JMEPEG (2009) 18:754–759
DOI: 10.1007/s11665-009-9404-z

1059-9495/$19.00

The Effect of Exposure to Simulated Body Fluids on Breakdown Potentials

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(Submitted September 12, 2008)

Current methods to evaluate the corrosion resistance of small medical implants are typically based on short-term in vitro tests. While the duration of these tests is kept to a minimum to make it feasible to evaluate a large number of samples in a reasonable time, these methods do not account for the long-term changes that can occur in the oxides of metals exposed to biological fluids. Given other electrochemical changes to these materials with time in solution, it is a reasonable question to consider whether breakdown potentials are a fundamental parameter of a material and surface condition. Data on 316L and nitinol wire samples, and nitinol stents, show that breakdown potentials increase with time in solution up to 28 days. The difference between the breakdown potential and rest potentials either increased or exhibited no change.

Keywords biomaterials, corrosion testing, material selection

1. Introduction

Evaluation of the corrosion resistance of medical implants is a complicated subject. Modern materials utilized in devices, such as 316L stainless steel, MP35N, and nitinol, are inherently resistant to uniform corrosion. Assessment of corrosion resistance then moves to concerns such as pitting, crevice, galvanic and fretting corrosion. Part of the complication in characterizing the corrosion resistance of a device is the inherent stochastic nature of pitting corrosion; the other is the complexity of modern devices.

There are a number of standards that can be used to evaluate devices, such as ASTM F2129 (Ref 1), F746 (Ref 2), and G71 (Ref 3). However, minimum criteria have not been defined for some of these standards, particularly for ASTM F2129. One of the challenges in determining minimum criteria is that these methods are admittedly harsh. They are designed to make materials fail, so a failure in the test is not necessarily indicative that a device will fail in vivo. All of these tests were designed to enable a researcher to rank materials, rather than provide in vivo simulation for design verification testing. That leaves one with the need for in vivo failure data. Given a lack of real failure data in the literature to base criteria, there is significant ambiguity for manufacturers and testing laboratories in determining whether their devices are adequately corrosion-resistant based on these short-term electrochemical tests.

In this vacuum, criteria were proposed specifying an absolute breakdown potential (E_b) of 600 mV (all voltages versus SCE) for good performance and 300 mV as a minimum acceptable breakdown potential (Ref 4, 5). These criteria were suggested for cases where there were no corroborating data, such as explants or animal trial evaluations. The basis of these criteria was an adequate safety margin to the maximum values for in vivo open circuit potentials of a number of implant materials published in the literature (Ref 6, 7).

Discussion of these criteria by Pound (Ref 8) suggests that a fixed minimum potential may be too simplistic. Pound suggests that $E_b - E_r$ is a better predictor of the resistance to pitting corrosion because it takes into consideration the gap between the breakdown potential and the rest potential. This view is supported by the work of Wilde (Ref 9) and Silverman (Ref 10). Wilde showed that the difference between the breakdown potential and repassivation potential, and not absolute E_b, was correlated to mass loss due to crevice corrosion in environmental exposure testing.

One factor missing from the discussion of criteria in the literature is whether E_b is a constant or if it varies with immersion time. Several studies (Ref 6, 11-14) have demonstrated that the oxides of titanium and nitinol undergo considerable change with time in solution. The oxide dome structure on 316L stainless steel (Ref 11), titanium (Ref 12), and nitinol (Ref 13) have been shown to undergo significant morphological changes with time in solution. Other studies demonstrated electrical properties of the oxides, such as Er (Ref 6) and the polarization resistance (Ref 14), change over long periods of time. Given these observations, it is a reasonable question to ask whether E_b and $E_b - E_r$ are material constants or are dependant on time in solution. This paper will evaluate whether E_b and $E_b - E_r$ change with the length of time a sample is held in solution. This will be evaluated for 316LVM stainless steel wires, nitinol wires, and for nitinol stents.

