over our experimental parameters. Under certain circumstances, Equation (11) could be simplified by ignoring terms from the second element, resulting in Equation (2).

Since B is negative, the value calculated from Equation (9) must always be smaller than the value calculated from Equation (2). Also, the above derivations show that both cases are interrelated. Increasing the radioactivity amount in the plating chamber by either increasing the plating solution volume or increasing the solution radioactivity concentration will cause a change from Case 2 to the simpler Case 1, while maintaining the amount of radioactivity deposited onto the cathode. When the radioactivity that we want to deposit onto the cathode is lower than 12.5% of the total amount in the plating chamber, which is often required to optimize the expensive radioisotopes (at least in the case where we use larger activities for therapeutic applications), we will use Case 2 and Equation (9) for deposition control.



Hafeli was a postdoctoral fellow at the Joint Center for Radiation Therapy at Harvard University, Boston, MA. His research interests include the use of therapeutic radioisotopes for cancer therapy and the application of magnetic microspheres for site-directed smart drug targeting.

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