

Tantalum Radiopaque Coatings for Stents

D.A. Glocker and M.M. Romach, Isoflux Incorporated, Rochester, NY

ABSTRACT

Many stents are made of the shape memory alloy Nitinol. They can be compressed to a fraction of their normal size for delivery and can expand and maintain their shape once in place. However, Nitinol stents are typically not visible in X-rays and some manufacturers use small radiopaque markers so that surgeons can estimate the stent's position. Often these markers are made of tantalum because of its radiographic density and excellent biocompatibility. A radiopaque tantalum coating is a much more desirable solution but there are several challenges. It must be 5 to 10 microns thick and must adhere in spite of substrate strains as high as 10%. The coating must not interfere with the mechanical properties of the stent. The substrate temperatures must not exceed approximately 200°C during coating in order to preserve Nitinol's shape memory properties. And, the coating must be manufacturable at a reasonable cost. This paper describes the development of a porous, columnar tantalum coating that meets these requirements and is surprisingly able to accommodate the necessary handling and large strains without delamination. Batches of several dozen stents can be coated at rates of 30 nm per minute with a total cycle time of 5 to 6 hours using this process.

INTRODUCTION

Stents are now widely used to reopen blood vessels that have narrowed, or suffered stenosis. These fine metal scaffolds are compressed to a small diameter and introduced through an incision into an artery by means of a catheter. Once they have been properly placed by viewing the procedure with a fluoroscope they are expanded. Coronary stents used in the blood vessels in and around the heart are typically made from stainless steel or cobalt alloys and are expanded against the vessel wall with a balloon at the tip of the catheter. After placement they are well protected within the body and easily remain expanded. However, stents that are used in the peripheral vasculature, such as the carotid and superficial femoral arteries, are more exposed and must retain their shape in spite of external forces. Therefore, the nickel-titanium alloy Nitinol, which has the unusual properties of pseudoelasticity (or superelasticity) and shape memory, is widely used for peripheral vascular devices [1].

Pseudoelasticity and shape memory result from the fact that Nitinol exists in two crystallographic phases. Below a first

transition temperature, known as M_f , Nitinol is in the martensitic phase and is very ductile. Above a second transition temperature, known as A_f , it transforms to the austenitic phase. Device shapes are thermally "set" in the austenitic phase and if a stent is cooled below M_f and distorted it will recover its set shape when the temperature is raised above A_f . This is termed shape memory. In addition, in the austenitic phase applied stresses cause a partial transformation to the martensitic phase. This stress-induced phase change gives rise to an unusual stress-strain relationship at temperatures above A_f called pseudoelasticity, which is illustrated in Figure 1.

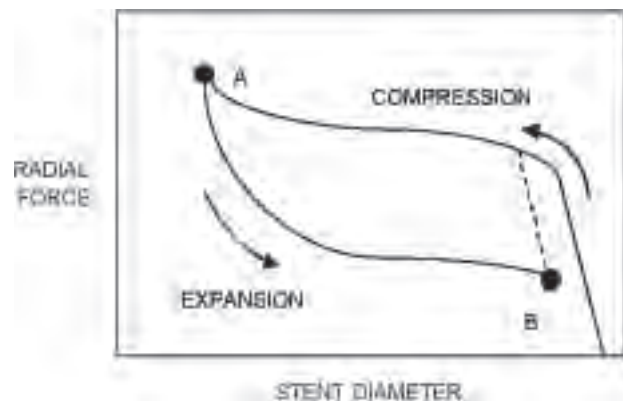


Figure 1: Stress-strain characteristics of Nitinol.

Nitinol device designers make use of the fact that the material can undergo pseudoelastic strains as high as 8%. The ability to recover from such high strains allows a stent to be compressed to a small fraction of its normal diameter, represented by point A in Figure 1, so that it can be loaded into a sheath at the catheter tip. When the stent is in position in the patient and the sheath is removed, it expands along a different path to almost its original size (the point marked B) where it exerts a gentle outward force on the vessel wall. However, its stiffness at that point is determined by the slope of the dashed line in Figure 1. These unique characteristics make Nitinol devices with A_f values below normal body temperature ideal in this application.