2. Materials and Methods

All experiments were performed on commercially available 316LVM stainless steel and nitinol wires. The 316LVM

This article is an invited paper selected from presentations at Shape Memory and Superelastic Technologies 2008, held September 21-25, 2008, in Stresa, Italy, and has been expanded from the original presentation.

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wire was acquired in a spring temper condition with an as-drawn surface condition and a 0.254 mm nominal diameter. Two lots of nitinol wire with a nominal composition of 56.0 wt.% Ni and balance Ti were acquired. One lot was acquired in a straight annealed condition with a black oxide surface condition and was used for testing with straight wire samples with no further processing. Sections of a second lot of nitinol wire were electropolished, wound on mandrels, and then heat-treated in air to form stents. The aim of the processing was to produce a stent with a thermally grown oxide on the surface. Both nitinol surface conditions were created with the intention that the samples would exhibit pitting corrosion in the cyclic potentiodynamic polarization (CPP) test.

All cyclic potentiodynamic experiments followed ASTM F2129 with the exception of changes to the open circuit hold time, and a reverse scan rate of 10 mV/s. Electrochemical experiments were performed with a Gamry Instruments PCI-4/300™ potentiostat and Gamry Framework™ software. Tests were performed in a standard 1 L corrosion cell utilizing a saturated calomel electrode (SCE) for a reference electrode and graphite rods for counter electrodes. All tests were performed in phosphate buffered saline at pH 7.4, 37 °C and under nitrogen purge. A forward scan rate of 1.0 mV/s, a reverse scan rate of 10 mV/s, and an initial potential equal to the rest potential were used for all experiments. Temperature was maintained with a hot water bath.

In the first series of experiments with straight wire samples, two open circuit potential (OCP) hold times were used: 1 and 66 h. Up to 30 samples were tested per combination of material and OCP hold technique, with one notable exception being the nitinol wire samples held for 66 h where 8 samples were tested due to a limited supply of that lot of material.

Stent samples were tested to the ASTM F2129 test method, again varying the OCP hold time. The first 15 samples followed ASTM F2129 using a 1 h OCP hold. The other half used a modified protocol where the samples were held for 672 h (28 days) at OCP before the CPP portion of the test. A Gamry Instruments ECM8™ multiplexer was used to record the open circuit potential of 5 samples at a time in order to test 15 samples with this protocol. Each sample was tested in an independent corrosion cell with its own reference electrode and counter electrode. Once the OCP hold was completed, the CPP portion of the experiment was run sequentially, one cell at a time.

Statistical analyses of breakdown potentials (E_b) and the difference between the breakdown potential and the rest potential ($E_b - E_r$) were performed using JMP™ version 7.0.1. Statistical evaluation was performed using the Wilcoxon/Kruskal-Wallis test with normal approximation, a non-parametric test, with a 95% confidence level used for statistical significance in all analyses.

3. Results

The changes in rest potentials and breakdown potentials for stainless steel samples are shown as a function of OCP hold time in Fig. 1. Rest potentials increased from a mean of −81 to 33 mV and breakdown potentials increased from 613 to 961 mV. Mean and standard deviations for E_r, E_b, and $E_b - E_r$ for all materials are listed in Table 1. While E_r and E_b values increased with increasing hold time, the change in E_b was greater than for E_r as can be seen by the increase in $E_b - E_r$ with increasing OCP hold time in Fig. 3. The mean $E_b - E_r$ increased from 694 mV with a 1 h OCP hold to 928 mV at 66 h. Increases to E_r, E_b, and $E_b - E_r$ for stainless steel samples were all statistically significant as can be seen by the Wilcoxon p-values listed in Table 2.

