Utilisation of first Polish multifunctional 3D bioprinter BioCloner Desktop for printing hydrogel cell scaffolds in controlled clean environment – case study

Wykorzystanie pierwszej polskiej wielofunkcyjnej biodrukarki 3D BioCloner Desktop do druku hydrożelowych rusztowań komórkowych w kontrolowanych warunkach o podwyższonej czystości – studium przypadku

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In this article novel technological solutions for applying additive manufacturing technologies in the biomedical and biotechnological industry are showcased. The BioCloner Desktop (referred to as 'Desktop') is a miniaturised version of an industrial printer developed as part of a project regarding utilising additive manufacturing technologies for manufacturing of bioresorbable implants. In the years 2016–2019, the project was financed from EU resources (project number POIR.01.01.01-00-0044/16-00). During this project, industrial-sized solutions dedicated for medical and pharmaceutical applications were developed.

The Desktop was developed as a way of expanding the possibilities of research and development in a standard biomedical laboratory. The size of the described printer allows it to be placed inside a laminar flow cabinet.

The Desktop is a device which meets the growing need for multipurpose compact desktop bioprinters dedicated for research and development applications. Currently, commercially available laboratory-scale machines lack an open architecture, which puts boundaries on research. Miniaturisation of the BioCloner bioprinter did not sacrifice its key feature of supporting multitool print and convenience of construction for further specialisation.

The BioCloner project, besides bioprinters, also includes dedicated slicing and printer control software. Thanks to its multiplatform compatibility, it is possible to easily increase the scale of production directly after the research process.

The Desktop is equipped with printheads that facilitate multiple methods of 3D printing. From the most popular fused filament fabrication (FFF) to the versatile fused granulate fabrication (FGF) to highly specialised printheads for bioprinting, designed to dispense hydrogels via pressure extrusion. The printheads have also additional features required in the bioprinting process, such as UV crosslinking lights and temperature control (heating as well as cooling). In this article, key features of both the BioCloner Desktop bioprinter and the dedicated BioCloner 3D slicing-operating software are outlined. Its second part is a report on the bioprinter's usage in the Biomedical Engineering Laboratory, named after E.J. Brzeziński, located at Faculty of Mechanical and Industrial Engineering of Warsaw University of Technology. During the study, hydrogel cell scaffolds for culturing WEHI-164 mouse fibroblasts were produced. The structures were obtained using a gelatin methacrylate (GelMa)-based commercially available bioink deposited directly into a cell culture vessel. The structures were fully crosslinked immediately after printing.

All printed scaffolds supported cell proliferation. There were no observed signs of contamination, and the conducted field tests confirmed the assumed functionality of the BioCloner Desktop bioprinter.

KEYWORDS: 3D printing, 3D bioprinting, cell scaffolds, tissue engineering, additive manufacturing

W artykule przedstawiono nowatorskie rozwiązania techniczne pozwalające na wykorzystanie technologii addytywnego wytwarzania w branżach biomedycznej i biotechnologicznej. BioCloner Desktop (dalej: „Desktop") jest zminiaturyzowanym rozwiązaniem opracowanym w ramach trwającego od 2016 r. projektu BioCloner, mającego na celu wdrożenie technik przyrostowych w procesie produkcji implantów wchłanialnych. Projekt ten w latach 2016–2019 był finansowany ze środków UE (projekt POIR.01.01.01-00-0044/16-00 – Pierwsza polska

