Multi-layer Electroplating of Au-Co/^{188}Re-Au on Stents for Lung Cancer Treatment

by Huixiong John Zhang[1*] & Urs O. Häfeli[2]
[1]School of Life Science and Technology, University of Electronic Science and Technology of China, Chendu, China
[2] Division of Pharmaceutics and Biopharmaceutics, University of British Columbia, Vancouver, Canada

This is a continuation of the work we reported earlier in this journal.[1] Multi-layer electroplating, namely gold striking, cobalt/rhenium-188 alloy plating and acid gold over-coating on the stent wire surface were performed. The initial gold strike step pre-coated the stent wire surface with a thin layer of gold and was crucial for good material adhesion between the stent wire basis metal and the following cobalt/rhenium alloy layer. The cobalt/rhenium-188 alloy layer contains the radioactive isotope rhenium-188 (^{188}Re) which would allow such stents not only to be used for mechanical support, e.g., in patients with lung cancer growing into the main bronchi, but also possibly for local cancer irradiation. The third and outermost gold over-coating layer serves to improve biocompatibility and maintain the stent-bound radioactivity in stable form. Scanning electron microscopy (SEM) and x-ray diffraction were used to characterize the electroplated layers. The working electroplating conditions for this multi-layer electroplating process were applied to a fully automated process for the preparation of radioactive ^{188}Re stents for in-vivo testing.

Keywords: *electrodeposition, electroplating, radioactivity, rhenium-188, stent*

Introduction

Lung cancer patients often have a tumor which grows into the main bronchial airways and severely constricts 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.[2] We investigated ways of further improving the situation and attempting to get rid of the tumor cells by making the stents radioactive and thus locally irradiating the cancerous tissue. For this purpose, radioactive rhenium-188 (^{188}Re) was electroplated together with cobalt onto stents in an automated fashion.[3-6]

A central issue in preparing radioactive stents as we addressed in an earlier paper[1] is to make sure that the final implanted product is within 10% of the target radioactivity, thus ensuring an appropriate and legal radiation dose deposition.[1,6] This is especially important when a short-lived radioisotope such as the beta-emitter ^{188}Re with a half-life of 17 hours is used. Any delay of more than three hours will make the radioactive implant worthless. Another critical issue is the mechanical strength and adherence of the electroplated layers. They must adhere well to the basis metal, with no peeling occurring during catheter mounting, implantation and residing in a patient's airways. In this paper, an overview of the experimental results for multilayer electrodeposition on stents is presented.

Experimental

All electroplating experiments were carried out with the automated electroplater shown in Fig. 1 which we developed and is described in detail elsewhere.[5,6] The system is capable of controlling electroplating current, plating time and can automatically change the plating solution and perform rinses. A user-friendly graphical interface developed with Visual Basic 6.0 software (Microsoft Corp., Redwood, Cal.) controls a data acquisition board (ADAC MF5500; IOtech Inc., Cleveland, Ohio), 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_3BO_3) with the radioactive isotope ^{188}Re in the form of perrhenate ReO_4^- at a concentration of up to 74 MBq/mL. The radioactive β-emitter ^{188}Re was eluted daily from a ^{188}W/^{188}Re-generator (Oak Ridge National Lab, Oak Ridge, Tenn.).[7]

The electroplating process was performed in a plating chamber, consisting of a 25 or 50 mL plastic syringe in which the anode made from platinum spirals along the wall and is protected from direct contact with the cathode (stent) by a layer of polyethylene mesh. The stents (Wallstents or Ultraflex stents from Boston Scientific, Natick, Mass.) were clamped directly to a small, gold-coated test clip connected to the cathode and hung in the center of the plating chamber. For the gold strike and cobalt/rhenium-188 electroplating processes, the current density was 100 A/m^2. For the acid gold over coating, the current density was 35 A/m^2. These current densities were selected after testing of a series of different values. They are working parameter values for our study, but might not be the only values that will work. The total time for the three electroplating layers is nominally less than 30 min. The automated electroplater supports currents up to 2000 mA with a resolution of 0.01 mA between 0 and 80 mA, and 0.5 mA between 80 and 2000 mA.

