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D5.3
Preliminary foot-controlled pneumatic flow for bioprinting

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Dissemination Level		
PU	Public	**X**
PP	Restricted to other programme participants (including the Commission Service)	
RE	Restricted to a group specified by the consortium (including the Commission Service)	
CO	Confidential, only for members of the consortium (including the Commission Service)	

Document History

Version	Date	Author	Summary of Main Changes
1	08/10/2019	Irene Bernardeschi, SSSA	First version of the template for project Deliverables
2	14/11/2019	Tomasz Gapinski, Vimex	First draft of the Deliverable
3	18/11/2019	Leonardo Ricotti, Irene Bernardeschi, SSSA	First revision for the Deliverable and request of additional contributions
4	29/11/2019	Tomasz Gapinski, Krzysztof Lenartowicz, Paulna Galas, Małgorzata Gonsior, Wojciech Kręciszek, Vimex	Revision including photographic documentation
5	30/11/2019	Leonardo Ricotti, Irene Bernardeschi, SSSA	Final revisions and Deliverable submission

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1 Executive summary

This deliverable reports a preliminary description of the handheld bioprinting system to be used for delivering the hydrogel containing ASC cells, carbon nanomaterials and piezoelectric particles into cartilage defects, by following a foot-controlled pneumatic printing strategy based on the specifications devised in the deliverable D2.1. Expected results are reported.

The concept design for the DEMONSTRATOR covers aspects related to:

- Determination of primary extrusion method
- Suitable design of the Control Unit to allow driving the extrusion as well as set different working parameters
- Definition of the cartridge geometry (i.e. commercially available syringe based solution)
- Design of the extrusion tube and tip geometry
- Design of a footswitch that will allow to use and to operate the system.

The aim is to build a basic system allowing extrusion of the nanocomposite hydrogel in conditions simulating the final application. The assumption is to regulate the speed of extruded material by means of 3 independent channels as well as to allow the switching between different modes (predefined or stored settings) of operation (3 modes for each channel). Fixing working settings for each of mode will be the matter of further investigations.

The bioprinting system overview is shown in Figure 1.

Figure 1: Bioprinting system overview

2 Foot-controlled pneumatic bioprinting handheld system

The whole handheld bioprinting system is composed of:

- The control unit, which allows to set working parameters and to monitor signals from the footswitch.
- The footswitch, which is driven by the user. Following user's intention, the control unit drives the handheld device to initiate the extrusion according to defined working parameters.
- Handheld device, which consists of the chamber and extrusion tube delivering the biomaterial directly into the cartilage lesion.

In **Error! Reference source not found.**2 is reported the general block diagram describing the functioning of the 3D bioprinting system.

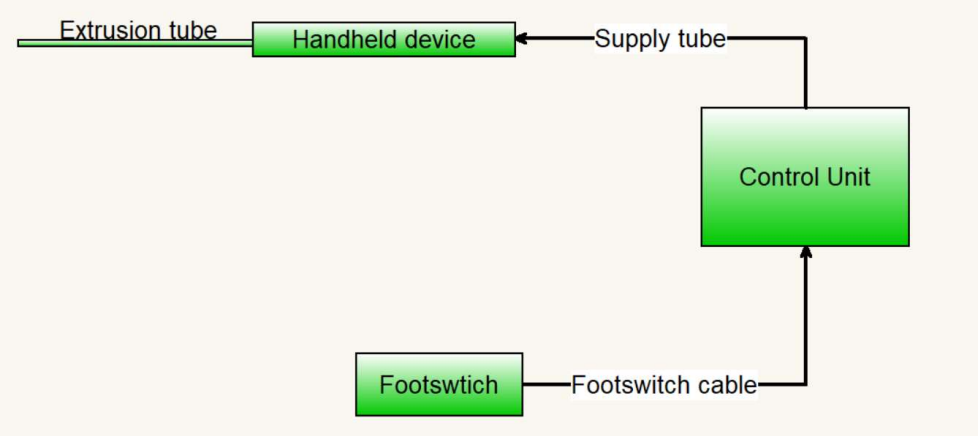

Figure 2: Block diagram of the system

2.1 Bioprinting strategy

The bioprinting strategy was defined considering the introduction of a pneumatic based system that causes the extrusion of the nanocomposite hydrogel by means of pressurised air delivered to the chamber/cartridge containing the hydrogel, as shown in **Error! Reference source not found.**In this way, it is assumed that the maximal pressure exerted on the piston, and thus on the biomaterial, is controlled. Such approach should also facilitate to constrain the shear stress applied to stem cells.

