Biological Design Doctoral Defense

Light-Activated Biomaterials for Soft Tissue Sealing and Wound Repair

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Abstract

Sutures, staples and tissue glues remain the primary means of tissue approximation and vessel ligation. Laser-activated tissue sealing is an alternative approach which conventionally employs light-absorbing chromophores and nanoparticles for converting near infrared (NIR) laser to heat. The local increase in temperature engenders interdigitation of sealant and tissue biomolecules, resulting in rapid tissue sealing. We developed light-activated sealants (LASE) in which indocyanine green (ICG) dye is embedded within a biopolymer matrix (silk or chitosan) for incisional defect repair. Light-activated tissue-integrating sutures (LATIS) that synergize the benefits of conventional suturing and laser sealing were also fabricated and demonstrated higher efficacies for tissue biomechanical recovery and repair in a full-thickness, dorsal surgical incision model in mice compared to commercial sutures and cyanoacrylate skin glue. Localized delivery of modulators of tissue repair, including histamine and copper, from LASE and LATIS further improved healed skin strength. In addition to incisional wounds, histamine co-delivered with silk fibroin LASE films accelerated the closure of full thickness, splinted excisional wounds in immunocompetent BALB/c mice and genetically obese and diabetic db/db mice, resulting in faster closure than Tegaderm wound dressing. Immunohistochemistry analyses showed LASE-histamine treatment enhanced wound repair involving mechanisms of neoangiogenesis, myofibroblast activation, transient epidermal EMT, and also improve healed skin biomechanical strength which are hallmarks of improved healing outcomes. We further investigated the benefit of temporal delivery of a second therapeutic (growth factor nanoparticles) in modulating wound healing outcomes in both acute and diabetic wounds. Our hypothesis of temporal delivery of second therapeutic around the 'transition period' in wounds further improve wound closure kinetics and biomechanical recovery of skin strength. Our results indicate that laser sealing and approximation, together with delivery of immunomodulatory mediators, can lead to faster healing and tissue repair, thus reducing wound dehiscence, preventing wounds moving towards chronicity and lowering incidence of surgical site infections, all of which can have significant impact in the clinic.

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Zoom Link: https://asu.zoom.us/j/8123453596