Injectable nanofibrous microscaffolds

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Minimally invasive surgeries are gaining significance, while their impact can be much more substantial with the adoption of novel injectable biomaterials for drug or cell delivery. Injectable biomaterials is a rapidly expanding field that may revolutionise medical treatments. Such biomaterials are particularly crucial in cell therapies, where low number of cells survive or remain at the site of injection, which significantly limits the therapeutic potential. Here we report on the laser-based fabrication of injectable electrospun nanofibers that deliver cells and drugs through the needle to the targeted tissue (Nakielski, 2022). We observed an efficient attachment of cells to the scaffold's surface, creating cell-populated microscaffolds (MS) that could be injected through 26G needles.

Electrospun PLLA nano- and microfibers were structured with a picosecond laser to make minimal changes to the polymer and thus preserve its biocompatibility. To increase the hydrophilicity of the MS, nanofibers were functionalised with natural polymer chitosan. We used Scanning Electron Microscopy (SEM) for morphological characterisation of MS with and without cells. The physico-chemical characterisation was done to analyse the impact of laser processing on polymer nanofibers. L929 cell line was used to assess the biocompatibility of produced MS and the possibility to inject as a biomaterial-cell construct.

The direct injection of cells into tissues faces several challenges. With the use of microscaffolds, the survival rate can be significantly increased, while the leakage of cells from the targeted tissue can be minimised. When using laser processing, any shape of microscaffolds can be created. The cytocompatibility assays show an increase in cell number with the culture time. L929 cells populated MS at each side, resulting in the formation of agglomerates. The injectability studies through 26G and 24G needles showed that the ejection rate was 92% and 97%, respectively. At the same time, the force needed to eject the load was around 25 N.

We developed a novel and straightforward method to fabricate microscaffolds from almost any type of electrospun material. The microscaffolds (MSs) are produced in a reliable way, with thousands of micro-objects formed in a matter of minutes. MSs are compatible with living tissues and readily populated with cells. By adjusting the surface chemistry of nanofibers, the physical and chemical structure of MSs can be customised to improve cell-MS interaction. The injectability studies show that PLLA-based MSs are injectable through the tested range of needle sizes and could be well-suited for minimally invasive cell delivery applications.

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References
Nakielski, P., Rinoldi, C., Pruchniewski, M., Pawłowska, S., Gazińska, M., Strojny, B., Rybak, D., Jezierska-Woźniak, K., Urbanek, O., Denis, P., Sinderewicz, E., Czelejewska, W., Staszkiewicz-Chodor, J., Grodzik, M., Ziai, Y., Barczewska, M., Maksymowicz, W. and Pierini, F. (2022) *Small*, **18**, 2104971.