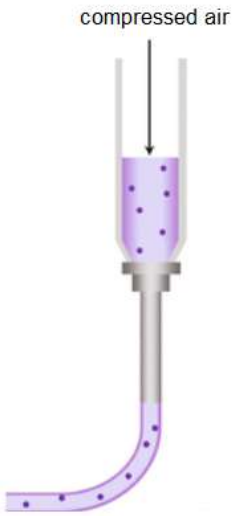

Figure 3: Pneumatic concept

2.2 Handheld device

The design of the handheld device is shown in **Error! Reference source not found.**, and consists of the following components:

- Extrusion tube and tip: channel for the delivery of the biomaterial to the operating area (i.e. lesions or cartilage defects).
- Chamber/cartridge: syringe based cartridge with floating piston and suitable connectors for the extrusion tube and compression system.
- Floating piston: piston that moves the biomaterial towards the extrusion as a result of the force applied from the compressed air.
- Supply tube with connectors: pneumatic system delivering the pressurised air to the chamber to allow pushing of the floating piston. It has been assumed that such approach should allow to constrain the shear stress exerted on stem cells contained within the hydrogel. It has to be investigated the amount of compression pressure delivered to the floating piston, which might not influence viability of stem cells.
- Adequate printing resolution.

Figure 5 shows the developed prototype of the handheld device:

