Fabrication of electrospun scaffolds with cell laden hydrogel for cartilage tissue engineering

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***Abstract*— Tissue engineering strategies create artificial substitutes for the regeneration of damaged tissues, beginning with the fabrication of scaffolds moving then to cell incorporation onto those scaffolds and subsequent tissue growth *in vitro*. Cell seeding techniques, unfortunately, are usually ineffective to develop scaffolds with homogenous cell distribution, resulting in non-functional tissue formation** [1]**. With electrospun scaffolds, cell incorporation becomes even more challenging. Electrospun scaffolds are a very tightly packed layer of fibers with small pores, that makes difficult the migration of cells onto the scaffolds, as well as, the diffusion of nutrients and wastes. To overcome this drawback, the direct incorporation of cells, using electrospraying technique, onto the scaffolds during the electrospinning process has been reported. Cell electrospraying is a jet-based technique that allows the spray of living cells onto the materials by applying an electric charge in a cellular suspension** [2]**. Several studies have proved that cells can survive and proliferate after electrospraying process** [3], [4]**. Still, previous work has shown that while uniformly distributed cell-laden scaffolds can be fabricated using this technique, some issues remain. Cell desiccation on top of the fibers due to longer duration of the experiment and inadequate cell environment – low temperature and CO_2 concentration – and solvent toxicity are the main limitations for the optimal efficiency of cell electrospray process onto electrospun fibers.**

In this regard, in this work, the production of electrospun scaffolds was combined with the electrospray of chondrocyte laden hydrogel creating a shield/protection around the cells during and after the electrospray process, preventing its dehydration. For that, a polymeric solution of polycaprolactone (PCL) and gelatin was electrospun alternately with a chondrocyte-laden sodium alginate hydrogel electrospray. Sodium alginate is a natural polymer widely used in biomedical engineering due to its biocompatibility, biodegradability and ability to form hydrogels [5]**. The prepared scaffolds were then cultured for 7 days and the respective cell viability assessed. The percentage of viability was calculated as a ratio of the metabolic activity of the electrosprayed chondrocytes and the metabolic activity of chondrocytes that did not underwent any process. The chondrocyte distribution was also evaluated.**

On the first day of culture, the results showed that the cellular viability was higher than the one previous reported, demonstrating that the alginate hydrogel allowed the cells to survive and helps in its attachment. After 7 days of culture, cells continue alive with considerable viability increasing. It was also shown that it was possible to incorporate cells homogenously distributed by electrospraying process using the chondrocyte laden hydrogel. These results emphasize the potential value that the hydrogels can have on the electrospraying process with the electrospun scaffolds.

Keywords*— *Cell laden hydrogel; Electrospun scaffolds; Cartilage tissue engineering

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TOPIC

2) a.: Multiscale technologies and devices for medicine, environment and energy

REFERENCES

[1] T. L. Akentjew *et al.*, "Rapid fabrication of reinforced and cell-laden vascular grafts structurally inspired by human coronary arteries," *Nat. Commun.*, vol. 10, no. 1, pp. 1–15, 2019.

[2] S. N. Jayasinghe and A. Townsend-Nicholson, "Stable electric-field driven cone-jetting of concentrated biosuspensions," *Lab Chip*, vol. 6, no. 8, pp. 1086–1090, 2006.

[3] J. J. Stankus, J. Guan, K. Fujimoto, and W. R. Wagner, "Microintegrating smooth muscle cells into a biodegradable, elastomeric fiber matrix," *Biomaterials*, vol. 27, no. 5, pp. 735–744, 2006.

[4] J. R. J. Paletta *et al.*, "Incorporation of osteoblasts (MG63) into 3D nanofibre matrices by simultaneous electrospinning and spraying in bone tissue engineering," *Eur. Cells Mater.*, vol. 21, pp. 384–395, 2011.

[5] A. D. Augst, H. J. Kong, and D. J. Mooney, "Alginate hydrogels as biomaterials," *Macromol. Biosci.*, vol. 6, no. 8, pp. 623–633, 2006.