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biodrukarka dedykowana do implantów wchłanialnych – BioCloner). W ramach projektu BioCloner opracowano rozwiązania wielkogabarytowe przeznaczone do zastosowania w branży medycznej i farmaceutycznej.
Desktop został opracowany z myślą o poszerzeniu możliwości prac badawczo-rozwojowych w typowym laboratorium biomedycznym. Wymiary drukarki BioCloner Desktop pozwalają na pracę w warunkach podwyższonej czystości oraz wewnątrz komory laminarnej. Desktop stanowi odpowiedź na rosnące wymagania stawiane przed kompaktowymi drukarkami nabiurkowymi wykorzystywanymi w pracach badawczo-rozwojowych. Dostępne na rynku urządzenia przeznaczone do biodruku w skali laboratoryjnej nie posiadają otwartej architektury, przez co ograniczają zakres prowadzonych prac badawczo-rozwojowych. Przy zmniejszeniu biodrukarki 3D zachowano wyróżniające BioCloner cechy – wsparcie druku wielogłowicowego oraz otwartość konstrukcji, która pozwala na rozwijanie kompatybilnych głowic i akcesoriów wspierających proces biodrukowania 3D. Projekt BioCloner poza wymienionymi biodrukarkami 3D obejmuje również dedykowane oprogramowanie sterujące zawierające kluczowe z perspektywy biodruku funkcjonalności. Dzięki międzyplatformowej kompatybilności sterowników możliwe będzie szybkie zwiększenie skali produkcji po zakończeniu prac badawczo-rozwojowych.
Desktop jest wyposażony w głowice wspierające różne metody druku przestrzennego. Od najpopularniejszego druku termoplastycznym filamentem *fused filament fabrication* (FFF), poprzez druk wykorzystujący nadtopiony granulat fused granulate fabrication (FGF), po głowice ciśnieniowe opracowane specjalnie do wymagań stawianych przez biodruk. Przykładem tego są głowice przeznaczone do ekstruzji ciśnieniowej hydrożeli z wieloma dodatkowymi funkcjami, takimi jak sieciowanie UV oraz kontrola temperatury (zarówno grzanie, jak i chłodzenie).
Opisywana w artykule drukarka została przetestowana w Laboratorium Inżynierii Biomedycznej im. E.J. Brzezińskiego mieszczącym się na Wydziale Mechanicznym Technologicznym Politechniki Warszawskiej. Wytworzono w nim rusztowania do hodowli fibroblastów mysich WEHI-164. Struktury zostały wydrukowane z hydrożelu bazującego na metakrylowanej żelatynie (GelMa), bezpośrednio w naczyniu przeznaczonym do dalszej inkubacji hodowli. Wszystkie otrzymane struktury pozwalały na zagnieżdżenie się i proliferację rozważanych w badaniu komórek. Nie zaobserwowano oznak zakażenia w trakcie hodowli. Przeprowadzone testy potwierdzają zakładaną funkcjonalność biodrukarki Desktop.
SŁOWA KLUCZOWE: druk 3D, biodruk 3D, rusztowania komórkowe, inżynieria tkankowa, metody przyrostowe

Introduction

A 3D printer could be defined as a device that facilitates methods of additive manufacturing during production, usually referred to as the 'layer by layer' method. Currently, the most widely used desktop 3D printers are based on technology developed during the 90s using the controlled extrusion of melted thermoplastic fed to a moving printhead in the form of a wire. This method allows for the preplanned deposition of fused material in the 3D printer's workspace [8].

3D printing is a method of manufacturing which, thanks to the nature of the additive manufacturing process, allows the designer to work outside of limitations set by conventional manufacturing methods. Thanks to this, 3D printing is used in a growing number of areas in industry, including the biomedical sector [2].

One key advantage of 3D printing methods, compared to other manufacturing methods, is the ability to precisely control and the rapid modification of printed models without the need for costly and time-consuming modification of production device. This provides the possibility of easy and low-cost production of product prototypes. Additive manufacturing methods also stand out with high efficiency thanks to low material losses [1].

Combining methods of 3D printing with advanced imaging technologies (such as 3D scanners, magnetic resonance, computed tomography, ultrasound imaging) makes it possible to create models with unmet resemblance to real objects. Thanks to this synergy, 3D printing has found many applications in the medical field, especially when highly personalised treatment is needed. It is used in manufacturing anatomical models for educational and procedure planning purposes, in dentistry, prosthetics, and in creating surgical guides for faster and more reliable surgical procedures [3].

3D bioprinting could be defined as applying methods of 3D printing to creating objects using biomaterials. Bioprinting requires treatment of highly specialised materials that are unsuitable for conventional 3D printing methods [4]. This highlights the need for 3D printers specially designed for printing with biomaterials as the source material to achieve the best result of the bioprinting process.

Such a bioprinter, besides compatibility with biomaterials, should also meet the following criteria [16]:
- high print resolution,
- biocompatibility of the finished print and every part of the device that comes into contact with the print,
- repeatability of the process,
- possibility of controlled extrusion of materials with changing rheology.

The bioprinter should also support the requirements originating from the cleanliness of biomedical products. The machine should be easy to clean and resistant to the widely used sterilisation agents used in microbiology laboratories. It should also support printing on the different print beds used during typical cell culture processes, such as petri dishes and multi-well plates. This feature would minimise the chance of contaminating or destroying fragile structures during transport from the printing location to the incubator.

