3D BIOPRINTING HANDHELD TOOL CONCEPT FOR INNOVATIVE OSTEOARTHRITIS TREATMENT WITH STEM CELLS UTILIZATION

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Introduction

Osteoarthritis (OA) is the most common chronic joint disease involving progressive damage and loss of cartilage, remodelling of subchondral bone, osteophyte formation, weakening of periarticular muscles and thickening of the joint capsule[1]. Over the next decade, the number of people affected by OA is expected to double due to population ageing and increased rate of obesity. Novel nanocomposite responsive materials combined with adipose tissue-derived stem cells (ASCs) and a remotely controllable ultrasound (US) treatment is developed within the H2020 project. Materials and cells will be delivered in situ through an innovative handheld 3D bioprinter, introduced to the operating area during an arthroscopic treatment through available port.

Materials and Methods

Before the pneumatic flow for bioprinting preliminary concept design, two different materials were tested in order to analyse the extrusion parameters to sketch structural features of 3D bioprinting device: PEG-fibrinogen - Pluronic and PBS - Pluronic based thermosensitive and UVA curable hydrogel precursors (manufactured by: REGENTIS Biomaterials, Israel).
The material in the volume of 5 ml was storage up to room temperature (20-22°C) and stabilized within 1 hour. Different needle's diameter dimensions were used 0,4; 0,6; 0,8 and 1,0mm. The following parameters were evaluated: pressure force on the syringe plunger necessary to begin the extrusion process as well as the extrusion velocity (ml/min) in the constant force with reference to the needle diameter.
Basing on the test results the first 3D bioprinting handheld device preliminary concept was designed to print the nanocomposite hydrogel and the ASCs directly onto the cartilage site to be treated – lesions in advance processed by the surgeon during an arthroscopic procedure.

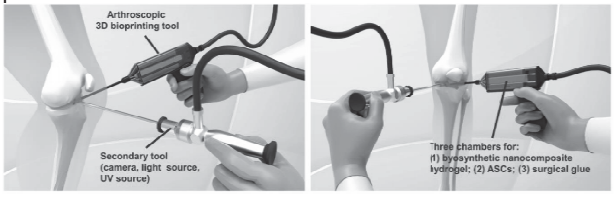

FIG. 1. 3D Bioprinting Handheld Tool Concept For Innovative Osteoarthritis Treatment.

Results and Discussion

Characteristic showing dependence of the velocity of hydrogel extrusion versus pressure force have allowed to evaluate the extrusion time in regard to tip diameter and choose the proper parameters of the cartridge chamber mechanism for 3D bioprinting tool. The 3D handheld bioprinter preliminary concept was developed including: chambers (cartridges), control unit, driving method, handheld device and single-purpose extrusion tips.
The number of chambers/cartridges (nanocomposite hydrogel without cells, nanocomposite hydrogel with cells embedded, the primer) were defined together with the main features: cylindrical shape, volume up to 10ml. The chambers are made from biocompatible material and easily pluggable within the handheld device.
An additional tool holding a camera and a light source will provide UV light in situ to promote hydrogel crosslinking.
Cells could be mixed with the nanocomposite hydrogel before loading the cartridge, or within the instrument, before printing. A deep investigation of the hydrogel/cell mixing mechanism within the arthroscopic tool will be carried out in the future to choose one of the possible strategies: targeting the formation of a core-shell structure, in which cells are in the core and the crosslinked hydrogel constitutes the external shell of the structure or targeting a different and novel printing strategy and structure architecture.
Control unit is expected to be equipped with ergonomic and usable user interface. Working parameters values (START/STOP, flow rate [%], active tool and auxiliary device activation e.g. light source) are going to be presented on the interface in a transparent and clear way to be easily recognized by the operator.
The handheld device is controlled by firmware installed in microcontroller to execute a particular printing process and also enabling presentation of printing-related functions such as initialization, direct motion control, printing start/stop.
Consequently, the device dimensions are assumed to be designed to be as versatile as possible respect to the different hydrogel viscosity values that may be obtained, keeping in mind the shear stress level harmless for stem cells survivability.
Extrusion tips were designed to deposit the bio ink with right shape and diameter without exerting excessive stress to cells (max. 15-25 kPa). For such reason, clogging inside the nozzle tip must be avoided and the flow was optimized considering the diameter of the tip. Fabrication of tolerances on the nozzle is important, and for each different dispensing tip mounted, calibration of the valve may be needed, especially for very long-dispensing tips.

Conclusions

In the next project stage, the hydrogel which confirms good results will be extruded with ASCs, repeating the experiments for comparing the pressure force and the extrusion velocity.
The prototype of bioprinting handheld system will be developed as a device which should assist the surgeon in depositing the bio inks during arthroscopy in a well-controlled shape according to the patient's cartilage anatomy. The prototype will be evaluated within the in-vitro and in-vivo test.
Then the final bioprinting handheld system will be designed and tested in the usability tests on human volunteers.

Acknowledgments

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