One disadvantage of Nitinol devices of typical dimensions is that they are difficult to see under fluoroscopy because of their fine structures and low radiographic densities. Therefore, many manufacturers attach markers made from materials

such as gold or tantalum to Nitinol stents to allow doctors to determine their position during deployment. However, the images formed this way are sometimes less than ideal and a fully radiopaque device would be preferable [1,2]. One way of producing radiopacity is a 5-10 micron thick conformal coating of a material having a high radiographic density, but there are several challenges in this application.

1. The coating must adhere under the extremely high strains the devices undergo during crimping and expansion as well as under the normal strains within the vessel.
2. Sustained temperatures above about 200°C will increase A_f unacceptably, so a relatively low temperature coating process is needed.
3. The added stiffness of the coating cannot change the mechanical properties of the underlying Nitinol.

Gold is an obvious choice in this application because it has a high radiographic density and is relatively ductile. However, in the body gold reacts electrochemically with Nitinol leading to corrosion. Tantalum, in contrast, also has a high radiographic density but is electrochemically compatible with Nitinol and is widely used in medical devices because of its biocompatibility. The purpose of this work, therefore, was to develop a process for radiopaque tantalum coatings on Nitinol that would not change the underlying device properties and which would adhere during the large strains in use.

EXPERIMENTAL METHODS

A dual inverted cylindrical magnetron sputtering system having two commercially pure tantalum targets, each 34 cm in diameter and 10 cm high and separated by 10 cm, was used for the runs reported here. Numerous coatings were deposited under a variety of conditions, but this paper will focus on the results of a one-half fractional factorial experiment that illustrate our major findings. There were four independent factors in that experiment. The two tantalum targets were driven with DC power or with AC power at 40 kHz in a dual cathode arrangement. Either xenon or krypton was used as the sputter gas rather than argon in order to reduce the incident energy flux at the substrates. The total power to both cathodes was 2 kW or 4 kW and a bias of either -50 V or -150 V was applied to the stents during coating. The base pressure before starting the process was below 5×10^{-6} Torr and the sputtering pressure was fixed at 3.8 mTorr as measured by a convectron gauge. The deposition rate at a total DC power of 2 kW in krypton was 33 nm per minute and the times were adjusted to give a coating thickness of approximately 10 microns for all of the runs.

Electropolished Nitinol stents between 6 and 10 mm in diameter were used in the experiment and the A_f values before coating were approximately 24°C. In each run stents were placed at several locations, as shown in Figure 2, and were held by small clips in such a way that they were thermally isolated.

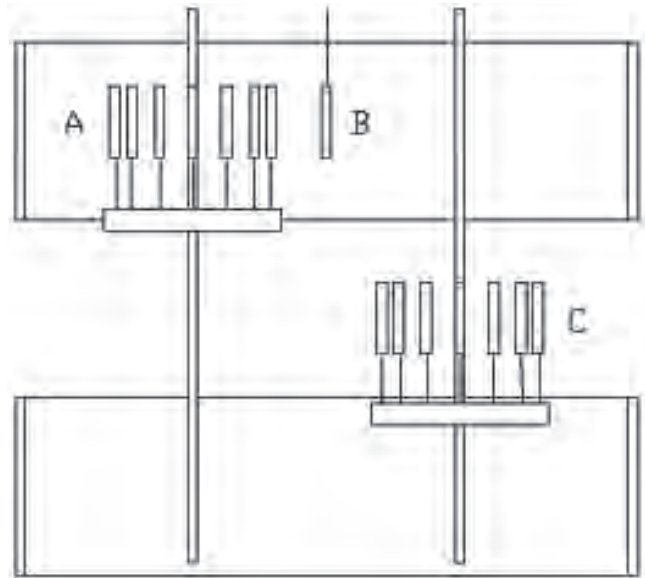


Figure 2: Substrate fixturing and locations.

In position A the stents were on the perimeter of a 10 cm diameter fixture that rotated about a vertical axis, which was approximately 7 cm from the cathode centerline. The vertical position of the stents was in the center of the upper cathode and each stent was periodically rotated about its own axis by a small “kicker.” In position B the stents were simply supported from a rotating rod that was approximately 7 cm from the cathode centerline and the vertical position of the stents was in the center of the upper cathode. In several runs stents were also placed in position C where they underwent planetary rotation like those in position A, but their vertical location was in the center of the chamber midway between the upper and lower cathodes.

