Degradation of PLGA Scaffolds Under Dynamic Loading

The Challenge:

To Determine Degradation of PLGA Scaffolds Subjected to Unsteady Mechanical Loading

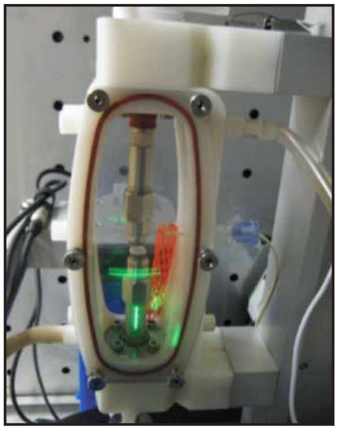
Background

PLGA is a commonly chosen material for many biomedical applications due to its biocompatibility and biodegradability. Many studies have been developed to determine the degradation rate of PLGA under static loading conditions and in the presence of common solvents. However, few studies have investigated the effect of dynamic mechanical loading on scaffold degradation, a relationship that needs to be investigated, as PLGA scaffolds are subjected to dynamic mechanical forces in many in vivo applications.

Figure 1 – The degradation of a disc PLGA scaffold was investigated under dynamic loading conditions.

In this study, the ElectroForce® 5110 BioDynamic® test instrument was used to impose cyclic loading on a standard, disc PLGA scaffold (Figure 1) while changes in sample geometry were monitored over time.

Meeting the Challenge



The ElectroForce BioDynamic 5110 test instrument is ideal for in vitro scaffold degradation studies because it applies axial loading, such as compression, and fluid perfusion all inside of a sterile culture chamber (Figure 2). In this study, the chamber was used with porous platens for compression experiments and fluid perfusion.

Figure 2 – The PLGA sample was mounted between two porous platens inside of a BioDynamic® chamber. The ElectroForce® BioDynamic 5110 test instrument can be used to apply dynamic loading (such as compression) and fluid perfusion.

To mimic the dynamic loading conditions that are seen in vivo, PLGA scaffolds were stimulated with cyclic strain for 8 days while axial displacement, load, chamber pressure, and scaffold diameter were recorded once every hour. During the experiment, the chamber was perfused with saline at a rate of 5 mL/ min to maintain scaffold hydration (Exp Group). Three additional groups without axial loading were used for control comparisons:

- Dry scaffolds (Ctrl Group)
- Hydrated scaffolds with perfusion only (+Perf Group)
- Hydrated scaffolds without perfusion or axial loading (-Perf Group)

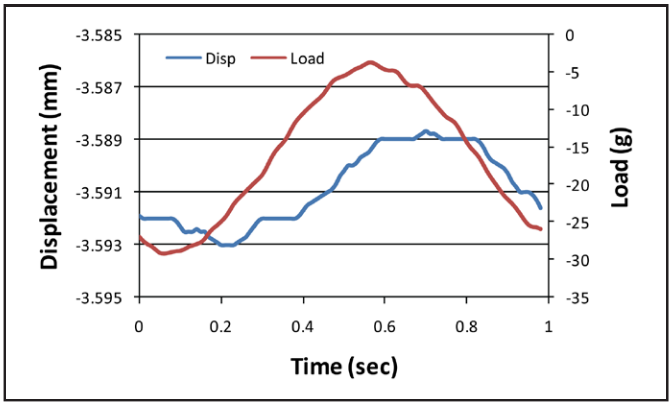


Figure 3 – The PLGA scaffold in the Exp. Group was subjected to sinusoidal loading from 5 to 30 grams at a frequency of 1 Hz.

The cyclically loaded PLGA scaffold (Exp) was subjected to a 1 Hz sinusoidal load compressing the sample from 5 to 30 grams (Figure 3). This data, collected over 8 days, was used to calculate the PLGA modulus as a function of time (Figure 4). The displacement curve shown in Figure 4 is representative of the absolute mover position as it relates to the total travel of the motor. During experimental straining, the bottom platen was moved while the top platen remained in a fixed position (-5.1 mm absolute).

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As the scaffold height was reduced over the eight test days, the displacement of the bottom platen increased to maintain the defined loads. This degradation-related change in scaffold geometry is associated with a decreasing modulus over time. A dramatic decrease in the modulus can be seen during the first two days of the loading period, but this time-dependent effect appeared to stabilize by the eighth experimental day.