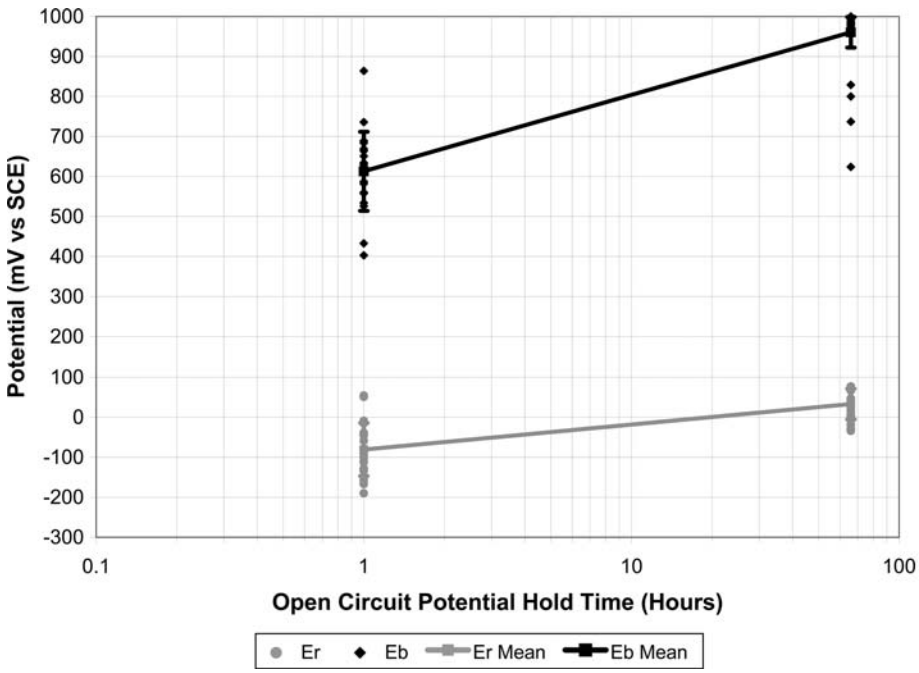

Fig. 1 Rest potentials and breakdown potentials as a function of open circuit potential hold time for stainless steel straight wire samples. Means are connected by the lines

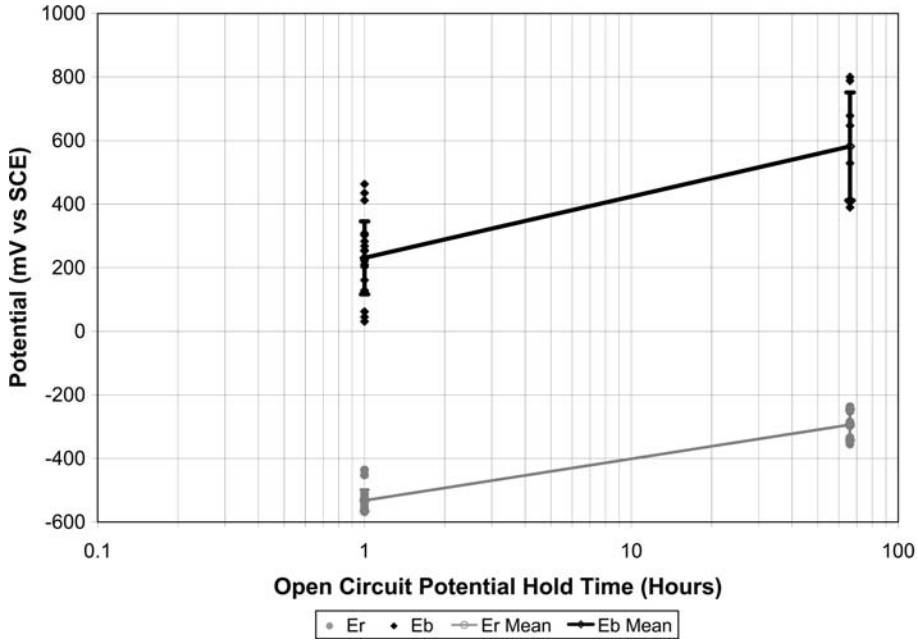

Fig. 2 Rest potentials and breakdown potentials as a function of open circuit potential hold time for nitinol straight wire samples. Means are connected by the lines