The stents were cleaned ultrasonically in an alkaline aqueous detergent and de-ionized water. Prior to coating, the targets were burned-in under the operating conditions for that run for 10 minutes while a cylindrical shutter isolated the stents. There was no adhesion promotion layer used and once the shutter was opened the tantalum nucleated directly on the stents.

The coating adhesion was determined by straining the stents to their maximum extent pseudoelastically and examining them for coating removal. A tape test was also done, but the strain test always produced more coating failure than the tape test and was used to discriminate between the coatings. The approximate coating removal was ranked from 0 (no removal) to 5 (greater than 10% removal). An adhesion rank of 1 indicated that there was an occasional area of removal but less than approximately 0.1% of the coated area flaked and an adhesion rank of 4 indicated that between 5% and 10% of the coated area flaked. Samples that had a score of 0 were further tested by crimping them around a 1.1 mm diameter mandrel in a dry ice and alcohol bath at a temperature below

M_f and letting them expand to their full size several times to confirm that the coating survived this operation. In all cases stents with scores of 0 in the strain test also survived multiple crimp tests with no removal as well.

The A_f values after coating were determined by cooling the samples below M_p , straining them, then immersing the strained samples in a water bath and measuring the temperature at which they recovered their original size and shape.

Once the optimum coating conditions were found for adhesion and A_p , several additional measurements and tests were done on stents coated under those conditions. The process temperature was determined during deposition in a number of runs (without rotation) by using ultra-fine chromel-alumel thermocouples attached to the stents. Potentiodynamic polarization measurements were also done to confirm that the corrosion resistance of the underlying stents was not compromised by the process or the coating. Finally, thirty-day and six-month animal studies were done comparing 10 coated and 10 uncoated stents in a porcine model to determine if there were any differences in the histopathology of stented arteries due to the coating.

EXPERIMENTAL RESULTS

Figure 3 is a radiograph of a stent with a 10 micron thick tantalum coating (right) and a similar uncoated stent (left), illustrating the effective radiopacity of the coatings in this study.



Figure 3: Radiograph of an uncoated stent (left) and coated stent (right).

The adhesion and A_f results were very similar for stents coated in positions A and B in each run and were averaged to produce the summary shown in Table 1.

It can be seen from the data in Table 1 that substrate bias had a major impact on coating adhesion. In every case in which the bias was -150 V there was no coating removal or extremely minor removal and in all but one case in which the bias was -50 V there was extensive removal. However, conditions that

Table 1: Run conditions and results for substrates in A & B positions

Run No	Power	Gas	Bias	AC/DC	Adhesion	Af
1	2 kW	Xe	50	AC	5	29
2	2 kW	Kr	150	AC	0	59
2R	2 kW	Kr	150	AC	0	48
3	4 kW	Kr	50	AC	4	57
4	4 kW	Xe	150	AC	0	>57
4R	4 kW	Xe	150	AC	0	>57
5	2 kW	Kr	50	DC	0	23
6	2 kW	Xe	150	DC	0	27
7	4 kW	Xe	50	DC	4	32
8	4 kW	Kr	150	DC	1	38

resulted in excellent coating adhesion were usually associated with an unacceptable rise in A_f . Run 5, which had excellent adhesion and the lowest A_f value, was an important exception to these results. It is worth noting that stents coated under the conditions of Run 5 were black in appearance.

The results for the stents in position C were also interesting when compared with those for the stents in positions A and B and they are summarized in Table 2.

As can be seen from Table 2, the stents in position C had very good adhesion overall, even in Runs 1 and 7 that produced poor adhesion in positions A and B. Because of their location and movement, for a given set of conditions these stents received a more oblique and lower energy coating flux than stents in positions A and B.

