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On-line monitoring of oxygen as a non-destructive method to quantify cells in engineered 3D tissue constructs

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Abstract:

Regulatory guidelines have established the importance of introducing quantitative quality controls during the production and/or at the time of release of cellular grafts for clinical applications. In this study we aimed to determine whether on-line measurements of oxygen can be used as a non-destructive method to estimate the number of chondrocytes within an engineered cartilage graft. Human chondrocytes were seeded and cultured in a perfusion bioreactor, and oxygen levels in the culture medium were continuously monitored at the inlet and outlet of the bioreactor chamber throughout the culture period. We found that the drop in oxygen across the perfused construct was linearly correlated with the number of cells per construct ($R^2 = 0.82$, $p < 0.0001$). The method was valid for a wide range of cell numbers, including cell densities currently used in the manufacture of cartilage grafts for clinical applications. Given that few or no non-destructive assays that quantitatively characterize an engineered construct currently exist, this non-invasive method could represent a relevant instrument in regulatory compliant manufacturing of engineered grafts meeting specific quality criteria.

Key-words: bioreactor, sensor, tissue engineering, quality control, perfusion, chondrocyte