Table 1 Mean and standard deviation for E_r, E_b, and $E_b - E_r$ values for stainless steel and nitinol straight wire samples

			E_r, mV		E_b, mV		$E_b - E_r$, mV	
Material	**OCP hold time, h**	**Number of samples**	**Mean**	**SD**	**Mean**	**SD**	**Mean**	**SD**
316 SS	1	21	−81	66	613	99	694	127
	66	30	33	38	961	38	928	89
Nitinol	1	22	−532	34	231	115	763	115
	66	8	−294	48	582	170	876	131
Nitinol stent	1	15	−106	23	446	148	553	150
	672	13	36	21	680	149	644	152

Table 2 p-Values for statistical comparisons of E_r, E_b, and $E_b - E_r$ vs. OCP hold time for 316 stainless steel and nitinol wire samples

Material	**Parameter**	**Wilcoxon p-value**
316 SS	E_r	<0.0001
	E_b	<0.0001
	$E_b - E_r$	<0.0001
Nitinol	E_r	<0.0001
	E_b	0.0002
	$E_b - E_r$	0.039
Nitinol stent	E_r	<0.0001
	E_b	0.0013
	$E_b - E_r$	0.1405

Nitinol straight wire samples performed similarly to the stainless steel samples. E_r and E_b increased with increasing OCP hold time as can be seen in Fig. 2. Mean rest potentials increased from −532 to −294 mV, while mean breakdown potentials increased from 231 to 582 mV. $E_b - E_r$ values also increased with increasing OCP hold time for the straight wire samples, as shown in Fig. 3. The change in $E_b - E_r$ was not as large as observed with the stainless steel samples, but the mean still increased from 763 to 876 mV. The changes in E_r, E_b, and $E_b - E_r$ were all statistically significant as can be seen by the Wilcoxon p-values shown in Table 2.

Rest potentials and breakdown potentials for the stent frames are shown in Fig. 4. As with the wire samples, breakdown potentials increased with increased open circuit potential hold in solution, in this case 672 h (28 days). Two samples in the 672 h hold period developed bubbles in the luggin probe which led to problems in the CPP test resulting in a set of 13 data points for the longer OCP hold. Figure 5 shows the open circuit potential as a function of time for one of the stent samples. Most of the changes in OCP occurred in the first 4 to 6 days with little subsequent change in the remaining 22 days of exposure. No significant transients were observed in the OCP traces, indicating that no metastable pitting occurred during the OCP hold. Mean rest potentials increased from −106 mV at 1 h to 36 mV at 672 h, and mean breakdown potentials increased from 446 to 680 mV. Increases in rest and breakdown potentials for the stents were statistically significant as shown by the p-values in Table 2. $E_b - E_r$ values are shown in Fig. 6, with the mean $E_b - E_r$ value increasing from 553 to 644 mV. However, the increase was not statistically significant

