Degradation and characterization of porous constructs for craniofacial space maintenance and antibiotic delivery

Allan M. Henslee, Sarita R. Shah, Patrick P. Spicer, Antonios G. Mikos, F. Kurtis Kasper
Department of Bioengineering, Rice University, Houston, TX

Statement of Purpose: Current clinical strategies to achieve soft tissue and bone repair in the craniofacial complex often include initial implantation of a solid space maintainer, designed to prevent soft tissue collapse into the bony defect until such time as a more definitive procedure such as autografting, can be performed. Current space maintainers composed of polymethylmethacrylate (PMMA) bone cement can be shaped to the defect *in situ* but are non-degradable, necessitating the need for an additional surgery to remove the implant. Additionally, these implants are non-porous, which has been shown to increase the incidence of wound dehiscence (opening of wound to the environment) when compared to porous implants. Therefore, the need exists for an *in situ* moldable implant with immediate porosity upon implantation and the ability to degrade over time. In this study, poly(propylene fumarate) (PPF), an osteoconductive polyester previously used in our laboratory for orthopaedic applications, was combined with carboxymethylcellulose (CMC) and poly(lactic-co-glycolic acid) (PLGA) microspheres that served as early and late stage porogens, respectively. PLGA has the additional advantage of providing a drug delivery platform. Based on previous studies, the PPF to crosslinking agent ratio and PLGA weight percentage were selected as parameters most likely to affect scaffold degradation. The objective of this study was to determine the effects of PPF to crosslinking agent ratio and PLGA weight percentage on the mass loss of scaffolds under accelerated (acidic) degradation conditions.

Methods: Poly(propylene fumarate) was synthesized as previously described[1] with a molecular weight of 1100 Da and a polydispersity of 1.4. CMC was purchased from Ashland and reconstituted in ddH_2O at 9 wt %. 50:50 PLGA was purchased from Lakeshore Biomaterials and formulated into microspheres using a water-in-oil-in-water double emulsion technique as previously described[2].

Parameter	High	Low
PPF:NVP ratio	3:2	2:3
PLGA wt %	40	30

Table 1: High and low values for each parameter.

Scaffold composites were fabricated by combining CMC at 40 wt %; PPF and its crosslinking agent, n-vinyl pyrrolidone (NVP); and PLGA at the relative amounts listed in Table 1. Composites were allowed to crosslink at 37°C for 24 hours, leached in deionized H_2O for 24 hours, and placed in ph 4.0 phosphate citrate saline at 37°C for accelerated degradation. Scaffolds were analyzed for mass loss at day 1 (after leaching), and at 2 and 4 weeks after fabrication. Scaffold images were generated using microCT and SEM analysis.

Results: Results are presented in Figure 1. MicroCT image analysis shows pores throughout each scaffold, while SEM shows pores can be found on the surface of each group. Gravimetric analysis shows significant mass loss for all groups at 4 weeks compared to day 1. The data also shows that the group with a 3:2 PPF:NVP ratio and 30% PLGA exhibited significantly less mass loss at 4 weeks when compared to all other groups.

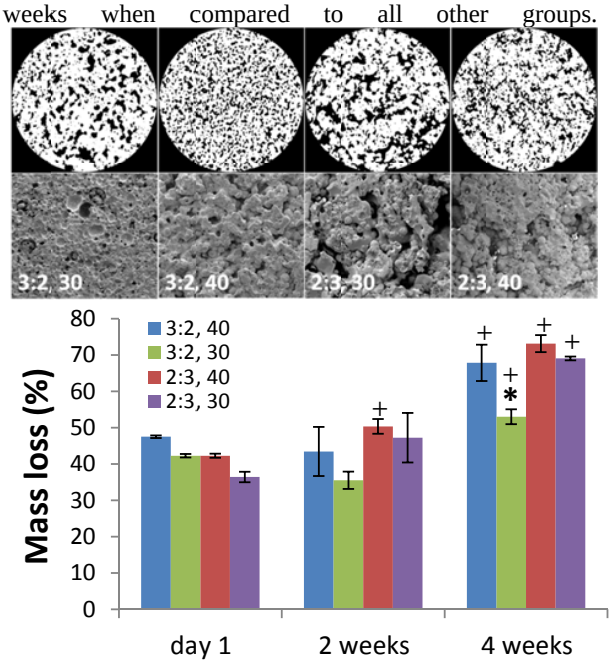

Figure 1: MicroCT (top) and SEM images (middle) of scaffolds at 2 weeks degradation. Mass loss (bottom) of scaffolds over 4 weeks as measured by gravimetric analysis. * indicates a significant difference between groups at that time point only, while + indicates a significant difference from the previous timepoint for that group, $p < 0.05$. Groups are named according to PPF:NVP ratio and 40 or 30 wt % of PLGA.

Conclusions: The results of the characterization show that all groups of scaffolds exhibit a porous structure from day 1. As previously mentioned, this aspect is important in reducing implant dehiscence as the pores are thought to provide "anchor points" for soft tissue to adhere. Under accelerated conditions, the results indicate that significant degradation is occurring, especially at the 4 week time point. Also the 3:2, 30 group exhibited significantly less mass loss at 4 weeks compared to other groups, perhaps because the ratio of PPF in conjunction with a low percentage of PLGA caused the PLGA microspheres to become completely entrapped by PPF, as evidenced by SEM. This entrapment may then have temporarily sequestered the PLGA from the surrounding media, thereby slowing early degradation of the PLGA. The mass loss observed in this group (3:2, 30) may impact its application in drug delivery. Therefore, future studies analyzing drug release from these scaffolds are warranted.

References:

1. Kasper FK. Nat Protoc 2009;4(4):518-525.
2. Henslee AM. Acta Biomat 2011;7(1):3627-3637.