Results and discussion

The mesh structure of stents results in many crossings of the same wire or different wires. The crossing points are problematic during the mechanical deformations that take place when the stent is mounted onto the catheter, following deployment into a patient's body, and subsequently the physiological movement introduced either by blood flow or breathing. The stent wires can slide

* Corresponding author:
Dr. Huixiong (John) Zhang
School of Life Science and Technology
University of Electronic Science and Technology of China
Chengdu, China 610054
E-mail: johnzhangwolf@gmail.com

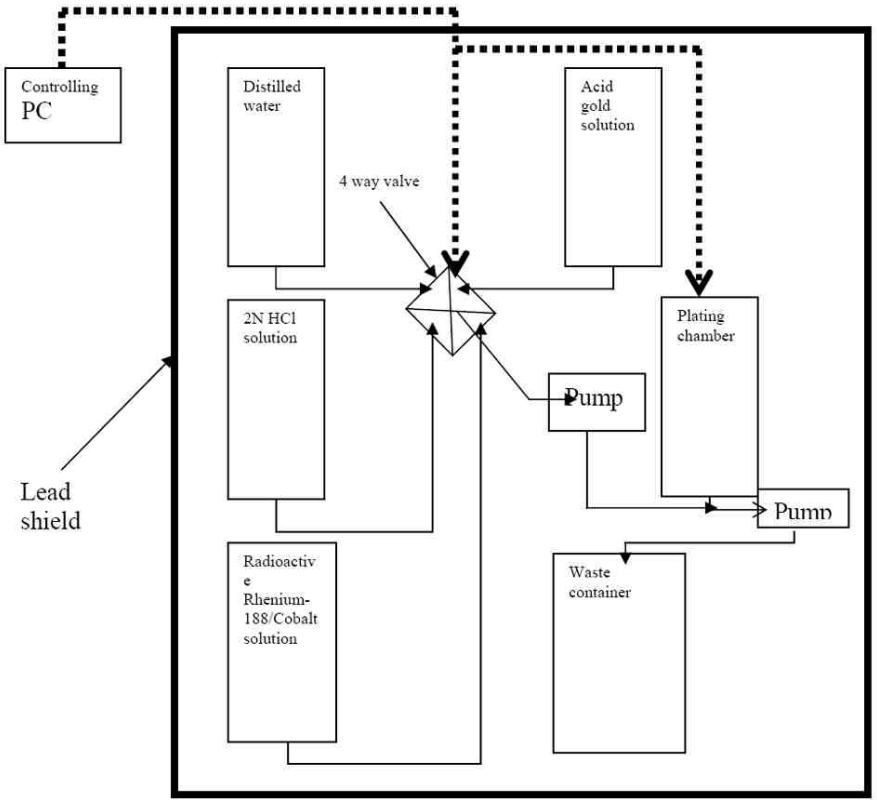


Figure 1—Overview of the experimental system- automated radioactive stent electroplater shielded by lead brick.

against one another, which could cause peeling if the layer is not mechanically strong or the adhesion to the base metal is not strong enough.

In order to optimize the plating procedure, the stents were cleaned with chloroform, acetone, 2N HCl and then water in an ultrasound bath, followed by the following plating procedure:

1. Gold strike
2. Co/^{188}Re alloy
3. Acid gold

The electroplating system was highly automated for two reasons. First, for safety considerations, we wanted to separate the radioactive electroplating solution and chambers from the operating stage and PC with a graphical user interface using lead bricks. The advantage for this design is that the exposure of the operator to irradiation during the process of preparing radioactive stents was minimized. Second, the automation provided precise control over the amount of radioactivity deposited on the stents despite the complicated multi-layer electroplating process. The process consisted of more than 20 steps, including rinsing, pumping in and out of different solutions, and even freshly mixing two solutions (2N HCl and acid gold) to prepare the "gold strike" solution just prior to its use in the plating chamber. The computer control made it possible that operating procedures, represented by the parameter values in the graphical user interface (GUI), can simply be saved to a parameter file and loaded again to repeat the process exactly. This automation also provides a convenient method for experimental documentation and process improvement. More details about the system can be found in our earlier papers.[5,6]

The electroplated layers should be strong and able to withstand operations such as catheter mounting and patient airway implantation. The critical step to realize this, as noted earlier, was to mix the gold strike solution freshly from the 2N HCl and acid gold solutions,[6] with the built-in pump of our system under program control, just before the gold strike process. The reason for freshly mixing instead of preparing in advance is because the gold strike solution we used is not stable and gold chloride will deposit after storing for several hours at room temperature. We chose the electroplating current for the 60 sec gold strike such that many gas bubbles developed on the stent wire surface. These bubbles helped to further clean the surface and keep the surface active. After the gold strike, a thin layer of gold was deposited on the stent surface and thus the stent was gold in color. This precoated thin gold layer improved the adhesion between the cobalt/rhenium alloy layer and the stent surface. The adhesion between the cobalt/rhenium alloy layer and the pre-coated gold layer and the over-coated gold layer was sufficiently strong and no exfoliation was observed after mechanical strength testing.[6]