A frequently emphasised direction of development in bioprinting technology is addressing the need for compact and versatile devices [7].

An especially interesting application of 3D bioprinting is the possibility of manufacturing cell culture scaffolds for tissue engineering and regenerative medicine. Hydrogel structures could be used as resorbable implants for bone regeneration [13].

3D bioprinter – BioCloner Desktop

The bioprinter used during the study (fig. 1) was produced by 45stages.

The BioCloner Desktop (referred to as 'Desktop') is equipped with a quick release printhead slot. This makes changing the printhead used during the printing process seamless. This ability to change the tool during the print creates the opportunity to use several materials in different forms in one process. Source materials can be fed in the form of filaments, granulates, powders, and a variety of fluids (such as liquids, gels, suspensions, and pastes). Thanks to the temperature-controlled printheads, it is also possible to process materials with narrow windows of printability influenced by temperature-sensitive behaviour. The currently supported printheads allow printing in a temperature range of 4–240 [°C]. The long list of supported printing technologies, combined with the quick-change feature, allows the user to easily print multi-material objects that are unobtainable from a generic bioprinter [6].

Microbiological cleanliness, inside the bioprinter, is easily obtainable by facilitating materials suitable for work in clean rooms in its design. The outer surfaces of the printer are made of flat, easily cleanable materials that are immune to the chemical cleaning agents used in a typical laboratory (such as a 70% solution of ethanol). The device and its workspace can also be sterilised by UV-C radiation.

The BioCloner Desktop bioprinter can be controlled in different ways: it can be operated through an integrated touchscreen or web interface accessible via a personal computer through an ethernet cable. Thanks to its web connectivity, the BioCloner 3D (dedicated slicing and process-controlling software) is suitable for bigger research facilities. After setting up the server environment, it is possible to control several printers from a single access point. Such an architecture makes it possible to create printer clusters that can rapidly scale-up the printing process as needed. Web-based process control is another improvement regarding printing carried out in clean rooms. Remote control over the printer minimises the need for direct physical contact between the operator and the machine during the printing process, which has a positive impact on maintaining high cleanliness in the vicinity of the printer, which is important as preventing contamination is a key feature in the manufacturing process of products for biomedical and biotechnological applications.

Fig. 1. BioCloner Desktop 3D bioprinter under laminar-flow hood

Thanks to its printhead offset calibration system, the Desktop supports the variety of different nozzles (diameter, length, shape) needed during the specific process, even those manufactured outside commonly used sizes. The option of using a custom-length nozzle is useful, especially when printing in restricted spaces. One example of such a process is printing in the commonly used multi-well plates and, something which is unique to bioprinting, the process facilitating a vessel containing a supporting and crosslinking bath, referred to as FRESH bioprinting [12].

By using a specialised head equipped with a touch sensor, it is possible to acquire a three-dimensional map of print bed. This is the core of the automated dynamic height compensation system. During printing, the table is moved on the *Z* axis in small adjustments to maintain the desired distance between the print surface and nozzle during every point of the process, which is essential for bioprinting. In comparison to conventional 3D printing, bioprinting requires greater control over the precise layer height. Differences between the desired geometry defined by the .STL file and the produced model that can be acceptable in conventional 3D printing are not always small enough to be ignored in biomedical applications. The dynamic height compensation system minimises the risk of inconsistency in each layer of the print, which is a crucial factor when printing resorbable implants. One of the key factors influencing the speed of decomposition of biodegradable objects is the area of the object's surface exposed to a breakdown agent [5]. This influence highlights how crucial the precise control over the final geometry of the printed structure is in maintaining the planned dynamic of decomposition of the resorbable implant inside the patient's body.

Incorporating the dynamic height compensation system also positively impacts one of the key elements of research studies – repeatability of prints – which lowers the overall cost of materials during development. Bioprinting, in contrast to conventional filament 3D printing, deals with expensive materials. Each failed print attempt represents a considerable loss of time and materials.

The printer, besides the heating function commonly found in 3D printers, supports additional accessories designed for bioprinting, such as mounting systems for laboratory glassware. The open architecture of the table allows for the installation of peripherals needed for specific processes.

Supported printheads

Pressure printing printhead (PPP)

A printhead (fig. 2) designed for pressure extrusion of hydrogels, liquids and suspensions (such as a cell

suspension in a culture medium) at ambient temperature. The design incorporates interchangeable distance rings, making it possible to use commercially available polymeric 3 ml and 5 ml cartridges with a luer-lock connection. The standardised nozzle connection allows the user to design a printing process using widely available and unified nozzles and medical syringes. The printhead's shell features a window that allows constant monitoring of the material level inside the translucent cartridge. The working pressure should be below 6 bar.

