Rapid and Precise Drop-on-Demand Bioprinting of Complex Structures with a Handheld System

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Abstract

This case study demonstrates the efficacy of a novel handheld bioprinting system for creating intricate biological constructs. Utilizing a Blue Drop Alginate bioink, structures were printed onto a $CaCl_2$-containing Blue Drop Agarose-based support layer in a glass petri dish. The system's optimized settings, including 37°C printhead temperature and 0.3 bar pneumatic pressure, allowed for the rapid fabrication of complex geometries in under two minutes. Furthermore, the handheld device exhibited remarkable precision, capable of fine detail printing by adjusting shooting modes. Its ergonomic design significantly enhances operability, making advanced bioprinting accessible and efficient for on-demand applications.

Introduction

Bioprinting has emerged as a revolutionary technology for tissue engineering and regenerative medicine, enabling the precise deposition of biomaterials and cells to create functional tissues and organs. However, existing bioprinting platforms often suffer from limitations such as large footprints, high costs, and restricted portability, which hinder their widespread adoption, particularly in point-ofcare settings or for immediate, on-site applications. Handheld bioprinters offer a promising solution to these challenges, providing flexibility and accessibility without compromising printing quality. This case study explores the capabilities of an advanced handheld bioprinting system, focusing on its performance in rapidly fabricating complex biomimetic structures with high precision, utilizing standard biomaterials.

Materials and Methods

Blue Drop Alginate was mixed with DMEM cell culture media to reach a final Alginate concentration of 2% (w/v). A crosslinking support gel was prepared by adding calcium chloride ($CaCl_2$) to a liquified (heated) Black Drop Agarose hydrogel to reach final concentrations of 20 mg/ml Agarose and 100 mg/ml $CaCl_2$. This solution was then cast into a standard glass petri dish to cool down, creating a stable crosslinking layer for bioink deposition and immediate Alginate crosslinking. The Black Drop Dropgun handheld bioprinting station was used for the printing experiments. A Drop-on-Demand (DoD) printhead was used with a 300 µm nozzle. The bioink was loaded into the device, and the printhead temperature was set to 37°C to ensure cell viability and optimal bioink rheology. Printing was performed with an air pressure of 0.3 bar. For continuous deposition, the constant shooting mode was activated with an opening time of 800 µm and a waiting time between drops of 100 ms. For achieving fine details and intricate patterns, the 'constant shooting' mode was deactivated, and a drop count of 1 was set, utilizing the device's instant shooting response. Complex biomimetic structures were bioprinted directly onto the crosslinking bioink layer within a glass petri dish. The handheld bioprinter was maneuvered manually to create the desired patterns (Figure 1).