We examined the stent surface (Fig. 2), the cobalt/rhenium alloy surface and the final gold over-coating surface with SEM and x-ray diffraction. The stent surface after the gold strike step was very similar to the clean stent surface due to the very small thickness of the gold layer. The only difference was the gold color. Under high

magnification (10,000×) with the SEM, we observed that under our operating conditions,[6] the cobalt/rhenium layer was amorphous (Fig. 3) and the gold layer overcoating consisted of small spherical structures (Fig. 4). The final electroplated stent was gold in color and no peeling was seen after ten cycles of squeezing to simulate the application environment (Fig. 5). Even cutting with a razor blade did not lead to peeling or separation of the individual layers.[6] An illustration of the cross section of a stent wire with the multi-layer electroplating process is shown in Fig. 6. The good stability made it possible to go a step further to test the radioactive stents in animal experiments (manuscript under preparation) and do clinical trial experiments on cancer patients.

Conclusions

We electroplated a gold (gold strike), Co/^{188}Re alloy and gold overcoating on medical stents. It was found that the precoating of a thin gold layer during the gold strike step greatly improved the adhesion between the electroplated cobalt/rhenium layer and the stent basis metal. We were able to prepare multi-layer electroplated radioactive stents with enough mechanical strength to be tested in animal experiments. The use of this electroplating technique can thus be used to deliver short half-life radioactive isotopes to the human body for cancer radiation therapy. However, its uses should not be limited to stents, and other objects, such as metal foils, can be radioactive electroplated for skin cancer treatment. The possibility of expanding this technique to other clinical useful short half-life radioactive isotopes, to plating techniques other than electroplating, and to materials other than metal, are to be pursued.

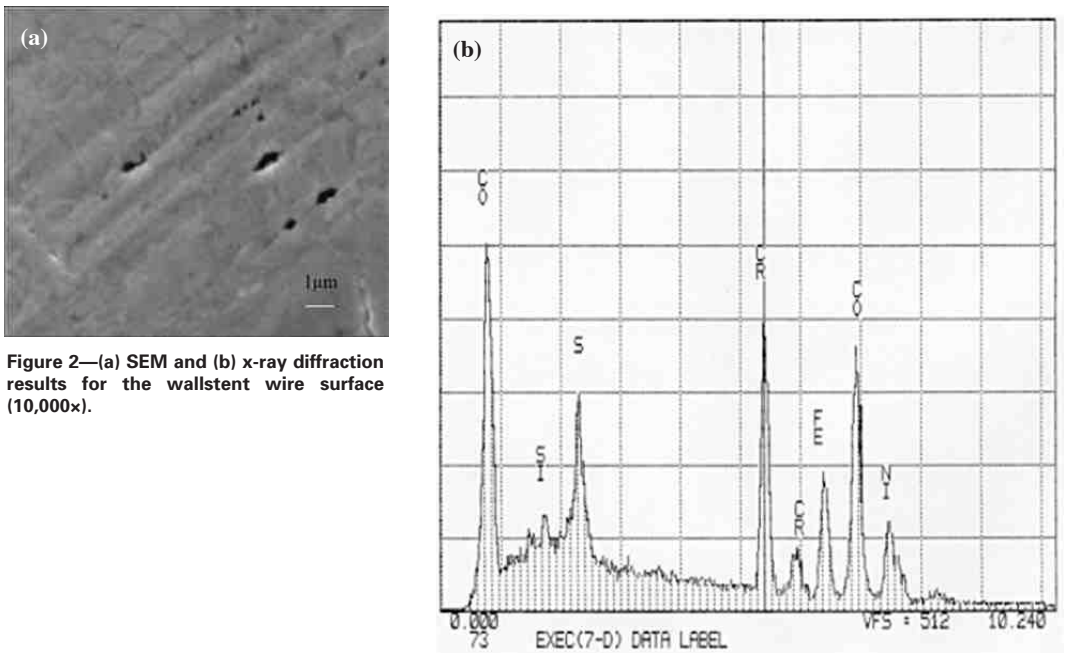


Figure 2—(a) SEM and (b) x-ray diffraction results for the wallstent wire surface (10,000×).

