

## Development of Polyelectrolyte Multilayer Coatings for Degradable Magnesium Alloys

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**Statement of Purpose:** The use of inert metallic implants for bone fixation and repair is wide spread in today's medical procedures. However, these implants are far from ideal, lacking certain benefits of polymeric and ceramic implants especially high biocompatibility and degradability. As an alternative to this, magnesium-based alloys are under development for bone fixation, drawing the attention of numerous researchers because of the inherent biodegradability of the magnesium metal. To-date, one of the main barriers to the implementation of these metals is the rapid degradation rate, producing undesirable hydrogen gas pockets and premature implant failure. Additionally, with *in vitro* culture studies, low cellular adhesion and proliferation is often observed, likely due to the rapid changes in substrate surface when first exposed to culture media preventing high cellular adhesion. In order to slow this degradation, as well as increase the implant interfacial interaction with native tissue, layer-by-layer polymeric coatings were implemented in this study. A series of composite degradable, inorganic conversion coatings paired with bioactive polyelectrolyte multilayer (PEM) coatings have been developed for the use on pure magnesium or magnesium-based alloys. Inorganic/PEM coatings may serve many purposes when applied to degradable magnesium implants, including improved biocompatibility and osseointegration, controlled corrosion resistance, and controlled delivery of drugs, growth factors or other biomolecules from the implant surface. Although previous coating research has attempted to address individual needs of alloy coatings, through ceramic or polymeric coatings, the inorganic/PEM composite coatings pose the potential to address numerous needs with one coating technology. The current work reports the fabrication of multilayered coatings, consisting of natural and synthetic polymers, assembled using layer by layer (LbL) technique under physiological conditions following pretreatment of alloy substrates under alkaline and/or fluorinating conditions.

**Methods:** PEM coating systems studied have covered a wide array of natural and synthetic polymers, including the use of alginate (ALG) coupled with poly-L-lysine (PLL) and poly (lactic-co-glycolic acid) (PLGA) or polycaprolactone (PCL) coupled with poly(allylamine hydrochloride) (PAH). First, magnesium alloy AZ31 substrates were ground and polished to remove the oxide layer and smooth the surface. Substrates were treated with NaOH or HF to create an inert inorganic layer on the alloy. Following this treatment, ceramic-coated substrates were subjected to a series of cationic and anionic polymer solutions. For all substrates, the first layer was polyethylenimine (PEI) which provided a strong cationic base layer. Subsequent to this, layering schemes included: alternating polycaprolactone with poly(allylamine hydrochloride) (PAH), poly (lactide-co-glycolide) (PLGA)

with poly(allylamine hydrochloride) (PAH), sodium alginate (ALG) with poly-L-lysine hydrobromide (PLL), and ALG-PLL coatings with subsequent cross-linked fibronectin layers. Buildup of coating layers was assessed using a combination of SEM, XRD, FTIR and AFM techniques. The initial corrosion resistance was assessed by measuring the electrochemical polarization curves and Nyquist plots as well as the hydrogen evolution in Hank's Solution and magnesium ion concentration released into cell culture media. The effect of the various coatings on MC3T3 pre-osteoblast and HMSC cell viability and morphology was tested with Live/Dead staining, DNA quantification and staining of cellular actin and nuclei.

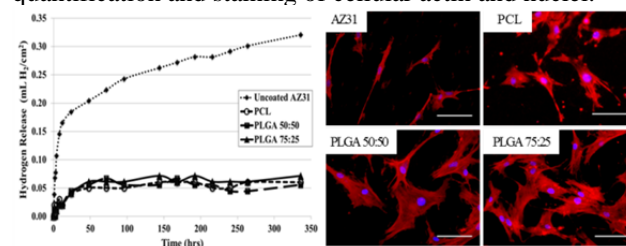


Fig 1: Hydrogen evolution (left) and HMSC morphology on AZ31-Mg(OH)<sub>2</sub>-Synthetic Polymer LBL composite coated substrates

**Results:** Testing from previous studies suggests the need to combine inorganic and highly adhesive organic coatings in order to create a coating which is stable for even a short period of time on the surface of a magnesium substrate. Results from the material characterization studies (AFM, XRD, SEM, FTIR) confirms the formation of the inorganic Mg(OH)<sub>2</sub> or MgF coatings on the AZ31 surface as well as the incremental build-up of the layer-by-layer coatings. Corrosion testing demonstrated that the all combined organic-inorganic coating combinations tested resulted in decreased corrosion of the AZ31 substrate, especially with respect to maintaining a low level of hydrogen release. Cytocompatibility studies showed improved cellular adhesion with the PCL, PLGA and fibronectin-coated substrates. Figure 1 shows the hydrogen evolution and corresponding HMSC cellular morphology on some of the synthetic polymer coated substrates.

**Conclusions:** The goal of these coatings is clearly not to fully prevent corrosion, but to temporarily suspend it so that the initial spike in corrosion, and corresponding hydrogen evolution, is not observed with the magnesium implant. Simultaneously, these coatings should improve the cellular integration and ultimate function to release pertinent drugs or growth factors which will aid in early time point healing mechanisms of the injured bone. Future studies will focus on the sustained release of drugs from PEM coatings.

**References:** The work discussed here is in part published as two recent articles. [1] Ostrowski N. *Acta Biomater* 2013; 9: 8704-8713 and [2] Kunjukunju S. *Acta Biomater* 2013; 9: 8690-8703.