Evaluation of Magnesium Alloys for Tracheal Stent Application

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Statement of Purpose: Tracheal stenting is used for successful management of adult airway obstructions; including tracheal stenosis.[1] The permanent nature of non-degradable tracheal stents makes them a last resort treatment option especially for pediatric patients. Complications related to stent removal and restenosis could be avoided with a degradable tracheal stent placement. Magnesium alloys in this regard have shown promise as degradable materials for orthopedic and cardiovascular applications.[2,3] In our previous study, AZ31 alloy exhibits the best overall degradation and biocompatibility in rat trachea model. In this study, we fabricated a novel ERC-P-06 alloy based on first principles calculations and explored the potential of this alloy for use as degradable tracheal stents.

Methods: Pure elemental metals used as initial materials were melted at 720°C. The ingots were T4 heat treated and extruded with an extrusion speed of 1 mm/s. To study the *in vitro* degradation behavior of ERC-P-06 alloy, samples were immersed in Hanks' solution for 1, 2 and 3 weeks according to the ASTM G31 protocol. Corrosion rate was calculated based on weight loss and the corrosion layer was assessed by SEM/EDX. Mechanical properties were further assessed based on ASTM E8 standard. For primary cytotoxicity evaluation, MTT test was conducted on BEAS-2B cell line (human bronchial epithelial cells). To further evaluate the feasibility of the new ERC-P-06 alloy, two ERC-P-06 alloy prototype stents as well as two AZ31 stents serving as controls were implanted into four New Zealand rabbits for 4 weeks. Following this, rabbit airway tissue response to the magnesium stents were measured by tracheal endoscope and histology analyses.

Results: The gran size (Figure 1) was greatly refined after extrusion. In the transverse direction, typical undefined grains characteristic of extrusion are visible due to severe plastic deformation. The grains were elongated as expected along the extrusion direction. The corrosion resistance of ERC-P-06 alloy was significantly improved after extrusion (Figure 2). Compared to AZ31, even though the corrosion rate was slightly higher, corrosion appears to be more uniform for ERC-P-06 alloy. Due to grain refinement, the strength and ductility were significantly improved after hot extrusion.

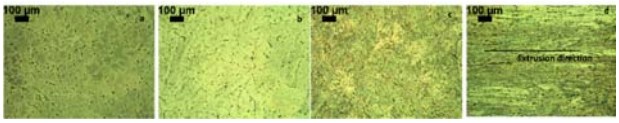

Figure 1. Microstructure of ERC-P-06 alloy (a) as cast, (b) T4 treated, (c) as extruded, transverse section, and (d) as extruded, longitudinal direction.

MTT test showed relative high cell viability after the extract of ERC-P-06 alloy was diluted more than 50% (Figure 3) which implies that the degradation product of Mg stents would not negatively affect the tissue when diluted by mucus in airway upon implantation.

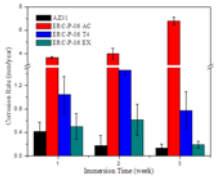

Figure 2. In vitro degradation behaviour of ERC-P-06 alloy in Hank's solution.

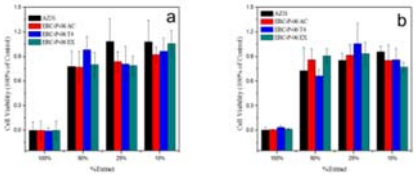

Figure 3. Cell viability of BEAS-2B cells cultured for (a) 1 day, (b) 3 days.

Prototype stents (Figure 4a.) were made by CNC machining. All the rabbits recovered very well after implantation surgery. However, some rabbits experienced respiratory distress later. Two rabbits implanted with AZ31 stents were euthanized two week post-surgery. The endoscope image shows that all the stents were covered with whitish gel after two weeks of implantation.

Figure 4. (a) The image of prototype stent and (b) the histology analysis of ERC-P-06 stent after 4 weeks of implantation (40X). ST=stent, DL=degradation layer.

H&E staining of tracheal tissue (Figure 4b) showed that the epithelium layer of tracheal lumen remain intact, however, some parts of epithelium layer did thicken, which could be caused by implant irritation. Histology image also indicated that the size of the stents is smaller than the lumen, which could cause respiratory distress.

Conclusions: ERC-P-06 alloy exhibits potential for use as degradable tracheal stents for tracheal obstruction. Extruded alloy shows less pitting, higher corrosion resistance and optimized mechanical properties. *In vitro* and *in vivo* test shows promising data for conducting future pre-clinical study in large animal models.

References: 1 Saito Y., Imamura H. Surgery today 2005;35:265-70. 2 Walker J., Shadanbaz S. *et al* J Biomed Mater Res B 2014;102:1316-31. 3 Haude M, Erbel R., Lancet. 2003; 381:836-44.