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Determination of Oxygen Gradients in Engineered Tissue Using a Fluorescent Sensor

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Abstract:

Nutrient and oxygen supply of cells are crucial to tissue engineering in general. If a sufficient supply cannot be maintained, the development of the tissue will slow down or even fail completely. Previous studies on oxygen supply have focused on measurement of oxygen partial pressures (pO_2) in culture media or described the use of invasive techniques with spatially limited resolution. The experimental setup described here allows for continuous, non-invasive, high-resolution pO_2 measurements over the cross-section of cultivated tissues. Applying a recently developed technique for time-resolved pO_2 sensing using optical sensor foils, containing luminescent O_2-sensitive indicator dyes, we were able to monitor and analyze gradients in the oxygen supply in a tissue over a 3-week culture period. Cylindrical tissue samples were immobilized on top of the sensors. By measuring the luminescence decay time, two-dimensional pO_2 distributions across the tissue section in contact with the foil surface were determined. We applied this technique to cartilage explants and to tissue-engineered cartilage. For both tissue types, changes were detected in monotonously decreasing gradients of pO_2 from the surface with high pO_2 to minimum pO_2 values in the center of the samples. Nearly anoxic conditions were observed in tissue constructs (~0 Torr) but not in excised cartilage discs (~20 Torr) after 1 day. Furthermore, the oxygen supply seemed to strongly depend on cell density and cell function. Additionally, histological analysis revealed a maximum depth of ~1.3 mm of regular cartilage development in constructs grown under the applied culture conditions. Correlating analytical and histological analysis with the oxygen distributions, we found that pO_2 values below 11 Torr might impair proper tissue development in the center. The results illustrate that the method developed is an ideal one to precisely assess the oxygen demand of cartilage cultures.

Keywords: Cartilage, Oxygen, Tissue engineering, Optical Oxygen Sensor