Chromophore-free Tissue Sealing and Repair using Mid Infrared Lasers

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Statement of Purpose: Sutures, staple, and conventional glues are commonly used to approximate tissue edges in surgery and wound healing. However, poor strength, infection, dehiscence, leakage, and / or acute inflammation are common complications associated with these methods. Laser-activated tissue sealing, in which, laser light energy is used to facilitate biomaterial incorporation with the tissue, provides an alternative approach for wound closure. Traditionally, light-absorbing chromophores and nanoparticles have been employed for converting near infrared (NIR) laser light to heat, resulting in the photothermal fusion of the sealant biomaterial with soft tissues. We now demonstrate a novel approach for sealing tissues without the need for chromophores using mid infrared (midIR) laser light. We characterized the absorption of midIR light by several different biomaterials and investigated the rise in local temperature at different laser powers. Optimal operating conditions were employed for midIR based photothermal sealing of incised / ruptured tissue ex vivo and using different skin surgical models in live mice. Recovery of mechanical properties including tensile strength and burst and leak pressures, in concert with histopathology analyses, were employed to determine the efficacy of the seal. The effect of midIR light on cell and tissue viability was also determined. Our results demonstrate that midIR lasers can be used for rapid sealing of soft tissues using conventional biomaterials without the need for chromophores or nanoparticles, which is a significant advantage for rapidly translating this technology in the clinic.

Methods: Chitosan, silk, alginate and cellulose films were investigated as the laser activated sealant regarding their photothermal behavior and adhesiveness to the tissue after laser exposure. Mathematical model as developed to study the temperature change along the sealant and underlying tissue. For ex-viv studies, robustness and mechanical strength of porcine intestine tissue segments following laser tissue sealing were measured and compared to incised and intact tissue. Along with mechanical strength of the sealed wound, leak and burst pressure of the porcine was performed following closure of incision od porcine intestine. Fibroblast cells were also exposed to the laser with different laser density and exposure time. MTT assay carried out for assessing cell viability. in-vivo studies were performed creating 1-cm full thickness incision was made on the back of the mice and the wound was closed using mid-infrared laser tissue sealing and silk suture as the control. The mechanical strength, digital image correlation analysis for strain mapping of the skin and histopathology assessment of the wound was performed on day 3.

Results: Chitosan laser activated sealant provided highest ultimate tensile strength and modulus of toughness among all used hydrogels. Moreover, those hydrogels provided immediate water tight sealing based on leak pressure measurement compare to suture. The proposed model was able to predict the temperature change within the tissue during laser tissue sealing. MTT assay did not show any cell death of any conditioned compared to untreated fibroblast cells. the ultimate tensile strength and modulus of toughness for laser sealed tissue was highly significant compared to incised tissue and similar to sutured closed incisions. Histological evaluation of the wounded area on 3^{th} post healing showed comparable result in angiogenesis and enhanced collagen formation compared to traditional techniques like suturing. Moreover, the digital image correlation analysis showed Laser tissue sealing method can hold the wound better and isolates the wound from nonuniform strains across the incision act as tension shielding without allowing higher shear strain across the incision that might would result in reduced scar formation.

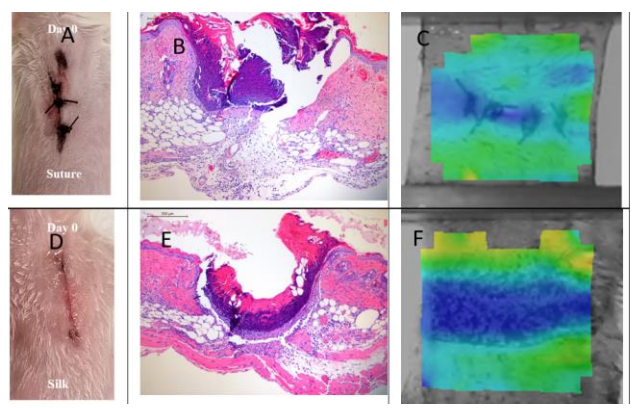

Figure 1. A: incision closed with suture on murine model, B: histological assessment of the incision after 3 days, C: strain distribution on the mouse sin closed with the suture. D: incision closed with laser tissue sealing on murine model. E: histological assessment of the incision after 3 days, F: strain distribution on the mouse skin closed with the laser tissue sealing.

Conclusions: In this study, transparent hydrogel films without any chromophores or nanoparticles were investigated as the sealant material for rapid sealing of soft tissues. The hydrogel provided a watertight seal immediately after surgery, which is a significant advantage for rapidly translating this technology in the clinic. This novel approach is easy to perform and regarding cosmetic aspect of wound healing provides a better option compared to sutures and staples.