Fused filament fabrication (FFF)

A printhead (fig. 3) dedicated to printing with thermoplastic materials fed in the form of a filament with a diameter of 1.75 mm. It is equipped with a direct drive motor and additional fan for cooling down the print and is compatible with conventional 3D printing nozzles with a metric thread. The option of using materials in filament form makes it possible to produce prints quickly from the widely available and cheap materials found in conventional 3D printing, and also with highly specialised filaments manufactured from biomaterials. The heating unit can achieve a stable working temperature up to 240°C.

High temperature pressure (HTP)

A printhead (fig. 4) dedicated to the pressure extrusion of molten thermoplastic materials, designed for work with medical grade polymers, with a maximum working temperature of 210°C. The printhead uses stainless steel cartridges with a luer-lock connection. It allows the user to print models out of biomedical polymers usually commercially available only in granulate form. The ability to print directly from the source form of the material eliminates the need to create filament for a conventional FFF printhead. This increases the quality of the final print by mitigating the chance of thermal degradation by minimising the number of thermal treatments need to obtain the final product [10] – printing with the HTP printhead requires only a single melting of the thermoplastic material.

Ultraviolet pressure (UVP)

A printhead (fig. 5.) designed for the pressure extrusion of UV-curable ceramic pastes. This printhead is suitable for the extrusion of materials requiring higher temperatures for printability. Its heating unit can maintain a temperature of up to 60°C and it is equipped with three ultraviolet LED lights with a controllable output power of up to 9 W each. LED lights emit light with a wavelength of 365 nm, which is suitable for crosslinking commonly used UV-curable materials in tissue engineering and regenerative medicine [9]. This printhead is designed for standard 3 ml luer-lock cartridges and features a level-checking window located on the front of the printhead.

Controlled temperature pressure (CTP)

A printhead (fig. 6.) designed for pressure extrusion of hydrogels for which their printability strongly depends on their temperature. An integrated cooling-heating unit maintains stable working conditions in the range of 4–60°C. The physical properties of many hydrogels used in bioprinting are influenced by the temperature, therefore a key parameter of their printability is the temperature at which the used hydrogel undergoes the sol-gel transition. Precise temperature control of the printhead's source material allows for controlled extrusion of partially liquified materials. Any deviation from within that tight thermal printability window results in either uncontrolled over-extrusion of the material or failure to extrude due to the material's resistance and clogged nozzle [15]. This printhead is compatible with 3 ml luer-lock cartridges.

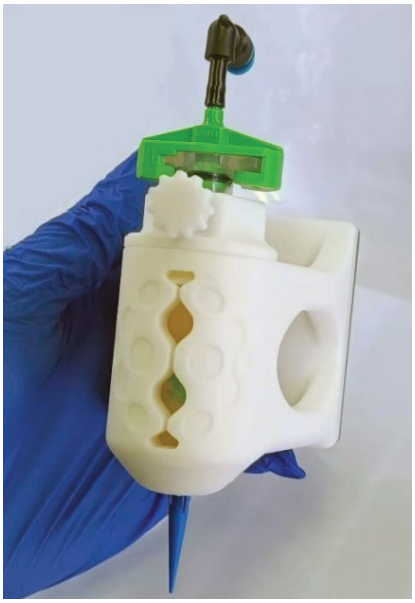

Fig. 2. Pressure printing printhead

Fig. 3. Fused filament fabrication printhead

Fig. 4. High temperature pressure printhead

Fig. 5. UVP printhead

Fig. 6. CTP printhead

External printheads

The BioCloner Desktop bioprinter, thanks to the above-mentioned quick release mounting slot, is compatible with existing systems of 3D bioprinting manufactured by external producers. The Puredyne printhead is an example of an external bioprinting system suitable for printing with the Desktop printer.

Bioprinting software – BioCloner 3D

The BioCloner project, besides the bioprinting devices, also features dedicated software. BioCloner 3D serves as both the slicing software needed when designing the 3D printing process and the device controlling software during the printing process.