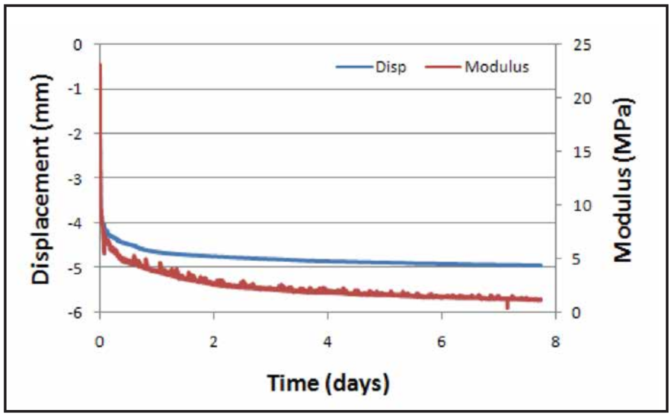

Figure 4 – When cyclic loading was applied to the PLGA, the scaffold modulus decreased over the 8 day test period. Sample thickness decreased during the test period, so to maintain loading, the absolute mover displacement increased over time.

End point testing was then performed to compare the degradation of the experimental group (Exp) to the three control groups (Ctrl, -Perf, and +Perf). A stress-strain analysis was selected to account for any alterations in sample geometry due to extended loading that would not be represented accurately with a force-displacement analysis. The Green strain and 1st Piola-Kirchhoff stress, respectively, are given by:

$$E_{zz} = \frac{1}{2}(\lambda_z^2 - 1) \text{ and } t_{zz} = \frac{F_z}{A_c}$$

where the stretch ratio is $\lambda_z = l/L_o$ with the loading height, l, and unloaded height L_o; F_z is the current force; and A_c is the contacted area.

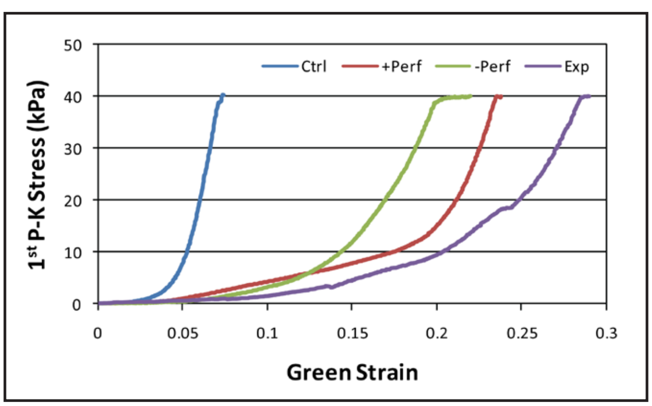

Figure 5 – Stress-strain data showed that axial compression and liquid perfusion resulted in the most compliant scaffold group (Exp) and dry scaffolds were stiffer than any hydrated groups (Ctrl).

The stress-strain analysis of the four PLGA sample groups indicated that full dynamic loading with axial compression and fluid perfusion (Exp) increased sample compliance, as compared to the unloaded states (Ctrl and –Perf, respectively) (Figure 5). Fluid perfusion alone (+Perf) was also shown to increase compliance (degradation) as compared to hydration alone (-Perf). Finally, dynamic loading through cyclic compression (Exp) led to increased scaffold degradation, or compliance, as compared to static loading through fluid perfusion. Ultimately, these results indicate that studying only the effects of static loading on scaffold degradation is insufficient to fully capture the degradation characteristics of the scaffold material. Dynamic loading protocols that mimic the dynamic stress state of the body must also be applied to properly characterize scaffolds.

Summary

In this study, the ElectroForce® 5110 BioDynamic® test instrument (Figure 6) was used to precisely load PLGA scaffolds and record finite changes in the sample material response and geometry. Scaffold degradation, indicated by increased compliance, was greater when dynamic loading was applied to hydrated samples, as compared to dry, unloaded controls. Dynamic loading with cyclic compression and fluid perfusion was also shown to increase scaffold degradation, as compared to static loading with fluid perfusion alone.

The BioDynamic system is ideal for scaffold characterization applications that require highly-controlled sample stimulation in a sterile, cell culture environment. The system's automated control mechanisms, accessible through the user-friendly WinTest® software package, allow researchers to generate reliable results without the need to constantly adjust or monitor an experiment. The frictionless design of the patented Bose® linear motor assures precisely-controlled compressive (or tensile) loading over billions of cycles.

Figure 6 – ElectroForce® BioDynamic® 5110 Test Instrument

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