Light-Activated Sealants for Skin Sealing and Repair

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Statement of Purpose: Despite their widespread use, conventional tissue approximation devices such as sutures and staples suffer from poor initial strength and inconsistent tissue interaction resulting in wound reopening and susceptibility to infection. Also, biomechanical mismatch between skin and sutures or staples can lead to extensive scarring. Laser-activated tissue sealing is an alternative approach that employs light-absorbing chromophores for converting near-infrared (NIR) laser light to heat, resulting in molecular interdigitation of proteins in the tissue and sealant resulting in rapid tissue sealing. Here, we demonstrate a multifunctional technology in which light-activated biomaterials were employed for soft tissue sealing and repair, including in combination with bioactives. We developed light-activated sealant (LASE) biomaterials consisting of NIR laser energy-absorbing chromophores including gold nanorods (GNRs), indocyanine green (ICG) dye, copper chloride ($CuCl_2$), or silver nanoprisms (AgNPr) embedded within a biopolymer matrix (silk) using film casting methods. LASEs were formulated with $CuCl_2$ and AgNPr because of their ability to combat surgical site bacterial (e.g., MRSA) infections, in addition to their ability to convert laser energy to heat. The role of bioactives, e.g. histamine, on LASE-mediated tissue repair was also investigated.

The efficacy of LASE-mediated tissue sealing and repair was determined using i) ultimate tensile strength (UTS) of the healed skin and ii) transepidermal water loss (TEWL) on day 2 and day 7 post surgery and compared with suture-approximated skin (control). TEWL measures loss of water vapor loss from the epidermis and dermal discontinuity due to wounding elevates these values because of the loss of barrier function of the skin. TEWL values that are comparable to the unwounded skin indicate restoration of the barrier function.

Methods: Silk fibroin, enriched from silkworm cocoons, was loaded with ICG, GNRs, $CuCl_2$, or PVP-AgNPr and cast as LASE films using solvent evaporation methods. The photothermal response of sealants, irradiated with lasers at different power densities, was determined using an infrared camera. LASEs that demonstrated temperature increase in the range of 55-65°C were employed for sealing full-thickness incisional wounds in immunocompetent Balb/c, immunodeficient Balb/c SCID, and diabetic and obese db/db mice. In studies involving histamine, the histamine solution was directly loaded into the incision before LASE-mediated sealing. TEWL measurements were performed on days 2 and 7 following sealing using a Delfin vapometer, and skin samples were either collected for histology or UTS measurements. UTS measurements were performed on the TA.XT Texture Analyzer with the clamp separation speed of 1 mm/s and the maximum force at which the tissue failure occurred was recorded as the UTS (in N). Skin samples collected for histopathology were analyzed hematoxylin and eosin (H&E) or Picrosirius red staining.

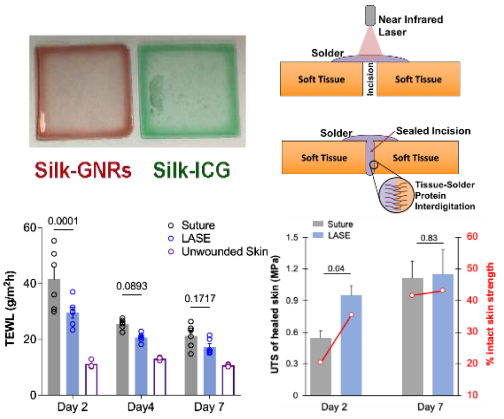

Figure 1. Top: GNR and ICG-LASEs (left); Top: Schematic of LASE sealing of soft tissues (right); Bottom: TEWL (left) and UTS (right)

Results: Skin incisions closed with chromophore-loaded silk films resulted in rapid sealing, enhanced recovery of biomechanical properties (UTS), and barrier function (TEWL) as early as 2 days post wounding in all three strains of mice investigated. Sealing with $CuCl_2$-silk LASEs resulted in TEWL values comparable to that with sutures, but AgNPr-silk LASEs resulted in significantly lower values, indicating better restoration of barrier function. Histopathology of silk-ICG treated incisions demonstrated equivalent tissue recovery by 7 days with an effect on coordinated neutrophil (Ly6G+ cells) spatial localization towards the LASE material instead of throughout the wound space at day 2 of healing with similar levels of resolution on day 7. Delivery of histamine resulted in further enhancement in skin tensile strength on day 3 post surgery, indicating the benefit of bioactive delivery during laser sealing. TEWL values of histamine-silk-ICG treated incisions were comparable with suture group.

Conclusions: Our results indicate that NIR laser sealing with LASEs led to improved healing outcomes in different strains of mice. This approach can have a significant clinical impact on routine surgeries, healing of acute wounds, and trauma management.