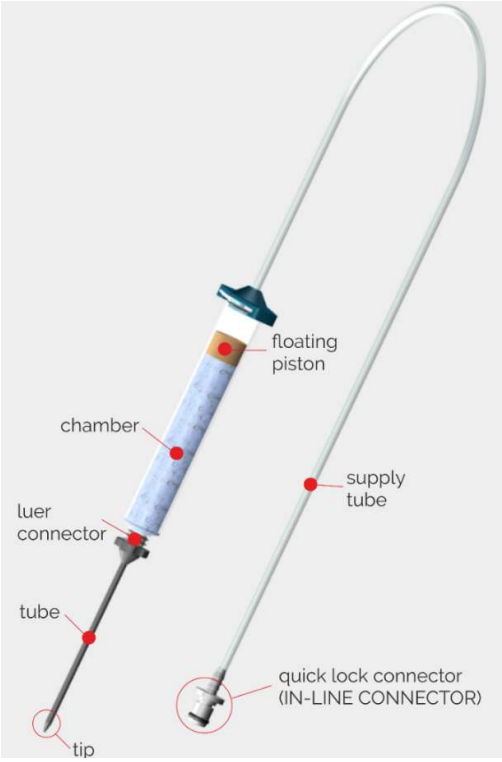

Figure 4: Handheld device concept

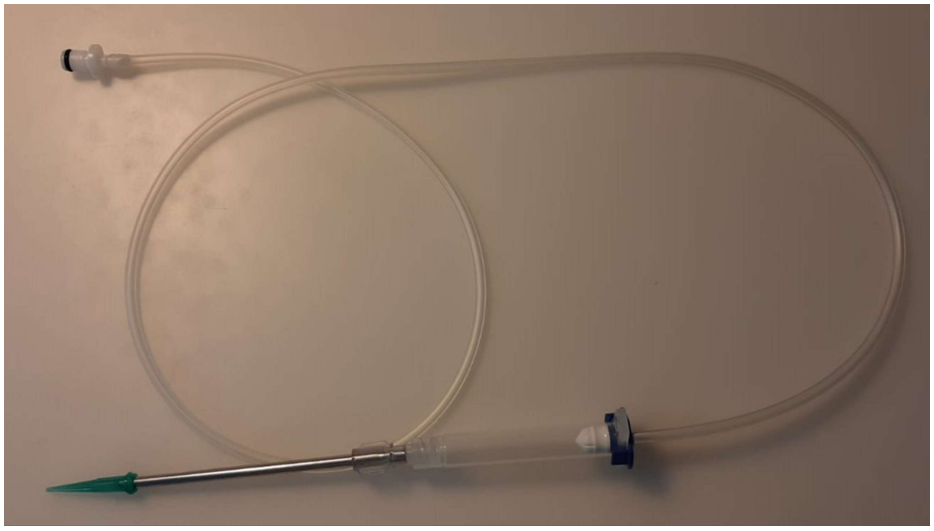

Figure 5: Handheld device

2.2.1 Chamber/cartridges in the 3D Bioprinter and extrusion tube

The primary design concept of the chamber/cartridge containing the nanocomposite hydrogel is a syringe-based system. This solution was chosen in order to match the assumption of a pneumatic driven extrusion. The cartridge, shown in Figure 6, has an appropriate connection for the supplying tube on the distal side and a luer connector (standard connection for medical

consumables) for the extrusion tube on the opposite part. Such solution will allow flexible manual connection of an extrusion tube to the chamber, thus facilitating testing of different extrusion tube dimensions during further testing phases.

Figure 6: Chamber / cartridge prototype

2.2.2 Extrusion tube and tips

A combined approach has been proposed and illustrated in Figure 7. The extrusion tube is made up from 304 alloy stainless steel (external diameter: 4.2 mm, internal diameter: 3.5 mm, length: 107 mm) and is combined with a separate tip (length: 31 mm, proximal internal diameter: 4.2 mm, distal internal diameter: 0.5 - 0.6 mm). For the proposed prototype one extrusion tube with chosen tip has been presented.

Figure 7: Tube with conical tip and luer-type connector for the cartridge

2.3 Footswitch design

The footswitch (Figure 8) allows the user to change current settings of extrusion speed, to change the mode of extrusion, to change active channel, to activate/deactivate the extrusion. Buttons "+" and "-" allow to increase/decrease the extrusion speed. The "CHANNEL" button allows to switch between the three available extrusion channels. The button "SET" allows to change predefined working parameters for the chosen channel. Pressing button "PRINT" initiates extrusion of biomaterial, while releasing the button stops the printing process.

Figure 8: Footswitch

2.4 Control unit design and pneumatic driving method

The designed controller (Figure 9) is an active device supplied by voltage (100-230 VAC, 50-60 Hz). It is equipped with connectors for handheld devices (handpieces) and a footswitch. For each channel independently it is assumed that the extrusion speed can be changed. Current settings are shown in 1 to 100% scale or by showing working pressure (1% corresponds to 0.45 kPa, 100% corresponds to 45 kPa with a tolerance of +/- 10%). The device will also allow to define mode of operation (e.g. adjustment of parameters for specific tip type) as well as activation/deactivation of working channel. The user interface will also illustrate the active channel. Activated extrusion will be indicated by the icon  . An example of user interface for a single channel is shown in Figure 10:

Figure 9: Control Unit

Figure 10: User interface view for a single channel.

The basic principle of operation has been presented on the general block diagram shown in Figure 11, where the controller serves the user interface, and drives the pneumatic system by monitoring its parameters and by driving suitable valves. Such approach will allow real-time measurements and observations during the normal device operation.