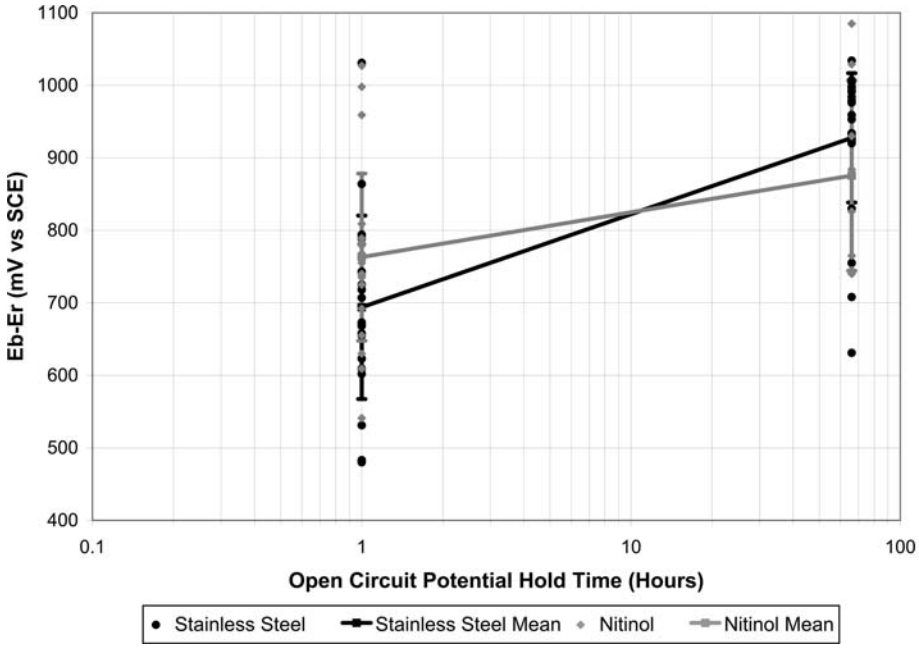

Fig. 3 $E_b - E_r$ as a function of open circuit potential hold time for stainless steel and nitinol straight wire samples. Means are connected by the lines

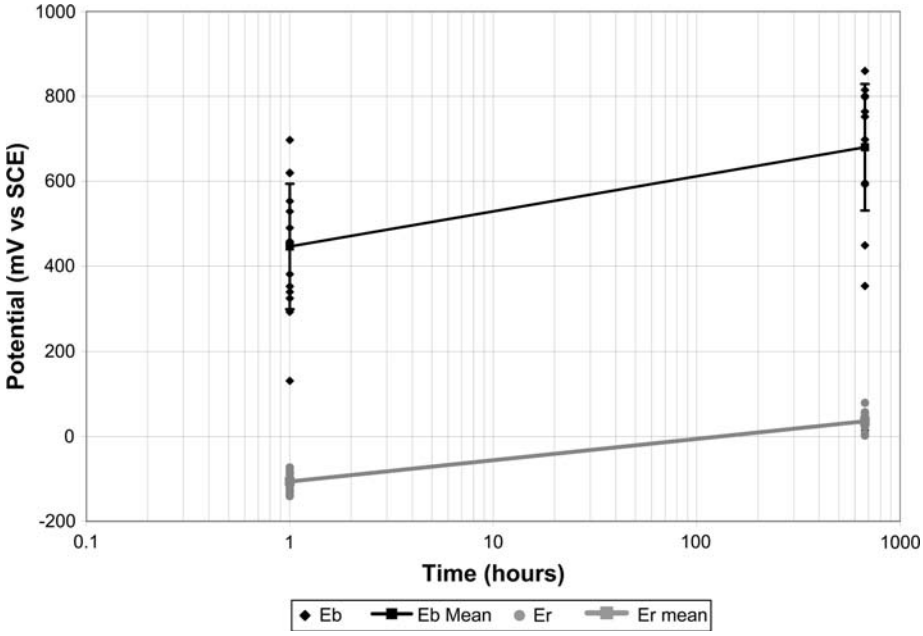

Fig. 4 Rest potentials and breakdown potentials as function of open circuit potential hold time for nitinol stents. Means are connected by the lines

as shown by the Wilcoxon p-value of 0.1344. Typical cyclic polarization curves for 1 h and 28 day OCP hold samples are shown in Fig. 7. The 28 day hold samples exhibited a decrease in current density in the passive region of between 1 and 1.5 orders of magnitude from that of the 1 h OCP hold samples. Additionally, it should be noted that none of the longer hold samples exhibited a repassivation potential on the reverse curve, while 13 of 15 of the 1 h hold samples did repassivate.

