Final Report

Project acronym: *ISIDE*
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Publishable project summary

The increase of pathologies affecting bone tissue and requiring invasive surgery (cancer, osteomyelitis, osteoporosis or traumatic bone lesions) together with the progressive aging of the population (leading to degenerative bone diseases) have significantly increased the market for bone substitutes, prostheses and implants. ***ISIDE*** aims to give a strong breakthrough in this scenario, by developing innovative resorbable and corrosion-controlled customized prostheses. A multidisciplinary approach has been proposed, involving a team composed of medical and material scientists, manufacturing and chemistry engineers, biochemists, biologists, and biomechanical engineers.

ISIDE aims to get "smart" and translational solutions to the major challenges of biomedical prostheses and biomaterials based on the possibility to:

- reduce implant failure due to bacterial infection,
- improve the implant surface features for quicker and better osteogenesis.

ISIDE also aims to innovate biomedical prostheses characterised by a controlled degradation rate, which do not need any second surgery to be removed and which have shapes perfectly fitting the patient's anatomy.

During the ***ISIDE***, commercial AZ31B and custom ZX31 alloys were produced by hot rolling and shaped by innovative production methodologies (i.e. Single Point Incremental Forming, SPIF and Super Plastic Forming, SPF) and treated by an alternative way of functionalisation and coating. The custom alloy was based on rigorous studies on the recent literature on the various effects of additive elements. For example, Al present in large proportions in AZ series alloys are suitable for mechanical improvements but is potentially cytotoxic due to its well documented adverse effect on the permeability of membranes of mitochondria. Hence, it was replaced with Ca in the custom alloy, increasing Zn concentration to 3% compared to AZ31. This was hypothesized to enhance the properties of the alloys from many aspects including its biocompatibility, toughess, ease of manufacturing to name a few. Experimental results confirmed the validity of the hypothesis.

Concerning the manufacturing processes, a wide experimental investigation allowed us to identify the correlation between the process parameters both mechanical performance and corrosive behaviour of the magnesium substrates. According to that, for SPIF and SPF a good knowledge of the optimal process configuration that improves the coating performance and the prosthesis degradation phenomena was developed within the ***ISIDE*** framework.

Furthermore, to change the degradation behaviour of AZ31B alloy, various type of coatings based hydroxyapatite (HAp) were developed by RF magnetron sputtering. These coatings are: Hydroxyapatite undoaped and doped with Si, Mg or Si+Mg. Because the HAp properties depend on the deposition temperature, the effect of deposition temperature on the properties of the coated AZ31B alloy was evaluated in the range of RT- 400 °C. As a conclusion, HAp coatings can be used to improve the properties of AZ31B alloys, but just up to 200 °C; beyond this temperature, the mechanical and the anticorrosion properties are lost. Regarding the dopant, the HAp properties are the best when the dopant is a combination of Si and Mg.

During the ISIDE project, biomedical investigations were conducted on magnesium devices manufactured using the processes mentioned above. These investigations focused on evaluating their cytotoxicity, osteogenic/osteoinductive potential and antibacterial properties, allowing us to identify novel Mg devices characterized by improved biological properties. Biochemical coating of the different alloys has been successfully achieved by using mussle-derived peptides additionally equipped with on-demand releasable antibiotics. It has been proven that this biochemical coating improves the biomaterials significantly.