The slicing part of BioCloner 3D, besides the standard features found in this type of software, contains additional add-ons dedicated to bioprinting. A key aspect is the support of pressure extrusion printheads. BioCloner 3D also supports multi-tool printing, making it possible to print structures from several varied materials in one process. For example, the user can manufacture a structure that has an outer shell made from a thermoplastic polymer printed with the FFF printhead and a soft silicone infill printed with the PPP printhead.

BioCloner 3D can divide one base .STL model into smaller independent submodels. Each of these submodels can then be given its own print parameters and infill/shell printhead combination. One example of the application of this feature is the manufacturing process of a three-layered structure, consisting of a lower layer with a solid infill made from hydrogel (A), a middle part with a porous infill made of hydrogel (B) and highest cover part made from a solid hydrogel (A) layer.

The software also provides control over the UV crosslinking process. It is possible to order crosslinking material during extrusion, after selected layers, or after the whole print.

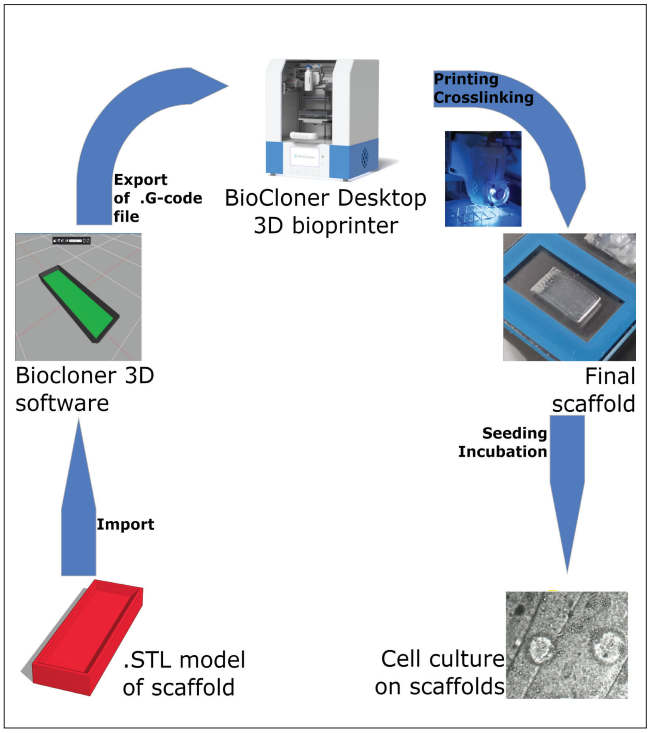

Fig. 7. Diagram of the workflow

Field test in biomedical engineering laboratory

To validate the bioprinting capabilities of the Desktop bioprinter, the device was installed in the Biomedical Engineering Laboratory, named after E.J. Brzeziński located within the Faculty of Mechanical and Industrial Engineering of Warsaw University of Technology.

The proposed protocol of the field test had the primary goal of verifying the applicability of the BioCloner Desktop bioprinter in a functioning biomedical engineering laboratory (fig. 7).

The test started with the preparation of an .STL file describing the outer geometry of a scaffold according to specific needs followed by importing the .STL file into the BioCloner 3D software and defining the print process parameters (speed of printhead during extrusion, temperature of the heating unit, extrusion pressure, crosslinking parameters) alongside the internal geometry of the scaffold (infill). The printer was set up inside laminar flow hood and connected to an external air compressor available in the laboratory. The whole room, including the printer and all the necessary equipment, was then sterilised. The UVP printhead was loaded with bioink and printing was commenced. Scaffolds were printed directly onto microscope slides equipped with side walls, acting as small, multi-well plates. Crosslinking commenced directly after printing. The finished hydrogel scaffolds were seeded with cells without the need for these scaffolds to leave the clean zone of the laminar flow cabinet. After the introduction of the cell culture, the chambered slides were covered and transported into an incubator for 48 hours.

An outcome fulfilling two requirements would be considered a positive result. The first was maintaining high enough cleanliness during the entire process to prevent microbiological contamination from occurring. The second condition was observing cell proliferation on the printed scaffolds.

Materials

The bioink used for the scaffolds was the commercially available photocurable GelMa-based BioINX EasyGel ×100. This bioink uses Lithium Phenyl (2,4,6-Trimethylbenzoyl) (LAP) as the photoinitiator.

The bioink was extruded through a stainless-steel nozzle, gauge 24 (internal diameter of 0.311 mm) with a length of 1 inch (25.4 mm) by FISNAR.

The scaffolds were printed on Nun Lab-Tek II Chamber Slide System microscope slides by Thermo Scientific.

