ROLE OF MODELING IN THE DESIGN AND PLANNING OF EXPERIMENTS FOR AUTOLOGOUS CHONDROCYTES KNEE IMPLANTS & ASSESMENT OF RISK IN THE DEVELOPMENT OF THE DEVICE

EXECUTIVE SUMMARY

Damage to hyaline articular cartilage in the knee is a major health problem that currently has no reliable treatment. This medical condition affects thousands of Americans annually and could be solved with a tissue engineering solution. This project investigates a novel tissue engineering technique that uses autologous chondrocyte and mesenchymal stem cells imbedded in a cross-linkable polymer to repair and regenerate damaged cartilage and bone within the knee. Two papers were written. The first addresses the technical details of this treatment and discusses the contribution of mathematical modeling to product development. The second addresses the financial details and risk associated with developing this treatment for clinical use and develops a general model for use with any new medical device.

Technical Paper
Articular cartilage has remarkable properties that are imperative for joint function. The proposed tissue engineering solution involves autologous cells encapsulated in gelatin microcapsules. These microcapsules as well as growth factor microspheres will be included within a polypropylene fumarate blend and it will be cross-linked *in vivo* in two parts, a bone replacement and a cartilage replacement. This treatment requires extensive experimentation before marketing. In order to reduce the cost associated with experimentation, mathematical modeling can help to guide experimental decisions. Three models were developed. The temperature profile during polymerization was modeled and showed that temperature increase would not contribute to significant cell death. The dependency of mechanical strength on porosity was determined for the bone replacement, and the maximum allowable porosity was found, while porosity in the cartilage replacement was determined to be unnecessary. The interdependence of degradation rate and cell growth rate was also discussed.

Financial Paper
Introducing a new medical device into the market involves a great deal of risk. A general model taking a medical device through the FDA process was developed and applied to this specific example. First and second stage decisions were considered to model the risk associated with market introduction. The risk of FDA approval can be decreased by increasing the knowledge of the device before entry into the process and by increasing the number of workers conducting FDA experiments. An economic pricing model was used to estimate the product profitability based on various market and product conditions, along with the effect of deviations in these conditions. These profitability estimates were then combined with the FDA analysis to find the possible values of the product NPW along with associated probabilities.