4. Discussion

Data from both wire samples and stents show that E_r and E_b values increased with increasing open circuit potential hold time for all the materials evaluated in this study. The increase in E_b values with time is an interesting and new finding. $E_b - E_r$ values either stayed constant or increased with increasing open circuit hold time. What is most significant

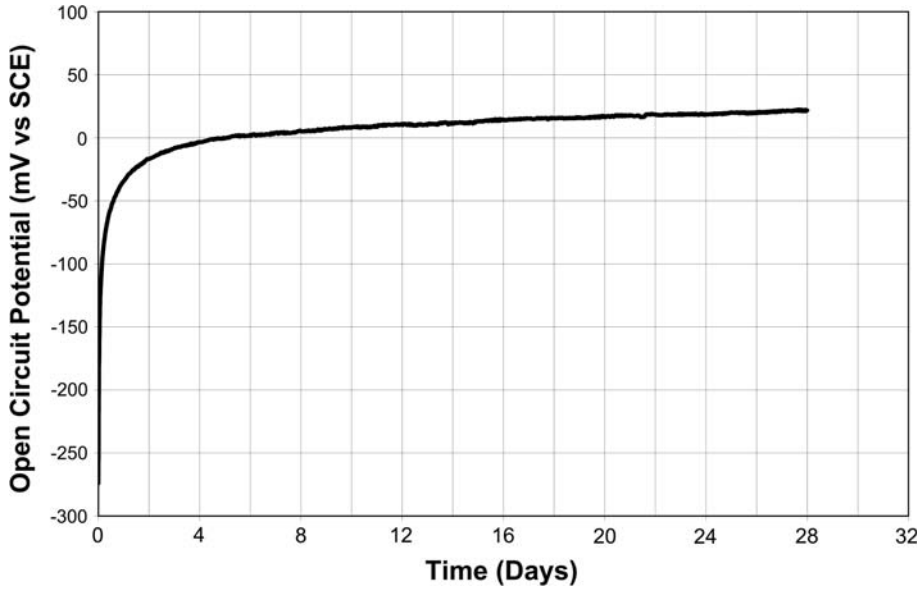

Fig. 5 Open circuit potential data from one representative sample showing increasing potential in the first 4 days with very little subsequent change

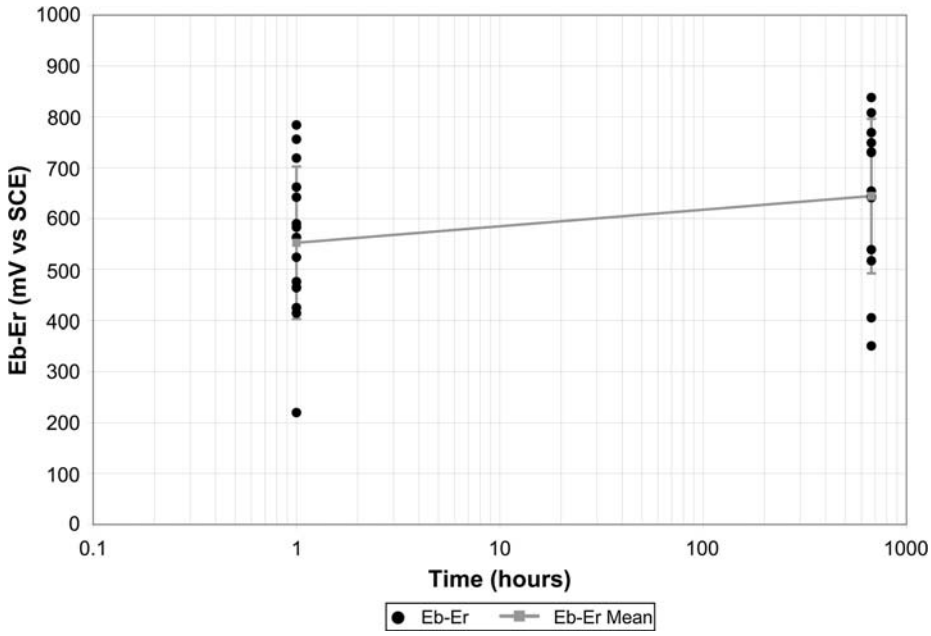

Fig. 6 $E_b - E_r$ as a function of open circuit potential hold time for nitinol stents. Means are connected by the line

here is that $E_b - E_r$ did not decrease with increasing time in solution.