The cells used for the culture were mouse fibroblast, cell line WEHI-164, obtained from Sigma-Aldrich.

Phosphate buffer solution (PBS) was prepared from a concentrated ×10 solution provided by Polbionica.

The cells were cultivated in MegaCell™ RPMI-1640 base medium enriched with 2 mM glutamine and 10% fetal bovine serum (FBS) and 1% Penicillin-Streptomycin antibiotics.

Designing of scaffolds

Starting from the .STL file, which depicted cuboids with dimensions of 6 mm × 15 mm × 1.86 mm (W, L, H). G-code files were prepared using the BioCloner 3D software. Two variants of scaffolds with different infills were designed; a basic variant (fig. 8) with a solid infill and a secondary variant with a lattice infill (fig. 9) were designed in a way that the axis of the infill lines were 0.93 mm apart, which corresponds to a distance three times greater than the inside diameter of the nozzle used. In each variant, the layer height was set to be equal to the value of the inside diameter of the nozzle: 0.31 mm. During first the attempts, it was decided that the models should also have a rim to serve as a pour guide (fig. 14). This rim was incorporated by removing infill from the top three layers without affecting the walls. This modification of the original file is described in the 'Ability to quickly modify print parameters' subsection of the 'Results and discussion' section. This resulted in a every structure having six layers of walls and three layers of infill.

Printing

Whole printing process occurred under an MSC Advantage laminar flow cabinet by Thermo Scientific. Before printing, the inside of the laminar flow cabinet was disinfected for 30 min with UV-C radiation from an integrated lamp. During this time, the stainless

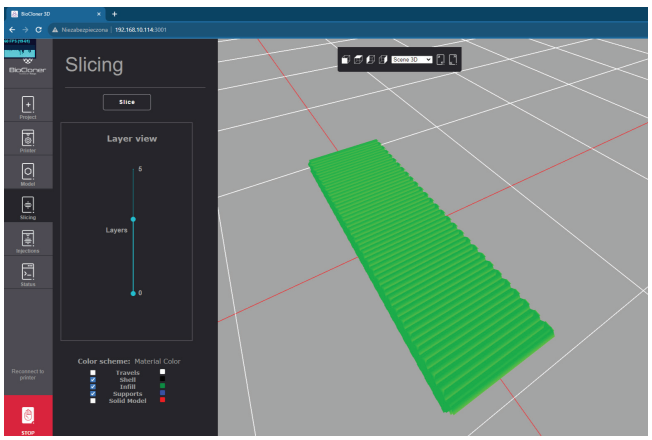

Fig. 8. Model of solid scaffold without visible walls

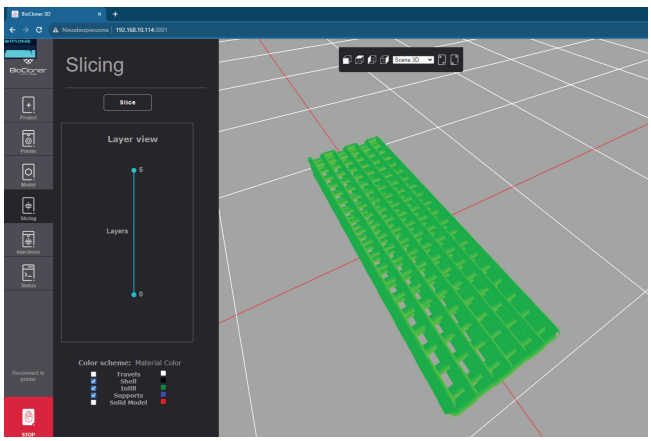

Fig. 9. Model of lattice scaffold without visible walls

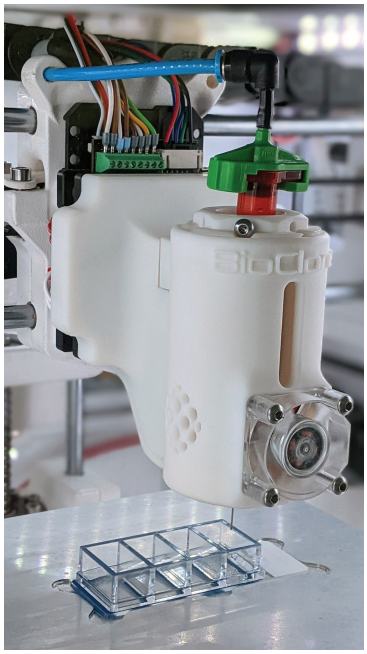

Fig. 10. UVP printhead and chamber slide mounted in dedicated holder inside the printer's workspace

steel nozzles were disinfected in a NUVE NC 40M autoclave.