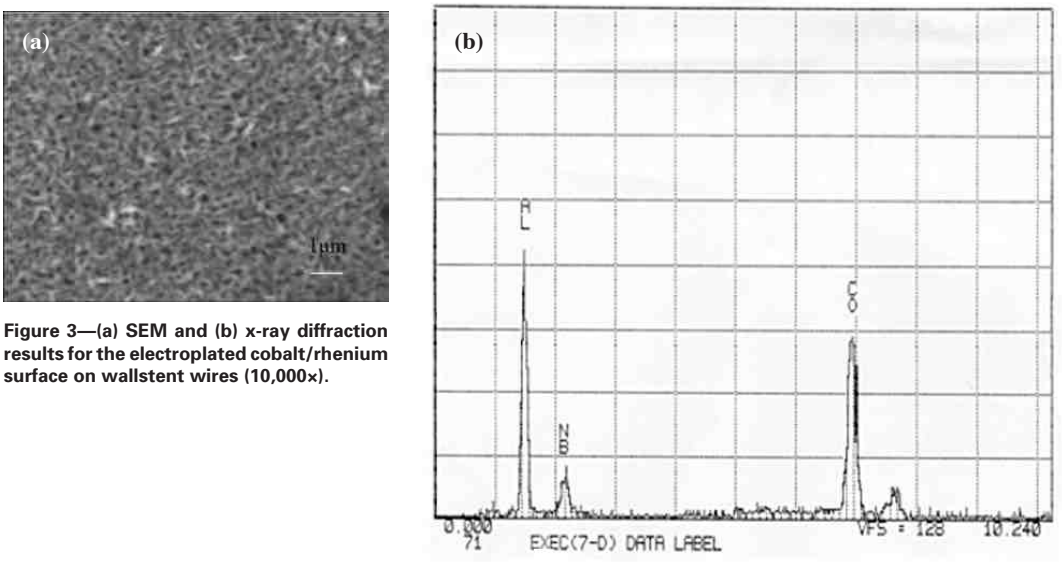
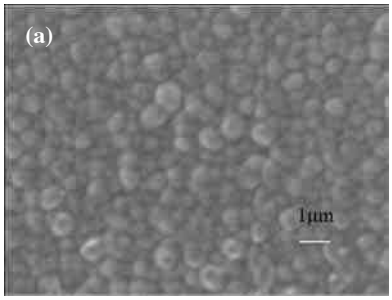


Figure 3—(a) SEM and (b) x-ray diffraction results for the electroplated cobalt/rhenium surface on wallstent wires (10,000×).



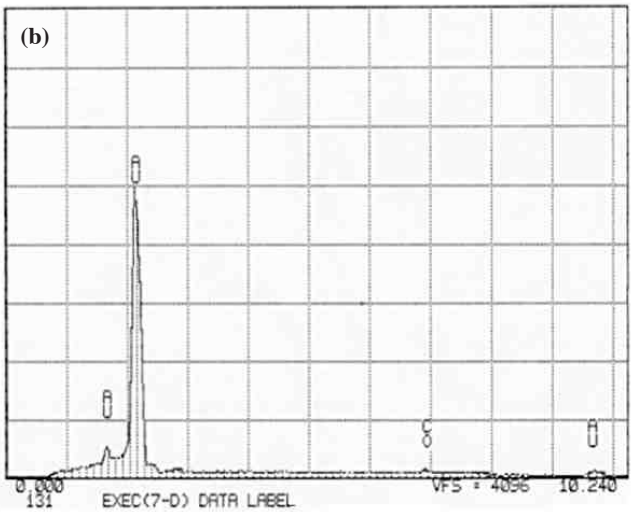


Figure 4—(a) SEM and (b) x-ray diffraction results for the final gold over coating on wallstent wires (10,000×).

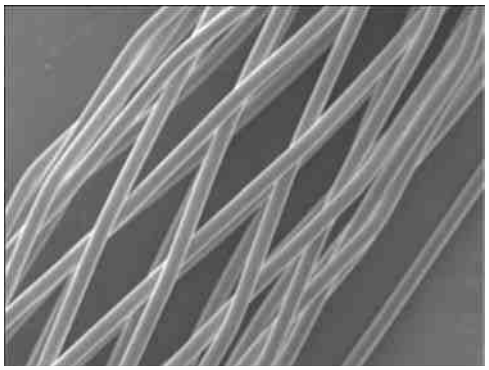


Figure 5—SEM of a wallstent after going through the three-layer electroplating process and after being mechanically squeezed ten times.