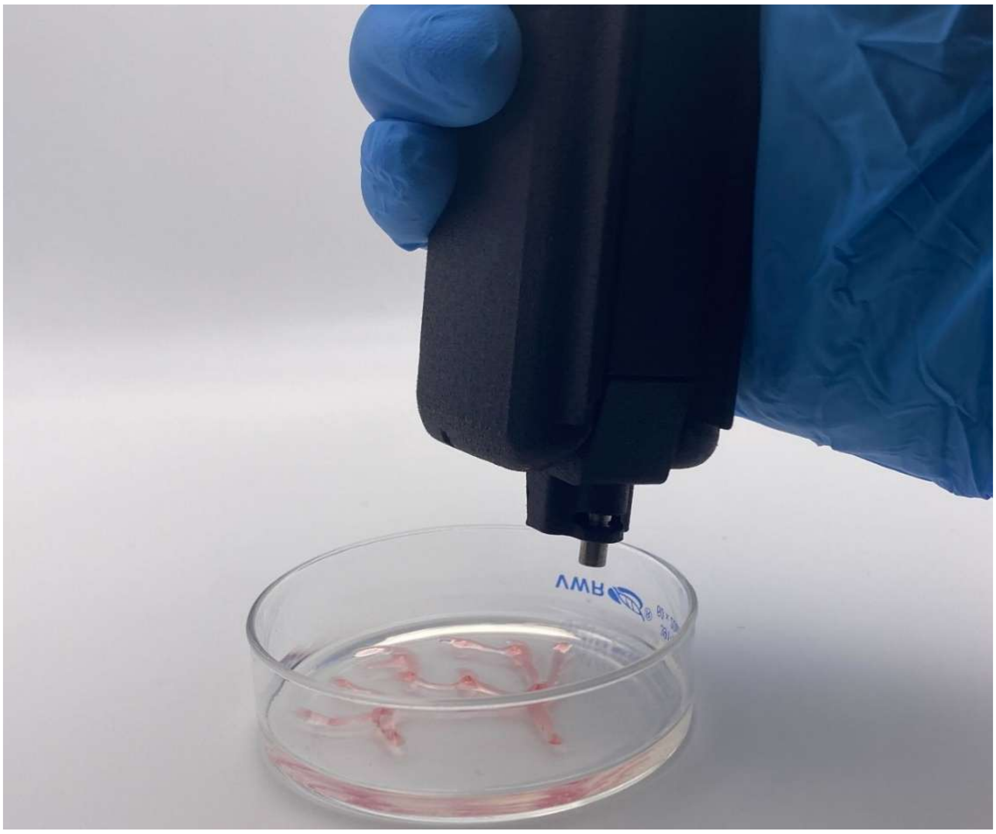

Figure 1: The handheld bioprinter positioned above a petri dish, actively depositing bioink to construct a complex structure.

Results

The handheld bioprinting system enabled the easy fabrication of complex, free-standing biomimetic structures onto a solidified, $CaCl_2$-containing Blue Drop Agarose base layer (Figure 2). The use of 2% Blue Drop Alginate bioink allowed for the creation of stable structures upon contact with the crosslinking base layer. A notable achievement was the speed of fabrication; the entire printing process for a detailed structure was completed in under two minutes, demonstrating significant efficiency compared to conventional benchtop bioprinters. The optimized printing settings (Table 1) facilitated consistent and controlled bioink extrusion, leading to well-defined geometries. Furthermore, the system demonstrated excellent precision for fine detail work. By deactivating the 'constant shooting' mode and setting a drop count of 1, the instantaneous shooting response upon button press enabled the creation of intricate features, confirming the device's capability for accurate, user-controlled deposition.

Figure 2: A biomimetic structure bioprinted using a handheld DoD printhead, illustrating the intricate details achievable with the handheld system.

Opening time	800 µs
Waiting time between drops	100 ms
Constant shooting	ON
Temperature	37 °C
Air Pressure	0.3 bar

Table 1: Optimized settings of the Black Drop Dropgun handheld station.

Discussion

This study highlights the significant advantages of employing a handheld bioprinting system for rapid and precise biofabrication. The ability to print complex structures in under two minutes with viscous biomaterials underscores the potential of such devices for accelerating research timelines and enabling on-demand applications, particularly where speed is critical. The detailed control over printing parameters, including the distinct modes for continuous printing and single-drop deposition, allowed for both rapid bulk fabrication and the creation of fine details, which is crucial for replicating intricate biological architectures. The ergonomic design of the handheld bioprinter was also identified as a key factor contributing to its ease of operation, which in turn enhances user control and accuracy during manual manipulation. This ease of use, combined with its portability, positions handheld bioprinters as a valuable tool for decentralized bioprinting, education, and potentially even intraoperative applications. Future work will focus on integrating live cell viability studies and exploring a broader range of biomaterials.

Conclusion

In conclusion, this case study successfully demonstrated the capabilities of a handheld bioprinting system for creating complex and detailed biological structures with remarkable speed and precision. The system's efficient operation, rapid fabrication time (under 2 minutes), and ability to achieve fine details through controlled deposition modes underscore its potential. The ergonomic design further enhances its usability, making advanced bioprinting more accessible and adaptable for various applications in regenerative medicine and tissue engineering.