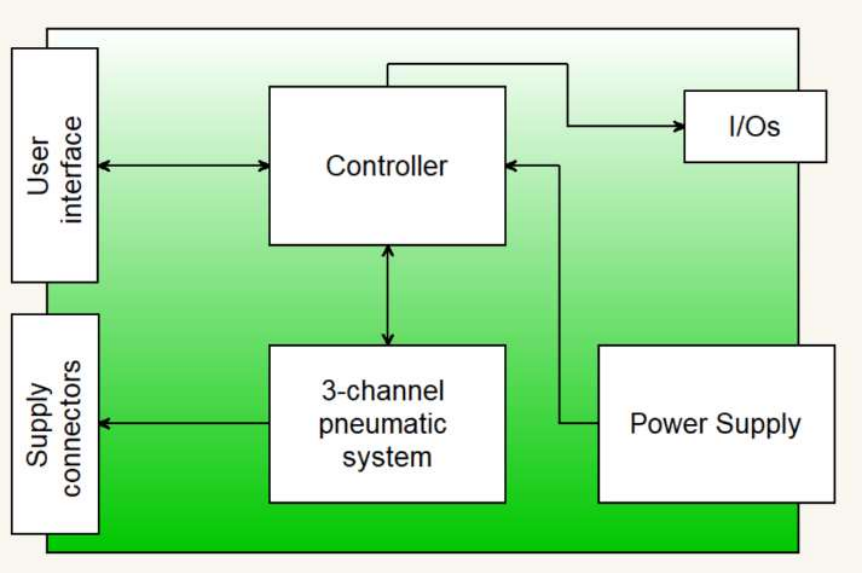

Figure 11: Block diagram of the Control Unit

2.5 Testing stand

The following pictures (Figure 12, Figure 13, Figure 14 and Figure 15) illustrate the testing stand consisting of vision system (camera, light source, endoscope, light guide cable, arthroscopic sheath/trocar) as well as the bioprinter (control unit, footswitch and handheld device), knee phantom and a monitor.

Figure 12: Testing stand

Figure 13: Testing stand - Monitor, control unit, phantom, light source, handheld device, camera

Figure 14: Testing stand - Monitor, control unit, phantom, light source, handheld device footswitch

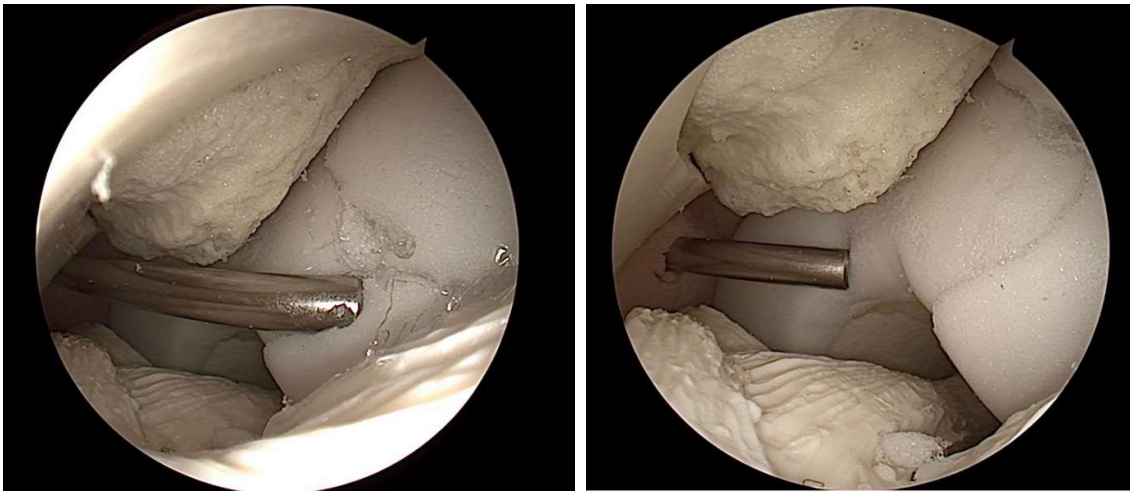

Figure 15: View inside the phantom

2.6 Extrusion

The following pictures show phases of hydrogel (PBS and Pluronic based thermosensitive and UV curable hydrogel precursor with no protein) delivery from the instrument, in different extrusion conditions: extrusion from the tube without the tip (Figure 16), extrusion from the tip connected to the tube (Figure 17), extrusion from the tip directly connected to the cartridge (Figure 18):