The cartridge containing the bioink was disinfected by direct spraying of a 70% solution of ethanol before it was transferred into the laminar flow cabinet.

Printing was conducted with a UVP printhead heated up to 35°C. Before printing and after inserting the bioink cartridge, the hydrogel within was allowed to heat up for 15 min.

A sterile chamber slide was placed in a dedicated aluminium slide holder placed inside the print bed. The printhead during printing can be seen in fig. 10.

The printing was carried out with a constant printhead speed of 2 mm/s during extrusion with a pressure of 1.1 bar.

While printing the last layer of each scaffold, the UV crosslinking unit was activated with full power for the initial solidification of the material. After printing the series of four scaffolds, every model was subjected to final crosslinking carried out by ten sweeping movements over the microscope slide. One movement took 75 seconds to complete.

The finished models (fig. 11) were submerged in a solution of PBS and kept at room temperature inside the laminar flow cabinet before seeding.

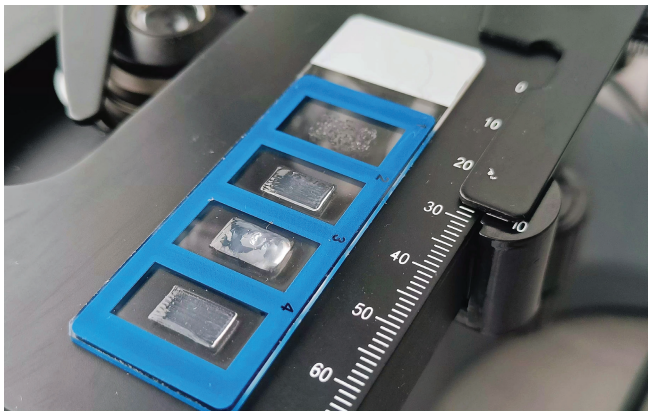

Fig. 11. Test hydrogel scaffolds

Seeding of cells and incubation

A seeding suspension of cells with a density of 10^4 cells in 2 ml of fresh medium was used per each scaffold and the seeded scaffolds were placed inside a Steri-Cycle i160 CO_2 Incubator made by Thermo Scientific for 48 hours with the temperature set to 36°C. The atmosphere inside the incubator contained 5% CO_2.

Results and discussion

Cell culture on hydrogel scaffolds

A visible monolayer culture formed on every scaffold. In fig. 12, partially adhered cells can be seen and the parallel structure of the solid infill scaffold can be observed. The culture seeded on a lattice scaffold (fig. 13) stood out with a denser population of adhered cells, which is consistent with the phenomenon of the scaffold structure impacting the density of the cell culture, as reported in the literature [14]. The pictures were taken on a NanoEntek Digital Bio JuLI FL smart fluorescent cell analyser.