The black appearance of the best coatings and the generally good adhesion of stents coated in position C suggest that porosity may play a role in the results. Figure 4 is a plan view scanning electron microscope image of a coating made at position C under Run 5 conditions in which the porous structure is clearly visible. The surprisingly good adhesion of such a coating may be due to the fact that the porosity leads to good strain accommodation. Nevertheless, the ability to withstand strains of up to 8% as well as the surface forces associated with the crimping operation is quite surprising. After confirming the reproducibility of the process, we focused further testing on coatings done under these conditions and multiple crimp and expansion steps and A_f measurements on hundreds of stents have continued to produce excellent results.

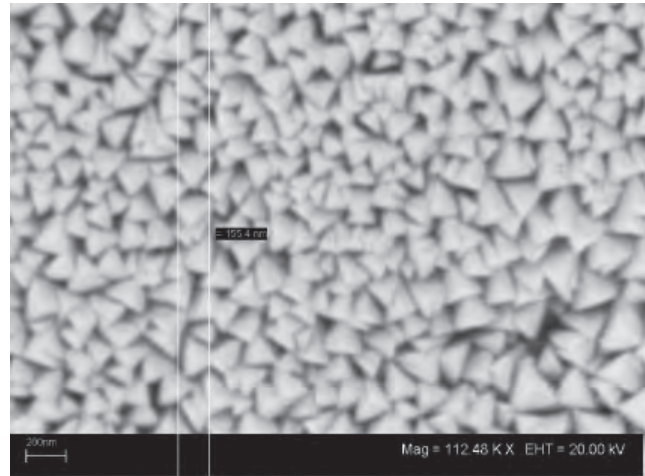


Figure 4: Plan view of 6 micron thick tantalum coating. The white lines are 155 nm apart.

Figure 5 shows the substrate temperature as a function of time for a stent coated under the optimum conditions. The arrows indicate when the shutter was opened and when the process was turned off and the thickness of this coating was 6.0 microns.

Table 2: Run conditions and results for substrates in C position

Run No	Power	Gas	Bias	AC/DC	Adhesion	A_f
1	2 kW	Xe	50	AC	0	30
2	2 kW	Kr	150	AC	0	42
2R	2 kW	Kr	150	AC	0	38
3	4 kW	Kr	50	AC	-	-
4	4 kW	Xe	150	AC	-	-
4R	4 kW	Xe	150	AC	-	-
5	2 kW	Kr	50	DC	0	24
6	2 kW	Xe	150	DC	1	25

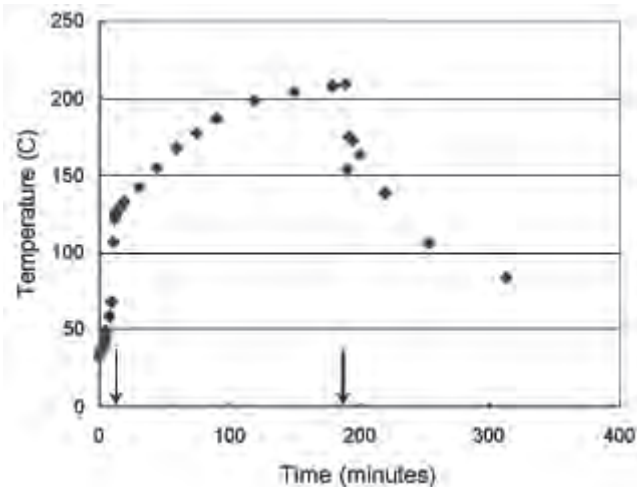


Figure 5: Stent temperature during the coating process.

The mass of a typical stent used in these experiments is 166 mg and the mass of the same type of stent with a 10 micron thick tantalum coating produced under the optimum conditions is 225 mg. The temperature rise seen in Figure 5 is surprisingly little for a tantalum coating deposited at 33 nm/min that adds this much mass relative to that of the small, thermally isolated device. The measured emissivity of this coating is greater than 98% across the visible spectrum and into the near infrared, which may account for the small rise. Because the wall of the chamber is water cooled and also has a relatively high emissivity, radiative cooling of the device may be playing an important part in keeping the temperature low.

Figure 6 shows the results of the potentiodynamic measurements for four stents coated under the optimum conditions. The breakdown voltage for bare Nitinol stents of the same type is approximately 800 mV v. SCE and for the coated stents the measured value was 905 +/- 191 mV v. SCE. These data show that the corrosion resistance of the tantalum coated stents is at least as good as that of the underlying material.