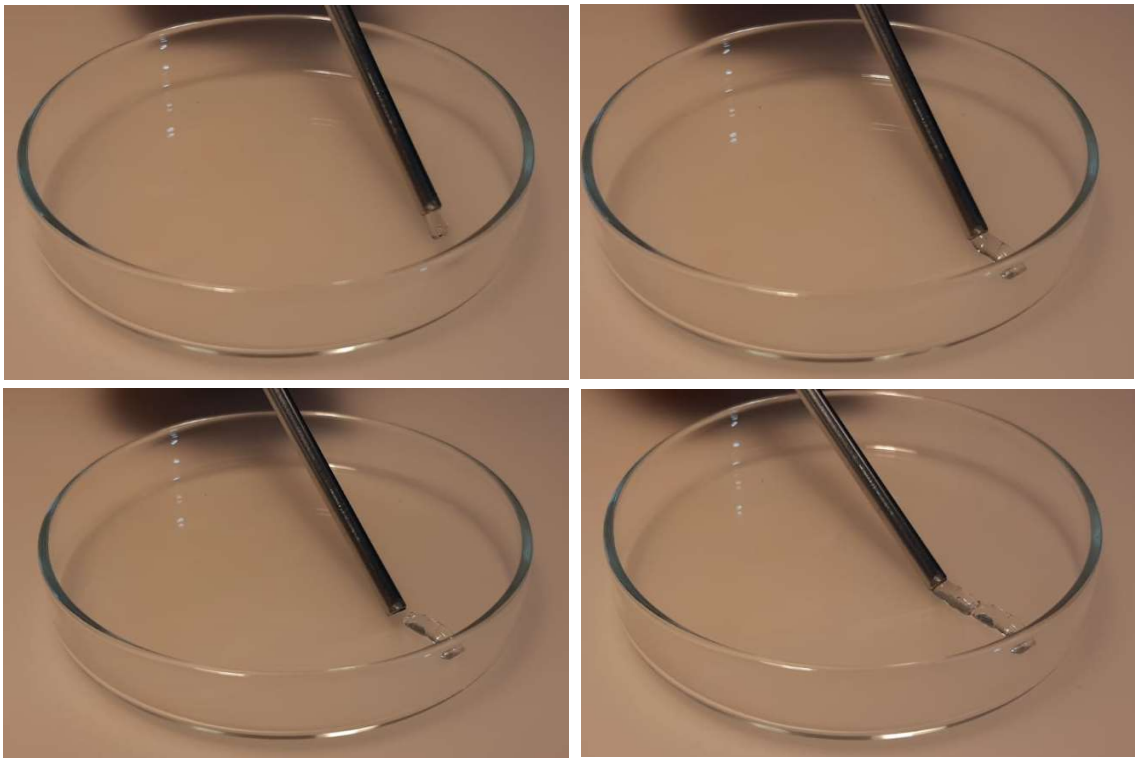

Figure 16: Extrusion from the tube without tip

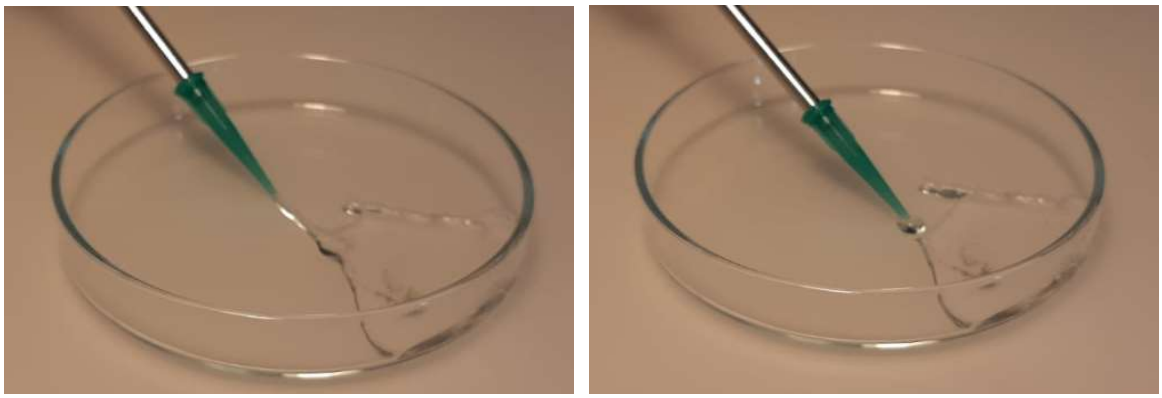

Figure 17: Extrusion from the tube with tip

Figure 18: Extrusion from a tip directly connected to the cartridge

3 Conclusions

This deliverable describes the first demonstrator of the platform developed for extruding the nanocomposite hydrogel. The key aspects (e.g. controlled pneumatic actuation, respect of dimensional constraints, etc.) were demonstrated. The platform also allowed the real-time monitoring of working parameters for the proposed system.

A flexible testing stand has been also proposed, which comprises:

- Knee phantom
- Endoscopic camera
- Endoscopic instruments (sheath, scopes, probes, etc.)
- Light source (daylight) with accessories
- Other elements

Such system will allow to investigate and optimize in the next months:

- Software/firmware design and development
- Determination of the bioprinting resolution
- Determination of the influence of the driving pressure on cells viability
- Measurements and testing of working parameters
- Learning about the relation between the compression pressure and shear stress for particular tip geometries and hydrogel types