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WHAT IS TISSUE ENGINEERING? WHAT IS ISOTT'S ROLE?

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1. INTRODUCTION

Tissue Engineering is still a developing field with its definition being "in the mind of the researcher." Presently there are a plethora of explications for this cutting edge medical technology. While serving at the National Science Foundation (NSF) in the late 1980s we attempted to define Tissue Engineering by sponsoring a national meeting of researchers in La Jolla, CA for this purpose. At that time I proposed that the first real tissue engineers were Dr. August Krogh and Mr. Erlang in 1919. Engineering typically involves system quantification *via* mathematics, which they accomplished with the definition of the Krogh Capillary Tissue Cylinder and the first mathematical model representing the tissue oxygen distribution.

ISOTT objectives include the investigation of tissue and organ function, repair, renewal and replacement *in vitro* and *in vivo*. For example, angiogenesis and blood hemostatis are essential considerations for oxygen and nutrient supply and metabolic byproduct removal from tissue. Oxygen tension measurement and prediction are necessary tools to determine the health of individual cells and organs in the body. In this paper, the "Bruley Template" will be used to illustrate the interaction of Bioprocess Engineering and Biomedical Engineering and the interface with clinical practice for Tissue Engineering applications. Other scientific and engineering challenges will be discussed including various problems that might be encountered in the commercialization of engineered tissue.

2. HISTORICAL BACKGROUND

Tissue Engineering is evolving as an important discipline with potential ubiquitous clinical impact that some researchers estimate could involve as many as thirty-two

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million procedures per year with a one-hundred billion dollar market for engineered tissues. Some of these tissues might include kidney, urethra, pancreas, liver, blood vessels, bone and cartilage, etc. Various investigators have used different names that include, in my view, a narrow definition of tissue engineering. The terms *regenerative medicine* and *reparative medicine* are used in some circles.

It is my opinion that tissue engineering was first defined through the work of Dr. August Krogh and the mathematician Mr. Agner K. Erlang (Figure 1, Equation 1). Engineering involves the quantification of systems *via* mathematical modeling. This was accomplished in the early 1900s when Dr. Krogh conceptualized the capillary tissue system and Mr. Erlang derived a mathematical model describing oxygen transport in the tissue. This linear model led to an analytical solution for which in part Dr. Krogh received the Nobel Prize in 1919.[1,2,3,4] In reality, vascular beds and the microcirculation are found to be a tortuous network that defies a single capillary solution. However, much valuable insight and information can be gained from simplified models of the complex structure.

Many investigators advanced this initial study by increasing the complexity of the mathematical models. Two of the most significant early works in the analytical modeling arena were accomplished by the work of Opitz and Schneider[5] and Gerard Thews.[6] For conservation of space, I will now use my own work to represent studies that I feel should be included in the definition of "Tissue Engineering." Certainly many other ISOTT investigators have contributed through theoretical and experimental research. In 1962, I met Dr. Melvin H. Knisely in the anatomy department of the medical school of South

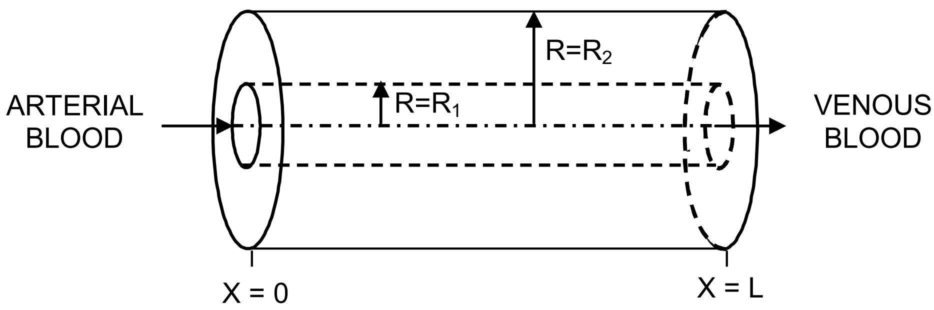

Figure 1. The Krogh Tissue Cylinder

$$\alpha_t \frac{\partial P_t}{\partial t} = k\left[\frac{1}{r}\frac{\partial}{\partial r} r \frac{\partial P_t}{\partial r} + \frac{\partial^2 P_t}{\partial z^2}\right] - M$$

Equation 1. The approximate Krogh-Erlang Tissue Model