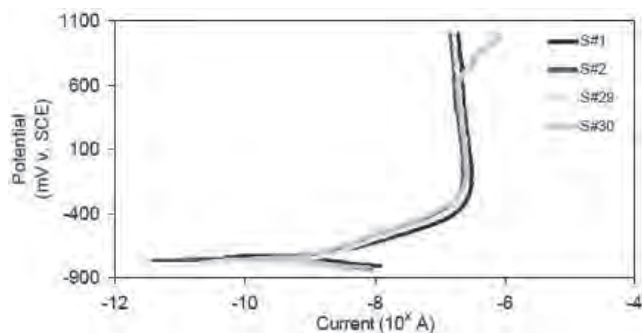


Figure 6: Corrosion measurements for four coated stents.

Thirty-day and six-month porcine studies were done comparing 10 tantalum coated Nitinol stents with 10 uncoated Nitinol stents. After euthanizing the animals the histomorphometry and histopathology of the stented arteries were examined. A typical photomicrograph from the six-month study is shown in Figure 7, in which the cross-section of the stent struts can be seen. The conclusion of these studies was that there was no statistical difference in stenosis, intimal thickness, or inflammation score between the results for the coated stents and those for the uncoated stents in both studies. There was also no difference in the injury score between coated and uncoated stents in the thirty-day study, but there was a very small but statistically significant difference in the six-month study. On a scale of 0 to 3, the mean injury score in the six-month study was 0.58 +/- 0.315 for coated stents and 0.24 +/- 0.254 for uncoated stents, which is significant for $p < 0.05$.

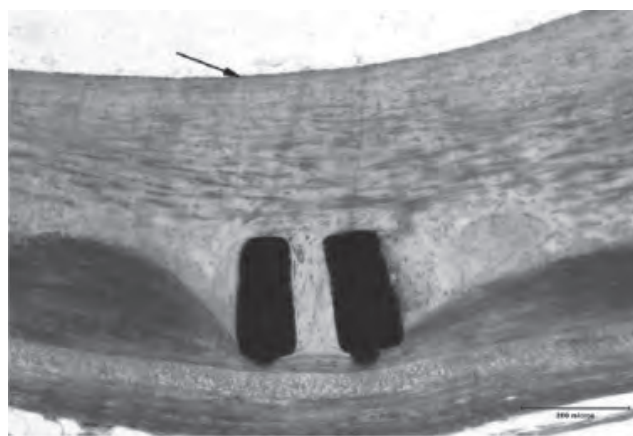


Figure 7: Typical histology of coated stents in animal trials.

The equipment used in these experiments can accommodate batch sizes of 50 to 100 stents depending on their dimensions and numerous large batches have been coated. The cycle time for the process is approximately 6 hours air-to-air for a 6 micron thick coating. Under these conditions the cost of a tantalum coating on a 10 mm diameter by 50 mm long Nitinol stent is comparable to the cost of rivets or markers.

CONCLUSIONS

Previous work on radiopaque coatings for intraluminal devices such as stents, stent grafts and vena cava filters has emphasized the need for energetic coating processes in order to achieve the excellent adhesion necessary [2]. Our work confirms that energetic coating conditions, such as those produced with dual cathode AC power and substrate bias, do result in good adhesion. However, those conditions can also produce thermal damage, particularly in temperature sensi-

tive materials such as Nitinol. We have found that a porous, columnar tantalum coating that withstands the strains in use surprisingly well can be deposited at temperatures that do not change the thermomechanical properties of Nitinol devices. These coatings have been shown to be corrosion resistant and animal trials have demonstrated their biocompatibility. The manufacturing cost for these coatings on typical devices is comparable to the cost of adding markers or rivets.

REFERENCES

1. D. Stoeckle, A. Pelton and T. Duerig, "Self-expanding Nitinol Stents: Material and Design Considerations," *Eur. Radiol.* (2004) 14:292–301.
2. R. Sahagian, "Radiopaque Coatings-Critical Insight: Marking Devices with Radiopaque Coatings," *Medical Device and Diagnostics Industry*, May 1999.