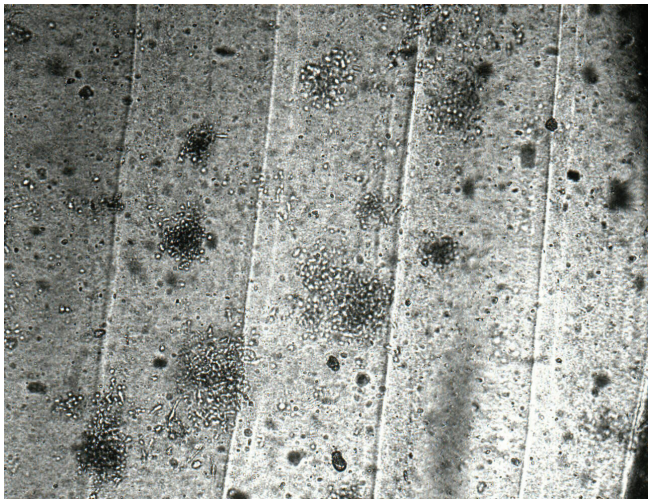

Fig. 12. Cell culture of WEHI-164 line on solid scaffold 48h after seeding

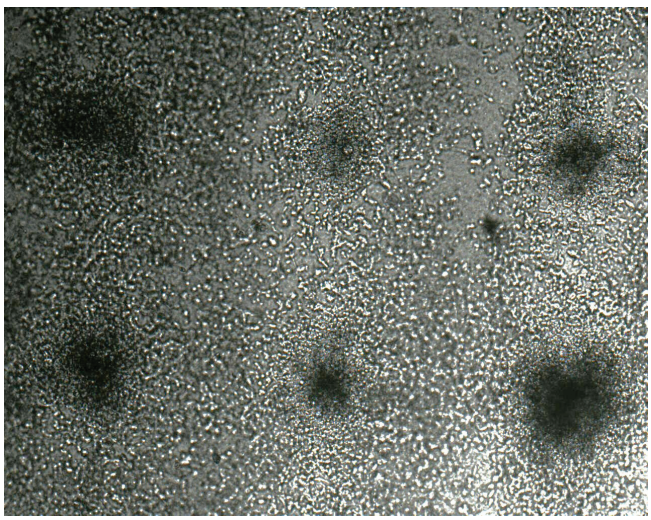

Fig. 13. Cell culture of WEHI-164 line on lattice scaffold 48h after seeding

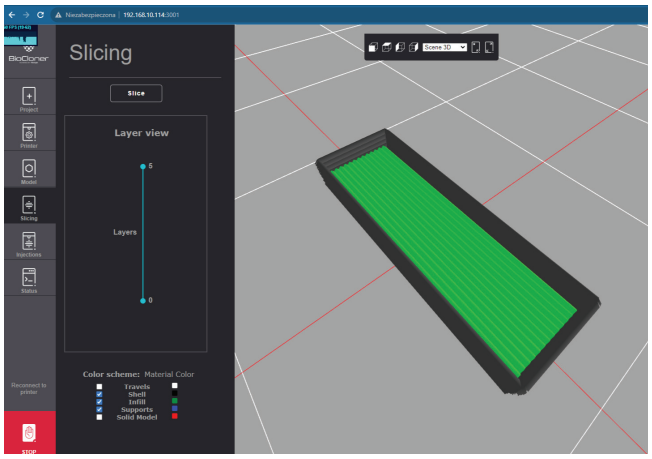

Fig. 14. Model of solid scaffold with extended walls

Ability to quickly modify print parameters

During the printing process, we noticed that there could be a potential problem with seeding the cell culture onto solid infill scaffolds, caused by the seeding suspension flowing from the top layer of the crosslinked hydrogel scaffold. To prevent such an outcome, it was decided to modify the .STL file describing the scaffolds by relatively extending vertically the walls of the prints (fig. 14) by removing half of the infill of the whole model (top 3 layers of print consisted of only walls). This improvement made the seeding process quicker and easier. As there was a computer featuring the proper software set up inside the laboratory, the change to the geometry was applied without the need to leave the clean zone, which reduced the time needed to implement the update of process design. It also did not increase the chance of contamination. It can also be speculated that adding pour guides reduces the overall risk of contamination by lowering the time needed to execute the seeding operation by allowing the lab operator to discharge the pipette faster. It should be noted that skipping the infill in top layers also shortened the print time.

Conclusions

The BioCloner Desktop bioprinter can manufacture biocompatible hydrogel cell culture scaffolds in a sterile environment.

The lack of evidence indicating contamination of the produced scaffolds shows that during the process, cleanliness was sustained.

Manufacturing of cell scaffolds directly into the culture vessel lowers the risk of contamination by eliminating the need to transfer the uncovered scaffold from the printer's workspace to a suitable vessel. It shortens the time needed to carry out the whole procedure and eliminates the need for additional sterilisation of printed structures before seeding. The direct printing approach also makes it possible to use delicate scaffolds, which could be subjected to degradation during a sterilisation process, especially during thermal sterilisation [11].

The proposed method could be used to manufacture scaffold from hydrogels mixed with cells, which would allow controlled deposition of cells in a three-dimensional culture space.

Printed scaffolds adhere to the print surface, which prevents uncontrolled floating of hydrogel objects in the cell medium during incubation, which further increases the repeatability of the printing process.

The ability to quickly modify the process was demonstrated. This makes it possible to apply any necessary modifications without the operator having to leave the clean environment. Every movement from and into the clean laboratory is a time-consuming process that increases the chance of contamination occurring.

It is possible to use the described bioprinter inside clean rooms. Its external dimensions and mass allow it to be installed inside an unmodified commercially available laminar flow cabinet by a single person, while not having to disassemble any essential lab and airlock elements favourably influences the costs of setting up the bioprinting workstation.

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