Beyond the changes to E_r and E_b, there were additional changes observed in the CPP curves. The difference in current density in the passive region suggests a greater polarization resistance with time in solution. This corresponds well with the increased polarization resistance found in F138 and nitinol observed by Rondelli (Ref 14) through EIS studies with immersions of up to 1 week.

The results here have interesting implications to the discussion on criteria for ASTM F2129. Referring back to the stent data in Fig. 4, the mean breakdown potential of 446 mV is clearly below the 600 mV criterion proposed for good material and some of the values fall below the 300 mV minimum criterion suggested by Corbett (Ref 4). However, with increasing time in solution, E_bs climbed to a mean of 680 mV and a minimum value of around 400 mV showing acceptable performance by Corbett's suggested criteria. Data from longer immersions show that Corbett's criteria would provide a conservative evaluation of the corrosion resistance of these devices. In contrast, $E_b - E_r$ values taken at 1 h are consistent with longer term data, showing that $E_b - E_r$ may be a better

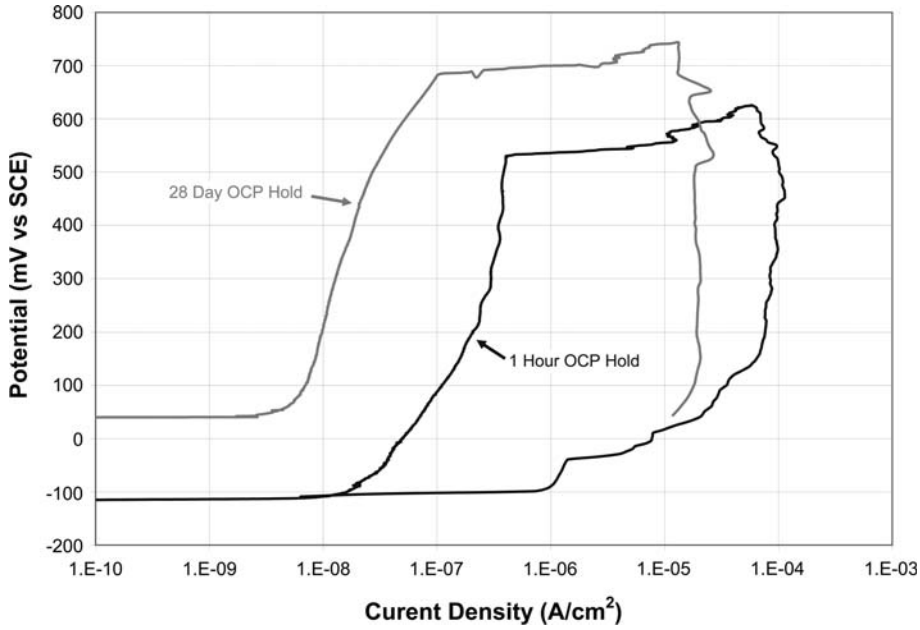

Fig. 7 Typical cyclic potentiodynamic polarization curves for 1 h and 28 day OCP hold times on nitinol stents

parameter due to its consistency. Others (Ref 8-10) have suggested that $E_b - E_r$ is a more relevant parameter for the prediction of corrosion performance from in vitro test data. Overall, this suggests that $E_b - E_r$ is a better parameter for evaluation of the resistance to pitting corrosion of implant devices than a fixed value of E_b.

5. Conclusions

- Rest potentials and breakdown potentials increased with increasing open circuit potential hold time. Changes were statistically significant for 316L stainless steel wires, nitinol wires, and nitinol stents.
- Statistically significant increases were observed for $E_b - E_r$ with increasing open circuit potential hold times for 316L stainless steel wires and nitinol wires.
- No statistically significant change was observed to $E_b - E_r$ with increasing open circuit potential hold times up to 28 days for nitinol stents.

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