Photochemical Modulation of Hydrogel Scaffolds and Nanoindenter-based Stiffness Quantification

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Biomechanical properties of the extracellular matrix, such as stiffness and porosity, are known to influence cell adhesion, migration, and differentiation. A key area of interest in tissue engineering is developing 3D *in vitro* models that recapitulate the ECM to better understand how these properties contribute to development and disease. Here, we present an approach to modulate the stiffness of a 3D hydrogel scaffold that relies on photochemical reactions and the electronic excitation of a photosensitizer. Using benzoporphyrin-derivative (BPD)-mediated photodegradation and riboflavin (RF)-mediated photocrosslinking, we photochemically modulated the stiffness of Matrigel hydrogels and quantified these changes using nanoindentation. Despite challenges with a poor signal-to-noise ratio, we demonstrated a significant decrease in stiffness between control groups and groups with BPD and 20 J/cm2 of light that followed a similar trend to bulk rheology measurements. We also found a significant increase in stiffness between control groups and groups with RF and 10 J/cm2 of light. However, the heterogeneous composition and batch-to-batch variability of Matrigel may influence the extent and replicability of this stiffness modulation. Despite these limitations, the spatiotemporal resolution of these light-based modalities has significant potential for further optimization in different hydrogels and future work with optical patterning.