Introduction

Bioartificial livers (BALs) aim to support liver function until a patient can receive a transplanted organ or make a recovery. Several BALs have been tested in clinical trials but as yet none are routinely used in practice\(^1\). As liver cells are highly metabolic and often separated from the plasma stream by a hollow fiber membrane, oxygen mass transport is critical to the viability of the BAL. The oxygen gradients within the bioreactor should also match the situation \textit{in vivo} as oxygen tension is an important modulator of liver function\(^2\). Oxygen tension delineates three metabolic zones along the liver lobule. To investigate these phenomena, a mathematical model is applied to describe oxygen mass transport in a BAL. ‘Operating Region’ charts describe the range of viable BAL designs. The range of size of the metabolic zones within the operating regions is also determined.

Materials and Methods

Using the Krogh cylinder method\(^3\), a model was applied to describe oxygen transport to liver cells in the extracapillary space of a hollow fiber bioreactor. The modeling equations were solved using the finite element software, Comsol Multiphysics 3.5a (Comsol AB). Two operating constraints were defined on the BAL – oxygen tension must be maintained above 2 mmHg for cell survival and the attachment area of the hollow fibers must be adequate to support at least 10 billion cells (the absolute minimum required for the BAL to be therapeutically effective). Modeling results were used to create operating region charts which display where the constraints can be satisfied. Within the region, the size of each of the metabolic zones will have implications on the functionality of the BAL.

Results

| Each of the operating constraints is represented by a maximum or minimum fiber number as a function of fiber lumen radius. They can be represented graphically to produce an operating region chart (Fig. 1). A flow rate of 200 ml/min was enough to adequately oxygenate a population of 10 billion cells, or 10% of the adult liver cell mass. It is possible to support a cell population of almost double this size using the technical maximum flow rate of 300 ml/min. Fiber length, lumen radius and membrane thickness also have implications on the position and size of the operating region. Within the operating region, the metabolic zone sizes vary over a large range (Fig. 2). Under certain conditions the zones are of equal size or may be absent completely, e.g. the perivenous zone under high flow rate conditions. |

Discussion and Conclusions

The operating regions allow, at a glance, the feasibility of designs to be assessed. The results show that in some cases even when enough oxygen can be provided to sustain the cell mass, the resulting gradient causes an imbalance in the metabolic zones. Through judicious choice of operating and design parameters we have shown it is possible to control the zone distribution and create a situation where each zone occupies an equal proportion of the BAL.

References List


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Disclosures

The authors have nothing to disclose

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