**Synergistic Interaction Between Corrosion-Fatigue of Nitinol and the Atherosclerotic Lesion Environment**

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**Introduction:** Stent fracture remains a significant problem when nitinol stents are implanted in arteries with high mobility such as the superior femoral artery. Understanding the effect of the unique mechanical and biological environments of these mobile arteries may hold the key to improving stent patency. We hypothesize that repetitive mechanical stresses interact synergistically with the cellular atherosclerotic lesion environment causing stent oxide damage and exposure of the base metal to macrophage-produced corrosive agents. This process ultimately leads to the fracture of stents. To test our hypothesis, we examined the effect of repetitive mechanical stress in the presence of acetylated-LDL activated macrophages on the open circuit potential (OCP), surface chemistry and roughness of nitinol. A more negative OCP is a sign of sensitization of the material to corrosion.

**Methods:** Repetitive four-point bending protocols were performed using a novel corrosion fatigue testing device (CF device) equipped with a sterile cell culture well in which OCP can be continuously monitored and recorded in real time. This method requires only two electrodes: the specimen and a (carbon) reference electrode. Data were collected using a high impedance (>10 GOhm) interface analog-digital converter device (National Instruments, USA). The data acquisition software is Labview Signal Express, USA. Measurement of OCP to assess stress corrosion of implantable metallic materials is a recognized method (ISO Standard 16429, © ISO, 2004). Prior to testing, flat nitinol coupons were pre-incubated for 24 h either in culture medium only, or in medium with acetylated-low density lipoprotein (Ac-LDL) activated THP-1 cells (A-MPh). Cells were activated in a 4h pre-incubation with 10µg/ml Ac-LDL. Three different bending load regimens (no strain; strain levels of 0.28% and 0.45%) at 1Hz load frequency were applied to these nitinol test samples for 5 days. This corresponds to nearly ½ million loading cycles, which is approximately the number of steps taken by a healthy individual in the course of 2 months.[1] The load level is below or near the published endurance limit of nitinol (200 MPa at zero mean stress)[2].

At the end of the stress regimen, specimens were inspected using reflective light microscopy. After cleaning, specimens were analyzed using XPS and AFM.

The specimens used in the experiments were prepared from 0.15 mm thick austenitic nitinol (Nitinol Devices Corporation, Fremont, CA); electropolished and passivated. This treatment results in surfaces that exhibit corrosion rates of about 9.4±4.4 nA/cm$^2$ (0.9% saline at 37$^o$C; Tafel method in an Avista type cell using a Gamry Femtostat; Gamry Instruments, Warminster, PA).

The CF device was built with autoclavable polycarbonate. The spot welded electrical contact areas of the specimens were coated with a lacquer film.

**Results:** We found that repetitive bending in the presence of activated macrophages has significant effects on the corrosion sensitivity, surface chemistry and roughness of nitinol.

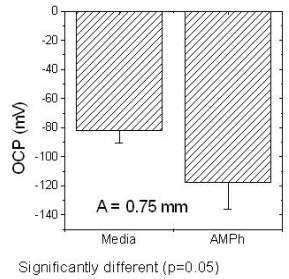


Figure 1. Effect of AMPh vs. media only on OCP after repetitive loading at 0.75mm amplitude (0.28% strain).

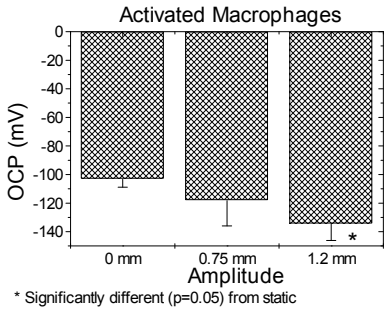


Figure 2. Effect of increasing amplitude when activated macrophages are seeded on the nitinol surface.

We observed significant ($p<.05$) sensitization of nitinol in the presence of adherent AMPh and repetitive loading compared to cell-free nitinol surfaces (Fig.1). We also observed increasing sensitization of nitinol with loading amplitude (strain) in the presence of adherent AMPh (Fig.2). Under similar loading at 1.2 mm in the presence of AMPh, we observed a decrease of the metal-bound oxygen component in the XPS spectra as compared to loading in media with no adherent cells or loading specimens with adherent cells at a lesser amplitude. Using AFM, we also observed a statistically significant increase of surface roughness on nitinol specimens with adherent cells subjected to the 1.2 mm bending protocol compared to the control conditions.

**Conclusions:** Acting synergistically, activated macrophages and repetitive bending at strain levels that are "safe" (below or near the endurance limit of nitinol) cause statistically significant corrosion sensitization of nitinol. This sensitization is likely to result from damage to the surface oxide. This effect appears at a relatively low number of loading cycles that corresponds to only 2 months of implant life. Also, the realistic strain levels for various arteries and stent designs must be determined, since they could be significantly above those tested.

1. Chen EH, Black J, J. Biomed. Mater. Res., 1980, 14**,** 567-86.
2. Pelton AR et al., in Materials and Processes for Medical Devices Conference, Anaheim, CA: ASM International, 2003, pp. 199–204.