Scaffold Size Versus Oxygen Tension: An Analytical Approach
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Introduction
It is widely recognised that a controllable oxygenation of tissue engineering (TE) constructs is essential for the development of clinically relevant grafts [1]. This study presents an analytical approach for predicting the maximum critical scaffold length in function of different in vitro culturing parameters, in order to ensure appropriate oxygen tension levels throughout the TE scaffold.

Materials and Methods
As a test case a regular Ti6Al4V scaffold with a porosity Φ of 61% was used. A 1D mathematical model, solving the mass conservation law and neglecting diffusive phenomena (Eq. 1), was used to predict the maximum critical scaffold length (Lmax):

$$\rho v_{in} A \frac{\partial c_{O_2}}{\partial x} = A \phi \rho_0$$

with the consumption $r_0$ following the Michaelis-Menten kinetics (Eq.2)

$$r_0 = v_{max,cell} \rho_{cell} \frac{c_{O_2}}{k_m + c_{O_2}}$$

The culture parameters that were varied in the analysis, were the maximum specific cell consumption rate ($v_{max,cell}$), inlet velocity ($v_{in}$), cell seeding density ($\rho_{cell}$), inlet ($c_{O_2in}$) and outlet ($c_{O_2out}$) oxygen tension. The scaffold area A equal to 3 mm$^2$, the medium density $\rho$ and $k_m$ were supposed to be constant (Fig 1). The validity of the 1D model was proven by comparison to 3D Computational Fluid Dynamics analyses.

![Scheme of the analytical model](image)

The oxygen range (Table 1) was selected to favour either cell proliferation ($c_{O_2in}$ 5% and $c_{O_2out}$ 1%) or differentiation ($c_{O_2in}$ 21% and $c_{O_2out}$ 10%).

<table>
<thead>
<tr>
<th>$v_{max,cell}$ [nmol/cellxh]</th>
<th>$v_{in}$ [mm/s]</th>
<th>$\rho_{cell}$ [10^6cells/ml]</th>
<th>$c_{O_2in}$ [%]</th>
<th>$c_{O_2out}$ [%]</th>
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</thead>
<tbody>
<tr>
<td>(1.08-1.37)x10^{-4}</td>
<td>0.03-0.1</td>
<td>(2.9-58)</td>
<td>5-21</td>
<td>1-10</td>
</tr>
</tbody>
</table>

Table 1: Value range of the culture parameters considered in the analysis

Results
Using chondrocytes with a $v_{max,cell}$ of 1.08x10$^{-4}$ nmol/cellxh [2] and a $v_{in}$ of 0.03 mm/s the model resulted in a $L_{max}$ – $\rho_{cell}$ behaviour as shown in Fig 2.

![Lmax as function of \(rho_{cell}\) in case of enhancement of proliferation or differentiation](image)

Discussion and Conclusions
For a scaffold seeded with 2.9x10^6 chondrocytes/ml the model predicted $L_{max}$ values of 8.9 cm and 3.8 cm respectively for the assumed oxygen ranges that favour either cell proliferation or differentiation. The presented methodology can provide an approach to optimise the tissue construct length and design in function of the desired oxygen tension.

References

Acknowledgments
This work is part of Prometheus, the Division of Skeletal Tissue Engineering of K.U.Leuven.

Disclosures
All authors declare the absence of any relationship with other people or organisations that could inappropriately influence their work.