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Multi-Nozzle Inkjet and its potential for the Industrialization of Bioprinting

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INTRODUCTION: Bioprinting, thanks to the unique flexibility and spatial accuracy it offers, has a promising future for the deposition of cells and extracellular matrices toward the fabrication of physiologically relevant 3D tissue models. Most bioprinting platforms offer switching single-nozzle printheads. In contrast, industrial inkjet printheads feature hundreds of nozzle in parallel while enabling the deposition of drops in physiologically relevant resolution. We hypothesize that this high-throughput industrial technology will enable the cost-effective fabrication of 3D tissue models, potentially leading to the industrialization of bioprinting. To test our hypothesis, we are investigating the reliability of the printing process, its throughput and its impact on cells.

METHODS: A 3D Bioprinting platform was developed and set up with a special Xaar 128 printhead compatible with water-based inks. Bioinks based on culture media with viscosity modifiers were prepared and characterized to improve the stability of the cell suspensions while remaining liquid enough for inkjet printing (<15mPa*s). 3T3 mouse fibroblast, A549 human alveolar basal epithelial and HUVEC were cultivated and suspended in bioinks (3x106cells/mL = 100% concentration) and their sedimentation rate measured. 7mL of the cell-loaded bioinks were fed into the ink system and were kept there for up to 35min of alternating sequences of purging, printing and settling at room temperature. Batches of cell-loaded bioinks were printed as one big drop in a petri dish that was subsequently divided into n=3 wells for culture. To quantify the stability of the process, cell concentration was measured after each batch printing. To measure the impact of the process on the cells, a viability test (Trypan Blue exclusion assays) was performed.

RESULTS & DISCUSSION: When using DMEM with 10%FBS as a bioink, suspended cell concentration in the printed batches dropped to 31% after 5min settling and sedimented cells were observed to clog the nozzles. Increasing the viscosity of the bioink by adding 5% Ficoll PM400 led to an increase of the cell concentration to 81% after 5 minutes settling while limiting the clogging of the nozzles. This indicates that the rheological properties of the bioink can be tuned to improve the stability of the printing process. Viability directly after printing and for up to 4 days culture remained over 85%, suggesting that the printing process and the addition of Ficoll has a limited impact on the cells (figure 1).

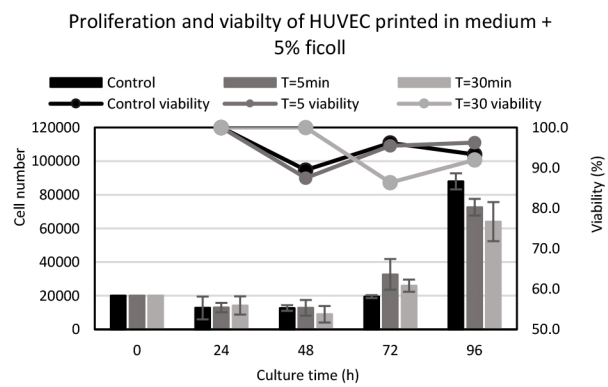

Figure 1: Proliferation and viability of HUVEC printed after T = 5 and 30 minutes settling in the printhead. The control was deposited by pipetting.

CONCLUSIONS: Our study demonstrates that high-throughput and reliable cell deposition can be achieved through industrial inkjet by modifying the rheological properties of the bioink.