

Tailoring Properties of Microsphere-Based Poly(lactic-co-glycolic acid) Scaffolds

Amanda Clark¹, Todd A. Milbrandt^{2,3}, and David A. Puleo¹

¹ Center for Biomedical Engineering, University of Kentucky, Lexington, KY, USA

² Department of Orthopaedic Surgery, University of Kentucky, Lexington, KY, USA

³ Shriners Hospital for Children, Lexington, KY, USA

Introduction: Biodegradable scaffolds are being used for tissue engineering applications to allow the body to heal naturally by creating a cell environment that promotes proliferation and differentiation (*J R Soc Interface* 6:331, 2009). Poly(lactic-co-glycolic acid) (PLGA) is commonly used in this application because it exhibits biodegradable and biocompatible properties. PLGA properties can be altered easily, allowing for finite control over the degradation, drug release and mechanical properties. One such property is the molecular weight. By varying the molecular weight in a uniform scaffold or in a mixed scaffold, which contains multiple molecular weights in the form of microspheres, gives the user the ability to tailor the properties for a desired outcome.

Methods: Uniform scaffolds (containing microspheres made from only one molecular weight of polymer) were made using a variation of the salt-leaching process, which allows for control of the pore size. The pore size was <150 μm , which was chosen based on previous work done. PLGA (50:50, acid-terminated) microspheres of varying molecular weight microspheres were prepared using the W/O/W double emulsion technique. The two molecular weights used were 12,000 Da, referred to as the low molecular weight (LMW) and 30,000 Da as the high molecular weight (HMW). The microspheres were sieved then mixed with 60 wt% of uniformly sized NaCl. After consolidation using a Carver press and “sintering” at a controlled temperature, described later, salt was leached in deionized water. The same process was followed to make mixed disks composed of microspheres made from two different molecular weights, in which various amounts of HMW microspheres were mixed with LMW microspheres before consolidation. The total mass of microspheres and NaCl per disk was constant. The sintering temperature used was 43 °C in all scaffolds except for 100% HMW scaffolds, which were sintered at 49 °C. The final scaffolds had a mass of approximately 44 mg and disk diameter of 6.0 mm.

To measure degradation, samples were shaken at 37 °C in 4 mL PBS, which was changed every two to three days. At each time point, disks were removed, lyophilized and the remaining mass was measured. A Bose ELF 3300 mechanical testing system was used to measure the compressive modulus of dry samples as well as samples incubated in PBS for five days. Morphology of samples was examined by scanning electron microscopy.

Results and Discussion: Preliminary studies showed that degradation of uniform LMW scaffolds was significantly different compared to HMW (Fig 1.). Ongoing studies

will determine the degradation of mixtures of the LMW and HMW microspheres, which are expected to fall somewhere in between the two curves shown in Fig. 1. Knowing the degradation rates will be an important factor in controlling the scaffold longevity and related drug release kinetics.

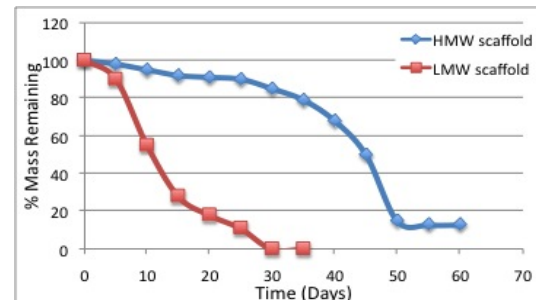


Figure 1. Degradation curves comparing LMW to HMW. Compression tests (Fig. 2) showed that the modulus was significantly different ($p < 0.01$) between the LMW scaffold and all other types, except the 75:25 due to large error. Modulus decreased with the addition of HMW microspheres, thought to be due to the sintering temperature being too low for the HMW microspheres to fuse together, creating discontinuities in the scaffold. This mechanical property is important for maintaining the necessary rigidity to allow for cell ingrowth and matrix without collapsing. Further studies are being done to measure properties at various degradation time points to ensure the modulus is not deteriorating too quickly.

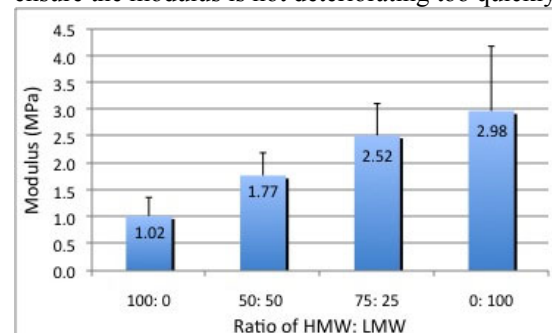


Figure 2. Compressive modulus for scaffolds (all disks sintered at 43 °C).

Conclusion: Degradation and mechanical properties of porous PLGA scaffolds can be changed by altering the composition of microspheres used to fabricate the scaffolds. By understanding how the properties vary, the scaffold can be tailored to specific needs depending on the application.

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