In-situ laser-assisted bioprinting of corneal pro-regeneration biomaterials

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Treating corneal wounds with corneal pro-regeneration biomaterials is an alternative to transplantation. To allow good vision, treated corneal wounds must be optically clear and their surface must be smooth. Currently, delivery methods for corneal pro-regeneration biomaterials rely on conventional syringe systems, lacking the precision needed to restore the pre-wound corneal topography. I will present a laser-based technology aiming to tackle this challenge. Our approach involves using our lab's drop-on-demand (DOD) bioprinting technology, known as laser-induced side transfer (LIST) [1-2], as a means to deliver biomaterials to corneal wounds in a precise and personalized manner. We have used LIST to achieve DOD printing of an acellular medium viscosity photo-crosslinkable ink based on Gelatin methacryloyl (GelMa). This formulation supports the growth of human corneal epithelial cells (HCEC) and stromal cells in an in-vitro environment (Fig. 1a). We established optimal printing conditions (Fig. 1b) and found that printed samples preserve their optical and biomechanical properties compared to control samples, including optical transmission (88±2% (printed) vs 90±1% (control)), diffuse reflectance (1.0±0.3% vs 0.3±0.1%), and storage modulus (1.9±0.1 kPa vs 2.1±0.1 kPa). We utilized optical coherence tomography (OCT) to characterize corneal wounds in cadaveric pig eyes (Fig. 1d-1e) and employed LIST for wound filling (Fig. 1f). After UV crosslinking, we observed uniform wound filling, resembling the pre-wound corneal topography with the absence of trapped bubbles or off-target material deposition (Fig. 1g-1h). The sealed wound withstands a pressure of 38±6 mm Hg, 2 times the average intraocular pressure (IOP). In conclusion, our results suggest that LIST printing can efficiently deliver corneal pro-regeneration biomaterials to precisely fill corneal wounds ex-vivo without compromising their optical and biomechanical properties. With further development, this technology could offer an alternative to transplantation for patients who would traditionally be put on corneal transplantation waiting lists.

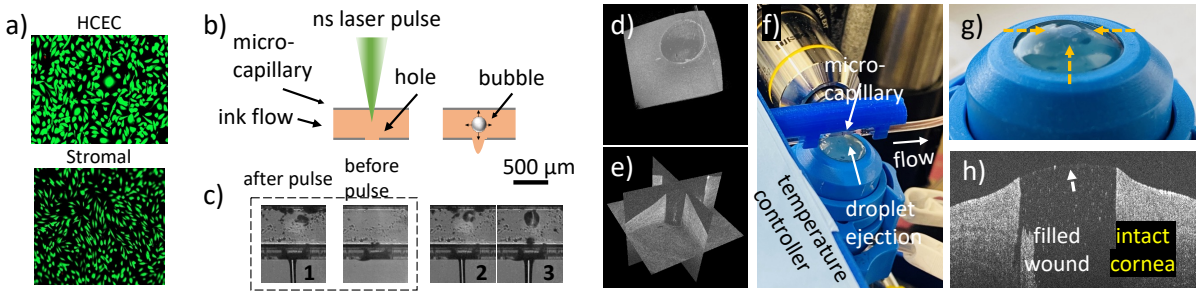

Figure 1: a) HCEC and stromal cell growth on GelMa-based sheets, b)-c) laser bioprinting, d-e) OCT mapping of corneal wounds, f) in-situ bioprinting, g)-h) images of a filled corneal wound.

References: [1] H. Ebrahimi Orimi, S. S. Hosseini Kolkooh, E. Hooker, S. Narayanswamy, B. Larrivee, C. Boutopoulos H. Ebrahimi Orimi et al., Sci Rep 10 (2020) 9730; [2] K. Roversi, H. Ebrahimi Orimi, M. Erfanian, S. Talbot, C. Boutopoulos, Bio Protoc 12 (2022) 1–12.