SMART Sensors for the Detection of Metal Ions in Orthopedic Patients: Initial Outcomes

Irene O’Hara 1, Dmitry Royzman 2, Divya Biju Kumar 3, Asimina Kiourt 3, Shalini Prasad 3, Joshua Jacobs 2, Mathew T. Mathew 2

1Marquette University, Milwaukee, WI; 2Rush University Medical Center, Chicago, IL; 3Ohio State University, Columbus, OH; 4University of Texas, Dallas, TX.

Email: mmathew@uic.edu

Disclosures: Irene O’Hara (N), Dmitry Royzman (N), Divya Biju Kumar (N), Asimina Kiourt (N), Shalini Prasad (N), Joshua Jacobs (N), Mathew T. Mathew (N)

INTRODUCTION: As per 2016 statistics, over 2.5 million Americans living with a total hip replacement are accompanied by a 10% implant failure rate [1]. These implant failures are often a result of trichoboration of the implant [2]. Trichoboration combines the mechanical process of wear and the chemical process of corrosion [2]. Artificial joints undergo continual tribological action—occurring mainly at joint articulations—in the corrosive internal biological environment. This continuous exposure results in complications or failure of an orthopedic device. Implant failure often occurs due to the release of metal ions from the implant into the body. Therefore there is an urgent need to develop an affordable, fast, and reliable technique to monitor metal ion levels in orthopedic patients. Our proposed solution is to develop a biosensor [3], calibrated to detect metal ions using electrochemical changes in a tested solution. This sensor will act as an effective diagnostic tool aiding in the clinical examination of the implant performance, as well as guiding the next steps in clinical care for patients with metal implants. Biosensor kits can be provided to the patients for routine diagnostic tools at home, similar to a glucometer for diabetic patients.

METHODS: This study is an extension of a previous collaborative project between UIC, Rush University, and UTD initiated in 2013 (Pentant-61/951,354,03/11/2014) [2, 3]. The previous study used a self-assembled monolayer immobilized gold micro electrode-based printed circuit board (PCB) biosensor based on the electrochemical impedance spectroscopy (EIS) to detect and quantify metal ions of Co, Cr, Mo and Ti—due to their involvement in the degradation of orthopedic implants (Fig 1). This recent study uses a commercially available biosensor, combined with a systematic approach to sensor calibration, testing, and validation [4]. Osteoarthritis was broken up into four stages: 1) Initial experimentation, 2) Calibration, 3) Validation and 4) Testing. Experiments were performed with a DropSens biosensor connected to a potentiostat in a three-electrode cell configuration. A standard protocol was used for the electrochemical testing. Electrochemical testing included open circuit potential test (OCP), and Electrochemical Impedance Spectroscopy (EIS) tests which were used to measure changes in the dissolved metal content in the tested solution. A DropSens strip with a 4mm gold working electrode, platinum reference electrode, and silver counter electrode were used for each test with 100µl of solution applied to the gold electrode. EIS data was also used to model the electrochemical process, to estimate the solution and polarization resistance, and to estimate double layer capacitance. During Stage 1, the sensor responses were standardized with known concentrations of metal content in phosphate-buffered saline and bovine calf serum (BCS). Detection was then optimized by testing a series of dilutions of known concentrations of metal content in BCS. These results were used to in regression analysis to form an equation that predicts the metal content in an unknown solution. During the validation stage, the results of the biosensor were compared with results of ICP-MS analysis. Lastly, the prediction equations were tested in Stage 4 during blind tests. A solution with unknown metal content was given by a third party and the solution’s recorded impedance was used in the previously formatted equations in an attempt to accurately predict the metal content in the solution.

RESULTS: The significant results in Stage 2 and 3 indicated that impedance values increased with increasing concentrations of metal ion species (Fig 2). Although overall impedance was lower in solutions with metal content than solutions without, such as the control BCS, there was a direct correlation between increasing metal content and impedance (R² = 0.96). However, when compared to validated ICP-MS values, the recorded impedance values were approximately the same. These impedance values were used in regression analysis to make prediction models. Blind tests using Na₂MoO₄ solutions statistically significantly predicted concentrations of metal ions- Mo ions (9 nm predicted vs 10 mM actual; Independent samples t-test).

DISCUSSION: There are multiple explanations for the direct correlation between impedance and metal ion content and basic principle of SMART biosensor. One explanation is interference of charge transfer due to the presence of wear particles on the interfacial boundary of the working electrode. Metal ions are more reactive than wear particles, which would cause differences in recorded values of impedance. An explanation is an electromagnetic phenomenon known as the “proximity effect.” [4] Since metal ions are conductors and were tested in such close proximity, this effect could apply. In this phenomenon, if a conductor carries an alternating current and the current flowing nearby, the current distribution in the first conductor is constrained to a smaller region. This current crowding, or proximity effect, gives an increase in the effective resistance of the circuit. When an alternating current flows through a conductor, it creates an associated alternating magnetic field around it. The magnetic fields induce Eddy currents in adjacent conductors. By Lenz’s law, an Eddy current creates a magnetic field that opposes the magnetic field that created it [5]. Eddy currents react back on the source of the magnetic field. These values were sufficient to create a valid prediction model, through regression analysis, and were used in blind tests to successfully predict metal concentrations.

Unfortunately, currently there is no fast, economic and efficient way of detecting metal ion levels in orthopedic patients. Currently, overactive metal ion release usually remains undetected until patients have reach their threshold of pain. The adverse biological side effects due to the degradation of orthopedic implants are all subject for concern given the recent reported increase in the incidences of these adverse tissue reactions [6]. An efficient testing method remains absent from the market. Since the SMART sensor is the first of its kind that has been proposed to noninvasively detect metal ion release from orthopedic implants, it provides an innovative solution to deliver increased care to those individuals suffering from implant-related side effects.

SIGNIFICANCE: The SMART biosensor will be a patient-driven technique that will allow orthopedic patients to have routine home check-ups for metal ion level in their body—very similar to a glucometer for diabetic patients. With proper calibration, these sensors could also be used for a variety of implants (knee, spine and dental implants). As an effective diagnostic tool to detect the on-set of implant failure, the SMART sensor will not only deliver relief to orthopedic patients, but also increase the quality of care delivered to these individuals. Further studies are required with patient samples and clinical trials with suitable modification with wireless technology.


ACKNOWLEDGEMENTS: Orthoillinois: Mark Barba, M.D.; NIH (AR064005 PI: Mathew) ; SMART Summer Program-UICOM-Rockford

Figure 1: Experimental set up for biosensor study.  
Figure 2: Impedance curve for CoCrMo and Na₂MoO₄ solutions (Validation)