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TOWARDS ENABLING OF ONLINE PERFUSED TE CONSTRUCT VISUALIZATION THROUGH THE DEVELOPMENT OF A MONITORED AND CONTROLLABLE BENCHTOP BIOREACTOR

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Summary: Tissue engineering (TE) aims to provide solutions for the regeneration or replacement of damaged organs and tissues. It has now long been recognized that technological innovations are lacking in the field, which hampers the robust production of high quality TE constructs [Talò et al, 2017]. In the case of bone TE, a common approach involves the perfusion culture of mesenchymal stem cell seeded on 3D scaffolds since perfusion enhances nutrient delivery to the cells [Martin et al, 2004]. However, the lack of monitoring and visualization of the structurally complex neo-tissue (cells + extracellular matrix) growing inside these constructs hampers the optimization and quality control of those bioprocesses. In the past we have shown that contrast-enhanced X-ray computed tomography (CE-CT) could be used as a non-destructive tool for neo-tissue visualization [Papantoniou et al, 2014]. However, that was in an off-line context whereas quality control relies on on-line measurements. In this study, our aim was to establish new tools for controlled and monitored 3D cell culturing.

In a first step, we developed a portable, benchtop perfusion bioreactor. This bioreactor allows precise monitoring and controllability of critical process parameters (pH, dO2 and T°), and fits inside an X-ray nanoCT device. Concomitantly, we tested the effect of an in-house developed X-ray contrast agent (CA) on 2D cultures of human periosteum derived cells (hPDCs). No significant effect on the metabolic activity and differentiation potential of the hPDCs was observed for different CA concentrations and staining times. Also for the cell exposure to a wide range of X-ray doses (40-60kV, 100-140µA, 8-20 min), no effect on cell proliferation was observed, not even for the highest X-ray dose. These results suggest that online administration of the CA during culture is feasible, and that the online exposition of hPDCs to X-rays does not lead to significant changes in cell proliferation. In a following step, these technologies will be combined and, together, will go one step further in the development of new solutions for online monitoring, control and visualization of perfused TE constructs, as well as in the development of automated bioprocesses.