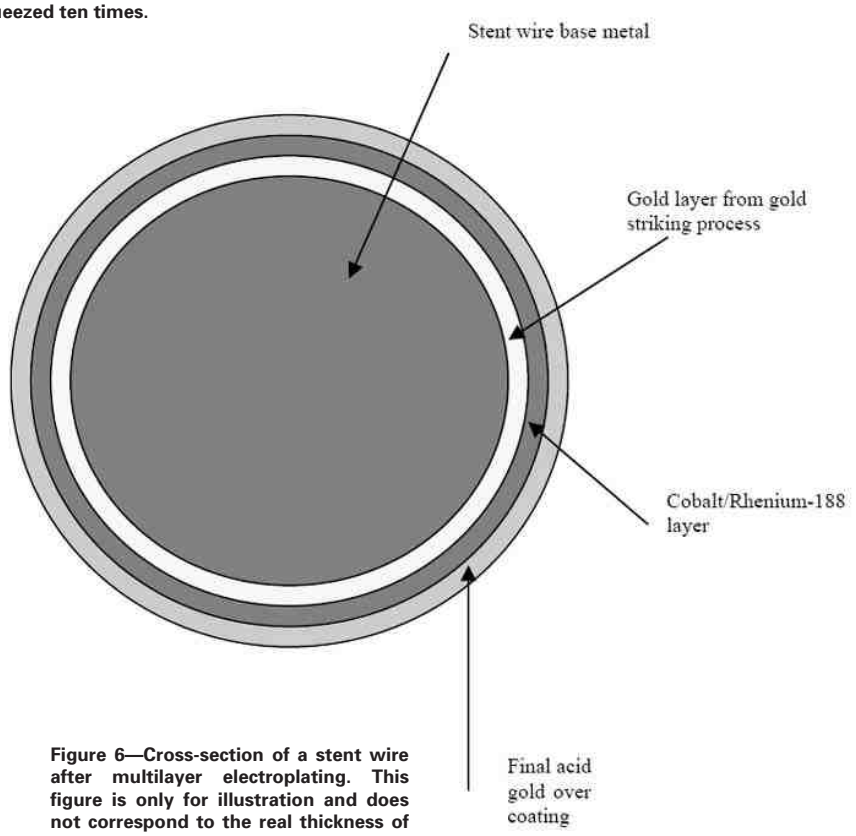


Figure 6—Cross-section of a stent wire after multilayer electroplating. This figure is only for illustration and does not correspond to the real thickness of the different layers.

Acknowledgments

We are very thankful to Bill Roberts from the Radiation Oncology Department at the Cleveland Clinic Foundation, as well as Dr. Ralph Gardner and Shuming Yang from the Chemistry Department at Cleveland State University for valuable discussions. This project was sponsored by the Department of the Army and National Medical Technology Testbed, Cooperative Agreement DAMD17-97-2-7016. The content of the information does not necessarily reflect the position or the policy of the government or NMTB, and no official endorsement should be inferred.

References

1. H. Zhang & U. H**ä**feli, *Plating & Surface Finishing*, **92** (3), 40 (2005).
2. A.C. Mehta & A. Dasgupta, *Clinics in Chest Medicine*, **20**, 139 (1999).
3. U.O. H**ä**feli, M.C. Warburton & U. Landau, *Biomaterials*, **19** (10), 925 (1998).
4. U.O. H**ä**feli, U. Landau & M.C. Warburton, U.S. Patent 6,077,413 (2000).
5. U.O. H**ä**feli, *et al*., *Applied Radiation and Isotopes*, **61** (6), 1313 (2004).
6. H. Zhang & U.O. H**ä**feli, *Journal of Medical Engineering and Technology*, **28** (5), 197 (2004).
7. F.F. Knapp, *et al*., *Anticancer Research*, **17**, 1783 (1997).

About the Authors

Dr. Huixiong (John) Zhang, PE is an associate professor at the School of Life Science and Technology, University of Electronic Science and Technology of China (UESTC), Chendu, China. He was formerly a Postdoctoral Research Fellow in the Radiation Oncology Department at the Cleveland Clinic Foundation. He holds a B.S. degree from Tianjin Institute of Light Industry in Tianjin, China, an M.S. degree from Tianjin University in Tianjin, China and a Ph.D. degree from Cleveland State 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.

Dr. Urs Häfeli is an assistant professor in the Division of Pharmaceutics and Biopharmaceutics at University of British Columbia in Vancouver, Canada. He holds a degree in Pharmaceutics from the Federal Institute of Technology, Zurich, Switzerland and a Ph.D. in Radiopharmaceuticals from the same institution and the Paul Scherrer Institute in Würenlingen, Switzerland. Dr. 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.